Patient Heterogeneity and Treatment Choices: Evidence from the Dialysis Industry*

Paul J. Eliason†, Benjamin Heebsh,‡ Riley J. League§, Ryan C. McDevitt¶, James W. Roberts‖

July 17, 2024

We study the use and effectiveness of epoetin alfa (EPO), historically one of Medicare's largest drug expenses. Using a novel instrumental variable based on elevation and a large payment reform, we estimate a model of providers' treatment decisions that incorporates the heterogeneous effect EPO has on patients. We find that increasing doses by 1% reduces anemia by 0.1%, on average, but increases heart attacks by 0.3% and mortality by 0.4%, with patients exhibiting substantial heterogeneity along these dimensions. Our counterfactual analysis shows that patients' well-being would decline considerably if providers disregarded their heterogeneous responses as mandated by some Medicare guidelines.

JEL Codes: D22, I11, I18, L20

*We thank nephrologists Matthew Ellis, Ruediger Lehrich, John Middleton, and Myles Wolf for providing valuable industry and medical insights. We gratefully acknowledge research support provided by the Social Sciences Research Institute, the National Science Foundation (SES 1850736 and 1851615), and the National Institute on Aging (T32-AG000186). We thank Jeffrey Hill, Alexander Marsh, Gabor Palinko, Lily Liu, Zilan Yang, Sungwoo Cho, and Hanmeng Wang for their research assistance. The data reported here have been supplied by the United States Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the U.S. government.

†David Eccles School of Business, University of Utah and NBER, paul.eliason@eccles.utah.edu

‡Federal Trade Commission, bheebsh.research@gmail.com. The views expressed in this article are those of the authors and do not represent the view of the Federal Trade Commission (FTC) or its commissioners.

§Gies College of Business, University of Illinois Urbana-Champaign, league@illinois.edu

¶Duke University and NBER, ryan.mcdevitt@duke.edu

‖Department of Economics, Duke University and NBER, j.roberts@duke.edu

1. Introduction

We study the use and effectiveness of epoetin alpha (EPO), a drug commonly prescribed to treat anemia among dialysis patients that was Medicare's largest Part B drug expense in the early 2000s (U.S. Government Accountability Office, 2012; Thamer et al., 2007). Prior to 2011, Medicare paid dialysis facilities on a fee-for-service basis for the EPO administered during treatment, providing an incentive to use large amounts of the drug and raising concerns that excessive doses increased the risk of mortality and cardiovascular events (Besarab et al., 1998; Singh et al., 2006). In response to the escalating costs of EPO and its potentially harmful effect on patients, Medicare switched to a prospective payment system (PPS) in 2011 to encourage providers to use the drug more judiciously, paying for both EPO and dialysis together at a uniform, predetermined rate. We use this payment reform, along with a structural model of providers' dosing decisions and a novel instrumental variable based on a facility's elevation, to estimate the heterogeneous effect of EPO on patients' health and evaluate several counterfactual policies related to providers' treatment decisions.

In our model, providers' dosing decisions depend on their own financial returns as well as the health of their patients. We capture these potentially conflicting incentives through a health production function that incorporates both observed and unobserved components of patients' health and allows EPO to have heterogeneous effects across patients in addition to nonlinear benefits across doses. Modeling the health effects of EPO in this way quantifies the tradeoffs faced by providers and allows us to demonstrate how they vary with facility attributes like corporate ownership and the costs of acquiring the drug, two fundamental features of the dialysis industry.

Identifying the parameters of the health production function is complicated by the fact that providers base their treatment decisions in part on patients' underlying health, so any correlation between doses and outcomes may be confounded by patients' unobserved attributes. Reflecting this possibility, OLS regressions of hemoglobin and blood transfusions on patients' EPO doses produce spurious negative and positive correlations, respectively, even though randomized controlled trials have shown the drug causes the opposite clinical response for these measures of anemia (Eschbach et al., 1989). Moreover, we cannot directly use the large drop in doses following the payment reform to identify the effect of EPO because it may be conflated with other contemporaneous changes in dialysis treatments and standards.

To overcome the empirical challenges associated with patients' unobserved health conditions and

coincidental changes in their level of care, we use a novel source of exogenous variation in providers' treatment decisions to identify the marginal effect of EPO on outcomes: patients living at higher elevations have less severe anemia at baseline and naturally require less EPO to manage their condition (Winkelmayer et al., 2009; Brookhart et al., 2011b). During the fee-for-service era, this physiological distinction made patients at higher elevations less profitable for providers, as they received smaller doses of EPO to keep their blood levels within clinical guidelines. After Medicare adopted the PPS, providers' financial incentives flipped, with patients at lower elevations becoming less lucrative for providers who no longer received separate payments corresponding to these patients' larger doses. As a result, the uniformly applied payment reform ultimately had different financial implications for facilities at different elevations and resulted in different changes in patients' doses of EPO.

Although promising as a source of exogenous variation, elevation may not be a valid instrument on its own; just as elevation directly affects anemia, it may also directly affect other health outcomes. In light of this potential confound, we estimate the causal effect of EPO using the interaction between elevation and the payment reform as an excluded instrument. By instrumenting for EPO doses in this way, our first stage resembles a difference-in-differences estimation, where the first difference compares EPO doses at high-elevation facilities with those at lower elevations, while the second difference compares doses during the fee-for-service era, when financial incentives favored higher doses, with those administered during the PPS era when the financial incentives reversed.

We find that lower-elevation facilities both use more EPO and disproportionately reduced their doses after the payment reform, with the second stage then linking the change in EPO to its effect on outcomes. For this specification to have a causal interpretation, the interaction between a facility's elevation and Medicare's payment scheme must only affect health outcomes through its influence on EPO, conditional on controls, and several pieces of evidence suggest our setting satisfies this requirement, such as parallel pre-trends for patients' EPO doses across high and low elevations and no meaningful changes in observable patient characteristics or facility inputs like staffing levels.

To evaluate how providers balance their financial returns along with their patients' health, we use our instrument to identify the health production function and estimate a structural model of providers' dosing decisions. We find that, in equilibrium, patients exhibit substantial heterogeneity in their response to the drug, with patients at the 75th percentile responding more than four times as strongly as those at the 25th. The tradeoffs inherent in providers' treatment decisions also become readily ap-

parent, where a 1% increase in EPO reduces patients' anemia by 0.1%, on average, but at the same time increases the rate of cardiac hospitalization by 0.3% and mortality by 0.4%. How providers then weigh these tradeoffs against their own financial incentives ultimately determines the amount of EPO they administer to patients, which we capture in our model and use as the basis of our counterfactual analysis.

Beyond allowing us to identify the heterogeneous effect of EPO on various health outcomes, our approach also allows us to identify the extent to which giving providers the freedom to tailor their treatments to each patient's specific needs results in better outcomes. Before Medicare's move to a PPS, EPO had accounted for as much as 25% of revenue at DaVita, one of the nation's two largest dialysis chains, and up to 40% of its profits (DaVita, 2005), with lawsuits at the time alleging that the company developed a software application called Snappy to automatically increase doses so patients' blood levels hit the upper bound of clinical guidelines (Mueller, 2023). Due to the wide heterogeneity in the effects of EPO, however, we find that mandating uniform doses to prevent providers from indiscriminately overtreating patients would lead to worse outcomes overall: giving all patients the average health-maximizing dose would reduce their health by an amount valued at nearly $2300 per month, underscoring the important role of heterogeneity in our setting. Similarly, requiring all patients to receive enough EPO to achieve the minimum hemoglobin level recommended by clinical guidelines prior to the payment reform would also cause outcomes to decline. In light of such wide heterogeneity, our results demonstrate the need for providers to have discretion in their treatment decisions even when misaligned financial incentives might spur policymakers to impose guidelines to restrain costs and protect patients, similar to what Medicare has done recently through initiatives like the Quality Incentive Program in dialysis.

Our model's estimates also allow us to evaluate how heterogeneity across providers influences the care received by dialysis patients. With large chains such as DaVita and Fresenius now operating more than 80% of facilities nationwide, two factors in particular distinguish their treatment decisions from those of independent facilities. First, we find that chains put less emphasis on patients' well-being when administering EPO: patients' health would improve enough to close 63% of the gap between observed outcomes and the theoretical upper bound if chains had the same level of altruism as independent facilities. Conversely, chains' lower acquisition costs for EPO spur them to use larger doses, benefiting patients who might otherwise be undertreated due to the financial incentives of the PPS. By highlighting the interaction between Medicare's payment policies and the corporate ownership of facilities, our

findings provide novel insights for policymakers seeking to implement similar reforms given the growing prevalence of chains throughout the broader health care system.

Our study contributes to the large literature aimed at understanding the behavior of health care providers, including their treatment decisions, quality of care, and associated costs (McGuire, 2000). One strand of this work seeks to explain the wide variation in treatment decisions observed in practice (Chandra et al., 2012). Because this variation is often unrelated to providers' quality of care, some point to it as evidence of the health care system's inefficiency, although a more recent literature has shown that a meaningful portion of the variation stems from differences in providers' productivity (Chan et al., 2022; Silver, 2021; Chandra and Staiger, 2020; Currie and MacLeod, 2017; Abaluck et al., 2016). Advancing this literature, we emphasize the role of patients' heterogeneous response to treatments and how it relates to providers' and regulators' various objectives (Dafny, 2005; Clemens and Gottlieb, 2014; Einav et al., 2018; Eliason et al., 2018).

Using observed provider and patient behavior to study the effectiveness of EPO also contributes to a growing literature exploring the limitations of clinical trials for assessing interventions in the field. To highlight one such limitation, trial participants may differ from the general population and fail to represent important subgroups (e.g., Murthy et al., 2004; Chassang and Feng, 2022), with a failure to distinguish treatment effects for these groups potentially limiting our understanding of how an intervention will ultimately affect spending and outcomes (Green et al., 2022). Gaps in representation also contribute to disparities in care, including slower uptake of newly developed drugs among groups with less representation in the trials (Alsan et al., 2024) and limited guidance for how to adapt care for underrepresented populations (Cuddy and Currie, 2024). In addition, design features of controlled trials, such as site selection (Allcott, 2015) and adherence protocols (Al-Ubaydli et al., 2017a), may appear to enhance the effectiveness of an intervention and abstract away from institutional or equilibrium factors that arise only when the intervention is deployed at scale (Oostrom, 2022; Bold et al., 2018; Al-Ubaydli et al., 2017b). For dialysis in particular, clinical trials of EPO have demonstrated its ability to reduce anemia (Eschbach et al., 1987) as well as heightened concerns about adverse effects for certain groups of patients (Besarab et al., 1998; Singh et al., 2006). Our paper builds on this work by using data from outside a controlled environment, showing evidence of wide heterogeneity in treatment effects and highlighting the role of providers' incentives in shaping equilibrium outcomes. We also contribute to the understanding of why some patients exhibit a reduced responsiveness to EPO, confirming the hypothesis

that certain comorbid conditions, such as hypertension, can significantly diminish the effectiveness of the drug (Van der Putten et al., 2008).

Finally, our paper contributes to a recent literature focused on the economics of the dialysis industry (e.g., Eliason et al., 2020; Dai, 2014; Cutler et al., 2017; Dai and Tang, 2015; Grieco and McDevitt, 2017; Eliason, 2021; Wilson, 2016a,b), including research on the switch to a PPS (Chertow et al., 2016; Hirth et al., 2014). Of particular relevance, Gaynor et al. (2023) study how dialysis providers balance patients' health with the financial incentives for EPO using a structural model of dosing decisions. Using data from before the payment reform, they find that fee-for-service payments resulted in an excessive use of EPO, with doses falling by a third under the optimal linear contract. We complement their work by directly using the change in payments to identify a model of providers' treatment decisions and explore the role of patients' heterogeneity in determining their EPO doses.

Our paper proceeds with Section 2, which discusses the essential details of the U.S. dialysis industry. Section 3 describes our data and provides descriptive statistics. Section 4 lays out a model of providers' equilibrium dosing decisions and our instrumental variable. Section 5 presents our IV estimation results of EPO's effect on patients' outcomes. Section 6 uses the IV estimates of the health production function to estimate the remaining model parameters. Section 7 reports estimates from various counterfactual simulations. Section 8 concludes. The appendix contains supplementary material referenced throughout the paper.

