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Good Research Practices for Measuring Drug Costs in Cost-Effectiveness Analyses: Medicare, Medicaid and Other US Government Payers Perspectives: The ISPOR Drug Cost Task Force Report—Part IV

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ABSTRACT

Objectives: Public programs finance a large share of the US pharmaceutical expenditures. To date, there are not guidelines for estimating the cost of drugs financed by US public programs. The objective of this study was to provide standards for estimating the cost of drugs financed by US public programs for utilization in pharmacoeconomic evaluations.

Methods: This report was prepared by the ISPOR Task Force on Good Research Practices—Use of Drug Costs for Cost-Effectiveness Analysis Medicare, Medicaid, and other US Government Payers Subgroup. The Subgroup was convened to assess the methodological and practical issues confronted by researchers when estimating the cost of drugs financed by US public programs, and to propose standards for more transparent, accurate and consistent costing methods.

Results: The Subgroup proposed these recommendations: 1) researchers must consider regulation requirements that affect the drug cost paid by public programs; 2) drug cost must represent the actual acquisition cost, incorporating any rebates or discounts; 3) transparency with respect to cost inputs must be ensured; 4) inclusion of the public program's perspective is recommended; 5) high cost drugs require special attention, particularly when drugs represent a significant proportion of health-care expenditures for a specific disease; and 6) because of variations across public programs, sensitivity analyses for actual acquisition cost, real-world adherence, and generics availability are warranted. Specific recommendations also were proposed for the Medicare and Medicaid programs.

Conclusions: As pharmacoeconomic evaluations for coverage decisions made by US public programs grows, the need for precise and consistent estimation of drug costs is warranted. Application of the proposed recommendations will allow researchers to include accurate and unbiased cost estimates in pharmacoeconomic evaluations.

Keywords: cost study, drug cost, Medicaid, Medicare, pharmacoeconomic.

Background to the Task Force

The ISPOR Task Force on Good Research Practices—Use of Drug Costs for Cost-Effectiveness Analysis (DCTF) was recommended by the ISPOR Health Science Policy Council on December 13, 2004 and approved by the ISPOR Board of Directors May 15, 2005. Because how drug costs should be measured for cost-effectiveness analyses (CEAs) depend on the perspectives, five Task Force subgroups were created to develop drug costs standards from the societal, managed care, US government, industry, and international perspective. This report is Part IV: a US government perspective (one of six reports from this ISPOR Task Force on Good Research Practices—Use of DCTF. The other reports (Part I: issues and recommendations; Part II: a societal perspective; Part III: managed care; Part V: industry perspective; and Part VI: international perspective) are also published in this issue of *Value in Health* (Volume 13, Issue 1). This DCTF subgroup met to develop core assumptions and an outline before preparing a draft report. The Task Force subgroups held open forums and/or group leader breakfast meetings at the ISPOR Annual International Meetings and European Congresses. The draft report was circulated to 174 Task Force primary reviewers (who were self-identified from a broad range of perspectives). Following this review, a new draft was prepared and made accessible for broader review by all ISPOR members. Comments for these reports by Task Force primary reviewers and ISPOR membership are published at the ISPOR website. All opinions reflect those of the authors and not necessarily their affiliations.

Introduction

This article is part of a series that address the topic of estimating drug costs for pharmacoeconomic and outcomes research studies. The goal of this DCTF Subgroup was to focus on drug cost estimation from the perspectives of Medicare, Medicaid, and other government payers in the United States for purposes of conducting pharmacoeconomic and cost studies.

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Drug Expenditures and Costs in the Public Sectors of the United States

Public pharmaceutical spending represents expenditures by Federal, State, and local governments. The largest public pharmaceutical programs are Medicare, Medicaid, and the State Children's Health Insurance Program. These programs are run by the Federal agency Centers for Medicare & Medicaid Services (CMS); however, Medicaid is administered by the States within broad Federal guidelines. Other public pharmaceutical programs include the Department of Defense, the Department of Veterans' Affairs (VA), Workers' Compensation programs, and State-only general assistance programs. The public sector also funds other programs that purchase pharmaceuticals including: maternal and child health services, school health programs, public hospitals and clinics, Indian health-care services, migrant health-care services, substance abuse and mental health activities, and medically related vocational rehabilitation services [1].

