Antihypertensive Drug Prescribing

Changes in Antihypertensive Prescribing During US Outpatient Visits for Uncomplicated Hypertension Between 1993 and 2004

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Abstract—Monitoring national patterns of antihypertensive drug therapy is essential to assessing adherence to treatment guidelines and the impact of major scientific publications on physician prescribing. We analyzed data from 2 US National Ambulatory Care Surveys to examine trends between 1993 and 2004 in the prescription of antihypertensive drug classes for uncomplicated hypertension and the association between thiazide and β-blocker prescribing and physician and patient characteristics. Diuretic prescriptions remained level through 2001 (39%; 95% CI: 34% to 44%) but increased to 53% (48% to 58%) in 2003, largely because of a 72% increase in thiazide prescriptions in the first quarter of 2003 (50%; 95% CI: 40% to 59%). However, these increases did not sustain in 2004. β-Blocker prescriptions increased modestly from 1993 (24%; 95% CI: 19% to 29%) to 2004 (33%; 95% CI: 28% to 39%). Prescription of calcium channel blockers and angiotensin-converting enzyme inhibitors declined significantly following the sixth Joint National Committee report, but both subsequently rebounded to prereport levels. Prescription of angiotensin II receptor blockers increased continuously from 1% in 1995 to 23% by 2004. Polytherapy prescriptions, particularly those involving ≥3 drug classes, became increasingly prevalent, accounting for 60% of antihypertensive drug visits by 2004. Prescriptions of thiazides and β-blockers were both more likely in 1998–2004 (versus 1993–1997). Blacks, women, and hospital outpatients were more likely to receive thiazides. Also, cardiologists were more likely to prescribe β-blockers. Evidence-based guidelines for antihypertensive drug therapy do impact physician prescribing, but the impact seems to be short lived. Future interventions are imperative for promoting long-term adherence to published guidelines.

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Key Words: antihypertensive prescribing ■ guideline adherence ■ NAMCS ■ NHAMCS

An estimated 65 million US adults have elevated blood pressure or hypertension with the number expected to rise as the obesity epidemic continues.1,2 Antihypertensive pharmacotherapy effectively reduces hypertension-related morbidity and mortality.3,4 Appropriate pharmacotherapy for uncomplicated hypertension assumes paramount importance to public health because ≈70% of US hypertensive adults lack comorbidities that complicate the use of certain antihypertensive drug classes.5

The US Joint National Committee (JNC) has published a series of guidelines that recommend appropriate antihypertensive therapy based on the best available evidence. JNC-recommended first-line drug therapy for uncomplicated hypertension has evolved over time. Both JNC-56 and JNC-63 recommended diuretics and β-blockers as preferred first-line therapies. More recently, major study findings from the Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT)7 and a meta-analysis of 42 clinical trials by Psaty et al8 concluded that thiazide diuretics are equal or, in some cases, superior to other antihypertensive drugs in reducing cardiovascular events. Subsequently, the JNC released its seventh report in 2003, which recommended thiazide diuretics to be prescribed alone or as part of combination therapy for most hypertensive patients.4

The JNC guidelines are not accepted without controversy, however.9–13 The latest European guidelines did not endorse thiazide diuretics as first-line agents but instead considered all of the antihypertensive drug classes to be equivalent.14 Some researchers have questioned the long-term safety of thiazide diuretics5,17 and the efficacy of β-blockers.16,17 Other researchers have suggested that to maximally lower blood pressure, patients should be treated initially with combination drug therapy and that one of the drugs used should be a diuretic.13,18

Past studies tracking practice patterns show that calcium channel blockers (CCBs) and angiotensin-converting enzyme inhibitors (ACEIs) have increasingly supplanted diuretics and β-blockers since their market entry in the early 1980s.19 The uptake of angiotensin II receptor blockers (ARBs) also has been rapid since their debut in 1995.20 The growing use of these agents predated clinical evidence supporting their disease-preventing benefits in hypertensive patients.21–23

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They were often prescribed in situations where evidence is lacking that they produce effects superior to older and less expensive drugs. In addition, the long-term safety of ARBs is still under investigation. These data suggest limited impact of evidence-based guidelines on physician prescribing practice. However, more recent studies have found that physicians responded rapidly to the 2002 ALLHAT publication and that prescribing of thiazide diuretics increased immediately and significantly. Research also shows that adoption of recommended antihypertensive prescribing guidelines is not uniform but instead varies by patient and physician characteristics.

