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RESEARCH ARTICLE

Medicare Part D's Effects on Drug Utilization and Out-of-Pocket Costs: A Systematic Review

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Objective. To update a past systematic review on whether Medicare Part D changed drug utilization and out-of-pocket (OOP) costs overall and within subpopulations, and to identify evidence gaps.

Data Sources/Study Setting. Published and gray literature from 2010 to 2015 meeting prespecified screening criteria, including having a comparison group, and utilization or OOP cost outcomes.

Study Design. We conducted a systematic literature review with a quality assessment.

Data Collection/Extraction Methods. For each study, we extracted information on study design, data sources, analytic methods, outcomes, and limitations. Because outcome measures vary across studies, we did a qualitative synthesis rather than meta-analysis.

Principal Findings. Sixty-five studies met screening criteria. Overall, Medicare Part D enrollees have increased drug utilization and decreased OOP costs, but coverage gaps limit the program's impact. Beneficiaries whose insurance becomes more generous after enrollment had disproportionately increased drug utilization and decreased OOP costs. Outcomes among dual-eligibles were mixed.

Conclusions. There is strong evidence on how Medicare Part D and the donut hole coverage gap affect utilization and OOP costs, but weak evidence on how effects vary among dual-eligibles or across diseases. Findings suggest that the Affordable Care Act's provisions to expand coverage and reduce the donut hole should improve patient outcomes.

Key Words. Medicare Part D, drug utilization, out-of-pocket costs, coverage gap, systematic review

The Medicare Part D prescription drug program, implemented in 2006, aimed to increase drug utilization and lower Medicare and Medicaid participants' out-of-pocket (OOP) prescription drug costs, thereby improving access (Oliver, Lee, and Lipton 2004). However, a major limitation is the "donut hole" coverage gap, in which beneficiaries pay all annual expenses between $3,310 and $4,850 in 2016. Additionally, dual-eligibles may face more stringent formularies during the transition from Medicaid to privately administered prescription drug

plans and complicated coordination of benefits between Medicare, Medicaid, and Part D plans (The Henry J. Kaiser Family Foundation 2006). A previous 2010 systematic review found that Medicare Part D increased drug utilization and decreased OOP costs; but the donut hole unfavorably impacted drug utilization, medication adherence, and OOP costs (Polinski et al. 2010). There were no observed changes in dual-eligibles' behaviors, whereas vulnerable populations such as those with HIV or mental illness experienced difficulties during the transition period. A major limitation of this previous review is the short time frame. Since Medicare Part D was implemented in January 2006, researchers were unable to evaluate long-term policy effects, including the donut hole. Second, existing studies did not specify the impact on dual-eligibles. We updated the previous systematic review (Polinski et al. 2010), focusing on long-term impacts and heterogeneous effects on subpopulations including dual enrollees and with different health conditions.

METHODS

We followed the Institute of Medicine's systematic review guidelines (Institute of Medicine 2011). Notable differences were one reviewer (YP) doing the extraction, with ongoing discussion with EGM about screening and extraction; these adaptations follow the updated guidance from the Patient-Centered Outcomes Research Institute (PCORI Methodology Committee 2013).

Search Strategy

A reference librarian was consulted on the bibliographic databases and search terms. To minimize publication bias, both published and gray literature such as conference papers, and working papers were searched via PubMed/MEDLINE, EconLit/EBSCO, Social Services Abstracts/ProQuest, PAIS International/ProQuest, Business Source Complete/EBSCO, PsycINFO, Scopus, Grey Literature Report by New York Academy of Medicine, the Kaiser Family Foundation, and the National Bureau of Economic Research. We searched for: (1) Medicare [Medicare], (2) Part D [Part D, prescription drug, drug

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benefi*], and (3) drug utilization or out-of-pocket costs [use, utilization*, adherence*, non adherence*, compliance*, noncompliance*; cost*, spending*, expenditure*]. We combined three words, one per category (e.g., [Medicare] AND [Part D] AND [use]). The last access date was November 7, 2015. Additional eligible studies were identified by hand searching of reference lists from primary articles and relevant reviews.

Review Process. Studies were eligible if they met prespecified exclusion and inclusion criteria. Exclusion criteria were intervention (non-Medicare Part D) and non-U.S. setting. Inclusion criteria were time horizon (published after 2010), English language, original research (not review articles or commentaries), population (eligible for Medicare Part D), presence of a comparison group, and outcomes (drug utilization or OOP costs). Eligibility was determined in two stages. First, titles, abstracts, and subject terms were screened for the exclusion criteria. Second, full text was reviewed for inclusion criteria. *EndNote* (version X7; Thomson Reuters, New York, NY, USA) was used to manage citations and full-text articles, and inclusion and exclusion criteria were tracked in Excel. Eligibility assessment was performed by YP and discussed with EGM.

Data Extraction

Study data were extracted by YP with results reviewed by EGM. The following information was extracted: research question, study design (data years, geographic location, population, treatment group, comparison group, time period, data sources, number of observations, and data analysis method), drug utilization, and OOP cost outcomes, and limitations. We did not do a meta-analysis because outcome measures vary across studies: drug utilization outcomes included pill-days per patient year, prescriptions per patient year, and different measures of cost-related nonadherence. The studies also varied with their comparison groups, time periods, health conditions, and analytic methods. For studies with similar outcomes, we qualitatively synthesize the findings and report the range of effect sizes.

Quality Assessment

We used predefined criteria and a fixed coding guide (see Appendix SA2) to systematically assess the risk of bias in each study. As the Institute of Medicine

does not provide a universal checklist to evaluate bias (Institute of Medicine 2011), our rubric included bias common to observational studies (Szklo and Nieto 2004; Higgins and Green 2008; Centre for Reviews and Dissemination 2009; Institute of Medicine 2011): comparability between intervention and control groups, attrition, data collection and quality, measurement error, missing data, and reliability and validity of the outcome measures. This rubric was pretested on five articles, and each reviewer subsequently scored articles on each dimension and an overall score for the total risk of bias. Scores were compared between reviewers, with discrepancies resolved through consensus.

RESULTS

Flow of Information

Following the protocol, 2,473 publications were initially identified. After screening, 2,055 articles were removed following exclusion criteria and 353 additional articles were removed following inclusion criteria. Sixty-five studies were eligible for reviews (see Appendix SA3).

Description of Studies

There was more evidence for drug utilization (62 studies) than OOP costs (24 studies). Most publications have sample sizes below 50,000, and use claims or survey data. More than half (40) of the articles are nationally representative, using claims data from national pharmacy chains or insurance companies, or nationally representative surveys.

Many observational studies used a nonequivalent control group design with a variety of control groups: near-elderly, veterans aged 65 years or older, or beneficiaries with low-income subsidies, or employer-sponsored coverage. Other study designs included single group pre/post comparisons and statistical predictions.

Overall Impact of Medicare Part D on Drug Utilization

Studies consistently found that Medicare Part D increased drug utilization in the general population across numerous outcomes, including medication persistence, number of days with possession of at least 1 drug within a class (Nair et al. 2010; Yala et al. 2014), annual prescription fills per person (Briesacher et al. 2011; Liu et al. 2011; Kaestner and Nasreen 2012; Yala et al. 2014), drug

access (Chen, Rizzo, and Ortega 2011; Urmie et al. 2011), and cost-related behavior changes such as medication cessation, applying to pharmaceutical assistance programs, and receiving free prescription samples (Urmie et al. 2011). Table 1 summarizes these findings.

The strongest effect sizes were for medication use. For example, Nair et al. (2010) and Zimmer (2015) found a 17.5–20 percent increase in prescriptions, Briesacher et al. (2011) estimated that annual prescription fills per person increased from 1.8 to 3.4, and Kaestner and Nasreen (2012) observed a 30 percent increase in annual prescriptions. Increases were highest among beneficiaries receiving low-income subsidies (Yala et al. 2014). There were smaller effects for cost-related nonadherence. Urmie et al. (2011) observed that fewer participants stopped taking prescriptions due to cost (from 8.9 to 7.6 percent), applied for pharmaceutical manufacturer assistance (from 6.4 to 2.7 percent), or had limited prescription access (from 23.0 to 18.6 percent); yet two studies did not find statistically significant changes in delaying or foregoing prescriptions (Chen, Rizzo, and Ortega 2011) or cost-related problems in accessing prescription drugs (Chakravarty et al. 2015).

Preconditions such as insurance types, coverage, and spending led to differential program impacts. Seniors newly gaining coverage or with improved coverage experienced reduced cost-related nonadherence (Safran et al. (2010): from 26.0 to 19.4 percent; Kennedy et al. (2011): from 22.1 to 14.3 percent). However, those who transitioned from employer-based prescription coverage to Part D plans with less generous coverage had increased cost-related nonadherence (OR = 1.7) (Safran et al. 2010). Drug utilization increased most among beneficiaries whose benefits become more generous: seniors transitioning from generic-only to no-gap coverage had 106 more days supply than those experiencing a coverage decrease (Ettner et al. 2011). Higher users experienced disproportionate impacts: Those with the highest pre–Part D OOP drug spending experienced a 4.0 percent relative increase in drug utilization (Mott et al. 2010).