In 2007, the CMS served approximately 93 million beneficiaries outlaying approximately $570.5 billion dollars [2]. CMS provides pharmaceutical coverage through its various benefit programs of Medicare and Medicaid. A description of the Medicaid and Medicare programs, including the prescription drug components, are summarized in Table 1. In addition to Medicare and Medicaid, there are a number of other public payers in the United States. In 2008, CMS projects that 46% of health-care expenditures and 35% of drug expenditures in the United States will be paid by public payers [3]. This is a substantial increase from prior years and, as a result, estimating pharmaceutical expenditures and the value of prescription medicines from a US public payer perspective is increasingly important.

As the public sector pays for a greater proportion of drug expenditures, there is an increasing desire for price transparency and more focus on discriminatory pricing. Discriminatory pricing occurs when pharmaceutical companies charge different prices to different groups of consumers (e.g., Medicare and Medicaid enrollees vs. enrollees of a managed care organization [MCO]) for identical pharmaceuticals. Traditionally, average wholesale price (AWP) was the most commonly used mechanism for pharmacy reimbursement, but the wide variations in discounts of AWP led to many controversies regarding the differences in pharmaceutical prices across payers.

Congress introduced a new average sales price (ASP) to standardize the reimbursement process and to minimize variation in pharmaceutical prices paid by Medicare for certain medications used in physician offices beginning January 1, 2005 [4]. Congress has also approved the use of the average manufacturer price (AMP) for Medicaid fee-for-service outpatient drug reimbursement. The ASP is a computed average manufacturer transaction price, calculated using sales data for all multiple source products available in the market for that drug, i.e., the payments that manufacturers received for their products. It is the weighted average of all non-Federal sales to wholesalers and is net of charge backs, discounts, rebates, and other benefits tied to the purchase of the drug product, whether it is paid to the wholesaler or to the retailer [4]. Thus, the ASP for drug products that have generic competition is very low. The ASP and the AMP were expected to be the future established reimbursement basis for Federal and possible even non-Federal insurers, but the use of AMP for Medicaid outpatient pharmacy reimbursement has been challenged. Thus, researchers and decision-makers need to better understand the mechanisms and implications of the evolving pharmaceutical cost structure for public payers. In this article, we aim to provide guidance for estimating drug costs to be used in cost-effectiveness and health economics studies from a public payer perspective.

Table 1 Features of Medicare and Medicaid programs [10,25,26]

Feature	Medicare	Medicaid
1. Enacted in 1965	Federal health insurance program covers acute inpatient (through Part A) and post–acute outpatient care (through Part B); and since 2006 covers outpatient prescription drugs (through prescription drug insurance, Part D).	Federal and state joint health insurance program; provides health and long-term care coverage, and prescription drugs, which are covered although not mandated.
2. Financing	Federal government funding through taxes, income and premiums.	Federal and state spending with Federal government funding 57% in 2006. States pay back Medicare for Part D prescription drug coverage for their dual eligible.
3. Eligibility	Aged 65 and above, disabled and those with end stage renal disease of any age; 44 million elderly and disabled Americans in 2006.	Welfare population of a particular Federal poverty level (single parents with dependent children, aged, blind, disabled); over 52 million low-income people including over 6 million Medicare beneficiaries, the dual eligible in 2006.
4. Patient cost sharing and variation in coverage	All costs vary by the type of service, and the plan the beneficiary enrolls into and the level and duration of service received. For traditional Parts A and B services, patients may or may not pay a premium and deductible and also may have a copayment or pay coinsurance. Compared with Part D beneficiaries above 150% of the Federal poverty level (FPL), those below the 150% FPL level may pay a lower premium or may not pay a premium and may have lower or no copayments or coinsurance. Part D beneficiaries who are below the 150% of the Federal poverty level (FPL) include dual eligibles on Medicare and Medicaid who will not have gaps in coverage; however part D beneficiaries above the 150% FPL will have gaps in coverage unless they enroll in high cost plans that cover drugs in the donut hole.	State Medicaid Programs are prohibited from imposing premiums or cost sharing for emergency room visits, family planning services, hospice care, and preferred drugs on certain groups including institutionalized persons, pregnant women, children and women in breast or cervical cancer programs.
5. Cost containment measures	Drug utilization controls by private drug plans—use of formulary based tiered prescription drug benefit structure by competing private insurance plans, manufacturer rebates, and reducing provider reimbursement.	Preferred drug lists, manufacturer rebates, State's maximum allowable cost, disease management, freezing or reducing provider reimbursements, reducing pharmacy dispensing fees, and increasing patient copayments.