2. Institutional Details of Dialysis

2.1. Kidney Failure, Anemia, and Dialysis

Kidneys filter wastes and toxins from the blood and produce erythropoietin, a hormone that stimulates red blood cell production. For patients with end-stage renal disease (ESRD), the kidneys no longer adequately perform these functions. To survive, those with ESRD must either receive a kidney transplant or go on dialysis, a medical treatment that clears wastes and toxins from the blood. The most common form of dialysis, hemodialysis, uses a machine to artificially clean blood outside the body, either at the patient's home or at a medical facility.[1] Because over 90% of dialysis patients in the U.S.

[1]For more information, please see `https://www.niddk.nih.gov`.

use in-center hemodialysis, we focus on that modality for our analysis.[2]

Dialysis patients primarily receive treatment at one of the more than 7,000 dedicated dialysis facilities across the country, where they typically go three times per week for treatment that lasts three to four hours each visit. These facilities are run by a mix of for-profit and non-profit firms, with the two largest for-profit chains, DaVita and Fresenius, controlling over 70% of facilities and earning 90% of the industry's revenue (United States Renal Data System, 2014; Baker, 2019). Independent facilities comprise most of the remainder.

Because patients with kidney failure no longer produce enough erythropoietin, nearly all suffer from anemia (Babitt and Lin, 2006), which stems from deficient or dysfunctional red blood cells and leads to reduced oxygen flow to the body's organs. Common symptoms of anemia relate mostly to a patient's quality of life, including fatigue, weakness, headaches, and insomnia, but in some cases anemia can contribute to a greater risk of serious heart conditions, hospitalization, and death (Kliger et al., 2013). To diagnose anemia and assess its severity, clinicians use either hematocrit or hemoglobin (HGB) concentration.[3] We focus on hemoglobin in this paper, with accepted guidelines defining anemia as a level below 14 g/dL for men and 12 g/dL for women.

Among dialysis patients, anemia is typically managed using a cocktail of drugs administered by the facility during their session. Chief among these is recombinant human erythropoietin, or epoetin alfa, a biologic commonly known as EPO. Manufactured by Amgen under the brand name EPOGEN, EPO was approved by the Food and Drug Administration (FDA) in 1989 to treat anemia in dialysis patients (Kalantar-Zadeh, 2017) and since then has become a standard of care for the condition, with those treated with EPO requiring fewer blood transfusions and reporting improved appetite, activity level, and sense of well-being (Eschbach et al., 1989; Valderrabano, 2000). By 2005, 99% of dialysis patients regularly received EPO, and in some years it was Medicare's largest Part B drug expense (Thamer et al., 2007).

By the mid-2000s, randomized controlled trials had begun to show that EPO may be harmful for certain types of patients. Besarab et al. (1998), for example, found that ESRD patients with congestive heart failure treated with EPO to achieve normal or high hematocrit levels had a higher probability of death and myocardial infarction, while Singh et al. (2006) found an increased risk of death and

[2]Please see Wang et al. (2018) for a discussion of the trends in dialysis modalities.

[3]Hematocrit is approximately equal to three times the measured hemoglobin level (Bain et al., 2017).

cardiovascular events among patients treated with EPO to normal or high hematocrit levels who were diagnosed with chronic kidney disease but not yet on dialysis. Although these trials focused on specific patient populations, they raised concerns about the use of EPO more broadly, and in March 2007 the FDA issued a public health advisory for EPO, mandating a black box warning and advising physicians to adjust doses to target hemoglobin levels between 10 to 12 g/dL (Thamer et al., 2013). Over this period, observational studies suggested similar adverse effects (Zhang et al., 2004; Bradbury et al., 2009; Brookhart et al., 2010), though they did not use a research design that allowed for causal estimates and providers did not change their doses much in response (Thamer et al., 2013). In June 2011, the FDA amended the original black box warning to include guidance about using a dose no higher than what would be necessary for the patient to avoid a blood transfusion.

Not all ESRD patients respond uniformly to EPO (Kalantar-Zadeh et al., 2009). Comorbid conditions like inflammation, for instance, depress the availability of iron and may dampen the effectiveness of EPO by directly limiting the ability of bone marrow to produce red blood cells (Ebben et al., 2006; Kalantar-Zadeh et al., 2003; Brookhart et al., 2011a). Observational studies in the medical literature have also shown a relationship between anemia and the elevation at which a patient resides. Brookhart et al. (2008), for example, found that patients living more than 6,000 feet above sea level receive 19% less EPO than patients residing at sea level but still achieve higher hemoglobin levels. Brookhart et al. (2011a) similarly find that patients moving from low to high elevations exhibit large increases in hematocrit even though they receive smaller doses of EPO. Clinical studies artificially replicating elevation-induced hypoxia have also shown that patients diagnosed with chronic kidney failure produce more natural erythropoietin at elevation (Bosman et al., 2002).[4]

2.2. Medicare Payment Reform

Since 1972, Medicare has extended full benefits to all patients with ESRD, regardless of age, paying for both dialysis and anemia treatment under Part B. Those enrolled in an employer group health plan when diagnosed with ESRD retain their commercial insurance as the primary payer for 33 months, during which time Medicare acts as a secondary payer (Lin, 2021; League et al., 2022).

From the early 1980s to 2010, Medicare paid providers a composite rate of approximately $128

[4]Please see Winkelmayer et al. (2009) and Brookhart et al. (2011b) for a more complete discussion of these physiological relationships.

per dialysis session, an amount intended to cover the labor, capital, and routine lab tests associated with each treatment. In addition, Medicare paid providers for EPO and other injectable drugs on a fee-for-service basis. Initially, Medicare set the payment rate for EPO at $10 per 1000 IUs and then updated the rate in 2005 based on the average sales price plus a 6% markup, resulting in a slight decline in payments to about $9.50 per 1000 IUs.[5] EPO doses and expenditures increased consistently during the fee-for-service era, with spending on erythropoietin stimulating agents such as EPO approaching $2.7 billion in 2007 (Whoriskey, 2012). Concerns that the distortionary incentives from fee-for-service payments resulted in excessive costs for Medicare and harm to patients motivated policymakers to include ESRD payment reform as part of the Medicare Improvements for Patients and Providers Act (MIPPA) in 2008.

MIPPA mandated the bundling of dialysis services and all injectable drugs and biologics used in the treatment of ESRD into a single prospective payment, to take effect in 2011. For the first year of the PPS, Medicare fixed payment for these services at about $230, a level chosen to reduce total federal payments to dialysis providers by 2%.[6] Although targeted primarily at EPO due to the drug's outsize impact on Medicare expenditures and patient outcomes, the original PPS also bundled together 21 other drugs, spanning anemia treatment, access management, and anti-infectives.[7]

To offset the incentives for providers to increase their profits by providing lower-quality care following the payment reform, MIPPA also mandated the development of the ESRD Quality Incentive Program (QIP), which reduces payments to providers who fail to meet certain clinical standards, such as hemoglobin levels and hospitalization rates. Although the specific criteria assessed in the QIP change from year to year, in its inaugural year, 2012, the QIP targeted patients' hemoglobin levels and urea reduction ratio, a measure of dialysis filtration. Under the QIP, Medicare reduces the annual payments to a facility by between 0.5% and 2.0% if, for instance, the HGB levels of too many patients fall outside the regulated standards, with the size of the penalty determined by the extent of the shortfall. We discuss the QIP further in Appendix B, where we provide evidence that it did not meaningfully contribute to the reduction in EPO administered during our sample period, and evaluate providers'

[5]For more details, please see `https://www.gao.gov/assets/260/253347.pdf`.

[6]See Federal Register, Volume 74, Issue 187, (September 29, 2009). Providers had the option to transition into the PPS either immediately in 2011 or gradually over four years starting in 2011. Over 90% opted for the immediate transition. In Appendix A, we demonstrate that our results are robust to using only the set of providers who opted in immediately.

[7]Since then, this list has been expanded to include over 50 products.

strategic responses to it in Bertuzzi et al. (2023).

3. Data, Descriptive Statistics, and Time Trends

The main dataset for our analysis comes from the U.S. Renal Data System (United States Renal Data System, 2019), a national clearinghouse that collects and manages data from a variety of sources relevant to ESRD patients and health care providers. Included in these data are Medicare claims, treatment histories, patient attributes, and annual facility surveys. In addition, CMS Form 2728, known as the Medical Evidence Form, provides data on the health and clinical attributes of patients when they begin dialysis. We also geocode facilities' addresses and extract their elevations using data from the U.S. Geological Survey (U.S. Geological Survey Center for Earth Resources Observation and Science, 2014).

Table 1 presents summary statistics for our variables of interest. We limit our sample to hemodialysis patients between the ages of 18 and 100 who have Medicare as their primary payer and no missing observations for the patient and facility characteristics used in our later analysis. These characteristics include demographic variables such as gender and age, comorbidities such as diabetes and cancer, patient behaviors such as smoking and drinking, and facility characteristics such as chain affiliation and elevation. We restrict our analysis to the years 2009–2012, a window centered narrowly around the start of the PPS, leaving us with approximately 10 million patient-month observations. As will be important for our instrumental variable analysis in Section 5, the elevation of facilities varies considerably, with a standard deviation of 924 ft. We present summary statistics by elevation in Appendix C.

The 2011 payment reform combined payments for dialysis treatments and injectable drugs into a single payment. Figure 1 shows the evolution of several aspects of these services, including the quantity and quality of anemia management and dialysis care, before and after the reform and across elevations. Measures of anemia management responded immediately to the payment change: EPO doses were relatively flat going into 2010 but decreased sharply starting midway through the year, moving in concert with the increase in transfusions shown in panel (b), a correlation consistent with EPO being used to increase patients' hemoglobin levels and reduce the need for transfusions. The sharp decline in EPO predates the payment reform in 2011 by a few months and matches Medicare's announcement of

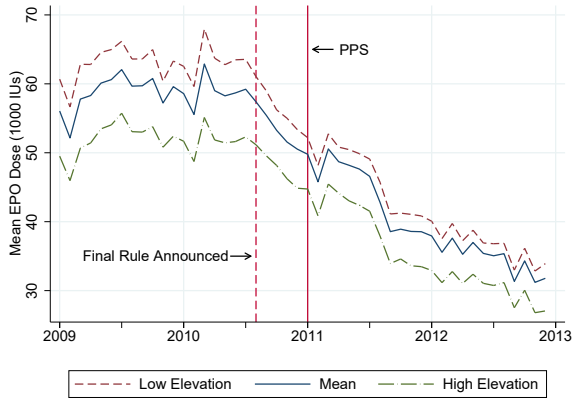
Table 1
Patient Descriptive Statistics

	Mean	Std. Dev.
Patient Characteristics		
Predicted Mortality	0.016	0.011
Age (Years)	63.40	14.57
Months with ESRD	45.08	38.01
Black	0.385	0.487
Male	0.552	0.497
Diabetic	0.540	0.498
Hypertensive	0.906	0.292
Incident Hemoglobin	9.853	1.674
Facility Characteristics		
Facility Elevation (ft)	638.1	923.5
Independent Ownership	0.197	0.397
EPO Use		
EPO Dose (1000 IUs)	48.50	64.11
Receives Any EPO	0.755	0.430
Health Outcomes		
Hemoglobin (g/dL)	11.12	1.22
Transfusions	0.028	0.166
Mortality	0.016	0.124
Hospitalizations		
Any Cause	0.1380	0.3449
Cardiac Event	0.0271	0.1625
Septicemia	0.0094	0.0965
Unique Patients	461,477	
Patient-Months	10,077,289	

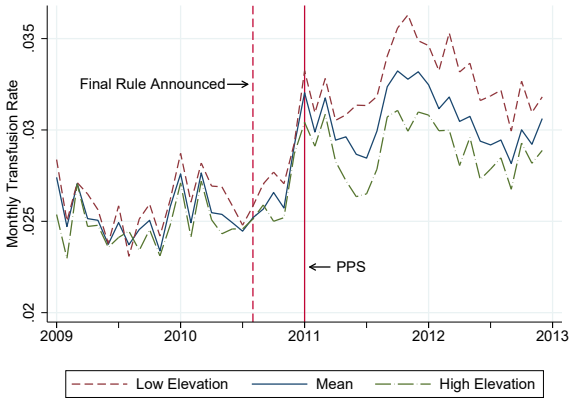
Notes: An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Predicted mortality is the predicted value for each observation using coefficients from a regression of mortality on patient controls and time fixed effects on observations from 2009 and 2010. Time fixed effects are not included in the prediction. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Transfusion and hospitalization variables are binary indicators. Facility elevation is measured in feet above sea level.