Although studies consistently found increased drug utilization among the elderly, there were no observed pre/post–Part D differences between nonelderly Medicare beneficiaries with disabilities and nonelderly individuals ineligible for Medicare (incidence rate ratio = 0.877) (Nelson et al. 2014).

Impact of Medicare Part D on Specific Drug Utilization

Medicare Part D significantly increased drug utilization among patients taking medications for heart disease (Donohue et al. 2010; Zhang et al. 2011),

Table 1: Overall Impact of Medicare Part D on Drug Utilization and Out-of-Pocket Costs

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Longitudinal data				
Briesacher et al. (2011)	Community-dwelling Part D enrollees from 2006–2007; compared to projected outcomes (N = 38,798)	Survey (Medicare Current Beneficiary Survey), 2000–2005	Annual prescription fills per person increased by 1.8 (95% CI: 1.1–2.5) in the first year after Part D implementation, and 3.4 fills (95% CI: 2.7–4.1) in the second year	Annual out-of-pocket (OOP) costs per person decreased $142 (95% CI: 103.1–182.5) in first year after Part D implementation, and sustained at $148 below predicted values (95% CI: 114.1–181.2) in second year
Chen, Rizzo, and Ortega (2011)	Medicare beneficiaries ≥65 (including dual-eligibles) during 2006–2007, compared to 2004–2005 (N = 12,073)	Survey (Medical Expenditure Panel Survey), 2004–2007	Insignificant change in delaying or foregoing prescriptions (β = 0.03, p = .83)	Decrease in OOP drug expenditures after January 2006 (β = −0.40 (natural log), p < .01)
Engelhardt and Gruber (2011)	Medicare-eligible individuals: (1) ages 65–70 and (2) all individuals ≥65 (N = 15,074 pre–Part D and 3,470 post–Part D); compared to (3) near-elderly ages 60–64, excluding those eligible for Medicare through disability insurance (N = 4,759 pre–Part D and 1,237 post–Part D)	Survey (Medical Expenditure Panel Survey), 2002–2007 excluding 2006	—	Small effect at low quantiles of household OOP prescription drug expenditures; effect grows consistently with higher baseline spending, with $180 and $800 reduced OOP spending at the 50th and 90th percentiles
Ettner et al. (2011)	Beneficiaries ≥65 from 8 western states continuously enrolled in Medicare Advantage with: (1) branded medication coverage with caps, (2) branded medication coverage without caps, or (3) generic-only gap coverage in 2005, compared to those who were continuously enrolled in Medicare Advantage with branded medication coverage in 2005 (N = 248,773)	Census and administrative data (enrollment and benefits files, medical encounters, inpatient outpatient and pharmacy claims), 2005–2007	All beneficiaries had increased supply days; those with the most improvements in benefit generosity experienced the largest increase (179.8, SE 1.7) compared to the comparison group (73.4, SE 1.9)	Mixed results for OOP changes, with trivial magnitudes for the reference group (whose drug coverage may have worsened post–Part D); other benefit design groups experienced significant reductions in OOP costs, with the largest reductions ($200–$300) among those newly acquiring branded drug coverage

Continued

Table 1. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Kaestner and Nasreen (2012)	Elderly who gained Part D prescription drug insurance, compared to elderly without prescription drug insurance in pre–Part D period (N = 42,639)	Survey (Medicare Current Beneficiary Survey), 2002–2007 excluding 2005	Gaining drug coverage associated with 30% increase in prescriptions per year	—
Kennedy et al. (2011)	Newly insured who lacked prescription coverage in 2005 but gained Part D coverage in 2006; compared to individuals (1) with continuous prescription coverage and (2) continuously uninsured without prescription coverage (N = 8,935)	Survey (Medicare Current Beneficiary Survey), 2005–2006	Cost-related nonadherence declined for all beneficiaries, with the greatest reductions (from 22.1 to 14.3%) for newly insured beneficiaries; newly insured more likely to have resolved cost-related nonadherence (aOR = 1.7; 95% CI: 1.3–2.2)	—
Liu et al. (2011)	Noninstitutionalized Medicare beneficiaries ≥65, compared to near-elderly aged 55–63 (N = 1,005)	Survey (Medical Expenditure Panel Survey), 2005–2006	Relative to the changes in the comparison group, those gaining Part D received 2.05 (p = .081) more prescriptions per patient year	Relative to the changes in the comparison group, those gaining Part D had $179.86 ($p$ = .034) lower OOP costs

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Table 1. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Mahmoudi and Jensen (2013)	Medicare beneficiaries ≥65, compared to near-elderly (55–63 years) without Medicare (N = 45,463)	Survey (Medical Expenditure Panel Survey), 2002–2009	Total prescriptions filled increased among elderly beneficiaries compared to the near-elderly for all race/ethnicity (white: 2.4% vs. −0.3%; African American: 1.1% vs. −0.8%; Hispanics: 4.2% vs. 0.7%)	OOP costs among elderly beneficiaries fell compared to the near-elderly for all race/ethnicity (white: $377.9 vs. $72.8; African American: $327.1 vs. $23.0; Hispanic: $322.0 vs. 159.8)
Millett et al. (2010)	Beneficiaries ≥65 without drug coverage in 2005 who enrolled in Part D in 2006 (N = 380);beneficiaries ≥65 without drug coverage in 2005 and 2006 (N = 286); beneficiaries ≥65 non-Medicaid drug coverage in 2005 and 2006 (N = 491)	Survey (Medical Expenditure Panel Survey), 2005–2006	—	Mean annual OOP expenditures decreased by 32% ($320, 95% CI: $250–$391) among all beneficiaries; mean annual OOP expenditures decreased by 49% ($748, 95% CI: $600–$897) among beneficiaries who enrolled in Part D; mean annual OOP expenditures decreased 32% ($353, 95% CI: $188–$518) among beneficiaries who did not enroll; no significant decrease among beneficiaries with drug coverage in both years
Mott et al. (2010)	Southeastern region seniors ≥65 eligible for Medicare coverage, compared to individuals aged 60–62 ineligible for Medicare coverage (N = 51,305)	Administrative (pharmacy claims), 2005–2007	Eligible seniors with the highest (>$469.61) and moderate ($66.0–469.61) OOP drug spending in 2005 increased their pill-days by 4.0 and 7.1% more than changes in the comparator group	For eligible seniors with the highest (>$469.61) OOP spending in 2005, OOP costs declined by 17.6% more than changes in the comparator group

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Table 1. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Nair et al. (2010)	Beneficiaries under the Medicare Advantage plan in 2006, compared to beneficiaries under the Medicare Choice plan in 2005, with a subset with hypertension, diabetes, dyslipidemia, or congestive heart failure (N = 6,876)	Administrative (enrollment data, pharmacy and medical claims), 2005–2006	Prescription use increased 17.5%, with 20.8 and 13.63% increases in the use of generic and brand-name medications	Mean monthly OOP expenditures increased 79.21% (from $45.66 to $81.83); members who did not reach the coverage gap still experienced a 12.76%, 6.27%, and 32.74% increase in OOP expenditures for all prescription, brand-name medications, and generic medication, respectively
Nelson et al. (2014)	Nonelderly disabled Medicare beneficiaries, compared to nonelderly non-Medicare beneficiaries (N = 9,935)	Survey (Medical Expenditure Panel Survey), from 2005 to 2006	Medicare Part D did not statistically increase number of prescriptions (incidence rate ratio = 0.877, p = .115)	Medicare Part D implementation decreased OOP costs ($\beta = -0.794$, $p < .001$)
Safran et al. (2010)	Seniors ≥65 who transitioned to Part D plans; compared to (1) seniors ≥65 with a consistent drug coverage source in 2003 and 2006 (employer or VA) and (2) seniors ≥65 without drug coverage in both 2003 and 2006 (N = 9,573)	Administrative and survey data from CMS, 2003 and 2006	Cost-related nonadherence declined from 26.0 to 19.4% ($p < .001$); among Part D enrollees, those who previously lacked prescription coverage or with prior coverage through a Medicare HMO or a Medigap/private plan experienced significant declines in cost-related nonadherence, while those who transitioned from employer-based prescription coverage to Part D plans had increased cost-related nonadherence in 2006 (OR = 1.7, $p < .01$)	OOP spending declined in all groups except those with prior employer-based coverage; adjusted odds of spending >$100/month reduced for Part D enrollees previously lacking coverage (OR = 0.3, $p < .001$) or who transitioned from Medicaid drug coverage (OR = 0.5, $p < .05$); individuals with employer-based coverage in 2003 had significantly higher OOP spending in 2006 irrespective of whether they retained employer-sponsored coverage or transitioned to Part D