Medicaid Program

Medicaid is a government-sponsored health insurance program that is administered at the state level and is available to certain low-income individuals/families that fit within an eligible group recognized by both Federal and State laws. Medicaid does not reimburse the beneficiaries directly. Instead, it reimburses their health-care providers directly. Depending on the state of residence and the eligibility status, the beneficiary may be required to provide a copayment for certain medical services and drugs.

A wide variety of individuals/families are covered by Medicaid. Requirements that must be met to be eligible for Medicaid coverage may include: whether one is pregnant, disabled, blind, or aged; the individual's income and resources; and whether one is a US citizen or a lawfully admitted immigrant. The rules concerning income and resources vary from state to state and from group to group. In addition, there are special rules for those who live in nursing homes and for disabled children living at home.

The Medicaid program pays for inpatient and outpatient prescription drugs. States maintain autonomy in setting the pharmacy payment rates for outpatient prescription drugs [5]. There are three components in the Medicaid drugs cost: 1) the estimated drug acquisition cost that the state pays the pharmacies; 2) the dispensing fee that the state pays the pharmacies; and 3) the drug rebates that the Medicaid Program receives from the drug manufacturers [6]. This rebates applies only to outpatient drugs purchased by the program on a fee-for-service basis [6]. When drugs are purchased through capitated MCOs, the MCOs may negotiate their own rebates and discounts [6]. Some states negotiate supplemental rebates directly with manufacturers [5]. Their leverage for doing this comes from each state Medicaid's preferred drug list [6]. In addition to the cost of the drug, Medicaid law allows states to pay a dispensing fee to the pharmacies. Nevertheless, Federal regulations do not specify its exact amount, so the dispensing fee that the states pay varies significantly.

Traditionally, Medicaid payments for approximately 400 multisource drugs are subject to Federal upper limits (FUL) set at 150% of the lowest published price for equivalent drugs [5,7]. States also may have their own maximum allowable cost list for multisource drugs [5].

The 2005 Deficit Reduction Act (DRA) changed the way state Medicaid programs pay pharmacies from being based on listed prices AWP and wholesale acquisition cost (WAC) to being based on the AMP [8]. The DRA set the FUL at 250% of the AMP for multiple source drugs, as calculated without regard to customary prompt pay discounts to wholesalers [8]. AMP is defined by DRA as the average price that a manufacturer receives for a drug in a given quarter for sales to the retail pharmacy class of trade [8]. According to DRA, the retail pharmacy class of trade is defined as chain pharmacies, independent pharmacies, mail order pharmacies, and other outlets that purchase or arrange for the purchase of drugs from a wholesaler or manufacturer [5]. The DRA AMP regulations have not been implemented to date because of a preliminary court injunction that enjoins CMS from implementing the final rule with comment concerning AMP to the extent that it affects Medicaid reimbursement rates for outpatient pharmacy [9].

AMP is expected to be significantly lower than the listed prices [5]. Thus, the change from listed prices to AMP is expected to decrease Medicaid payments for estimated drug acquisition costs to pharmacies [10]. Indeed, the average FUL before the DRA was approximately five times higher than the proposed AMP [5]. The AMP was confidential, but such information is required by DRA to be posted on CMS's website and made available to the public and states [8].

The prescription drugs used in institutions such as nursing homes, hospitals, Intermediate Care Facilities for the Mentally Retarded, and mental health institutions comprise a significant proportion of overall state drug spending [6]. Most states pay for these prescription drugs in one of two ways: they may purchase drugs on a fee-for-service basis, separate from an institutional payment rate; or they may include drug spending in the bundled institutional payment rate [6].