Figure 1
Time Trends in Treatments and Outcomes, by Elevation

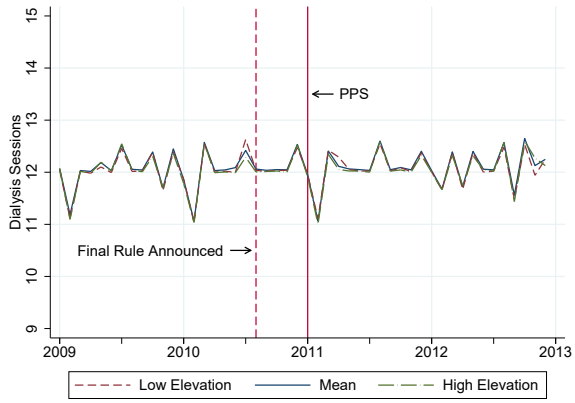
(a) Monthly EPO Dose



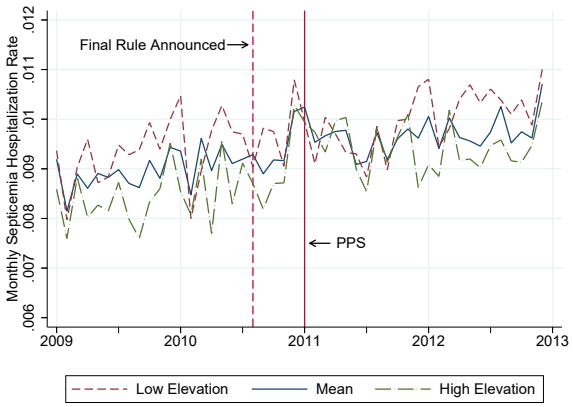
(b) Transfusion Rate



(c) Monthly Dialysis Sessions



(d) Hospitalizations for Septicemia



Notes: An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Transfusion and hospitalization variables are binary indicators. High (low) elevation denotes facility elevation in the fifth (first) quintile. This corresponds to being above 870 (below 73) feet above sea level. The solid vertical line indicates the start of the PPS in January 2011, while the dashed vertical line indicates the announcement of the final rule for the PPS.

the final PPS rule.[8,9]

The dashed lines in Figure 1 show how treatment evolved for patients residing in the first and fifth elevation quintiles. Patients at high elevations received smaller doses of EPO in both the pre- and post-2011 periods, as shown in panel (a), while those at lower elevations experienced a much larger decline following the payment reform. Directly related to the drop in EPO, panel (b) shows a much larger increase in transfusions for patients at lower elevations despite having a rate similar to those at higher elevations prior to 2011.

In contrast to the changes in patients' treatment for anemia, we find little evidence that dialysis care itself changed in response to the payment reform, providing reassurance that we can use the switch to prospective payments to identify the health effects of EPO. As examples, the average number of dialysis sessions per patient in panel (c) remained steady each month throughout the payment reform, and hospitalizations for septicemia in panel (d), a class of infections that can arise from improper cleaning of dialysis facilities and reflects low-quality care, did not change.

4. Model of Provider's Treatment Decisions

4.1. Model Primitives

Our descriptive results from Section 3 suggest the payment reform had a large impact on the amount of EPO administered to dialysis patients and their corresponding measures of anemia management. Despite the decline in hemoglobin levels and increase in transfusion rates, however, the reduction in EPO may have improved patients' health overall given the widespread concern about EPO's adverse effect on cardiac events and mortality (Besarab et al., 1998; Singh et al., 2006). To better understand how EPO influences these various components of health, as well as the tradeoffs providers make between their own financial returns and their patients' well-being, we consider a stylized model of providers' dosing decisions that incorporates the key factors governing these choices.

[8] We show in Appendix D that our results are robust to changing the treatment period to also include the anticipatory period between the announcement and the implementation of the payment reform. For more details, please see `https://www.gao.gov/assets/gao-13-190r.pdf`.

[9] As discussed in Section 2, two other policy changes occurred during this period, a black box warning and the QIP. In Appendix B, we present evidence that these changes do not explain the decline in EPO doses in Figure 1 — if anything, they would make our estimate of the change in EPO doses attributable to the payment reform conservative.

Suppose a provider's utility from administering EPO can be described by the objective function

$$U(epo; p, X, a, u) = epo * p + h(epo, X, a, u),$$

where *epo* is the amount of EPO administered, p is the profit margin from a dose of EPO, a is the elevation of the facility, X is a vector of other observable patient characteristics, and u is a vector of unobserved patient characteristics. When deciding how much EPO to administer to a patient, the provider takes into account both the profit margin of EPO and the patient's health, given by the function

$$h(epo, X, a, u) = \sum_c \beta_c h_c(epo, X, a, u) - \beta_f f(epo, X, a, u) + H(X, a, u),$$

where h_c consists of observable components of health, f is an unobservable health cost, and H is a patient's unobserved baseline health status that does not depend on EPO. The weights β_c and β_f represent the value providers put on each component of health relative to the financial returns from EPO, with larger βs implying greater altruism. For each observable component of health, we have

$$h_c(epo, X, a, u) = \alpha_c(epo, X, u) + b_c(X, a, u),$$

where α_c represents the health production function that captures the potentially heterogeneous effect of EPO on outcome c, and b_c is the baseline level of the health component. Here we allow the baseline health level b_c to differ by elevation, reflecting past work in the medical literature showing that dialysis patients residing at higher elevations have higher baseline levels of hemoglobin (Brookhart et al., 2008). At the same time, we do not allow the effect of EPO on observed health to differ by elevation — that is, a does not enter $\alpha_c(\cdot)$. As the medical literature has not reached a consensus on this relationship, we provide empirical evidence supporting this assumption in Appendix E.3. Additionally, we allow elevation to enter the unobserved health costs, $f()$, as shown below.

Our stylized model highlights several important aspects of a provider's dosing decision. Notably, the first-order condition,

$$g(epo^*; p, X, a, u) = p + \sum_c \beta_c \frac{\partial \alpha_c}{\partial epo^*} - \beta_f \frac{\partial f}{\partial epo^*} = 0, \tag{1}$$

shows that a financially motivated provider will overtreat patients if the profit margin of EPO is positive and undertreat them if it is negative. This relationship mirrors policymakers' concerns both before the payment reform, when they suspected providers administered excessive doses of EPO to generate more revenue, and after, when they feared the reform would result in insufficient doses by making the drug an uncompensated cost for providers.

The model also highlights the role of heterogeneity in patients' responsiveness to EPO. Using the implicit function theorem, the equilibrium level of EPO changes with respect to its profit margin at the rate[10]

$$\frac{\partial epo^*}{\partial p} = -\left(\frac{\partial^2 h}{\partial epo^* \partial epo^*}\right)^{-1} = -\left(\sum_c \beta_c \frac{\partial^2 \alpha_c}{\partial epo^* \partial epo^*} - \beta_f \frac{\partial^2 f}{\partial epo^* \partial epo^*}\right)^{-1}. \tag{2}$$

From the equation, two factors dictate the extent to which EPO doses adjust in response to a payment change: the adjustment depends on both how providers value patients' health, with more-altruistic providers responding less strongly, as well as the curvature of the health function with respect to EPO, where more rapidly diminishing returns to health result in a weaker response. The first point is well understood — health care providers are known to respond to financial incentives to varying degrees — whereas the second is not. If the second derivatives of the health function with respect to treatment vary across patients for any reason, providers will respond to payment changes differently for different types of patients. And, because health is multidimensional, providers must also potentially trade off the positive effect of EPO on one health outcome against its negative effect on another.

The data clearly reflect this heterogeneity. Panel (a) of Figure 1, for instance, shows the change in EPO doses differed across elevations following the payment reform, suggesting that $\frac{\partial^2 h}{\partial epo\ \partial epo}$ depends on elevation. Furthermore, with the influence of elevation on providers' responses to their financial incentives given by

$$\frac{\partial^2 epo^*}{\partial p \partial a} = -\beta_f \frac{\partial^3 f}{\partial epo^* \partial epo^* \partial a} \left(\frac{\partial epo^*}{\partial p}\right)^2, \tag{3}$$

the smaller change in EPO doses for patients at higher elevations in Figure 1 reveals this value is negative. Assuming EPO has decreasing marginal benefits in terms of unobserved health, this implies the marginal benefit from EPO at higher elevations decreases more rapidly than the marginal benefit at

[10]Here we assume differentiability of $g(\cdot)$ with respect to a, X, u, and p around epo^*.

lower elevations, perhaps because physiological differences at high elevations make excessive EPO doses especially harmful. In short, the observed differences in how providers respond to payment changes demonstrate that the heterogeneous relationship between health and EPO influences their response. Beyond elevation, other relevant sources of heterogeneity could include patient comorbidities like obesity or heart disease that may similarly impact the effectiveness or risks of EPO and therefore also influence providers' dosing decisions.

4.2. Identification of the Health Production Function

A key component of our model is the health production function, which describes the effect of EPO on patients' health and allows us to estimate the respective weights providers place on various health outcomes. Although the results from clinical trials could serve as a basis for these relationships, they do not account for the influence of providers' financial incentives in determining doses nor the full spectrum of heterogeneity among patients, making them ill suited for such an exercise. Instead, we use a novel instrumental variable to identify the causal effect of EPO in a way that incorporates important features of the dialysis industry.

To motivate our approach for estimating the health production function, we first use our instrument to recover the local average causal effect of EPO on the most prominent observable dimensions of health. We then use this same strategy to estimate our production function to allow for a greater degree of heterogeneity. Because estimating the average treatment effect of EPO does not depend on the functional form assumptions we make when estimating our structural model, this first approach grounds and enriches our understanding of EPO's effect on patients' outcomes beyond what can be learned from the narrow scope of clinical trials.

We denote the local average treatment effect of EPO on observable health outcome c as α_c^{IV}, with our estimation approach captured by

$$y_{ijt}^c = \alpha_0 + \alpha_c^{IV} EPO_{ijt} + X_{ijt} b_c + \varepsilon_{ijt}, \tag{4}$$

where y_{ijt}^c is the health outcome c of patient i treated at facility j in month t and X_{ijt} is a vector

of observable patient and facility characteristics, including facility and time fixed effects.[11] The main challenges with identifying the causal effect of EPO stem from reverse causality and simultaneity, which could bias OLS estimates in ambiguous ways. The estimates would be biased upward, for example, if only the healthiest patients receive EPO, or a downward bias could emerge if unobserved confounds like rapidly deteriorating kidneys lead to both high doses of EPO to combat anemia along with low survival rates due to the patient's declining health.

To overcome these empirical challenges, we use two independent sources of variation in EPO doses within an instrumental variables regression that, under a standard set of assumptions, returns an average treatment effect. First, we use the time-series variation in EPO payments associated with Medicare's payment reform. As Medicare imposed the change uniformly across all providers, rather than targeting specific payment changes to specific facilities, the switch to prospective payments introduced a plausibly exogenous shock to EPO doses due to the change in providers' financial incentives. Second, we use a novel source of variation based on a physiological aspect of anemia management: patients living at higher elevations have higher baseline levels of hemoglobin and therefore require smaller doses of EPO to manage their anemia. With facilities considering both their own financial returns as well as their patients' well-being when administering EPO, those at lower elevations reduced their doses comparatively more after the PPS eliminated fee-for-service payments. Putting these two institutional details together, patients at low elevations experienced a larger shock to their EPO doses than patients at higher elevations did, and we can use the cross-sectional variation from patients' elevations along with the time-series variation induced by the payment reform to identify the causal effect of EPO on outcomes.

We cannot simply use the switch to prospective payments directly as an instrument, however, as doing so may violate the exclusion restriction if trends like updated dialysis standards and related medical advances coincide with the payment reform. Similarly, just as elevation directly affects patients' hemoglobin levels, it may also directly affect their health in other ways. Instead, we use the interaction of a post-PPS indicator variable and a facility's elevation as an instrument for EPO doses while controlling directly for time fixed effects and elevation in our first- and second-stage regressions. Our empirical strategy of interacting one variable with time-series variation and another with cross-sectional variation

[11] The regression coefficient capturing the differences in the outcome by patient and facility characteristics is denoted b_c to emphasize the fact that this coefficient captures the baseline health differences that do not depend on EPO doses also captured by $b_c(\cdot)$ in the theoretical model.

was first introduced by Bartik (1991) and is closely related to the approaches later used by Card (1995) to study the returns to education, Nunn and Qian (2014) to study the impact of food aid, and Bettinger et al. (2017) to study the effectiveness of online college courses.