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Table 1. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Yala et al. (2014)	Medicare Part D beneficiaries in eight states (AZ, CA, CO, NV, OK, OR, TX, WA) not receiving low-income subsidies (1) with or (2) without gap coverage, compared to (3) those receiving low-income subsidies ($N = 344,817$)	Administrative data (health plan data: enrollment files, pharmacy claims, and medical claims), from 2005 to 2006	Low-income subsidy group had more prescriptions, compared to non-low-income subsidy with or without gap coverage (38.1 vs. 25.1 vs. 26.5, $p < .05$)	Low-income subsidy group had lower OOP costs, compared to nonlow-income subsidy with or without gap coverage ($148 vs. $546 vs. $570, $p < .05$)
Zhang et al. (2010b)	Pennsylvania elderly ≥65 with no or limited drug coverage ($150 or $350 caps), who then received Medicare Advantage coverage in 2006; compared to elderly ≥65 with stable drug coverage and no caps through retiree health insurance ($N = 34,176$)	Administrative data (insurance claims), 2004–2007	—	Relative to those with stable coverage, Part D reduced OOP spending by 13.4% (95% CI: 9.1–17.1%) among those with no prior coverage and 15.9% (95% CI: 12.8–19.1%) among those with limited coverage of $150 quarterly caps
Zimmer (2015)	Medicare beneficiaries aged 65–74; compared to near-elderly aged 55–64 (36,141)	Survey (Medical Expenditure Panel Survey), from 2000 to 2004 and 2006 to 2008	Post–Part D, 4.82 more prescriptions per person were filled, representing a 20% increase, relative to pre–Part D elderly	Post–Part D, OOP spending was reduced by 20%, relative to pre–Part D elderly

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Table 1. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Repeated cross-sectional data				
Chakravarty et al. (2015)	New Jersey Medicare beneficiaries ≥65, compared to near-elderly aged 50–64 (N = 6,466 (2001); 6,319 (2009))	Survey (New Jersey Family Health Survey), 2001 and 2009	Prescription drug access among elderly decreased overall (OR = 1.8, p = .02), although relative decrease compared to nonelderly population not statistically significant (rOR = 1.55, p = .16)	—
Urmie et al. (2011)	Medicare enrollees ≥65, surveyed post–Part D, compared to pre–Part D (N = 2,244)	Survey (Harris Poll Online Panel), 2005–2007	Reduction in cost-related nonadherence (8.9% vs. 7.6%), applications to assistance programs (state/local government assistance, 5.2% vs. 3.9%; pharmaceutical manufacturer assistance, 6.4% vs. 2.7%), receipts of free prescription samples (57.2% vs. 49.5%), limited prescription access (23.0% vs. 18.6%)	—

arthritis or other rheumatic conditions (Cheng and Rascati 2012; Yazdany, Tonner, and Schmajuk 2015), bacterial infections (Zhang, Lee, and Donohue 2010c), dementia (Fowler et al. 2013), glaucoma (Blumberg et al. 2015), coronary heart disease and/or diabetes mellitus (Hanlon 2013), hyperlipidemia, hypertension, and/or diabetes (Zhang et al. 2010a), kidney disease (Yusuf et al. 2014), or with coronary stent placements (Duru et al. 2014). It also reduced cost-related nonadherence among beneficiaries with glaucoma (Blumberg et al. 2015) and with coronary stent placements (Duru et al. 2014). Table 2 summarizes these findings.

It is difficult to compare statistically the magnitude of these effects across diseases, as most studies restrict their populations to narrow disease groups. A notable exception is Zhang et al. (2010a), who evaluated the impact of among those with hyperlipidemia, diabetes, and hypertension, finding that medication possession ratios improved the most among diabetics (17.9 percentage points). When comparing studies qualitatively, the most robust increase was observed in individuals with heart disease without prior drug coverage (Donohue et al. (2010): six more heart failure prescription annually; Zhang et al. (2011): higher likelihood of antihypertensive utilization (OR = 1.4); Hanlon et al. (2013): findings on antilipemic use consistent across race).

Although utilization increased for most disease-specific studies, some studies had mixed outcomes. Most studies found increased utilization of diabetes-related medications (Vaidya, Blazejewski, and Pinto (2012): 55.1–61.3 percent increase in statin use; Gellad et al. (2013): 2 to 3 times higher utilization of oral hypoglycemics, statins, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and brand-name insulin analogs). However, beneficiaries with cancer (Kircher et al. 2014) and depression (Lim, Jung, and Shi 2013) did not have significantly different drug utilization.

Impact of Donut Hole Coverage Gap on Drug Utilization

Medicare Part D coverage gaps negatively impacted drug utilization (see Table 3). Polinski et al. (2011) found that beneficiaries without financial assistance in the gap were more likely to discontinue (hazard ratio = 2.0). Compared to those with gap coverage, beneficiaries on plans without gap coverage had higher cost-related nonadherence regardless of whether they experienced the gap (OR = 5.75) or not (OR = 2.78) (Bakk 2015).

Although the magnitude of the coverage gap impact varies across studies, investigators consistently showed that these gaps significantly limit the program's impact among patients with diabetes (Duru et al. 2010; Gu et al.

Table 2: The Impact of Medicare Part D on Specific Drug Utilization and Out-of-Pocket Costs

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Longitudinal data				
Cheng and Rascati (2012)	Medicare beneficiaries ≥65 with arthritis in 2008, compared to 2005 (N = 2,484)	Survey (Medical Expenditure Panel Survey), 2005–2008	Median prescription fills per year increased from 28.4 to 32.6. (14.6% change, p = .014)	Median out-of-pocket (OOP) drug expenditures decreased by $151 (25.2% change, p < .001)
Donohue et al. (2010)	Pennsylvania beneficiaries ≥65 with diagnosed heart failure who transitioned from no or limited drug coverage ($150 or $350 caps) to Part D coverage, compared to those with continuous no-cap employer-sponsored coverage (total N = 6,950)	Administrative (pharmacy and medical claims, enrollment data), 2003–2007	Relative to the comparison group, individuals who previously lacked drug coverage filled 6 more cardiovascular prescriptions annually (adjusted ratio of prescription counts = 1.36, 95% CI: 1.29–1.44, p < .001) and the no-coverage group experienced significant increases (p = .01 or lower) in the likelihood of good adherence to all drug classes and combinations, except for aldosterone-inhibiting diuretics (p = .85)	—
Duru et al. (2014)	Beneficiaries ≥65 with a coronary stent placement not receiving low-income subsidies with or without gap coverage, compared to those receiving low-income subsidies (N = 2,967)	Administrative (pharmacy claims), 2007	Low-income subsidy enrollees were had higher proportions of days covered overall and for those with stents (>80% adherence overall: 54.8% vs. 47.6%, p = .008; >80% adherence among patients with drug-eluting stents, 59.1% vs. 51.7%, p = .022); no statistically significant differences in early discontinuation of clopidogrel after coronary stent placement	—

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Table 2. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Fowler et al. (2013)	Pennsylvania community-dwelling Medicare Advantage enrollees ≥65 with three types of continuous coverage: (1) no-gap coverage, (2) $150 cap, and (3) $350 cap; compared to those with generous employer-sponsored coverage without a cap from 2004 to 2007	Administrative (pharmacy and medical claims, enrollment data), 2004–2007	Antidementia prescriptions per month increased in all coverage groups ($p < .001$); compared to those with generous insurance, beneficiaries with no-gap coverage increased annual antidementia prescriptions filled by 38% ($p < .001$); compared to the no-cap group, those without any coverage or with a $350 cap pre–Part D had a 36% ($p = .002$) and 15% ($p = .003$) increase in any antidementia prescription use	—
Kircher et al. (2014)	Medicare beneficiaries ≥65 with cancer, compared to near-elderly aged 55–63 with cancer ($N = 6{,}607$)	Survey (Medical Expenditure Panel Survey), from 2002 to 2010	No statistically significant differences in utilization	Compared to changes among near-elderly, OOP costs among beneficiaries decreased by $356 per person ($p = .02$)
Lim, Jung, and Shi (2013)	Medicare beneficiaries with depression, compared to (1) Medicaid beneficiaries, (2) dual-eligibles, and (3) those with private coverage ($N = 22{,}592$)	Survey (Medical Expenditure Panel Survey), from 1997 to 2009	Compared to Medicaid beneficiaries, Medicare beneficiaries' antidepressant use increased post–Part D ((aOR) = 1.35, CI = 1.05–1.72); no significant changes compared to other control groups	—
Vaidya, Blazejewski, and Pinto (2012)	Diabetic patients ≥65, compared to near-elderly patients aged 57–64 ($N = 5{,}961$)	Survey (Medical Expenditure Panel Survey), 2004–2008	The percentage of elderly patients prescribed statins increased significantly from 55.05 to 61.25% ($p = .002$), while there was no significant increase in statin prescriptions among the near-elderly	—