The Medicaid Drug Rebate Program

The Medicaid Drug Rebate Program was created by the Omnibus Reconciliation Act of 1990 (OBRA '90), which added Section 1927 to the Social Security Act [8]. OBRA '90 became effective in early 1991. The rebate regulations were modified by the Medicare Modernization Act (MMA) and DRA. The Program requires drug manufacturers to enter into a rebate agreements with the Department of Health and Human Services in order to receive Federal funding for fee-for-service outpatient drugs dispensed to Medicaid patients [5,8,11]. Manufacturers that do not sign a rebate agreement with CMS are not eligible for Federal Medicaid reimbursement for their products [11].

For innovator drugs, the amount that manufacturers rebate to Medicaid is the larger of 15.1% of AMP or the difference between the AMP and the best price per unit and adjusted by the Consumer Price Index-Urban (CPI-U) [5,12]. The rebate amount for non-innovator drugs is currently 11% of the AMP per unit [5,12].

The best price is defined as the lowest manufacturer price available to private and public purchasers [5,8]. Nevertheless, drug prices for certain public entities such as the Indian Health Service, Department of Defense, and Department of Veterans Affairs are not considered in establishing best prices [8].

According to OBRA '90 manufacturer rebates were confidential; DRA provisions—not implemented to date—request the AMP to be disclosed to states and the public. The DRA also has provisions to secure rebates for certain physician-administered drugs [8]. It also has provisions regarding the inclusion of authorized generic drugs when calculating the AMP and the best price for drugs [8].

Medicare Program

Medicare was enacted by Congress in 1965 to provide health insurance primarily for the nation's elderly. In 1973, the entitlement was expanded to include certain groups with disabilities or end stage renal disease. Part A of Medicare provides hospital inpatient and outpatient services, nursing home care, home health care, hospice care, and skilled nursing facilities. The hospital inpatient services are paid through a prospective payment system that covers all services through the diagnostic related groups.

Medicare Part B covers physician supplies, medical supplies, some oral cancer therapies, and physician office services. Pharmaceuticals provided in the outpatient setting are paid through an outpatient prospective payment system (OPPS) and classified into ambulatory payment classifications similar to the inpatient system. The difference is a drug-specific payment for outpatient drugs and pharmaceutical beyond a cost of $55 which is the threshold to receive separate payments.

Medicare Part C earlier known as Medicare + Choice (M + C) programs are now known as Medicare Advantage plans as part of the Medicare Prescription Drug and Modernization

Act of 2003 (MMA). These were developed by private health plan sponsors that provide managed Medicare services to enrollees and receive payments from Medicare. The original intent was to establish and provide access to private plan options similar to the health maintenance organizations and preferred provider organizations that operate in a competitive marketplace, reduce patient cost sharing for Medicare benefits, and cover additional services that traditional Medicare is not authorized to offer [13].

The Medicare Modernization Act of 2003

The MMA, which was passed in 2003, was designed to provide access for senior citizens at low prices by encouraging competition across Medicare drug plan providers. Drug coverage under Medicare Part D began on January 1, 2006. Medicare Part D covers prescription drugs and certain related services in the ambulatory setting. Enrollees pay a premium and participate in cost sharing. Enrollees may opt for a stand alone prescription drug plan, known as a Medicare prescription drug plan (PDP) or through a Medicare Advantage plan, known as a Medicare Advantage Prescription Drug (MAPD) plan. The plans provide the drugs through a formulary as approved by CMS. The plans assume financial risk under the conditions established by MMA. As a result of the fact that net prices include rebates and the fact that drug companies enter confidential contracts with Medicare Plans that provide legal confidentiality agreements, there is no publicly available indicator of the industry's actual cost [14].

ASP

In response to inflationary pressures in spending for Medicare Part B covered drugs (from $6.5 billion in 2001 to $10.9 billion in 2004) [15]. The MMA moved from the AWP to the ASP method of reimbursement for physician-administered drugs. The ASP-based reimbursement method was instituted by Medicare beginning in January 1, 2005.