Adapting this approach to our setting, we have a first-stage specification of

$$EPO_{ijt} = \psi_1 Elevation_j + \psi_2 PPS_t + \psi_3 Elevation_j \times PPS_t + X_{ijt}\Psi_c + \upsilon_{ijt}, \tag{5}$$

where the instrument $Elevation_j \times PPS_t$ varies by facility and time period, allowing us to include month-year fixed effects. By instrumenting for EPO doses with the interaction term, our first stage resembles a difference-in-differences estimation, comparing EPO doses at facilities that typically use less of the drug due to their high elevation with those at lower elevations that typically use more of it, during the fee-for-service era when financial incentives favored higher doses relative to the PPS era when the financial incentives reversed. As outlined in Nunn and Qian (2014), the main distinction between this strategy and a typical difference-in-differences estimation is the continuous treatment variable.

For our second stage to have a causal interpretation, the interaction between a facility's elevation and Medicare's payment policy must only affect health outcomes through its influence on EPO doses, conditional on the controls. In our setting, this requires that (i) any other mechanism through which elevation affects patients is constant over time and (ii) any other mechanism causing health outcomes to differ before and after the payment reform affects patients uniformly with respect to their elevation. As discussed above, using elevation as an instrument by itself would mean the reduced-form slope captures both the effect of EPO as well as other plausible mechanisms that affect health outcomes, such as patients living at higher elevations having more-active lifestyles (e.g., hiking and skiing) or elevation having direct consequences for patients' health. By interacting the two variables, however, the reduced-form coefficient measures only how the slope between elevation and outcomes changes when the payment policy changes — the main effect of elevation included in both the first and second stages differences out any other plausible mechanisms that remain constant across the different payment schemes.

Although not directly testable, several pieces of evidence suggest our empirical strategy satisfies these two requirements. In the same spirit as a traditional difference-in-differences estimation, the plot of EPO doses for the first and fifth elevation quintiles in the first panel of Figure 1 shows parallel trends

in EPO doses prior to the payment reform.[12] On average, low-elevation patients received higher doses of EPO before prospective payments, with the difference between the two groups remaining constant during this period.[13] After the payment reform, average EPO doses declined in both quintiles, but the decline was much larger for those at lower elevations. The second stage then links the change in EPO to the corresponding health outcomes like transfusions, with the right panel showing a larger increase for patients at lower elevations commensurate with their larger reductions in EPO.

A related threat to identification would be omitted variables that change disproportionately across elevations over time. Although some differences across elevations do exist and change over time, as shown in the balance tables for observable patient characteristics at each elevation quintile in Appendix C, the changes are not systematically moving toward better or worse outcomes. To assess more formally whether changes in unobserved patient characteristics might confound our analysis, we create a composite measure of a patient's health status using the coefficients from an OLS regression of mortality on observable patient characteristics and month-year fixed effects to predict a patient's mortality risk. This predicted mortality variable is likely correlated with unobserved characteristics that affect patients' health, and we can detect changes in the composition of the patient population by testing if predicted mortality changed differentially by elevation after the payment reform. Estimating equation (5) with predicted mortality as the dependent variable, we show in Table 2 that the differential change by elevation is a precisely estimated zero, suggesting that a changing mix of patients across elevations is unlikely to confound our analysis.[14,15]

Another violation of the exclusion restriction could come from facilities reinvesting the additional profits they earn from administering less EPO after the payment reform. Facilities at higher elevations received a larger financial gain from Medicare's switch to prospective payments, for instance, and may have reinvested their windfall in ways that improved patient care. As shown in Table 3, however, we

[12] As discussed in Christian and Barrett (2017), non-parallel pre-trends would have suggested our difference-in-differences analog violated the exclusion restriction.

[13] A regression of EPO on facility elevation, a time trend, and the interaction of the two along with patient and facility controls using data prior to prospective payments indicates that the difference in time trends is small and not statistically significant (p=0.5777).

[14] As the purpose of these regressions is to assess how predicted mortality correlates with the instrument, and predicted mortality is constructed as a direct function of patient comorbidities and demographics, we omit these patient controls from the specifications in Table 2.

[15] Column (3) of Table 2 shows that, while facility fixed effects absorb most of the variation in facility elevation, some small portion remains. Within-facility variation in elevation arises from some measurement error arising from geocoding locations and on rare occasions facilities moving physical locations. Because the magnitude of such variation is small, we omit the time dimension from the subscript of $Elevation_j$ in equation (5).

Table 2
Predicted Mortality by Elevation

	(1) Predicted Mortality	(2) Predicted Mortality	(3) Predicted Mortality
Facility Elevation	0.000000182**	0.000000165**	0.000000100
	(5.95e-08)	(6.05e-08)	(0.000000175)
Elevation × PPS	-7.62e-08***	-4.43e-08^{+}	-3.20e-08
	(2.03e-08)	(2.37e-08)	(1.98e-08)
Year-Month FE	0	1	1
Pat/Fac Controls	0	0	0
Facility FE	0	0	1
R-squared	0.000167	0.000431	0.134
Dep. Var. Mean	0.0164	0.0164	0.0164
Observations	10077289	10077289	10077264

Notes: OLS estimates from equation (5). Dependent variable is predicted mortality. Predicted mortality is the predicted value for each observation using coefficients from a regression of mortality on patient controls and time fixed effects on observations from 2009 and 2010. Time fixed effects are not included in the prediction. PPS is an indicator variable for January 2011 or later. Facility elevation is measured in feet above sea level. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

Table 3
Facility Inputs by Elevation

	(1) Nurses Per Technician	(2) Patients Per Employee	(3) Patients Per Station	(4) Employees Per Station	(5) Hosp., Septicemia
Facility Elevation	-0.00000513	-0.0000503	-0.0000399	-0.00000351	-0.000000699***
	(0.0000142)	(0.0000335)	(0.0000588)	(0.0000123)	(0.000000129)
Elevation × PPS	0.00000767	0.0000226	-0.00000837	-0.00000573	0.0000000336
	(0.00000856)	(0.0000231)	(0.0000169)	(0.00000373)	(0.0000000786)
Year-Month FE	1	1	1	1	1
Pat/Fac Controls	1	1	1	1	1
Facility FE	0	0	0	0	0
R-squared	0.226	0.155	0.0866	0.0676	0.00283
Dep. Var. Mean	0.910	5.402	3.988	0.766	0.00939
Observations	242917	254307	256712	256173	10077289

Notes: OLS estimates from equation (5). Dependent variables in columns (1)–(4) are facility-level ratios. Dependent variable in column (5) is an indicator for hospitalization with a primary diagnosis of septicemia. PPS is an indicator variable for January 2011 or later. Facility elevation is measured in feet above sea level. For columns (1)–(4) an observation is a facility-month. For column (5) an observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility to freestanding or hospital-based, and chain ownership status, as well as geographic information about the patient's residence, including state and average income in the ZIP code. For columns (1)–(4) controls are facility-month-level means of the patient-level controls. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

do not find evidence of such behavior, as conventional measures of a facility's investment in providing high-quality care, such as the number of patients per staff, the number of patients per station, and the number of infections per patient, did not change across elevations after the payment reform. Appendix E investigates other potential violations of the exclusion restriction related to the use of drugs other than EPO and changes in dialysis modalities.

With the approach outlined above, our IV estimand recovers the average equilibrium marginal effect of EPO on observable health outcomes, expressed as

$$\alpha_c^{IV} = \frac{\frac{\partial^2 h_c^*}{\partial p \partial a}}{\frac{\partial^2 epo^*}{\partial p \partial a}} = \frac{\frac{\partial^2 h_c}{\partial epo^* \partial a}\frac{\partial epo^*}{\partial p} + \frac{\partial h_c}{\partial epo^*}\frac{\partial^2 epo^*}{\partial p \partial a}}{\frac{\partial^2 epo^*}{\partial p \partial a}} = \frac{\partial h_c}{\partial epo^*} = \frac{\partial \alpha_c}{\partial epo^*}, \tag{6}$$

where the third equality holds because $\frac{\partial^2 h_c}{\partial epo^* \partial a} = 0$. Using two-stage least squares with a continuous treatment variable, this estimator can be interpreted as a weighted average of the unit causal effects of EPO along the support of EPO doses, with the weights of each incremental level of EPO coming from

the size of the complier group at that level. In Appendix E, we provide evidence that the compliers with our instrument are drawn from the entire distribution of EPO doses and find little evidence of unobserved heterogeneity in the effect of EPO on observable health outcomes, both of which suggest our IV estimand captures the average treatment effect of EPO over the entire patient population.

We can extend our analysis to estimate the heterogeneous effects of EPO by estimating the same IV regression within cells of patients who have identical observable characteristics or, more simply, by interacting observable characteristics with our baseline instrument, allowing us to recover not only the overall local average treatment effect of EPO, but also the heterogeneity in the treatment effect based on differences in patients' observable characteristics like age, gender, and comorbidities. To do so, we estimate the second-stage equation

$$y_{ijt}^{c} = \alpha_0 + \alpha_{c,1}^{IV} EPO_{ijt} + X_{it} b_{c,X} + EPO_{ijt} \times X_{it} \alpha_{c,X}^{IV} + F_{jt} b_{c,F} + \varepsilon_{ijt}, \tag{7}$$

where F_{jt} represents facility characteristics that may affect the baseline level of health and

$$\mathbb{E}\left[\frac{\partial \alpha_c}{\partial epo^*} | X_{it} = x_{it}\right] = \alpha_{c,1}^{IV} + x_{it} \alpha_{c,X}^{IV}$$

gives the average marginal effect of EPO on patients with observable characteristics X_{it}.[16] To estimate equation (7), we extend our IV strategy from above using two-stage least squares and treating EPO_{ijt} as an endogenous variable while interacting EPO_{ijt} with all patient attributes in the data. To instrument for these interactions, we use the natural extension of our original instrument by interacting it with each patient attribute and then use these interactions as a new set of instruments. For example, we instrument for the difference in the marginal effect of EPO for men and women using the differential change for men and women after the start of PPS and across elevations. Using analogous instruments for all components of $EPO_{ijt} \times X_{it}$, we estimate equation (7) and obtain the average marginal effect of EPO for patients with heterogeneous observable characteristics.

[16] This specification only allows the returns from EPO to vary by patient attributes, not by facility characteristics. Different facilities may have production possibilities frontiers that are level-shifts of one another, but the slope does not change. Put differently, if a patient were to move from one facility to another, the level of the health outcome y_{ijt}^{c} could change as facility characteristics enter the $b_c(\cdot)$ function, but the marginal effect of EPO ($\frac{\partial \alpha_c}{\partial epo^*}$) could not. This simplification reflects the physiological and institutional details of anemia treatment. The EPO molecule is the same across providers, and a patient's physiological reaction to a given amount of that molecule will be the same irrespective of which facility administers it.

5. Instrumental Variable Estimation Results

5.1. Estimated Treatment Effects

We present results from our first-stage estimates in Table 4, with an F-statistic of 49.1 demonstrating the instrument's relevance. Given the body's physiological response to elevation, EPO doses decrease with elevation in the expected way, but the rate of this decrease falls by over a quarter after the payment reform. Estimates from our preferred specification presented in column (3) indicate that patients at sea level had their average monthly EPO dose reduced by 1400 IUs more than patients living 1000 feet above sea level. Following the first-stage estimates, we recover the local average treatment effect of EPO on patient outcomes using two-stage least squares. In addition to instrumenting for EPO_{ijt}, we control for several patient covariates, month-year fixed effects, and facility fixed effects, estimating this equation for the main outcomes of interest: HGB levels, blood transfusions, hospitalizations, and mortality.