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Table 2. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Yusuf et al. (2014)	Medicare Part D beneficiaries on dialysis not receiving low-income subsidies, compared to those receiving low-income subsidies (N = 198,349 (2007); 209,972 (2008); 220,051 (2009); 231,320 (2010))	Administrative (Center for Medicare and Medicaid U.S. Renal Data System), from 2007 to 2010	The odds of using phosphate binders, intravenous vitamin D analogs, and calcimimetic are higher among patients with low-income subsidies (OR = 1.17–2.38); yet the odds of using oral vitamin D analog is lower among patients with low-income subsidies (OR = 0.70–0.96)	Patients without low-income subsidy pays higher OOP costs for all medications (2007: $113 vs. $8.15; 2008: $115.44 vs. $8.03; 2009: $112.46 vs. $8.26; 2010: $111.51 vs. $8.74)
Zhang et al. (2010a)	Pennsylvania beneficiaries ≥65 with: (1) no drug coverage, (2) relatively poor coverage ($150 quarterly cap, with $600 annual maximum), or (3) relatively good coverage ($350 quarterly cap) pre–Part D; compared to those with continuous retiree health benefits with no deductible and $10/$20 copayments irrespective of their total drug spending (N = 20,889)	Administrative (enrollment data and pharmacy and medical claims), 2003–2007	Relative to the changes in the comparison group, medication possession ratios improved 13.4 (95% CI: 10.1–16.8), 17.9 (95% CI: 13.7–22.1) and 13.5 (95% CI: 11.5–15.5) percentage points among those with hyperlipidemia, diabetes, and hypertension in the group without prior drug coverage; less improvement among those with limited prior drug benefits; drug adherence increased after Part D among beneficiaries without prior coverage with hyperlipidemia (OR = 1.67, 95% CI: 1.35–2.07), diabetes (OR = 2.36, 95% CI: 1.81–3.08), and hypertension (OR = 2.09, 95% CI: 1.82–2.4)	—

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Table 2. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Zhang et al. (2011)	Pennsylvania beneficiaries ≥65 with hypertension and continuous coverage from a single health insurer; coverage types included: (1) no-gap coverage, (2) $150 cap, and (3) $350 cap, compared to those with employer-sponsored coverage without a coverage gap (N = 16,002)	Administrative (pharmacy claims and enrollment data), 2004–2007	Relative to the changes in the comparison group, those without prior drug coverage had the largest increase in use of antihypertensive medications (likelihood of use, OR = 1.40, 95% CI: 1.25–1.56; number of pills per day, 0.29, 95% CI: 0.24–0.33)	—
Zhang, Lee, and Donohue (2010c)	Pennsylvania beneficiaries ≥65 with: (1) no-gap coverage, (2) $150 cap, and (3) $350 cap who then received Medicare Advantage in 2006, compared to enrollees with stable drug coverage and no caps (N = 35,102)	Administrative (insurance claims), 2004–2007	Largest increase in antibiotic use among those without prior drug coverage (OR = 1.58, 95% CI: 1.36–1.85); largest increases in antibiotic subclasses of quinolones (OR = 1.70, 95% CI: 1.35–2.15) especially among those without prior drug coverage and with $150-caps; pneumonia-related ambulatory antibiotic use increased (OR = 3.60, 95% CI: 2.35–5.53) more than use associated with other acute respiratory tract infections (OR = 2.29, 95% CI: 1.85–2.83)	—
Repeated cross-sectional				
Blumberg et al. (2015)	Beneficiaries with glaucoma before Part D, compared to after Part D (N = 20,688)	Survey and administrative (Medicare Current Beneficiary Survey and Medicare claims), from 2004 to 2009	Cost-related nonadherence declined (taking smaller doses: 9.4% vs. 2.7%, $p < .001$; skipping doses due to cost: 8.2% vs. 2.8%, $p < .001$)	—

Continued

Table 2. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Hanlon et al. (2013)	Black and white Medicare beneficiaries ≥70 years with coronary heart disease and/or diabetes mellitus, post–Part D; compared pre–Part D (N = 1,091)	Survey (Health Aging and Body Composition Study), 2002–2008	Prior to Part D, blacks were less likely to take an antilipemic (32.7% vs. 49.4%); antilpemics use increased after Part D (blacks 48.3%, whites 64.6%)	—
Cross-sectional data				
Gellad et al. (2013)	Part D beneficiaries ≥65 with diabetes, compared to veterans ≥65 with diabetes (N = 1,571,580)	Administrative (Medicare Prescription Drug Event files; Veterans Administration outpatient and prescription claims, and enrollment data), 2008	Higher brand-name drug use among Part D beneficiaries (hypoglycemics: 35.3% vs. 12.7%, statins: 50.7% vs. 18.2%, angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers: 42.5% vs. 20.8%, insulin analogs: 75.1% vs. 27.0%)	—
Stuart et al. (2011)	Diabetic Medicare beneficiaries enrolled in Part D, compared to those in retiree drug subside plans (N = 257,532)	Administrative data (Chronic Condition Warehouse, MarketScan Medicare Supplemental and Coordination of Benefits database), 2006	Except insulin use (18.8% vs. 17.7%), the treatment group showed lower use of antidiabetic agent (73.7% vs. 75.9%), oral antidiabetic (65.5% vs. 67.4%), renin–angiotensin–aldosterone system inhibitors (66.6% vs. 67.3%), and antihyperlipidemics (60.5% vs. 69.4%) at $p < .0001$	—
Yazdany, Tonner, and Schmajuk (2015)	Medicare beneficiaries ≥65 using biologic drugs for rheumatoid arthritis without low-income subsidies (with or without gap coverage), compared to those receiving low-income subsidies (N = 6,932)	Administrative (claims), 2009	Beneficiaries with low-income subsidies more likely to obtain biologics (relative risk ratio = 2.98, 95% CI: 2.50–2.56)	Beneficiaries with low-income subsidies pay lower OOP costs ($72 vs. $3,751)

Table 3: The Impact of the Donut Hole Coverage Gap on Drug Utilization and Out-of-Pocket Costs

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Longitudinal data				
Baik et al. (2012)	Part D beneficiaries with depression and heart failure, who had: (1) no coverage or (2) coverage for generic medications only in the gap; compared to those with low-income subsidies ($N = 552{,}956$)	Administrative (Chronic Conditions Warehouse), 2007	Beneficiaries without drug coverage had 5.0% (95% CI: 1.7–8.2%) and 9.4% (95% CI: 7.2–11.5%) lower use of antidepressants and heart failure drugs after entering the coverage gap; those with generic coverage had a larger reductions in using branded drugs but did not switch to generic formulations; although adherence to antidepressants did not change after the gap, adherence to heart failure drugs reduced by 2.5% (95% CI: 1.2–3.7%) and 2.6% (95% CI: 1.3–3.9%) in the no-coverage and generic coverage groups	—
Donohue et al. (2011)	Pennsylvania beneficiaries with limited ($150 or $350 quarterly caps) or no drug coverage in 2004–2005, but obtained Part D benefits in 2006; compared to stable employer-sponsored coverage ($N = 15{,}080$)	Administrative (prescription drug, medical claims, and enrollment data), 2004–2007	Those without prior coverage had increased odds of antidepressant use after Part D (OR = 1.61, 95% CI: 1.41–1.85), and this increase was higher than changes in the employer-sponsored reference group (ratio of OR = 1.67, 95% CI: 1.40–1.99) or those with limited prior coverage (no change); all three treatment groups had increased odds of ≥80% days covered with an antidepressant (no prior coverage, $150 cap, $350 cap groups: OR = 1.86, 95% CI: 1.44–2.39; OR = 1.74, 95% CI: 1.25–3.42; OR = 1.19, 95% CI: 1.06–1.34), which was larger than changes in the employer-sponsored reference group (ratio of ORs = 2.17, 2.03 and 1.39, respectively)	—