The ASP is based on a computed average transaction price, i.e., the payments that manufacturers received for their products. It is the weighted average of all non-Federal sales to wholesalers and is net of chargeback, discounts, rebates, and other benefits tied to the purchase of the drug product, whether it is paid to the wholesaler or the retailer. Of note, there are exceptions to this general rule. Researchers are invited to refer to these exceptions listed in the latest ASP quarterly change request document [16]. Nevertheless, ASP is calculated using sales data for all drug products, branded and generic, available in the market for that drug. Thus, the ASP for drug products that have generic competition is very low. The reimbursement rate to providers for single-source drugs is the lower of 106% of ASP or WAC [17].

Medicare Payment for Cancer Therapies and Biologics

Medicare part B covers certain cancer drugs that have to be administered in a physician's office [18]. Chemotherapy and other oncology drug costs are of particular concern to Medicare because more than 60% of new cancer diagnoses occur in the elderly. Of the top 20 outpatient drugs that Medicare Part B covered in 2005, 16 treat cancer or chemotherapy-related side effects [19]. In the first year of Medicare Part D, 16 of the top 20 drugs based upon Medicare expenditure were drugs to treat cancer or the side effects of chemotherapy [19]. While innovation is commonly associated with better clinical outcomes and survival, its fiscal burden on payers is considerable. For instance, the emergence of new drugs on the market for treatment of metastatic colorectal cancer has been associated with a significant increase in drug costs [20]. In addition to the complexity of coverage under Part B versus Part D, the shift to ASP pricing had a significant impact on medical oncologists, urologists, rheumatologists, and infectious disease specialists. As of 2006, all end-stage renal disease drugs, and drugs and biologics with "pass-through" designation under the OPPS are reimbursed based on ASP [16].

Patient Cost Sharing and Variation in Coverage

The cost sharing for Medicare beneficiaries varies by type of service, and by the type of plan (e.g., PDP or MAPD that the beneficiary enrolls into), and by the levels and duration of service received. Medicare Part A is automatic, whereas Part B is optional and most beneficiaries pay a premium and deductible; in addition, individuals may opt for a Medigap insurance policy, which covers Medicare eligible expense not reimbursed by Medicare. Part D beneficiaries who are above the 150% of the Federal poverty level pay a premium and participate in cost sharing annually; 25% cost sharing where they initially get partial coverage for their drug costs for up to 75%, followed by 100% cost sharing because of the gap in coverage when they will pay full drug costs, and finally 5% cost-sharing when they reach a set catastrophic level of maximum coverage for 95% of their drug costs. Beneficiaries below the 150% Federal poverty level include dual eligible on Medicare and Medicaid and pay lower or no premiums and lower or no copayments or coinsurance and have no gap in coverage.

State Medicaid Programs require nominal cost sharing for prescription drugs for certain patient populations except children and pregnant women. Cost sharing is also not widely variable as for Medicare beneficiaries. Cost sharing is prohibited for emergency room visits, family planning services and hospice care.

Other Public Programs

A variety of Federal agencies and state and local governments purchase pharmaceuticals through different procurement methods, distribution systems and dispensing channels [18–20]. The other public programs account 7% of overall spending for retail prescription drugs during 2006 [21]. Veteran Affairs, Department of Defense, Public Health and Coast Guard (The Big Four) are the largest Federal purchasers of pharmaceuticals aside from Medicare and Medicaid. In order to provide an integrated, comprehensive, portable, high quality national drug plan for Veterans, the VA established the Pharmacy Benefits Management Strategic Healthcare Group (PBM-SHG) in 1995 [22].

The Federal government publishes several price lists that apply to the different Federal agencies [23]. These prices apply to drugs used in community and institutional pharmacy. Federal Supply Schedule prices are available to all Federal agencies. Other prices may be restricted to the Big Four or to specific Federal agencies. Federal listed prices generally include drug product and distribution costs.

Federal listed prices may be subject to minimum quantity purchase. Discounts may be available for prompt payment, and rebates may be available for formulary placement and market share. Individual Federal providers may negotiate lower prices for drugs included in Federal schedules and prices for drugs not included in those schedules.

Multiple outpatient pharmacy programs operate at the state level such as workers' compensation, prisoners, disease specific programs (e.g., mental health, HIV/AIDS), and other assistance programs. States may also manage drug discount programs for uninsured low income patients. Programs may participate in intrastate or multistate purchasing pools.