The results for HGB levels highlight the importance of our empirical strategy. Although randomized controlled trials have shown that EPO increases HGB levels, the OLS results in Table 5 suggest the opposite effect due to the nonrandom assignment of EPO: more-anemic patients with lower HGB levels tend to be prescribed higher doses of EPO, inducing a negative correlation between HGB and EPO if relevant patient attributes are not observed in the data. Our IV strategy corrects for these endogenous treatment decisions, as shown in column (2), where increasing EPO doses by 1000 IUs per month increases a patient's HGB by 0.0208 g/dL, on average, for an implied elasticity of HGB with respect to EPO of 0.09, and confirms the established medical fact that EPO effectively treats anemia. Table 5 also shows results with transfusions as the dependent variable. As with HGB, the OLS coefficient contradicts established medical evidence by suggesting that more EPO is associated with the need for more blood transfusions, whereas correcting for endogenous dosing decisions using our IV strategy reveals that larger EPO doses do indeed reduce the likelihood of receiving a transfusion.

Table 6 shows the primary adverse effects of larger EPO doses — they lead to more hospitalizations for cardiac events as well as higher mortality rates. For both all-cause and cardiac hospitalizations, the OLS and IV results suggest a positive correlation with EPO doses, although this effect does not remain statistically significant for all-cause hospitalizations in the IV specification. For mortality, the

Table 4
First Stage Regression

	(1) EPO	(2) EPO	(3) EPO
Facility Elevation	-0.00477***	-0.00353***	-0.00542***
	(0.000341)	(0.000401)	(0.00157)
Elevation × PPS	0.00144***	0.00133***	0.00140***
	(0.000214)	(0.000203)	(0.000200)
Year-Month FE	1	1	1
Pat/Fac Controls	0	1	1
Facility FE	0	0	1
R-squared	0.0297	0.0835	0.139
Dep. Var. Mean	48.50	48.50	48.50
Observations	10077289	10077289	10077264

Notes: OLS estimates from equation (5). Dependent variable is monthly EPO dose. EPO doses are censored at the 99th percentile and measured in 1000 IUs. PPS is an indicator variable for January 2011 or later. Facility elevation is measured in feet above sea level. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

OLS estimates show a statistically significant, negative correlation with EPO, but the effect becomes positive while remaining statistically significant when we use our instrument. Our IV estimates imply that a 1% increase in EPO raises the rate of cardiac hospitalization by 0.3% and mortality by 0.4%, validating the concerns of policymakers who advocated for the FDA's black box warning and Medicare's adoption of the PPS to reduce the widespread use of EPO among dialysis patients.[17]

As a placebo test, we also estimate equation (4) with septicemia as the dependent variable. Because

[17]For comparison, Besarab et al. (1998) conducted a randomized control trial where dialysis patients with heart conditions were randomized into two EPO treatment arms targeting different hematocrit levels. They found that patients treated most intensely suffered 22% more deaths and 29% more nonfatal heart attacks than those targeting a lower hematocrit level. In comparison to such findings, the substantial drops in mortality and cardiac hospitalizations that we estimate seem quite reasonable.

Table 5
The Effect of EPO on Hemoglobin Levels and Transfusions

	HGB		Transfusion	
	(1) OLS	(2) IV	(3) OLS	(4) IV
EPO	-0.00303***	0.0208***	0.000132***	-0.000574***
	(0.0000254)	(0.00542)	(0.00000256)	(0.000153)
Implied Elasticity	-0.0132	0.0908	0.227	-0.989
Year-Month FE	1	1	1	1
Pat/Fac Controls	1	1	1	1
Facility FE	1	1	1	1
Dep. Var. Mean	11.12	11.12	0.0282	0.0282
Observations	8181736	8181736	10077264	10077264
First-Stage F-statistic		33.41		49.11

Notes: OLS and IV estimates from equation (4). Dependent variable in columns (1)–(2) is hemoglobin. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Dependent variable in columns (3)–(4) is a binary variable for receiving a blood transfusion. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Implied elasticities are calculated using the reported linear effect of EPO along with the average outcome value and EPO dose reported in Table 1. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

Table 6
THE EFFECT OF EPO ON HOSPITALIZATIONS AND MORTALITY

	Hosp., Any Cause		Hosp., Cardiac Event		Hosp., Septicemia		Mortality	
	(1) OLS	(2) IV	(3) OLS	(4) IV	(5) OLS	(6) IV	(7) OLS	(8) IV
EPO	0.000154***	0.000201	0.0000153***	0.000181+	-0.000000269	0.0000351	-0.000112***	0.000126*
	(0.00000348)	(0.000249)	(0.00000121)	(0.0000942)	(0.000000602)	(0.0000538)	(0.000000893)	(0.0000631)
Implied Elasticity	0.0541	0.0707	0.0273	0.323	-0.00139	0.181	-0.345	0.388
Year-Month FE	1	1	1	1	1	1	1	1
Pat/Fac Controls	1	1	1	1	1	1	1	1
Facility FE	1	1	1	1	1	1	1	1
Dep. Var. Mean	0.138	0.138	0.0271	0.0271	0.00939	0.00939	0.0157	0.0157
Observations	10077264	10077264	10077264	10077264	10077264	10077264	10077264	10077264
First-Stage F-statistic		49.11		49.11		49.11		49.11

Notes: OLS and IV estimates from equation (4). Dependent variables are binary outcomes. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Implied elasticities are calculated using the reported linear effect of EPO along with the average outcome value and EPO dose reported in Table 1. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. +, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

septicemia, a severe blood infection resulting from facilities' poor cleaning protocols, has no known relation to EPO, a statistically significant effect of EPO on septicemia would suggest an omitted variable confounds our analysis. As shown in Table 6, however, we do not find a causal effect of EPO on septicemia in our IV specification, providing further reassurance in our identification strategy.

Figure 2 shows the distribution of the marginal effects of EPO from estimating equation (7) on each of the outcomes we consider for all patient-month observations, and Table 7 reports summary statistics for these distributions.[18] For each outcome, the average of the marginal effects is similar to the local average treatment effects reported in Tables 5 and 6, while the wide variation in patients' responsiveness to EPO has important practical implications: the marginal effect of EPO on HGB, for example, is more than twice as large for a patient one standard deviation more responsive than the mean compared to a patient one standard deviation less responsive. Similarly, the effect of EPO on transfusions is 2.3 times greater, the effect on cardiac hospitalizations is 4.3 times greater, and the effect on mortality is 2.6 times greater. Given the correlation between this treatment effect and the levels of EPO and HGB, the third quartile of the elasticity of HGB with respect to EPO is 4.5 times greater than the first quartile. In the model, the large degree of heterogeneity means providers must trade off their financial considerations against the ways in which EPO either helps or harms each patient individually, resulting in different equilibrium levels of EPO and health effects across patients.

In Appendix E.4, we consider the possibility that doses are also related to unobserved heterogeneity,

[18]The coefficients on specific interactions are provided in Appendix F.

Table 7
Summary Statistics of Estimated Heterogeneous Effects of EPO

	Mean	Std. Dev.	25th Percentile	Median	75th Percentile
HGB	0.0158	0.0055	0.0122	0.0156	0.0192
HGB Elasticity	0.0943	0.1069	0.0268	0.0586	0.1203
Transfusion	-0.000563	0.000220	-0.000697	-0.000580	-0.000430
Hosp., Any Cause	0.000467	0.000421	0.000203	0.000442	0.000719
Hosp., Cardiac Event	0.000238	0.000149	0.000142	0.000234	0.000330
Mortality	0.000162	0.000071	0.000116	0.000155	0.000201
Observations	10077289				

Notes: Summary statistics for $\mathbb{E}\left[\frac{\partial \alpha_c}{\partial epo^*}|X_{it} = x_{it}\right]$ using IV estimates of equation (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Transfusion and hospitalization variables are binary indicators. HGB elasticity reports the patient-month-level implied elasticity of HGB with respect to EPO using the causal effect reported here along with the observed level of EPO and HGB.

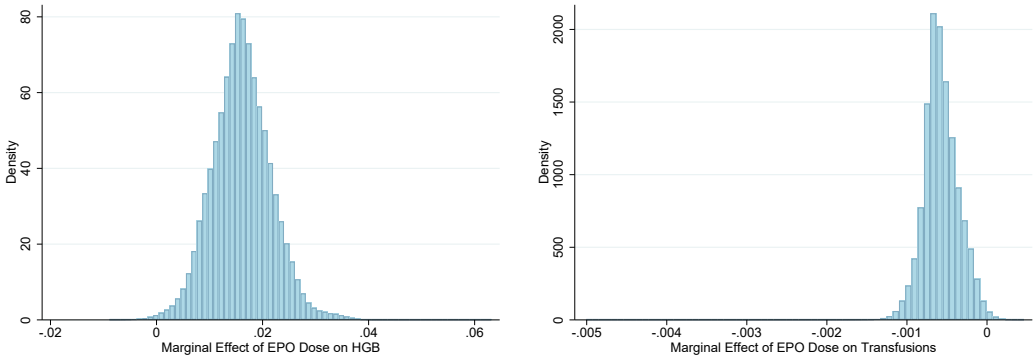
finding no empirical evidence suggesting that they are. As such, the estimates recovered from our IV approach can be interpreted as average treatment effects, even if the complier group is not wholly representative of the overall population, and can be used to assess counterfactual policies that may shift treatment in a way that does not line up perfectly with how compliers responded to the instrument (Heckman and Vytlacil, 2007).

Taken together, our results highlight the clinical tradeoffs associated with using EPO. Although EPO effectively treats patients' anemia, as reflected by higher HGB levels and fewer blood transfusions, these improvements must be weighed against a higher risk of cardiac events and death, where the wide heterogeneity in the effect of EPO means these tradeoffs are not uniform across patients.

5.2. Comparison to Clinical Trials

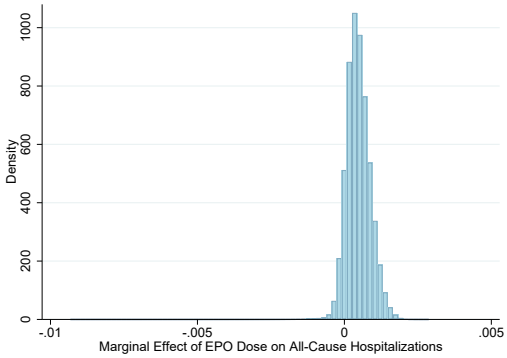
Given providers' equilibrium dosing decisions, our estimates of EPO's effectiveness stand in contrast to those measured in clinical trials. The original Phase III trial, for example, found an average effect per 1000 IUs of EPO of 0.0271 (Eschbach et al., 1989), an effect 30.2% larger than our estimate from Table 5. In addition, the aggregated results from multiple clinical trials in Tonelli et al. (2003) found even larger estimates of the average marginal effect, ranging from 0.0338 to 0.0896, while the heterogenous

Figure 2
Histogram of Estimated Marginal Effects of EPO

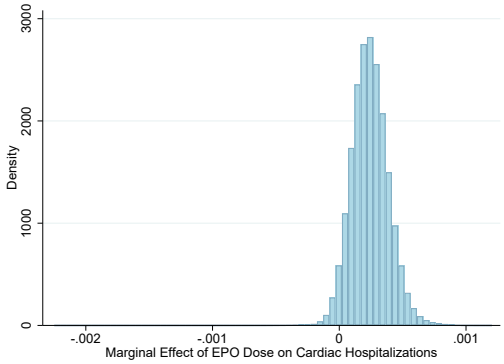


(a) HGB

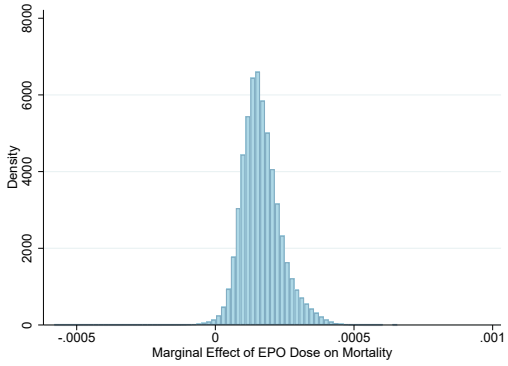
(b) Transfusions



(c) All-Cause Hospitalization



(d) Cardiac Hospitalization



(e) Mortality

Notes: Estimated marginal effects come from IV estimates of equation (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Transfusion and hospitalization variables are binary indicators.

treatment effects from the first panel of Figure 2 show that the equilibrium marginal effects of EPO generally fall below those found in clinical trials.