Continued

Table 3. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Fung et al. (2010)	California diabetic beneficiaries ≥65 in: (1) an integrated Medicare Advantage plan with a gap and (2) a network model Medicare Advantage plan with a gap; compared to (3) those with no gap [compared to (1)] and (4) those with generic-only coverage during the gap [compared to (2)]	Administrative (pharmacy claims), 2005–2006	In the integrated model, adherence to three chronic drug classes was lower among those with a gap versus no gap (OR = 0.83, 95% CI: 0.79–9.88 for oral diabetes drugs; OR = 0.78, 95% CI: 0.74–0.83 for hypertension drugs; OR = 0.69, 965% CI: 0.65–0.73 for lipid drugs); no statistically significant differences in adherence between network model beneficiaries with a gap versus generic-only gap coverage	In the integrated model, gap beneficiaries had 189% (95% CI: 185–193%) higher out-of-pocket (OOP) expenditures for all drugs; network beneficiaries with a gap had 14% (95% CI: 10–17%) higher OOP expenditures; integrated plan beneficiaries who reached the gap threshold had 284% (95% CI: 277–293%) higher OOP expenditures; network plan beneficiaries who reached the gap threshold had 23% (95% CI: 19–27%) higher OOP expenditures
Gu et al. (2010)	Diabetic beneficiaries with: (1) no-gap coverage or (2) generic drug coverage in gap; compared to those with brand-name coverage in gap (N = 12,881)	Administrative (pharmacy claims data), 2007–2008	Beneficiaries with no coverage (OR = 0.617, 95% CI: 0.523–0.728) or generic-only coverage (OR = 0.702, 95% CI: 0.604–0.816) were less likely to be adherent after entering the donut hole, although no difference in adherence between treatment groups (p = .1586)	—
Hales and George (2010)	Prescription drug-only plan beneficiaries without gap coverage; compared to Medicare Advantage beneficiaries with gap coverage taking at least one cardiovascular medication (N = 750)	Administrative (pharmacy adjudication records), 2006	Part D enrollees who entered the donut hole were more likely to delay (OR = 1.54, 95% CI: 0.924–2.562), switch and delay (OR = 1.52, 95% CI: 0.532–4.322), and delay and stop (OR = 2.30, 95% CI: 1.134–4.673) their cardiovascular prescriptions	—

Continued

Table 3. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Joyce, Zissimopoulos, and Goldman (2013)	Beneficiaries ≥65 with diabetes not receiving low-income subsidies with or without gap coverage, compared to those receiving low-income subsidies (N = 609,723 (2006); 673,646 (2007); and 714,403 (2008))	Administrative (enrollment, Part A and B claims for fee-for-service Medicare enrollees, Part D claims), from 2006 to 2008	Statistically significant declines in medication use during the coverage gap, with higher declines for high cost medications (statins, antihypertensives, and oral hypoglycemics: 4–6%; antiasthmatics, antipsychotics, and other central nervous system drugs: 7–18%) than low cost medications (ACE inhibitors/ARBs, beta blockers, and diuretics: 2–4%, antidepressants, analgesics: 3–6%)	—
Li et al. (2012)	Part D plan enrollees with hypertension or hyperlipidemia ≥65 with: (1) no coverage, (2) generic-only coverage, or (3) both brand-name and generic coverage during the coverage gap in 2006; compared to those with low-income subsidy (N = 68,647)	Administrative (Medicare claims, Medicare Part D prescription drug event file), 2005–2006	Patients with no-gap coverage had decreased prescriptions per patient-month (antihypertensives: 4.8%, lipid-lowering agents: 7.2%), higher nonadherence (antihypertensives: OR = 1.60, 95% CI:1.50, 1.71; lipid-lowering agents: OR = 1.59, 95% CI:1.50, 1.68), and more medication gaps (antihypertensives: OR = 1.35, 95% CI:1.25, 1.45; lipid-lowering agents: OR = 1.38, 95% CI:1.29, 1.46), and smaller declines in use of pain relievers and antidepressants; patients with generic-only coverage had decreased use of cardiovascular medications only; those with complete coverage had no changes in use	—
Nair et al. (2011)	Medicare beneficiaries with a chronic condition (congestive heart failure, diabetes, dyslipidemia, or hypertension) who reached the Part D coverage gap (N = 4,509)	Administrative (insurance data), 2006	In the gap, brand-name medication use decreased by 9.3% ($p < .0001$) and generic medication use increased by 7.4% ($p < .0001$), compared to pre-gap phase	Beneficiaries faced a 60.7% increase (from $747 to $1,201) in OOP expenditures in the gap, with a $454 (95% CI: $425–$485) difference in OOP costs between pre-gap and gap phases

Continued

Table 3. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Park et al. (2014)	Medicare Part D beneficiaries on dialysis not receiving low-income subsidies with or without gap coverage, compared to those receiving low-income subsidies (N = 11,732)	Administrative (Center for Medicare and Medicaid U.S. Renal Data System), from 2006 to 2007	Beneficiaries without low-income subsidies had lower adherence for most drugs (antihyperglycemics: OR = 0.76, 95% CI: 0.63–0.92, antihypertensives: OR = 1.06, 95% CI: 0.94–1.19, antilipidemics: OR = 0.80, 95% CI = 0.67–0.95, phosphate binders: OR = 0.65, 95% CI = 0.55–0.76, cinacalcet: OR = 0.39, 95% CI = 0.30–0.49) and higher rates of discontinuation (antihyperglycemics: HR = 1.18, 95% CI: 1.06–1.31, antihypertensives: HR = 1.01, 95% CI: 0.93–1.10, antilipidemics: HR = 1.25, 95% CI: 1.12–1.40, phosphate binders: HR = 1.13, 95% CI: 1.05–1.21, cinacalcet: HR = 1.61, 95% CI: 1.75–1.82)	—
Polinski et al. (2011)	Community-dwelling fee-for-service beneficiaries without financial assistance for drug costs in the coverage gap, compared to those with financial assistance (full subsidy, partial subsidy, and retirees) (N = 217,131)	Administrative (prescription drug claims data and enrollment data), 2006–2007	After reaching the coverage gap, beneficiaries without financial assistance were twice as likely to discontinue medications (hazard ratio = 2.00, 95% CI: 1.64–2.43), less likely to switch (hazard ratio = 0.60, 95% CI: 0.46–0.78), and more likely to reduce adherence (OR = 1.07, 95% CI: 0.98–1.18)	—
Polinski et al. (2012b)	Beneficiaries ≥65 with a stand-alone Part D or retiree drug plan, a cardiovascular diagnosis, and reached the coverage gap without financial assistance; compared to those with financial assistance during the gap period (N = 7,960)	Administrative (prescription drug claims data and enrollment data), 2005–2007	Beneficiaries without financial assistance were more likely to discontinue cardiovascular drugs (hazard ratio = 1.57; 95% CI: 1.39–1.79; risk difference = 13.76 drugs/100 person-years; 95% CI: 10.99–16.54) but had no difference in likelihood of switching cardiovascular drugs	—

Continued

Table 3. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Stuart et al. (2013)	Part D beneficiaries hospitalized for acute myocardial infarction and survived at least 30 days after discharge, without a low-income subsidy; compared to those with a low-income subsidy (N = 8,900)	Administrative (inpatient claims), April 2006-December 2008	Seniors without subsidies had fewer mean percent of days covered after transitioning from the initial coverage phase into the Part D coverage gap (angiotensin-converting enzyme inhibitor/ angiotensin II receptor blockers: 5.1%, $p < .05$; beta blockers: 5.9%, $p < .05$; statins: 7.8%, $p < .05$; clopidogrel: 7.0%, $p < .05$); no changes in adherence after transitioning from the gap to the catastrophic coverage phase	—
Tamariz et al. (2011)	Patients with osteoporosis, rheumatoid arthritis, or multiple sclerosis enrolled in a "basic" Part D plan with a coverage gap; compared to those with a "complete" Part D plan without a coverage gap for generic and branded medications (N = 142,605)	Administrative (claims and enrollment data), 2006	For patients taking alendronate or teriparatide, discontinuation rates were higher in the basic plan (adjusted OR = 2.02 and 3.56, respectively)	—
Zhang et al. (2012)	Medicare Part D beneficiaries with depression and either (1) no coverage or (2) generic-only coverage in the coverage gap; compared to those with full coverage in the gap (N = 65,223)	Random sample of Medicare fee-for-services beneficiaries' claims, 2007	Relative to the changes in the comparison group, the no-gap coverage group had a 12.1% (95% CI: 9.9–14.3%), 12.9% (95% CI: 11.2–14.7%), and 13.4% (95% CI: 8.2–18.6%) reduction in monthly use of antidepressants, heart failure drugs, and oral antidiabetic drugs after reaching the gap, respectively; those with generic gap coverage had 6.9% (95% CI: 4.8–9.1%), 8.7% (95% CI: 7.0–10.4%), and 10.3% (6.0–14.6%) reductions in monthly use of antidepressants, heart failure drugs, and oral antibiotic drugs, respectively, attributable to reductions in using brand-name drugs	—