Local government may also have pharmacy programs at local health departments, jails, and detention centers, as well as assistance programs for specific populations.

Section 340B of the Public Health Service Act (340B) provides manufacturer discounts and rebates for covered outpatient drugs purchased by certain Federal grantees, state and local governments, Federally qualified health center, and qualified disproportionate share hospitals [24]. 340B prices are based on the Medicaid fee-for-service Federal rebate; manufacturers may provide further discounts.

Recommendations

Increasingly, Federal and state governments' interest in comparative effectiveness and pharmacoeconomic evaluations are expected to take center stage in the United States for coverage decisions made by Medicare, Medicaid, and other public payers. Therefore, these evaluations need to include accurate and unbiased effectiveness and cost estimates from clinical trials and real world effectiveness studies that are updated to reflect Medicare, Medicaid, or other public payer perspectives and experiences. With respect to pharmacoeconomic (e.g., cost-effectiveness) evaluations, our task was to focus narrowly on providing guidance for selecting and using drug cost input parameters for use in pharmacoeconomic models and evaluations. Recommendations for pharmacoeconomic evaluations to inform analyses from a Medicare or Medicaid perspective are summarized in Table 2. A more detailed list of recommendations follows in this section. Our recommendations also may apply to budget impact models, which are increasingly used to support decision-making for prescription drug coverage and benefit design.

The Medicare, Medicaid and other US Government Payers Subgroup of the ISPOR Task Force on Good Research Practices—Use of DCTF makes the following recommendations for research related to drug cost studies:

1. Researchers must be aware of legislation, eligibility and coverage requirements, and price increases that affect the actual prices paid for drugs by US government agencies. Legislation regarding Medicare drug prices includes but is not limited to information outlined in the MMA of 2003. Similarly, Medicaid and other governmental agencies have evolving policies and regulations that influence the prices they pay for drugs. Because drug companies and MCOs enter into confidential contracting arrangements, there are limited publicly available indicators of actual acquisition cost (AAC) for pharmaceuticals. We recommend the use of:
   - AAC paid by each public program, incorporating any rebates or discounts, if feasible. When several programs are evaluated in the economic evaluation, the weighted average of AAC of the programs should be estimated.
   - ASP for studies of Medicare Part B drugs.
   - AMP for studies of Medicaid fee-for-service outpatient drugs.
   - If program-specific costs are not available, the economic evaluation of 340B programs should use Medicaid outpatient fee-for-service price net of pharmacy discounts and Federal rebates to estimate the drug product cost.
2. Transparency with respect to price inputs is critical. Prices listed by public programs often exclude dispensing and administrative costs incurred by pharmacies. An economic evaluation should estimate and include these costs in the analysis.
3. The economic evaluation should include the US public programs' perspectives in the analysis. Using Medicare as one example of a public payer, there are multiple viewpoints (patient, private insurer, and governmental) that are reflected. Different perspectives can lead to sharply different estimates.
   - If the study is conducted from the patient perspective, the cost in the study should be the estimated out-of-pocket cost, which should include premiums and copayments and may include the deductible and likelihood of being in the donut hole and/or above the catastrophic threshold; these factors are dependent upon the type of plan in which the patient is enrolled.
   - If the study perspective is the private insurer administering the benefit, the cost should be AAC plus dispensing and administrative fees less estimated patient cost sharing. The cost will differ according to benefit structure because the cost to the plan would be different before and after patients spending more than the deductibles, reaching the donut hole, or within the range of catastrophic coverage.
   - The government's perspective should include all drug payments, regardless of source.
4. Drug costs for a Medicare study should consider whether the drug is covered under Parts A, B, C and/or Part D. The status of coverage would affect the relevant costs. Also, the likelihood of coverage and tier status, when applicable, should be incorporated into drug cost estimates.
5. With the advent of Medicare part D prescription data becoming available for Government and academic researchers, it is imperative that investigators understand the limitations of the data. Emerging Data on Medicare Part D for

Table 2 Standard recommendations for pharmacoeconomic studies from Medicare and Medicaid perspectives