The distinction between our estimates, which come from actual dosing decisions and reflect providers' equilibrium behavior, and those from randomized controlled trials suggests the need for field studies to complement the findings from more controlled environments, especially when the drug in question is the central target of a major payment reform like EPO in dialysis. As discussed above, various factors could contribute to a disparity between the treatment effects estimated in clinical trials and those experienced in practice, such as treatment effect heterogeneity, differences in patient groups, or distinct administration protocols. From the results below, the effectiveness of EPO outside of clinical trials also depends on how providers trade off their altruistic tendencies with their financial considerations as well as how they adjust to the heterogeneous responses of their patients. Quasi-experimental estimates can complement the evidence from trials by using data that account for these factors, especially when the complier group is more representative of the population than the trial's participants.

6. Structural Model Estimation Results

Having recovered the equilibrium effect of EPO on various health outcomes, we now put more structure on the model presented in Section 4 to recover the weights providers place on patients' health relative to their own financial returns and simulate how EPO doses and health outcomes would change under a number of counterfactual scenarios. To do so, we first move from our estimated distribution of average treatment effects to specify the form of the health production function by assuming (i) any heterogeneity in the effect of EPO on observable health outcomes flows only through observable patient characteristics — i.e., there is no unobserved heterogeneity[19] — and (ii) the marginal effect of EPO varies by patient characteristics linearly in an additively separable way. Under these assumptions, the health production function takes the form

$$\alpha_c(epo, X) = \left(\alpha_{c,1} + \sum_{x \in X} \alpha_{c,x} x\right) epo, \tag{8}$$

and the estimates of equation (7) return the parameter values $\alpha_{c,1}$ and $\alpha_{c,x}$ rather than merely the averages, where the estimates presented in Figure 2 show the heterogeneous treatment effect of EPO and

[19]Strictly speaking, we need only assume that providers do not make dosing decisions based on unobserved heterogeneity in the effect of EPO on observable health outcomes. We make the stronger assumption of no unobservable heterogeneity for expositional clarity. We further discuss this assumption and provide empirical support for it in Appendix E.

fully characterize the production function for observable components of health. For the observable health component c, we focus specifically on HGB levels, cardiac hospitalizations, and mortality because HGB levels can be viewed as a sufficient statistic for anemia management (i.e., as opposed to transfusions, it is the outcome directly targeted by facilities) and cardiac hospitalizations are more directly related to EPO than all-cause hospitalizations (i.e., a salient side effect of EPO is an elevated risk of heart attacks).

Next, we assume the effect of EPO on unobserved health costs is quadratic and depends on the ownership of the facility, elevation, and unobserved heterogeneity, taking the form

$$f(epo, a, u) = (\phi_j + \phi_{a,1} a + u)\, epo + (1 + \phi_{a,2} a)\, epo^2, \tag{9}$$

where the second term contains a normalization and ϕ_j differs by the ownership of the facility, allowing the productivity of EPO to differ in ways that correspond to the documented differences in dosing practices of large chains and independent facilities. Furthermore, because the influence of financial incentives on providers' dosing decisions depends only on the parameters of this function and the weight providers place on unobserved patient health relative to profits, we can estimate the unobserved health costs of EPO.

By way of simplification, consider that at $a = 0$ and $u = 0$, we have

$$\frac{\partial epo^*}{\partial p} = (2\beta_f)^{-1} \qquad \text{and} \qquad \frac{\partial^2 epo^*}{\partial p \partial a} = -(2\beta_f)^{-1} \phi_{a,2},$$

which means we can use OLS to estimate

$$EPO_{ijt} = \gamma_1 + \gamma_2 PPS_t + \gamma_{a,1} a_{ijt} + \gamma_{a,2} a_{ijt} PPS_t + X_{ijt}\Gamma + \varepsilon_{ijt} \tag{10}$$

and identify $\beta_f = \frac{\Delta p}{2\hat{\gamma}_2}$ and $\phi_{a,2} = -\frac{\hat{\gamma}_{a,2}}{\hat{\gamma}_2}$, where Δp is the change in the profit margin of EPO after the start of PPS.[20] In short, identification follows from (i) how responsive providers are to a change in financial incentives, where β_f tells us how much they value profits relative to unobserved patient health, and (ii) the variation in the responsiveness to financial incentives across different elevations, where $\phi_{a,2}$ tells us how the effect of EPO on unobserved health differs by elevation.

[20] Δp takes a value of \$9.51, the average payment stipulated by Medicare for 1000 IUs of EPO administered in 2010.

The first two columns of Table 8 present the estimated coefficients of equation (10) along with the implied parameter values. The regression includes the same patient and facility controls used in Section 5 along with facility fixed effects. We estimate $\beta_f > 0$, which means providers value avoiding unobserved health costs, and $\phi_{a,2} > 0$, which implies those costs increase more rapidly at higher elevations, both of which are as expected.[21]

We can also allow for heterogeneity in chain altruism by parameterizing the weight placed on unobserved health so that it depends on facility-type in the form of $(1+\delta_j)\beta_f$, where δ_j gives the chain-specific difference in altruism. Interacting PPS_t and elevation with chain ownership indicators, we can identify the values of δ_j, as the different response of each chain to the new payment policy indicates the relative weight they place on profits: more-responsive firms value their patients' health less than those with more-muted responses. The final two columns of Table 8 show that, relative to independent facilities, chains place about half as much weight on health outcomes, a finding consistent with previous reduced-form results (Eliason et al., 2020).

Using the estimated parameters of the health production function, we can then estimate the weights providers place on each observable component of health. Here, providers' dosing decisions reveal the relative importance they place on each outcome. For instance, if we observe that providers administer relatively smaller EPO doses to patients for whom EPO is very effective at increasing HGB levels but for whom it also increases the risk of death, then we infer that providers place more weight on avoiding mortality than combating anemia. To do this, we parameterize the profit margin of EPO for patient i at facility j at time t as

$$p_{ijt} = p_t - \bar{c} - F_{jt}\xi,$$

where p_t is the observed payment rate for EPO at time t (i.e., \$9.51 per 1000 IUs under fee-for-service and \$0 starting in 2011), $\bar{c}$ is the average cost to the facility of acquiring and administering a dose of EPO, and ξ captures variation from this mean acquisition cost along observable facility characteristics.

[21]Note that while the sign of β_f indicates that EPO imposes costs on unobserved health, the magnitude of β_f cannot be meaningfully interpreted alone. This is because $f(\cdot)$ contains a normalization to pin down the "units" of unobserved health. That said, $\beta_f f(\cdot)$ can together be interpreted as the unobserved health cost in dollars. This is because a one unit change in $\beta_f f(\cdot)$ has the same effect on provider utility as a $\beta_f f(\cdot)$ dollar decrease in provider profit.

Table 8
Estimates of Production Function of Unobserved Health

	No Heterogeneity by Chain		Heterogeneity by Chain	
	(1) EPO	(2) Implied Parameters	(3) EPO	(4) Implied Parameters
PPS	-17.83^{***}		-9.790^{***}	
	(0.440)		(0.894)	
PPS × DaVita			-11.25^{***}	
			(0.939)	
PPS × Fresenius			-8.957^{***}	
			(0.953)	
PPS × Other Chain			-9.574^{***}	
			(1.057)	
PPS × Elevation	0.00138^{***}		0.00268^{***}	
	(0.000203)		(0.000490)	
β_f		0.267^{***}		0.486^{***}
		(0.00659)		(0.0443)
δ_{DaVita}				-0.535^{***}
				(0.0416)
$\delta_{Fresenius}$				-0.478^{***}
				(0.0470)
$\delta_{OtherChain}$				-0.494^{***}
				(0.0469)
$\phi_{a,2}$		0.0000774^{***}		0.000274^{***}
		(0.0000109)		(0.0000423)
Year-Month FE	0		0	
Pat/Fac Controls	1		1	
Facility FE	1		1	
Dep. Var. Mean	48.50		48.50	
Observations	10077264		10077264	

Notes: OLS estimates from equation (10) and implied parameter values. Columns (3) and (4) present results allowing for heterogeneity in altruism by chain ownership, while columns (1) and (2) do not. Dependent variable is monthly EPO dose. EPO doses are censored at the 99th percentile and measured in 1000 IUs. PPS is an indicator variable for January 2011 or later. Facility elevation is measured in feet above sea level. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

Under this parameterization, the first-order condition from equation (1) in Section 4 is given by

$$\beta_f \left(\phi_1 + \phi_{a,1} a_{jt} + u_{ijt} + 2(1 + \phi_{a,2} a_{ijt}) epo_{ijt}\right) = p_t - \bar{c} - F_{jt}\xi + \sum_c \beta_c \left(\alpha_{c,1} + \sum_{x \in X} \alpha_{c,x} x_{it}\right),$$

where the left-hand side gives the marginal effect of EPO on unobserved health and the right-hand side gives the sum of the marginal financial benefit to the provider and the marginal benefit to the patient in terms of improved health along observable dimensions. Substituting in our previously estimated parameter values, including the marginal effect of EPO on observed and unobserved health outcomes, we can write this condition as the estimating equation

$$Y_{ijt} = \eta_1 + \eta_j^{Chain} Chain_{jt} + \sum_c \beta_c \left(\hat{\alpha}_{c,1} + \sum_{x \in X} \hat{\alpha}_{c,x} x_{it}\right) + \phi_{a,1} WtElev_{ijt} - F_{jt}\xi + \varepsilon_{ijt}, \tag{11}$$

where $Y_{ijt} \equiv 2\hat{\beta}_f(1+\hat{\phi}_{a,2} a_{ijt}) epo_{ijt} - p_t$, $\eta_1 + \eta_j^{Chain} Chain_{jt} \equiv -\bar{c} - \xi_j^{Chain} - \hat{\beta}_f \phi_j$, $WtElev_{ijt} \equiv -\hat{\beta}_f a_{ijt}$, and $\varepsilon_{ijt} \equiv -\beta_f u_{ijt}$. We estimate equation (11) by OLS.

Table 9 presents estimates of the weights placed on each of these outcomes in the patient health function. We find that each month providers are willing to pay \$13 to increase HGB 1g/dL, \$3,200 to avoid a heart attack, and \$11,500 to avoid a death.[22] As before, we can also allow for heterogeneity in altruism and EPO acquisition costs across chains by interacting chain-ownership indicators with X_{jt} and defining $Y_{ijt} \equiv 2\hat{\beta}_f(1+\hat{\phi}_{a,2} a_{ijt}) epo_{ijt} - (1+\hat{\delta}_j) p_t$. Using this specification, the parameter estimates in column (2) of Table 9 pertain to the preferences of independent facilities and can be translated into chain preferences using the corresponding $\hat{\delta}_j$. Comparing the results in columns (1) and (2) indicates that the weights placed on each observable component of health by independent facilities are roughly twice those from our estimates that do not allow for heterogeneous altruism. This echoes our estimates of $\hat{\delta}_j$ from Table 8, which revealed that chains are approximately half as altruistic as independent facilities.

Using our estimates that allow for heterogeneity in altruism by chain and calibrating $\bar{c}$ and ξ_j^{Chain} to match the average EPO acquisition costs in facilities' 2010 cost reports, we report our estimates of

[22] Our estimates for β_c for each observable health component c can be interpreted as the amount of profit a provider is willing to forego to increase the value of the outcome by 1 unit. This can be seen by noting that the derivative of the provider's utility function with respect to total profit ($epo * p$) is 1 while the derivative with respect to health component c is β_c. This implies the provider values both a β_c dollar change in profit and a one unit change in health component c at β_c dollars.

Table 9
Estimates of Weights on Observable Components of Health

	(1) No Heterogeneity by Chain	(2) Heterogeneity by Chain
β_{HGB}	12.64	33.43^{+}
	(9.094)	(18.40)
$\beta_{CardiacHosp.}$	-3229.8***	-6279.4***
	(386.0)	(773.1)
$\beta_{Mortality}$	-11520.0***	-23040.4***
	(724.3)	(1475.5)
$\phi_{a,1}$	0.000936	-0.0132***
	(0.000881)	(0.00129)
Year-Month FE	0	0
Facility Controls	1	1
Facility FE	0	0
Dep. Var. Mean	22.46	46.24
Observations	10077289	10077289

Notes: OLS estimates from equation (11). Column (2) presents results allowing for heterogeneity in altruism by chain ownership, while column (1) does not. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility to freestanding or hospital-based, and chain ownership status, as well as geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

the costs by chain in Table A17 in Appendix G. Consistent with greater buyer power allowing firms to negotiate substantial discounts from drug manufacturers, we estimate large chains purchase EPO at a much lower cost than independent facilities do.