In this study, we present trends in the prescribing of major antihypertensive drug classes for treating uncomplicated hypertension by US physicians in ambulatory care settings between 1993 and 2004. We also analyze the association between the prescribing of thiazide diuretics and β-blockers, respectively, and physician and patient characteristics. Based on the literature, we hypothesized a priori that these recommended antihypertensive drug therapies would be prescribed less frequently by noncardiologists and to men and ethnic minorities.

**Methods**

**Data Sources**

Annual data from 1993 to 2004 were obtained from the National Ambulatory Medical Care Survey (NAMCS) and the outpatient department component of the National Hospital Ambulatory Medical Care Survey (NHAMCS). The National Center for Health Statistics provides complete descriptions of both surveys and yearly data at http://www.cdc.gov/nchs/about/major/ahcd/ahcl1.htm. These surveys, particularly NAMCS, have been validated against other data sources and have also been used in past research of antihypertensive prescribing.

In brief, NAMCS captures healthcare services provided by office-based physicians, whereas NHAMCS assesses services offered at hospital outpatient departments. Both surveys use multistage probability sampling procedures, enabling the generation of nationally representative estimates. Between 1993 and 2004, annual participation rates among physicians selected for NAMCS averaged 70%, whereas the participation rate of selected hospitals with outpatient departments was 90% in NHAMCS.

Standard encounter forms were completed for a systematic random sample of patient visits during randomly assigned reporting periods. Yearly encounter forms varied slightly between NAMCS and NHAMCS and were revised every 2 years. Data used in our analyses were from domains common to NAMCS and NHAMCS across time, including patient demographics, visit characteristics, reasons for visit, diagnoses, and new and continuing medications. Nonresponse rates were mostly ≤5% in both surveys for all of the years.

**Study Sample**

**Uncomplicated Essential Hypertension**

The study sample consisted of ambulatory visits by men and women ≥20 years of age who had essential hypertension (International Classification of Disease Ninth Revision code 401) as the primary diagnosis and had no compelling comorbidities. We termed these patient visits as “hypertension visits.” Visits by patients with the following comorbidities were excluded from the analysis: hypertensive organ damage, coronary artery disease, diabetes mellitus, congestive heart failure, stroke, chronic renal disease, and pregnancy. Visits of patients having heart block or bronchospasm also were excluded given that they are contraindications for β-blockers. The exclusions were identified primarily by International Classification of Disease Ninth Revision codes, as well as by the appropriate reason-for-visit codes that are specific to NAMCS and NHAMCS. Patients whose encounter forms did not indicate the presence of a condition were assumed as not having that condition. The number of hypertension visits excluded because of relevant comorbidities ranged from a low of 200 in 1993 to a high of 449 in 2002. The resulting effective sample size for hypertension visits ranged from 2931 in 1993 to 3667 in 2004. After taking into account sampling weights, the estimated number of hypertension visits in the population ranged from 29.8 to 39.6 million.

**Patient Visit Characteristics**

Nonclinical characteristics included patient age, gender, race/ethnicity, medical insurance, visit status, US census region, metropolitan area status, physician specialty, and practice setting. Medical insurance was classified as private/commercial insurance, public insurance (ie, Medicare and Medicaid), and other insurance (eg, workers’ compensation and self-pay). Visit status distinguished first-time visits from return visits to a practice. Physician specialty was available only from NAMCS, which contributed >90% of weighted population estimates of hypertension visits in all of the study years. We categorized physician specialties into cardiology, internal medicine, general and family practice, and a category encompassing all others. This composite “other” category included primarily all of the hypertension visits in NHAMCS, as well as hypertension visits in NAMCS for which the physician specialty fell outside the 3 chosen categories. The weighted distribution of total hypertension visits by physician specialty was 7% in cardiology, 41% in internal medicine, 33% in general and family practice, and 19% in the other category. Of the hypertension visits in the other category, 42% were from NHAMCS, with nephrology and pulmonology the most predominant specialties listed for the rest.