Feature	Medicare	Medicaid
1. Perspectives for Pharmacoeconomic evaluations to inform cost containment	Medicare perspective, patient's perspective	Federal and State Medicaid perspective, patient's perspective
2. Cost and Effectiveness considerations for decision-analytic methods	1. Use actual acquisition cost (AAC) paid by each public program, incorporating any rebates or discounts; ASP for Medicare Part B drugs; AMP for Medicaid fee-for-service outpatient drugs; Medicaid outpatient fee-for-service price net of pharmacy discounts and Federal rebates 2. Include dispensing and administrative costs incurred by pharmacies and plans 3. Consider Budget impact analysis = cost analysis from the payer's perspective 4. Include effects of estimated acquisition cost (AWP minus discount, ASP, AMP), rebates, type of plan, benefit structure/tier status, generic drug (multisource drug) prices, and patients' real-world adherence in sensitivity analyses	

AWP, average wholesale price; ASP, average sales price; AMP, average manufacturer price.

Calendar Year 2006 should be used with caution as this was the first year that the drug benefit was administered and CMS has stated that the data for later years (i.e., 2007 and beyond) may be more valid and reliable for research purposes. For Medicare parts A, B and D, the investigator must understand the link between disease and resource use as it pertains to the way the benefit is administered.

6. Special attention has to be paid to cancer and other high cost drugs, particularly when the drug costs are a significant proportion of total health-care expenditures for a disease state. Medicare Part D has unique implication for cancer patients because some cancer drugs were already covered under Medicare Part B. Researchers should be kept abreast of new data that are available at the CMS website. Refer to the series of announcements regarding Medicare payment and coding for drugs and biologicals in the "Downloads" section of the ASP "Overview" page at: the following address: http://www.cms.hhs.gov/McrPartBDrugAvgSalesPrice/.
7. Weighted average drug cost across Medicaid delivery systems (fee-for-service and managed care; other Medicaid programs and dual eligible), and dispensing channels (hospital, long-term care, physician offices and outpatient clinics, outpatient pharmacy) should be presented when feasible.
8. Fee-for-service Medicaid pharmacy reimbursement should include an estimated average of drug acquisition cost and dispensing fee. FUL and state maximum allowable cost limits for multiple source drugs should be considered in the analysis. Federal and state rebates should be deducted from the pharmacy reimbursement amount to estimate the net drug product cost. Differences in calculation of innovator and multisource products rebates should be considered in the analysis.
9. Managed care recommendations should apply to Medicaid managed care. Medicare recommendations should apply for dual eligible beneficiaries, with exception of the payments made by the Medicaid program in substitution of dual eligible patients.
10. In general, adjustments for inflation should use the Consumer Price Index (CPI) All Urban Consumers for Prescription drugs. Exceptions occur in public programs. AMP of innovator drugs purchased by the Medicaid program should be adjusted by the CPI All Urban Consumers for All Items values based on launch date and current quarter AMP—42 U.S.C. 1396r-8(c)(2)(A)(ii)(II). Also drug procurement contracts of other public programs typically limit cost increases to the CPI All Urban All Items.
11. Budgetary impact analysis for private health plans participating in public programs will become increasingly popular and important in the future, therefore, it is critical that guidelines specific to this demand be developed.
12. Due to the possible wide variation in drug prices, producers of studies need to document the credible source(s) of their drug cost inputs.
13. Drug costs should be consistent with the time frame of the study. For example, if the time frame of the study is the lifetime of patients, drug costs should be calculated accordingly.
14. Due to the variation in coverage and benefit structure across plans, sensitivity analyses are warranted. When it comes to sensitivity analyses, the following should be taken into account:
    - AAC, rebates and discounts
    - For Medicare studies, variation in coverage based on drug costs under MMA, including the "standard" Medicare benefit of 25% copay for initial drug expenditures, 100% of cost in the donut hole where there is a gap in coverage, and then 5% copay during catastrophic coverage
    - The likelihood of coverage across different Plans and tier status for the drug should be specified
    - Due to the high proportion of total health-care costs attributable to drug costs among certain extremely ill patients (e.g., terminally ill cancer patients), the proportion of such terminally or severely ill patients should also be considered
    - The effect of generic prices when brand-name drugs are off-patent or likely to be off-patent should be incorporated.

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