Finally, our estimated model provides estimates of the unobserved health costs of EPO. Figure A12 in Appendix G presents the health costs that an average patient would endure at different doses of EPO, both by elevation and by chain. Although patients experience small health gains at low levels of EPO, the health costs grow rapidly at higher doses and accrue more quickly to patients at higher elevations. Because in equilibrium EPO is disproportionately given to patients with low health costs from EPO, we estimate that the average patient in our sample receives $4,055 of unobserved health benefits from the drug each month, split at $4,876 during the fee-for-service era and $3,298 after the payment reform.

7. Counterfactual Analysis

Our structural model allows us to assess counterfactual scenarios that illustrate how patient heterogeneity and financial incentives influence the care patients receive and their resulting health outcomes, as well as how they interact with important industry characteristics like chain ownership and drug acquisition costs. Our first counterfactual establishes a point of comparison by considering the health outcomes that could be achieved if providers simply administered the health-maximizing dose of EPO. We then consider two counterfactuals examining the role of patient heterogeneity in determining EPO doses, one in which all patients receive a uniform dose of EPO set equal to the average health-maximizing amount and another where all patients are treated to achieve the same targeted level of hemoglobin. Finally, we explore the role of dialysis chains in administering EPO by evaluating what would happen if chain facilities had the same level of altruism that we observe for independent facilities and if all facilities acquired EPO at the low cost negotiated by the largest chain. Our main set of counterfactual results are shown in Table 10, with supplemental results in Appendix G.

We first consider the health outcomes that could be achieved if facilities administered a dose to each patient that maximizes their total health, as would be the case if providers were perfectly altruistic or if Medicare set the per-dose payment equal to its cost. This counterfactual allows us to measure the extent to which financial incentives cause realized health outcomes to diverge from their hypothetical upper bound, with column (1) of Table 10 comparing outcomes under this scenario to those observed following the 2011 payment reform. We find that health-maximizing EPO doses are 26.5% higher, on average, than those observed under PPS, which suggests facilities now undertreat patients. The higher doses in this counterfactual come with adverse tradeoffs — mortality rates increase by 12.5% and cardiac hospitalization rates increase by 10.6% — but the negative effects are offset by better controlled anemia and gains in unobserved health, as reflected by higher HGB levels and fewer transfusions.[23] Overall, health-maximizing doses improve total health by an average of $117.5 per patient per month.[24]

To demonstrate the importance of accounting for patients' heterogeneity when making treatment

[23]Table 10 reports changes as a percentage of baseline levels for observable inputs and health outcomes. Table A18 reports the levels of these variables.

[24]These dollar amounts can be interpreted as the weight independent facilities put on outcomes. If patients value their own health more than the facilities do, these dollar amounts caould be scaled up by that difference. For example, if patients value their own health twice as much as an independent facility does, then the total health gains from the health-maximizing dose are twice the value given in Table 10.

decisions, we next consider what would happen if all patients received a uniform EPO dose set to the average health-maximizing level estimated in the previous counterfactual. Column (2) of Table 10 shows how these doses and the corresponding health outcomes compare to those we observe in the data. In this scenario, the average increase in EPO doses over observed doses is the same as the health-maximizing counterfactual by construction, but the standard deviation of EPO doses falls from 62 thousand IUs per patient-month to zero since all patients receive the same amount. As dosing decisions are not tailored to each patient's idiosyncratic needs in this counterfactual, they ignore the diverse tradeoffs incorporated into individualized treatment plans and fail to achieve the gains of the patient-specific health-maximizing dose. Similar to giving individualized health-maximizing doses, patients' anemia is better managed, but acute outcomes such as hospitalizations and mortality become worse. At the same time, the gains in terms of higher HGB levels are smaller than before and the costs in terms of adverse events are larger, while uniform doses impose large unobserved health costs equivalent to more than $2,000 per month. The overall impact amounts to a nearly $2,300 reduction in patient health per month even though doses were set to the average health-maximizing level. Because patients vary in the benefits they receive from EPO, this counterfactual underscores the importance of tailoring doses to each patient's specific needs rather than attempting to bring treatment to a single standard dose for all patients, even if that standard is, on average, a sensible one.

While the previous counterfactual reduced the heterogeneity in the amount of EPO administered to each patient, policymakers may instead want providers to target EPO doses to reduce heterogeneity in observed health outcomes. For example, the ESRD QIP began penalizing dialysis providers in 2012 for patients who failed to achieve a minimum HGB level of 10 g/dL (Centers for Medicare & Medicaid Services, 2010). Policies like the QIP that impose uniform targets for all patients ignore the possibility that the ideal outcome may differ across patients depending on their responsiveness to the treatment and sensitivity to its side effects. To evaluate this possibility, we consider the consequences of requiring all patients to achieve a minimum HGB level of 10. Column (3) of Table 10 shows that patients receive 17.5% more EPO and experience better anemia management in this counterfactual but at the same time accrue health costs that average over $500 per month, stemming from both unobserved health costs and an increased risk of adverse events. Although forcing patients to achieve a minimum HGB target is harmful on average, some patients are made better off — the financial incentives providers face under prospective payments lead them to undertreat patients, whereas requiring a minimum HGB level

works to partially offset this incentive. In particular, 34% of patients who previously failed to achieve the HGB target under PPS alone now see health improvements, particularly those who require only small increases in their EPO doses to hit the standard. These patients come closer to their own health-maximizing dose, while others overshoot theirs to reach the minimum level of HGB, worsening their overall health. Allowing heterogeneity in observed health outcomes while also motivating providers to administer sufficient EPO doses when they have no financial incentive to do so is a key tradeoff policymakers must balance in payment reforms, particularly when financial penalties are tied to health outcomes in programs like the QIP.

For our final set of counterfactuals, we consider the impact of for-profit chains on the dialysis industry, a long-standing concern for policymakers and patient advocates who contend that these providers prioritize profits over patients.[25] First, column (4) of Table 10 shows the results of setting chains' level of altruism to that of independent facilities, which reflects one primary reason chains may make different treatment decisions — their fiduciary duty to maximize profits. Because chains now place more weight on total patient health than in our original estimates, we find that average EPO doses increase 12% relative to the observed PPS baseline. Here, even though cardiac hospitalizations increase 4.6% and mortality increases 5.5%, overall patient health improves substantially. Compared to the health-maximizing counterfactual in column (1), setting the altruism of chains to that of independent facilities achieves 63% of patients' maximum possible increase in total health over observed outcomes.

In the last column of Table 10, we reduce the average acquisition cost of EPO for all chains to that of Fresenius, whose average cost is the lowest we observe in our data. This counterfactual highlights how large chains' purchasing power may influence their treatment decisions, an exercise inspired by recent proposals for Medicare to negotiate directly with manufacturers to procure drugs at a lower cost. Reducing the cost of EPO leads to a 1.6% increase in doses, which results in better overall health for patients but also a slightly higher risk of mortality and cardiac hospitalizations. Overall, these higher doses close 8% of the gap between observed patient health and the health-maximizing counterfactual, demonstrating a key tradeoff of allowing chains to provide dialysis: although large chains' lower levels of altruism may harm patients' health, their greater bargaining power over drug manufacturers serves to reduce the conflict between their financial incentives and patients' well-being.

[25] Table A19 presents counterfactual outcomes that do not allow for heterogeneity in chain altruism.

Table 10
Counterfactual Outcomes

	(1) Health-Maximizing EPO Dose	(2) Uniform EPO Dose	(3) Minimum HGB Target	(4) Chain Altruism Equal to Independent Altruism	(5) Lower Acquisition Cost of EPO
EPO Dose (%)	26.47	26.47	17.49	11.57	1.595
Hemoglobin (%)	1.720	0.699	1.118	0.786	0.108
Transfusion Rate (%)	-20.62	-20.92	-12.47	-9.017	-1.245
All-Cause Hospitalizations (%)	3.974	4.514	2.632	1.736	0.239
Cardiac Hospitalization (%)	10.57	11.70	6.463	4.583	0.636
Mortality (%)	12.52	13.59	8.264	5.456	0.752
Unobserved Health ($)	169.1	-2066.7	-389.2	92.90	12.34
Total Health ($)	117.5	-2295.7	-522.9	73.98	9.472

Notes: Change under counterfactual scenarios. Rows related to observable health outcomes (EPO dose to mortality) report percentage change relative to baseline while unobserved and total health report level change in dollars per patient month relative to baseline. The baseline for all columns is the simulated outcome under PPS. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Counterfactual EPO doses are restricted to the observed support of doses. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later.

8. Conclusion

We estimate a structural model of dialysis facilities' use of the anti-anemia drug epoetin alfa, historically one of Medicare's largest Part B drug expenses. Using a large payment reform and the elevation of facilities to construct an instrumental variable that identifies our model, we show that doses depend on both the clinical effectiveness of EPO as well as the financial incentives faced by providers, with the substantial heterogeneity in patients' responsiveness to the drug having a large influence on providers' dosing decisions. Although EPO successfully reduces anemia in dialysis patients, facilities must weigh that benefit against an elevated risk of heart attacks and mortality.

We use our model to demonstrate the extent to which the doses administered by providers diverge from those that would maximize a patient's health as well as how allowing providers to tailor treatments to their patients' specific needs results in substantially better outcomes. By contrast, policies that impose uniform health targets or standards of care may harm patients if they prevent providers from taking those specific needs into account. Finally, we show that the large chains that dominate the dialysis industry are less altruistic than independent facilities, but these chains' lower acquisition costs for EPO spur them to use more of the drug, benefiting patients on average.

The large drop in EPO following Medicare's adoption of prospective payments, together with the wide heterogeneity we estimate for the effect of EPO on patients' health, suggests the need for more work on how providers respond to alternative payment models like the PPS in dialysis and related pay-for-performance initiatives like the QIP. As of 2022, alternative payment models accounted for more than 40% of traditional Medicare spending and more than 45% of spending for commercial insurers (Health Care Payment Learning & Action Network., 2023). In light of their growing prevalence, more research focused on the tradeoffs inherent in alternative payment models, both for patients and for other parts of the health care system, would provide valuable guidance for policymakers seeking to restrain costs while at the same time maintaining high standards of care.

References

Abaluck, J., L. Agha, C. Kabrhel, A. Raja, and A. Venkatesh (2016). The Determinants of Productivity in Medical Testing: Intensity and Allocation of Care. *American Economic Review 106*, 3730–3764.

Al-Ubaydli, O., J. A. List, D. LoRe, and D. Suskind (2017a). Scaling for economists: Lessons from the non-adherence problem in the medical literature. *Journal of Economic Perspectives 31*(4), 125–144.

Al-Ubaydli, O., J. A. List, D. LoRe, and D. Suskind (2017b, May). What can we learn from experiments? understanding the threats to the scalability of experimental results. *American Economic Review 107*(5), 282–86.

Allcott, H. (2015). Site selection bias in program evaluation. *The Quarterly Journal of Economics 130*(3), 1117–1165.

Alsan, M., M. Durvasula, H. Gupta, J. Schwartzstein, and H. Williams (2024). Representation and extrapolation: evidence from clinical trials. *The quarterly journal of economics 139*(1), 575–635.

Andresen, M. E. (2018). Exploring marginal treatment effects: Flexible estimation using stata. *The Stata Journal 18*(1), 118–158.

Angrist, J. D. and J.-S. Pischke (2009). Mostly harmless econometrics: An empiricist's companion.

Babitt, J. L. and H. Y. Lin (2006). Mechanisms of Anemia in CKD. *Journal of the American Society of Nephrology 23*, 1631–1634.

Baicker, K. and T. Svoronos (2019). Testing the Validity of the Single Interrupted Time Series Design. *NBER Working Paper 26080*.

Bain, B. J., I. Bates, and M. A. Laffan (2017). *Dacie and Lewis Practical Haematology* (12 ed.).

Baker, S. (2019). The U.S. Health Care System is Full of Monopolies. *Axios*.

Bartik, T. J. (1991). *Who benefits from state and local economic development policies? Kalamazoo, MI: WE Upjohn Institute for Employment Research.*

Bertuzzi, L., P. Eliason, B. Heebsh, R. J. League, R. C. McDevitt, and J. W. Roberts (2023). Gaming and effort in performance pay. Technical report.