**Measures**

We defined “antihypertensive drug visits” as hypertension visits during which prescription of a generic or brand-name antihypertensive drug was mentioned. The JNC 5, JNC 6, and JNC 7 were used to identify and classify the antihypertensive drugs. For brand-name and combination antihypertensive agents, each generic name (active ingredient) component of the agent was counted separately. Then, each generic name was categorized into its major antihypertensive drug class. Polytherapy was defined as antihypertensive drug visits during which >1 active ingredient was mentioned either in 1 single combination pill or in multiple pills.

We examined the following antihypertensive drug classes: diuretics, β-blockers, CCB, ACEI, ARB, α-blockers, peripheral-acting antiadrenergic agents, and direct vasodilators. Diuretics were further categorized as thiazide diuretics and all other diuretics (ie, loop and potassium-sparing diuretics), and β-blockers included α-β blockers. Throughout the study period, peripheral-acting antiadrenergic agents and direct vasodilators were rarely mentioned, and α-blockers and central-acting agents were mentioned in <5% of antihypertensive drug visits in most years. Therefore, this article will not report specific information on these infrequently used drug classes. Of primary interest was the prescribing of each antihypertensive drug class as a percentage of antihypertensive drug visits and as related to patient visit characteristics.

**Analyses**

Statistical analyses were performed using SAS-callable SUDAAN software (Research Triangle Institute) to account for sampling weights and the complex survey designs. The unit of analysis was the patient visit. Comparisons of NAMCS and NHAMCS suggested limited differences on key outcome measures. We, therefore, combined the 2 surveys to obtain a wider range of outpatient settings and a broader socioeconomic spectrum of hypertensive patients seeking ambulatory care. SUDAAN PROC CROSSTAB generated parameter estimates for antihypertensive prescribing by class and corresponding 95% CIs from 1993 through 2004. In addition to temporal trends, we also investigated patient visit characteristics associated with the prescribing of thiazide diuretics and β-blockers. 2 preferred drug classes recommended in JNC...
6 and 7. χ² tests (PROC CROSSTAB) examined isolated association between prescribing of thiazide diuretics or β-blockers and each patient visit characteristics using combined 1993–2004 NAMCS and NHAMCS data. Two separate multiple logistic regression models then tested the independent effect of each patient visit characteristic on prescribing of either drug class after controlling for all of the other characteristics simultaneously. Time effect was modeled as 1999–2004 versus 1993–1998.

Results

Trends of Antihypertensive Prescribing by Drug Classes

The weighted number of ambulatory visits by adults having uncomplicated essential hypertension as the primary diagnosis (hypertension visits) increased 33% from 29.8 million in 1993 to 39.6 million in 2004. The proportion of hypertension visits in which antihypertensive drug therapy was prescribed (antihypertensive drug visits) remained stable between 1993 (74%; 95% CI: 69% to 79%) and 2004 (70%; 95% CI: 63% to 76%).

Temporal trends in prescribing between 1993 and 2004 varied across antihypertensive drug classes. In 1993, the most frequently prescribed drugs at antihypertensive drug visits were CCBs (44%; 95% CI: 39% to 50%) and ACEIs (36%; 95% CI: 31% to 41%) followed by diuretics (34%; 95% CI: 30% to 39%) and β-blockers (24%; 95% CI: 19% to 29%).

Prescription of CCBs remained stable through 1998 (42%; 95% CI: 37% to 48%; of antihypertensive drug visits) but then decreased to 29% (95% CI: 25% to 33%) in 2000 (Figure 1). Subsequent changes in prescription of CCBs did not reach statistical significance. Although prescription of ACEIs exhibited some fluctuations throughout the study period, they accounted for a largely stable percentage of total antihypertensive drug visits between 1993 (36%; 95% CI: 31% to 41%) and 2004 (35%; 95% CI: 30% to 41%). It is noteworthy, however, that prescription of ACEIs declined significantly from 42% (95% CI: 37% to 47%) in 1997 to 30% (95% CI: 26% to 35%) in 1999. Prescription of ARBs increased progressively from 1% (95% CI: 0% to 2%) of antihypertensive drug visits in their first year on the market in 1995 to 23% (95% CI: 18% to 29%) by 2004.