Continued

Table 3. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Zhang, Baik, and Lave (2013)	Medicare Advantage enrollees ≥65 continuously enrolled in stand-alone Part D plans with (1) no-gap coverage or (2) generic-only gap coverage; compared to those with full-gap coverage through Medicaid or a low-income subsidy (N = 139,958)	Administrative (enrollment data, prescription drug and medical claims), 2007	Relative to the changes in the comparison group, beneficiaries without gap or generic gap coverage had fewer monthly prescription fills (no coverage: 16.0%, 95% CI: 15.5–16.5%; generic gap coverage: 10.8%, 95% CI: 10.3–11.4%), with reductions mainly attributable to reduced use of brand-name drugs; beneficiaries with heart failure and diabetes had lower adherence (heart failure: 3.6%, 95% CI: 2.9–4.2%; diabetes: 10.3%, 95% CI: 9.4–11.3%)	—
Zissimopoulos et al. (2015)	Medicare beneficiaries ≥65 with diabetes not receiving low-income subsidies with no-gap coverage, compared to receiving low-income subsidies (N = 557,756)	Administrative (pharmacy claims data), from 2006 to 2008	Beneficiaries without low-income subsidies more likely to discontinue medication use after reaching the coverage gap, with variation across race/ethnicity (% difference in diabetes medications relative to control group: whites: 2.4%, black: 4.1%, Hispanic: 6.7%; % difference in nondiabetes medications relative to control group: white: 2.6%, black, 3.2%, Hispanic: 4.2%)	—
Cross-sectional data				
Bakk (2015)	Beneficiaries in the coverage gap, compared to beneficiaries not in the coverage gap (N = 1,157)	Survey (Health and Retirement Study), 2006	Compared to those without coverage gaps, beneficiaries who reached the gap or did not reach gap had higher cost-related nonadherence (OR = 5.75, $p < .001$ and OR = 2.78, $p < .01$)	—

Continued

Table 3. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Conwell et al. (2011)	Female beneficiaries ≥65 in prescription drug-only plans with: (1) no-gap coverage or (2) partial-gap coverage (generic-only); compared to those with low-income subsidies, retiree drug subsidy, or no-gap prescription drug-only plans (N = 39,399)	Administrative (pharmacy claims and enrollment data), 2007	Among teriparatide users, beneficiaries with retiree drug subsidies without gap coverage had 3 fewer fills per month ($p < .001$), but teriparatide users in other plan types or benefit designs experienced no changes; among non-teriparatide users with osteoporosis or other chronic conditions, retiree drug subsidy beneficiaries had 1.1 to 1.2 fewer fills per month ($p < .001$)	OOP costs increased among teriparatide users enrolled in partial-gap (121%, $300) or full-gap (186%, $349) exposure plans but decreased for those in no-gap (−49%, −$131) and retiree drug subsidy (−30%, −$40) plans; OOP costs for non-teriparatide users in partial- or full-gap exposure prescription drug plans increased by $144 and $176; for other chronic conditions (no-gap plan $2.80) ($p < .001$); OOP costs in partial- or full-gap plans increased by $124 and $151 (no-gap plan -$19.88) ($p < .001$)
Duru et al. (2010)	Multistate beneficiaries with diabetes mellitus and generic-only drug coverage; compared to those with no-gap coverage (N = 1,468)	Survey (Translating Research into action for Diabetes Study), 2007	Beneficiaries taking insulin with generic-only gap coverage self-reported lower cost-related nonadherence (16% vs. 29%, p = .03); no differences in cost-related nonadherence by type of gap coverage among beneficiaries not taking insulin	—

2010; Joyce, Zissimopoulos, and Goldman 2013; Zissimopoulos et al. 2015), cardiovascular disease (Hales and George 2010; Li et al. 2012; Polinski et al. 2012b; Stuart et al. 2013), osteoporosis and arthritis (Conwell et al. 2011; Tamariz et al. 2011), mental health (Donohue et al. 2011), and kidney disease (Park et al. 2014).

Although it is difficult to statistically compare effect sizes across studies that are limited to specific conditions, there is some evidence for lower utilization of cardiovascular drugs versus antidepressants in the coverage gap (Baik et al. [2012]: antidepressant and heart failure drug utilization decreased by 5.0 and 9.4 percent, respectively; Zhang et al. [2012]: beneficiaries with multiple chronic conditions reduced their monthly use of antidepressants, heart failure drugs, and antidiabetics by 12.1, 12.9, and 13.4 percent, respectively).

The coverage gap prompted some substitution of generic for brand-name drugs. Beneficiaries who reached the gap decreased their brand-name medication use by 9.3 percent, but increased generic medication use by 7.4 percent (Nair et al. 2011). Similarly, Zhang, Baik, and Lave (2013) found that beneficiaries without gap coverage or with generic-only gap coverage had fewer prescriptions filled per month, relative to the changes in the group with low-income subsidy (16.0 percent and 10.8 percent reduction). Those with generic-only coverage had larger declines in brand-name drug utilization (8.2 percent vs. 6.7 percent decrease), while those without any coverage had larger declines in generic medication utilization (5.2 percent vs. 2.4 percent decrease).

The Impact of Benzodiazepine Exclusion on Drug Utilization and Inappropriate Medication Use

Benzodiazepines are excluded from Medicare Part D coverage, although some states offer supplemental coverage through Medicaid. Table 4 summarizes findings from benzodiazepine exclusion studies. The benzodiazepine exclusion led to a 10 percentage point reduction in utilization, while its utilization remained stable in states with partial and complete coverage through Medicaid (Briesacher et al. 2010); and elderly Medicare Advantage enrollees had larger decreases in benzodiazepine utilization than the near-elderly (Ong et al. 2012a,b). Those losing benzodiazepine coverage when changing from private coverage to Medicare Part D increased their rates of fluid movement (switching on and off benzodiazepines; OR = 2.43), and switch patterns (substituting with other medications; OR = 2.09) (Chen and Kreling 2014). Although these studies consistently found that the benzodiazepine exclusion decreased benzodiazepine utilization, Lai et al. (2015) explained that

Table 4: The Impact of Benzodiazepine Exclusion on Drug Utilization, Inappropriate Medication Use, and Out-of-Pocket Costs

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Longitudinal data				
Briesacher et al. (2010)	Nursing home residents in states where Medicaid limits benzodiazepine coverage completely (1 state) or partially (6 states); compared to those in states with no Medicaid limits on benzodiazepine coverage (41 states) (N = 1,068,104)	Administrative (prescription drug dispensing record and Minimum Data Set), January 2005–June 2007	No-coverage policies immediately reduced benzodiazepine use from 27% to 17% after Part D (95% CI: −0.11, −0.09, $p < .001$); benzodiazepine use remained stable in the partial and complete coverage states	—
Chen and Kreling (2014)	Medicare beneficiaries using benzodiazepines from one southeastern state who changed from private coverage to Part D, compared to beneficiaries using benzodiazepines with continuous private coverage (N = 466)	Administrative (pharmacy data), from 2005 to 2006	Those losing benzodiazepine coverage had higher fluid movement (switching from a benzodiazepine to a substitute agent and back; OR = 2.43, $p < .05$) and switch patterns (OR = 2.09, $p < .05$)	—

Continued

Table 4. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Donohue et al. (2012)	Pennsylvania beneficiaries who transitioned from no or limited drug coverage ($150 or $350 caps) to Part D coverage in 2006, compared to beneficiaries with continuous no-cap coverage (total $N = 34{,}697$)	Administrative (pharmacy and medical claims, enrollment data from large health insurance company), 2004–2007	High-risk medication use increased from 15.7 to 17.6% among those gaining coverage but decreased from 21.0 to 18.3% among those continuously enrolled (ratio of ORs = 1.34, 95% CI: 1.22–1.48, $p < .001$); proportion of total drug use attributable to high-risk medications declined from 3.0 to 2.0% among those gaining coverage, a smaller decline relative to those continuously enrolled (ratio of ORs = 0.68, 95% CI: 0.59–0.78, $p < .0001$)	—
Fu et al. (2010)	Community-dwelling adults ≥65 enrolled in Part D in 2005 versus 2006; compared to those not enrolled in Part D ($N = 1{,}774$)	Survey (Medical Expenditure Panel Survey), 2005–2006	Enrollees used significantly more potentially inappropriate prescriptions in 2006 than nonenrollees (incidence rate ratio = 1.56, 95% CI: 1.08–2.25), but no significant difference in trends between Part D enrollees and nonenrollees	—
Lai et al. (2015)	Physician visits in which at least one benzodiazepine was prescribed before Medicare Part D, compared to after Medicare Part D ($N = 86.9$ million physician visits)	Survey (National Ambulatory Medical Care Survey), from 2005 to 2009	Benzodiazepine prescribing decreased by 1.83% ($p = .09$) from 2005 to 2006 after the Medicare Part D benzodiazepine exclusion, and increased by 21.66% from 2006 to 2007	—

Continued

Table 4. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Ong et al. (2012a)	Elderly Medicare Advantage beneficiaries who use benzodiazepines and subject to the benzodiazepine exclusion; compared to near-elderly benzodiazepine users enrolled in a managed care plan without a benzodiazepine exclusion ($N = 22{,}827$)	Administrative (medical and pharmacy claims and eligibility files), 2005–2007	Beneficiaries experiencing the benzodiazepine exclusion had lower benzodiazepine use (100–74.8%, $p < .001$) and increased use of other psychotropic drugs (39.6–45.1%, $p < .001$); those with no exclusion had a larger decline in benzodiazepine use (100–57.5%, $p < .001$) and decreased use of other psychotropic drugs (55.4–45.1%, $p < .001$)	—*
Ong et al. (2012b)	Elderly Medicare Advantage enrollees with new anxiety disorders, excluding dual-eligibles; compared to near-elderly aged 60–64	Administrative (behavioral, medical and pharmacy claims, and eligibility files) for the first 6 months of 2005, 2006, and 2007	Medicare Advantage enrollees had more covered claims for psychotropic drugs including benzodiazepines in 2005 versus 2006–2007 and declining days' supply of any psychotropic drug (2005: 124.9, 2006: 66.0, 2007: 76.1, $p < .001$), benzodiazepines (2005: 71.1, 2006: 1.1, 2007: 1.5, and 2007, $p < .001$); no significant differences in psychotropic medication use among the near-elderly	—*