Between 1993 and 2001, prescription of diuretics fluctuated but did not differ significantly, ranging from 34% to 43% of antihypertensive drug visits (Figure 2). In the next 2 years, prescription of diuretics rose successively from 43% (95% CI: 38% to 47%) in 2002 and 53% (95% CI: 48% to 58%) of total antihypertensive drug visits in 2003 and stabilized at 50% (95% CI: 45% to 55%) in 2004. The increase observed in 2003 resulted largely from increased prescriptions of thiazide diuretics, which reached 50% (95% CI: 40% to 59%) of antihypertensive drug visits in the first quarter of 2003 compared with 29% (95% CI: 22% to 37%) in the fourth quarter of 2002. However, this notable increase in the prescription of thiazide diuretics did not sustain in the remaining quarters of 2003. The relatively unchanged prescription rate for all diuretics until 2001 masked a progressively diverging pattern of use for thiazide versus other diuretics. The percentage of antihypertensive drug visits receiving thiazide diuretics doubled from 23% (95% CI: 19% to 28%) in 1993 to 46% (95% CI: 42% to 51%) in 2004, whereas the percentage receiving other diuretics declined from 23% (95% CI: 18% to 29%) to 15% (95% CI: 10% to 21%) during this period.

After a stable pattern between 1993 and 1996 (averaging 23% of antihypertensive drug visits), prescription of β-blockers exhibited a small and insignificant increase to 32% (95% CI: 27% to 37%) of total antihypertensive drug visits in 1997 (Figure 2). Thereafter, prescription of β-blockers remained essentially unchanged and accounted for 33% (95% CI: 28% to 39%) of total antihypertensive drug visits in 2004.

Trends of Polytherapy

Among antihypertensive drug visits, the mean number of antihypertensive drugs prescribed increased significantly from 1.7 (95% CI: 1.6 to 1.8) in 1993 to 2.1 (95% CI: 2.0 to 2.2) in 2003 and remained at 1.9 (95% CI: 1.8 to 2.0) in 2004. Polytherapy comprised 48% (95% CI: 43% to 54%) of total antihypertensive drug visits in 2004.
antihypertensive drug visits during 1993 and rose to 60% (95% CI: 54% to 66%) by 2004 (Figure 3). Most polytherapies were provided through multiple pills (rather than single-pill combination formulations), ranging from 68% (95% CI: 60% to 75%) of all polytherapy drug visits in 1993 to 64% (95% CI: 54% to 72%) in 2004.

Combinations of 2 antihypertensive drug classes remained the most common mode of polytherapy from 1993 (34%; 95% CI: 30% to 39%; of all antihypertensive drug visits) through 2004 (36%; 95% CI: 31% to 42%). Among all of the possible pairwise combinations of the major antihypertensive drug classes, significant increases were observed between 1993 and 2004 for prescription of an ACEI or ARB in combination with a diuretic (10% versus 27% of all antihypertensive drug visits), a CCB (8% versus 17%), or a β-blocker (6% versus 15%), as well as for combinations containing a diuretic and β-blocker (9% versus 16%; Figure 3).

Polytherapies containing ≥3 antihypertensive drug classes increased from 14% (95% CI: 10% to 20%) of all antihypertensive drug visits in 1993 to 24% (95% CI: 20% to 28%) in 2004. The 3 most common forms of these polytherapies in 2004 were combinations that included a diuretic. These were a diuretic, β-blocker, and ACEI/ARB (9%; 95% CI: 6% to 12% of all antihypertensive drug visits); a diuretic, CCB, and ACEI/ARB (8%; 95% CI: 6% to 11%); or a diuretic, β-blocker, and CCB (4%; 95% CI: 2% to 6%).

Among all of the polytherapy drug visits, a diuretic on average was present in 71% (ranging from 63% to 74%) of these combinations. The close connection between diuretics and polytherapy also was indicated by the common use of polytherapy in the prescribing of diuretics (mean: 85%; ranging from 79% to 100%). Likewise, polytherapy remained largely stable in the prescribing of β-blockers (mean: 69%; ranging from 61% to 79%). Polytherapy became increasingly dominant in the prescribing of ACEIs/ARBs and CCBs. The proportion of total drug use occurring as polytherapy increased from 53% (95% CI: 44% to 62%) in 1993 to 76% (95% CI: 69% to 81%) in 2004 for ACEIs/ARBs and from 51% (95% CI: 42% to 60%) to 80% (95% CI: 71% to 88%) for CCBs.