Continued

Table 4. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Polinski et al. (2012a)	(1) All patients ≥65 taking antipsychotic medications without drug insurance in 2005 and eligible for Part D ("policy model") and (2) patients ≥65 taking antipsychotic medications without drug insurance in 2005 and enrolled in Part D ("clinical model"); compared to their projected experiences if Part D had not been introduced ($N = 3{,}030$)	Administrative (pharmacy claims), 2005–2006	Among eligible patients (policy model), Part D associated with a 5% increase in days' supply in 2006 and monthly increases of 159 per 1,000 patients (95% CI: 90–227) in 2005, an immediate but nonsignificant temporary decrease in January 2006, and a 151 per 1,000 patients (95% CI: 49–254) increase in 2006; enrollees (clinical model) experienced decreases of 125 days' supply per 1,000 patients (95% CI: 45–205) in 2005, followed by an immediate increase of 8,007 per 1,000 patients (95% CI: 7,078–8,937) and a subsequent decrease of 227 per 1,000 patients (95% CI: 73–381)	Among all eligible patients (policy model), Part D associated with 37% lower out-of-pocket (OOP) costs per 30-day supply, with an immediate $31 decrease (95% CI: $25–$36) in January 2006 and an additional $2 decrease (95% CI: $1–$3) thereafter; enrolled patients (clinical model) had 62% lower OOP costs per 30-day supply, with an immediate $86 (95% CI: $76–$96) decrease in January 2006 and $4 (95% CI: $3–$5) increase thereafter

Note. *Total expenditures reported only, not OOP.

reductions were not only caused by formulary exclusions: prescribing decreased 1.83 percent from 2005 to 2006 after the Medicare Part D benzodiazepine exclusion, but increased 21.66 percent from 2006 to 2007.

Findings on potentially inappropriate medication use are mixed. Donohue et al. (2012) found that inappropriate drug utilization increased slightly among those moving from no coverage to Part D coverage (relative odds ratio = 1.3, $p < .001$). Similarly, Polinski et al. (2012a) projected that Medicare Part D implementation was associated with 5 percent increase in days' supply of antipsychotics. In contrast, Fu et al. (2010) found no significant difference in the likelihood of potentially inappropriate medication use between enrollees and nonenrollees.

Impact of Medicare Part D on Drug Utilization among Dual-eligibles

There is limited empirical evidence on Medicare Part D among dual-eligibles, summarized in Table 5. There is some evidence that elderly dual-eligibles did not experience changes in pill-days, total number of prescriptions (Basu, Yin, and Alexander 2010), or medication access (Domino and Farley 2010). A qualitative study (Hensley 2012) of elderly dual-eligibles with mental illness reported that beneficiaries did not experience access problems during the transition and their needs for psychotropic and other medications were met. However, nonelderly disabled dual enrollees with mental illness experienced differential antipsychotic treatments depending on whether they lived in strict-cap (low limits on monthly fills) or no-cap states: post–Part D use of medications to treat schizophrenia (17.69 percent) and bipolar disorder (35.47 percent) increased disproportionately in strict-cap states (Madden et al. 2015).

Out-of-Pocket Costs among the General Population

Most studies found that OOP costs among the general Medicare Part D population decreased, with estimates from $142 to $356 per person-year (Briesacher et al. 2011; Liu et al. 2011; Cheng and Rascati 2012; Kircher et al. 2014) or 20 percent (Zimmer 2015) (see Tables 1 and 2). These reductions in OOP costs were experienced across race/ethnicity (Mahmoudi and Jensen 2013), although more for African Americans (Chen, Rizzo, and Ortega 2011) and nonelderly beneficiaries ($\beta = -0.794$) (Nelson et al. 2014). This decline in OOP costs is supported by studies showing that beneficiaries with low-income subsidies had even lower OOP costs (Yala et al. 2014; Yusuf et al.

Table 5: The Impact of Medicare Part D on Dual-Eligibles

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Longitudinal data				
Basu, Yin, and Alexander (2010)	Dual-eligibles from 45 states, aged 65–78 years, compared to near-elderly patients with Medicaid coverage aged 60–63 (N = 177,331)	Administrative (pharmacy claims, Census 2000), January 2005–April 2007	No significant changes in trends in the dual-eligibles' pill-days or total number of prescription due to Part D	No significant changes in trends in the dual-eligibles' out-of-pocket (OOP) expenditures due to Part D
Domino and Farley (2010)	Medicare beneficiaries enrolled during 2005–2006 (panel 10); compared to 2004–2005 (panel 9) (N = 5,015)	Survey (Medical Expenditure Panel Survey), 2004–2006	Insignificant differences between panels, indicating Part D likely not associated with changes in access to protected psychotropic drug classes (antidepressant and antipsychotic medications) and nonpsychotropic classes (lipid-lowering and antihypertensive agents)	—
Madden et al. (2015)	Community-dwelling nonelderly disabled dual enrollees with schizophrenia or bipolar disorder who live in "strict-cap" states with low limits on monthly fills, compared to those living in "no-cap" states (N = 9,229)	Administrative (Medicaid and Medicare claims), from 2004 to 2007	Compared to changes in "no-cap" states, enrollees in "strict-cap" states with schizophrenia and bipolar disorder had 17.7 and 35.5% increases in overall medication use after Part D	—

Continued

Table 5. *Continued*

Citation	*Study Population*	*Data Sources*	*Drug Utilization Outcomes*	*Out-of-Pocket Cost Outcomes*
Millett et al. (2010)	Dual-eligibles ≥65 with drug coverage in both years but provided through Medicaid in 2005 and Part D in 2006 (N = 198)	Survey (Medical Expenditure Panel Survey), 2005–2006	—	No significant decrease in mean OOP expenditures among dual-eligibles or beneficiaries with drug coverage in both years
Cross-sectional data				
Hensley (2012)	Beneficiaries in Midwestern urban area with mental illness, describing post–Part D experiences; compared to pre–Part D (N = 26)	Qualitative interviews in psychosocial rehabilitation clubhouses, December 2007 to January 2008	Part D participants perceived that their medication needs (psychotropic and other) were met and did not experience serious access problems during the transition	Mixed opinions about whether the OOP costs for Part D were reasonable or a significant burden preventing them from obtaining other necessities

2014; Yazdany, Tonner, and Schmajuk 2015). Reductions in OOP costs grow consistently with baseline spending: Engelhardt and Gruber (2011) reported reductions of $180 at the median and $800 at the 90th percentile of baseline spending, and Mott et al. (2010) found that while seniors with lower pre–Part D spending had similar OOP costs, those with the highest pre–Part D spending had 17.6 percent fewer OOP costs. Yet not all studies documented reduced OOP costs: Nair et al. (2010) found that mean OOP expenditures increased from $45.66 to $81.83 per member per month, hypothesizing that this increase is due to the coverage gap when members paid 100 percent of medication costs.

When looking at subgroups with different sources of prescription coverage, all Part D beneficiaries except those previously reporting employer-based coverage reported lower OOP spending, and Medicare Part D beneficiaries who previously lacked coverage experienced the largest reductions (Safran et al. 2010). While annual OOP expenditures decreased by 32 percent ($320) for all Medicare beneficiaries, beneficiaries without previous drug coverage experienced a larger 49 percent decrease ($748) (Millett et al. 2010). Similarly, beneficiaries whose prescription insurance become more generous, in terms of previous insurance caps (Zhang et al. 2010b; Ettner et al. 2011) and branded versus generic-only coverage (Ettner et al. 2011), showed the highest reduction in OOP costs, with estimates of 15.9 percent (Zhang et al. 2010b) or around $200–300 (Ettner et al. 2011).

Out-of-Pocket Costs for Beneficiaries in Coverage Gap

Beneficiaries faced increased OOP expenditures in the gap (see Table 3). Nair et al. (2011) estimated an overall increase of 60.7 percent. These findings were consistent for beneficiaries with diabetes and osteoporosis. Fung et al. (2010) found that beneficiaries with diabetes had 189 percent higher OOP expenditures for all drugs compared to no-gap beneficiaries, and 14 percent higher OOP expenditures compared to those with generic-only gap coverage, and Conwell et al. (2011) found that OOP costs rose among teriparatide users enrolled in partial- or full-gap exposure plans (increases of 121 and 186 percent) but fell for those in no-gap exposure plans.