Figure 2. Trends of prescribing for diuretics (□) and β-blockers (△) as a percent of all hypertension visits in which an antihypertensive drug was reportedly prescribed.

Figure 3. Use of antihypertensive polytherapy among all hypertension visits in which an antihypertensive drug was reportedly prescribed. Error bars, 95% CIs. Categories for combinations of 2 antihypertensive drug classes are not mutually exclusive. BB indicates β-blocker.
Correlates of Prescribing of Thiazide Diuretics and β-Blockers

Prescription of thiazide diuretics and β-blockers was independently associated with a few patient visit characteristics after accounting for other covariates (Table). Compared with non-Hispanic whites, blacks were 1.4 (95% CI: 1.2 to 1.7) times more likely to receive a thiazide diuretic, whereas they were marginally less likely to receive a β-blocker (0.8; 95% CI: 0.7 to 1.0). The likelihood of receiving a thiazide diuretic was less for men than women (0.7; 95% CI: 0.6 to 0.8), whereas it was slightly greater for patients living in the West (versus the Northeast) or suburban areas. Also, physicians who practice in hospital outpatient departments were 1.6 (95% CI: 1.2 to 2.2) times more likely to prescribe thiazide diuretics than private practice physicians. Compared with cardiologists, internists, and general and family practitioners were 40% less likely to prescribe β-blockers.

The likelihood of receiving a thiazide diuretic or β-blocker for treating uncomplicated hypertension was significantly greater during 1999–2004 than during 1993–1998. Prescription of thiazide diuretics was 1.6 (95% CI: 1.4 to 1.8) times and prescription of β-blockers was 1.3 (95% CI: 1.1 to 1.5) times more likely in the latter time period.

Other patient visit characteristics were not associated with the likelihood of receiving a prescription for either a thiazide diuretic or β-blocker. These included age, medical insurance, and visit status.

Discussion

The prevalence of hypertension continues to rise in the United States. Appropriate antihypertensive drug therapy is important, because deviation from evidence-based guidelines in hypertension treatment contributes to the high cost of medications and create difficulties in providing affordable prescription drugs for patients diagnosed with hypertension. Monitoring national patterns of antihypertensive drug therapy is essential to assessing adherence to treatment guidelines and the impact of major scientific publications on physician prescribing.
Medication prescribing, particularly for a disease as prevalent as hypertension, is a complex practice for which evidence-based recommendations represent only 1 of many influencing factors. Other factors may include drug marketing, formularies, and drug price; a combination of these factors can act to mitigate the impact of guidelines on actual practice.\footnote{32,33} For instance, since the market entry of ACEIs and CCBs in 1980s, advertising for these drugs has increased dramatically, whereas that for diuretics has decreased sharply; physician prescribing subsequently increased for highly marketed drugs while decreasing for others.\footnote{32} In addition, when major brand drugs become available in generic form, market share often increases within 12 months for the generic form and decreases for the brand drug.\footnote{34,35} These are some of the factors that may also substantially impact prescribing patterns.

The release of evidence-based guidelines, such as JNC reports, should ideally guide physicians in their antihypertensive prescribing behavior. This study found changes in antihypertensive prescribing that are consistent with a response to the latest recommendations and clinical evidence for treating uncomplicated hypertension. Patients seen after 1998 were significantly more likely to receive thiazide diuretics and \(\beta\)-blockers compared with those seen before 1998. The proportion of total antihypertensive drug visits in which a thiazide diuretic was prescribed increased significantly immediately after the ALLHAT main publication. Prescription of both CCBs and ACEIs declined in the years immediately after the publication of JNC 6. Diuretics ranked the leading antihypertensive drug class for most of the years beginning in 1998 and were used predominantly in combination with other drug classes, particularly ACEIs and \(\beta\)-blockers, as the most common antihypertensive polytherapies. As suggested by guidelines, polytherapy has become increasingly prevalent, accounting for 60% of patient visits seen and treated for uncomplicated hypertension by 2004. The use of combinations of \(\geq 3\) antihypertensive drug classes is becoming more common.

This study also suggests, however, that changes in prescribing after the release of new treatment recommendations may be transitory, because prescribing patterns tended to subsequently regress toward their previous levels. For the adoption of treatment guidelines to become widespread and persistent, clinical evidence dissemination needs to be augmented by additional efforts, such as national health policies, local health initiatives, electronic prescribing decision support systems, favorable prescription copayments, and patient-friendly prescription drug information. Notwithstanding, uniform adoption of any recommendations may never be expected in the practice of medicine because of its inherent complexity and the importance of clinician judgment and patient preferences.

Prescribing practices are known to vary with physician and patient characteristics. Most recently, using the National Health and Nutrition Examination Survey (NHANES) data, Gu et al\footnote{36} concluded that variations in antihypertensive drug therapies by sociodemographic factors continue to exist, although such treatments among US hypertensive adults have improved considerably in the 1990s. In particular, Gu et al\footnote{36} found lower antihypertensive medication use among men, younger adults, and Mexican Americans in certain gender and age groups. In our study, we also found differences by gender in that men were less likely to receive thiazide diuretics, as well as differences by race/ethnicity, in that blacks were more likely to receive thiazide diuretics but less likely to receive \(\beta\)-blockers compared with non-Hispanic whites. Patterns of prescribing for blacks may be partly explained by physician response to the evidence that blacks have reduced responses to monotherapy of \(\beta\)-blockers, as well as ACEIs and ARBs, compared with diuretics.\footnote{34,36} Antihypertensive prescribing also varies by physician specialty and practice setting, with greater guideline adherence found among cardiologists (versus physicians in other specialties) and physicians in hospital outpatient departments (versus private practice physicians).

Our findings must be interpreted in the context of data limitations. Although NAMCS/NHAMCS are designed to produce national estimates with minimal biases, these estimates are not linked to individuals but to patient visits. Sicker patients and patients prescribed medications who require frequent follow-ups may be oversampled, resulting in an overestimation of the actual administration of antihypertensive medications. Underestimation also may be possible because of incomplete reporting of medications prescribed, which could be particularly problematic when a patient’s medications exceeded the allowed maximum spaces for reporting. However, we did not discern any indication of underreporting of antihypertensive prescribing among patient visits during which the maximum number of medications was reached. We found a comparable or greater proportion of antihypertensive drug visits among hypertension visits with a maximum number of medications reported versus among those without. Furthermore, although instructed to report both new and continued medications, physicians may selectively record new prescriptions, in the case of polytherapy, perhaps because the new additional medication is still being titrated. To the extent that this phenomenon exists, it would not only underestimate a given drug but would underestimate polytherapy and drug combinations.

Nonetheless, our results are comparable to those based on self-report data by individual participants in the NHANES.\footnote{36} Our ability to assess physician adherence to recommended first-line antihypertensive drug therapies is compromised by a lack of longitudinal patient-specific data regarding whether a reported medication is the first prescribed for the patient or a change in therapy. Physician adherence to practice guidelines is a complex issue that requires the measurement and inclusion of a range of other factors that influence medication prescribing, for which we do not have data in this study.

In conclusion, hypertension continues to affect a significant and growing proportion of the US population, and an increasing number of antihypertensive prescriptions are being given to hypertensive patients. Temporal trends in prescribing have remained largely consistent in the past decade for the treatment of uncomplicated essential hypertension in US ambulatory care settings. Evidence-based guidelines for antihypertensive drug therapy do impact physician prescribing; however, this impact seems to be short-lived.

**Perspectives**

Our examination of the prescribing of antihypertensive medication over a 12-year period suggests that evidence-based
guidelines alone are insufficient to induce lasting changes in physician prescribing practice. This observation is not unexpected given the increasing complexity of modern medicine. Acting as agents on behalf of their patients, today’s physicians face a range of factors in addition to clinical evidence that can influence the way they practice. These factors may include influences from the pharmaceutical and health insurance industries, physician desire to retain decision-making autonomy, and patient preferences. Scientific knowledge is still lacking with regard to the intertwining relationships of these factors and the net impact of each on physician practice. Efforts aimed at addressing these issues may help transform short-term changes in physician practice into long-term adherence to published guidelines and, therefore, improved quality of care.

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Disclosures
None.

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