Impact of the Benzodiazepine Exclusion on Out-of-Pocket Costs

While several studies (Ong et al. 2012a,b) evaluated the benzodiazepine exclusion's impact on patients' deductibles, copayments, and plan

reimbursements, only one study examined its effect on OOP costs (Polinski et al. 2012a) (see Table 4). Polinski et al. (2012a) estimated a 37–62 percent decrease in OOP costs for antipsychotics among uninsured elderly patients newly obtaining drug insurance.

Out-of-Pocket Costs for Dual-Eligibles

Two quantitative studies (Basu, Yin, and Alexander 2010; Millett et al. 2010) and one qualitative study (Hensley 2012) found mixed outcomes or no significant changes in OOP costs among dual-eligibles (see Table 5). Compared to near-elderly patients with Medicaid coverage (Basu, Yin, and Alexander 2010) or elderly beneficiaries with previous coverage through Medicaid (Millett et al. 2010), dual-eligibles did not have higher OOP costs. A qualitative study of adults with mental illness found mixed perceptions about the impact on OOP costs, with some interviewees expressing that Medicare Part D premiums and copayments were reasonable, while others revealing them to be a significant burden preventing them from obtaining other necessities (Hensley 2012).

Quality Assessment

We scored 51, 35, and 14 percent of studies as high, medium, and low quality, respectively (see Data S1). The strongest study designs used nonequivalent controls with differences-in-differences regression models to compare differential trends between those becoming eligible for Medicare Part D to similar ineligible individuals (such as near-elderly, veterans, or with employer-sponsored drug coverage). Almost all studies using claims data had no attrition because they restricted to individuals continuously enrolled in the full year, while many survey-based studies had low response rates (e.g., Safran et al. 2010; Chakravarty et al. 2015) or else did not report rates of nonresponse. Across studies, there was minimal bias from the intervention affecting the data collection and quality. Studies using claims data commonly suffered from moderate measurement error, as prescription claims may not reflect actual use. Survey-based studies often had recall bias, particularly where respondents reported experiences in the past year. However, the Medical Expenditure Panel Survey, commonly used in these studies, minimizes recall bias by requesting that participants bring medications to interviews and verifying responses with pharmacies. Only 10 studies provided sufficient information to evaluate the risk of bias from missing data; among these studies we concluded

that three had low bias along this dimension. Although most studies did not provide an extensive rationale for their choice of outcome measures and their validity/reliability, studies frequently used common measures (such as prescriptions per month, days of prescription filled, and OOP costs). Ten publications were linked studies reporting slightly different outcomes or patient populations; most notable was a study team analyzing administrative data from a large Pennsylvania health insurer (e.g., Donohue et al. 2010, 2011, 2012). These studies had a rigorous design, were all graded as high quality, and provided incremental evidence, but the large number of linked studies in which the same data sources and study design were used for multiple manuscripts focusing on slightly different outcomes or drug classes limits external validity.

DISCUSSION

We systematically reviewed evidence on how Medicare Part D impacted OOP costs and drug utilization since the last 2010 systematic review. In addition to reviewing new studies, we focused on the coverage gap and Medicare Part D's effects on diverse subpopulations such as dual-eligibles and those with specific conditions. There is strong and robust evidence for increased drug utilization and decreased OOP costs across different medications, using a range of data sources and study designs. However, the generosity of beneficiaries' pre–Part D insurance and drug spending strongly moderated the program's impact. We also found that the benzodiazepine exclusion decreased drug utilization and OOP costs. These findings are consistent with those from the prior systematic review (Polinski et al. 2010), although our findings demonstrate a longer term impact.

Despite the strong evidence for the overall effects of Medicare Part D and the coverage gap, there are three areas with weak evidence where further research is needed. First, there is limited research on how outcomes differ among dual-eligibles. This group was often deliberately excluded to reduce measurement error (such as procuring drugs from other coverage sources that are not available in the datasets) and internal validity (such as selection bias from individuals who transition across coverage sources). The few studies on this population found mixed outcomes, which could be due to the small and nonrepresentative samples (Millett et al. 2010; Hensley 2012). Future research with representative samples is needed to evaluate effects on dual-eligibles with various health conditions and level of prescription drug spending. A second

area with weak evidence is comparing findings across diseases or drug classes. With a few exceptions (Zhang et al. 2010a, 2012; Baik et al. 2012), most studies about specific conditions were restricted to narrowly defined clinical populations. Although these studies provide a deeper understanding of the impact of Medicare Part D, effect sizes cannot be statistically compared across studies. Future research comparing outcomes across diseases could elucidate whether some patient populations are more vulnerable to the coverage gap, thereby experiencing differential cost-related nonadherence. A third research gap is the long-term effect of Medicare Part D on drug utilization and OOP costs after the transition period.

There were some common study limitations that may have biased reported findings; yet with such a robust corpus of publications reporting similar effects using different study designs and data sources, we still conclude that there is a high-quality evidence for the overall effects of Medicare Part D on utilization and OOP costs. As this was a major policy change, there are no randomized controlled trials and all studies are observational. Most of the studies that we graded as high quality used a pre/post design with nonequivalent controls (such as near-elderly or individuals retaining employer-sponsored drug coverage) and a differences-in-differences framework. This analytic design should control for difference in groups as long as they have parallel trends in the prior to the policy intervention. However, as Stuart et al. (2013) noted, two sources of bias are that enrollees could have different OOP costs by changing their prescription filling behaviors, and there may be reverse causality because those with higher adherence will incur higher costs and thus be more likely to reach the gap. Many studies using this differences-in-difference design also did not explicitly test the parallel trends assumption. Second, a major source of measurement error with the 42 studies relying on claims data is that researchers cannot monitor whether beneficiaries consumed medications (actual vs. measured behavior) or whether beneficiaries received medications through other coverage sources such as pharmacy assistance programs. Claims data are also unable to provide information on reasons for reduced utilization; nonadherence (measured by fewer prescriptions) could be due to cost or else medical reasons such as side effects or the course of treatment ending (Chakravarty et al. 2015). The survey-based studies can track drug use across insurance coverage sources and elicit reasons for nonadherence but are susceptible to other measurement error such as recall and nonresponse bias. Third, many studies have poor external validity because they use data from a single pharmacy chain or prescription plan, and limit analyses to individuals maintaining continuous enrollment. Finally, some of these studies may

provide high quality evidence but were downgraded because we could only systematically evaluate the risk of bias based on the reported information. Information about missing data, attrition, and data collection procedures were commonly excluded. This highlights a broader need to clearly report study design, which researchers and medical journal editors are trying to improve through guidelines such as the Strengthening the Reporting of Observational Studies Statement (Vandenbroucke et al. 2007).

This systematic review has four limitations. Like all systematic reviews, it may suffer from the publication bias, which may overestimate effects. We could not compare results from published studies and gray literature as most gray literature meeting our inclusion criteria later became peer-reviewed articles and there was too much heterogeneity in study designs to do a statistical assessment. Second, the OOP cost savings represent the beneficiary, not societal perspective. Third, we did not review health outcomes, as most studies focused on utilization and OOP costs. Lastly, one reviewer (YP) identified studies and extracted data. This may lead to reviewer bias, although the new PCORI standards asserts that fact-checking may be sufficient (Hickam et al. 2013) and EGM was consulted on the study design and data synthesis.

More broadly, our findings can inform the potential impact of insurance market changes due to the Affordable Care Act (ACA). The ACA includes "essential health benefits," including drug benefits that plans must cover (HealthCare.gov, 2014). Over 8 million people selected plans with prescription drug benefits through the federal or state exchanges (Office of the Assistant Secretary for Planning and Evaluation (ASPE) May 1, 2014). Our findings suggest that these essential benefits provisions may increase drug utilization and decrease OOP costs among those gaining new or improved coverage; however, these outcomes may worsen among those selecting less expensive high-deductible plans. A second relevant policy change is that Medicare beneficiaries in the donut hole now only pay 45 percent for brand-name drug and 58 percent for generic drugs and the gap will be closed by 2020 (The Official U.S. Government Site for Medicare 2016). We found that this coverage gap has a negative impact on beneficiaries; eliminating it will likely improve drug utilization, medication discontinuation, and OOP costs, especially to seniors with multiple conditions. To improve the ACA's impact, it is important to enroll those without previous insurance and minimize the crowding-out of less generous private insurance among those previously insured. Following our review's findings on the importance of the coverage gap, the closing of the gap provides an opportunity for future research to assess the population impact of this altered policy design.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Appendix SA1: Author Matrix.

Appendix SA2: Quality of Study Assessment.

Appendix SA3: Summary of Evidence Search and Selection of Studies for Systematic Review of Medicare Part D's Effects on Drug Utilization and OOP Costs.

Data S1. Explanation of Coding Guide.