Besarab, A., W. Bolton, J. E. J. Browne, A. Nissenson, D. Okamoto, S. Schwab, and D. Goodkin (1998, August). The Effects of Normal as Compared with Low Hematocrit Values in Patients with Cardiac Disease Who Are Receiving Hemodialysis and Epoetin. *The New England Journal of Medicine 339*, 584–590.

Bettinger, E. P., L. Fox, S. Loeb, and E. S. Taylor (2017). Virtual Classrooms: How Online College Courses Affect Student Success. *American Economic Review 107*(9), 2855–2875.

Bold, T., M. Kimenyi, G. Mwabu, J. Sandefur, et al. (2018). Experimental evidence on scaling up education reforms in kenya. *Journal of Public Economics 168*, 1–20.

Bosman, D., C. Osborne, J. Marsden, I. Macdougall, W. Gardner, and P. Watkins (2002). Erythropoietin response to hypoxia in patients with diabetic autonomic neuropathy and non-diabetic chronic renal failure. *Diabetic Medicine 19*, 65–69.

Bradbury, B. D., M. D. Danese, M. Gleeson, and C. W. Critchlow (2009). Effect of Epoetin Alpha Dose Changes on Hemoglobin and Mortality in Hemodialysis Patients with Hemoglobin Levels Persistently below 11g/dL. *Clinical Journal of the American Society of Nephrology 4*, 630–637.

Brookhart, A., B. D. Bradbury, J. Avorn, S. Schneeweiss, and W. C. Winkelmayer (2011a). The Effect of Altitude Change on Anemia Treatment Response in Hemodialysis Patients. *American Journal of Epidemiology 173*(3), 768–777.

Brookhart, M., S. Schneeweiss, J. Avorn, B. Bradbury, J. Liu, and W. Winkelmayer (2010, March). Comparative Mortality Risk of Anemia Management Practices in Incident Hemodialysis Patients. *Journal of the American Medical Association 303*(9), 857–864.

Brookhart, M. A., B. D. Bradbury, J. Avorn, S. Schneeweiss, and W. C. Winkelmayer (2011b). The Effect of Altitude on Anemia Treatment Responses in Hemodialysis Patients. *American Journal of Epidemiology 173*, 768–777.

Brookhart, M. A., S. Schneeweiss, J. Avorn, B. D. Bradbury, K. J. Rothman, M. Fischer, J. Mehta, and W. C. Winkelmayer (2008). The Effect of Altitude on Dosing and Response to Erythropoietin in ESRD. *Journal of the American Society of Nephrology*, 1389–1395.

Brot-Goldberg, Z. C., A. Chandra, B. R. Handel, and J. T. Kolstad (2017, 04). What does a Deductible Do? The Impact of Cost-Sharing on Health Care Prices, Quantities, and Spending Dynamics. *The Quarterly Journal of Economics 132*(3), 1261–1318.

Card, D. (1995). *Aspects of Labour Market Behavior: Essays in Honor of John Vanderkamp*, Chapter Using Geographic Variation in College Proximity to Estiamte the Return to Schooling. Toronto: University of Toronto Press.

Centers for Medicare & Medicaid Services (2010, July). New Bundled Prospective Payment System for End-Stage Renal Disease Facilities Designed to Promote Efficient Care and Improve Patient Outcomes. Technical report, Department of Health & Human Services.

Chan, D. C., M. Gentzkow, and C. Yu (2022). Selection with variation in diagnostic skill: Evidence from radiologists. *The Quarterly Journal of Economics 137*(2), 729–783.

Chandra, A., D. Cutler, and Z. Song (2012). Who Ordered That? The Economics of Treatment Choices in Medical Care. *Handbook of Health Economics 2*, 397–432.

Chandra, A. and D. O. Staiger (2020). Identifying sources of inefficiency in healthcare. *The quarterly journal of economics 135*(2), 785–843.

Chassang, S. and R. Feng (2022). The Cost of Imbalance in Clinical Trials. *NBER Working Paper 30745*.

Chertow, G., J. Liu, K. Monda, D. Gilbertson, M. Brookhard, A. Beaurbrun, W. Winkelmayer, A. Pollock, C. Herzog, A. Ashfaq, T. Sturmer, K. Rothman, B. Bradbury, and A. Collins (2016). Epoetin Alfa and Outcomes in Dialysis amid Regulatory and Payment Reform. *Journal of the American Society of Nephrology 27*, 3129–3138.

Christian, P. and C. Barrett (2017). Revisiting the Effect of Food Aid on Conflict: A Methodological Caution. *World Bank Policy Research Working Paper No. 8171*.

Clemens, J. and J. Gottlieb (2014). Do Physicians' Financial Incentives Affect Medical Treatment and Patient Health? *American Economic Review 104*(4), 1320–1349.

Cuddy, E. and J. Currie (2024). Rules vs. discretion: Treatment of mental illness in us adolescents. *NBER Working Paper No. 27890*.

Currie, J. and W. B. MacLeod (2017). Diagnosing expertise: Human capital, decision making, and performance among physicians. *Journal of labor economics 35*(1), 1–43.

Cutler, D., L. Dafny, and C. Ody (2017). How Does Competition Impact the Quality of Price of Outpatient Service Facilities? A Case Study of the U.S. Dialysis Industry. Working Paper.

Dafny, L. (2005). How Do Hospitals Respond to Price Changes. *American Economic Review 95*, 1525–1547.

Dai, M. (2014). Product Choice Under Price Regulation: Evidence from Out-Patient Dialysis Markets. *International Journal of Industrial Organization 32*, 24–32.

Dai, M. and X. Tang (2015). Regulation and Capacity Competition in Health Care: Evidence from US Dialysis Markets. *The Review of Economics and Statistics 97*(5), 965–982.

DaVita (2005, May). DaVita 2004 Annual Report.

Ebben, J., D. Gilbertson, R. Foley, and A. Collins (2006). Hemoglobin level variability: Associations with comorbidity, intercurrent events, and hospitalizations. *Clinical Journal of the Americal Society of Nephrology 1*, 1205–1210.

Einav, L., A. Finkelstein, and N. Mahoney (2018). Provider Incentives and Healthcare Costs: Evidence from Long-Term Care Hospitals. *Econometrica 86*(6), 2161–2219.

Eliason, P. (2021). Price Regulation and Market Structure: Evidence from the Dialysis Industry. Working Paper.

Eliason, P. J., P. L. Grieco, R. C. McDevitt, and J. W. Roberts (2018). Strategic Patient Discharge: The Case of Long-Term Care Hospitals. *American Economic Review 108*(11), 3232–65.

Eliason, P. J., B. Heebsh, R. C. McDevitt, and J. W. Roberts (2020). How Acquisitions Affect Firm Behavior and Performance: Evidence from the Dialysis Industry. *The Quarterly Journal of Economics 135*(1), 221–267.

Eschbach, J., J. Egrie, M. Downing, J. Browne, and J. Adamson (1987). Correction of the Anemia of End-Stage Renal Disease with Recombinant Human Erythropoietin. *New England Journal of Medicine 316*, 73–78.

Eschbach, J. W., M. H. Abdulhadi, J. K. Browne, B. G. Delano, M. R. Downing, J. C. Egrie, R. W. Evans, E. A. Friedman, S. E. Graber, and N. R. Haley (1989). Recombinant human erythropoietin in anemic patients with end-stage renal disease. results of a phase iii multicenter clinical trial. *Annals of internal medicine 111 12*, 992–1000.

Gaynor, M., N. Mehta, and S. Richards-Shubik (2023). Optimal Contracting with Altruistic Agents: Medicare Payments for Dialysis Drugs. *American Economic Review 113*(6), 1530–1571.

Green, A., N. Trivedi, J. Hsu, N. Yu, P. Bach, and S. Chimonas (2022). Despite the fda's five-year plan, black patients remain inadequately represented in clinical trials for drugs. *Health Affairs 41*, 368–374.

Grieco, P. and R. C. McDevitt (2017). Productivity and Quality in Health Care: Evidence from the Dialysis Industry. *The Review of Economic Studies 84*(3), 1071–1105.

Health Care Payment Learning & Action Network. (2023). Apm measurement: Progress of alternative payment models.

Heckman, J. J., S. Urzua, and E. Vytlacil (2006). Understanding instrumental variables in models with essential heterogeneity. *The Review of Economics and Statistics 88*(3), 389–432.

Heckman, J. J. and E. Vytlacil (2005). Structural equations, treatment effects, and econometric policy evaluation. *Econometrica 73*(3), 669–738.

Heckman, J. J. and E. J. Vytlacil (2007). Econometric evaluation of social programs, part ii: Using the marginal treatment effect to organize alternative econometric estimators to evaluate social programs, and to forecast their effects in new environments. *Handbook of Econometrics 6*, 4875–5143.

Hirth, R., M. Turenne, A. Wilk, J. Wheeler, K. Sleeman, W. Zhang, M. Paul, T. Nahra, and J. Messana (2014). Blood Transfusion Practices in Dialysis Patients in a Dynamic Regulatory Environment. *American Journal of Kidney Disease 64*, 616–621.

Kalantar-Zadeh, K. (2017). History of Erythropoiesis-Stimulating Agents, the Development of Biosimilars, and the Future of Anemia Treatment in Nephrology. *American Journal of Nephrology 45*, 235–247.

Kalantar-Zadeh, K., G. Lee, J. Miller, J. Jing, J. Robertson, and C. Kovesdy (2009). Predictors of Hyporesponsiveness to Erythropoiesis-Stimulating Agents in Hemodialysis Patients. *American Journal of Kidney Disease 53*, 823–834.

Kalantar-Zadeh, K., C. McAllister, R. Lehn, G. Lee, A. Nissenson, and J. Kopple (2003). Effect of malnutrition-inflammation complex syndrome on epo hyporesponsivenes in maintenance hemodialysis patients. *American Journal of Kidney Disease 42*, 761–773.

Kliger, A. S., R. N. Foley, D. S. Goldfarb, S. L. Goldstein, K. Johansen, A. Singh, and L. Szczech (2013, November). KDOQI US Commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD. journal article.

League, R. J., P. Eliason, R. C. McDevitt, J. W. Roberts, and H. Wong (2022). Variability in prices paid for hemodialysis by employer-sponsored insurance in the us from 2012 to 2019. *JAMA Network Open 5*(2), e220562–e220562.

Lin, E. (2021, 03). The Cost of Transferring Dialysis Care From the Employer-Based Market to Medicare. *JAMA Network Open 4*(3), e212113–e212113.

McGuire, T. G. (2000). Physician agency.

Mueller, T. (2023). *How to Make a Killing: Blood, Death and Dollars in American Medicine*. W. W. Norton & Company.

Murthy, V. H., H. M. Krumholz, and C. P. Gross (2004). Participation in cancer clinical trials: race-, sex-, and age-based disparities. *Jama 291*(22), 2720–2726.

Nunn, N. and N. Qian (2014). US Food Aid and Civil Conflict. *American Economic Review 104*(6), 1630–1666.

Oostrom, T. (2022). Funding of Clinical Trials and Reported Drug Efficacy. *Working Paper*.

Silver, D. (2021). Haste or waste? peer pressure and productivity in the emergency department. *The Review of Economic Studies 88*(3), 1385–1417.

Singh, A., L. Szczech, K. Tang, H. Barnhart, S. Sapp, M. Wolfson, and D. Reddan (2006, November). Correction of Anemia with Epoeitin Alfa in Chronic Kidney Disease. *The New England Journal of Medicine 355*, 2085–2098.

Thamer, M., Y. Zhang, J. Kaufman, D. Cotter, F. Dong, and M. A. Hernan (2007). Dialysis Facility Ownership and Epoetin Dosing in Patients Receiving Hemodialysis. *Jama 297*(15), 1667–1674.

Thamer, M., Y. Zhang, D. Lai, O. Kshirsagar, and D. Cotter (2013). Influence of Safety Warnings on ESA Prescribing among Dialysis Patients Using an Interrupted Time Series. *BMC Nephrology 14*.

Tonelli, M., W. Winkelmayer, K. Jindal, W. Owen, and B. Manns (2003). The cost-effectiveness of maintaining higher hemoglobin targets with erythropoietin in hemodialysis patients. *Kidney International 64*, 295–304.

United States Renal Data System (2014). 2014 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Bethesda, MD.

United States Renal Data System (2019). USRDS 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Bethesda, MD.

U.S. Geological Survey Center for Earth Resources Observation and Science (2014). GTOPO30 Global 30 Arc-Second Elevation.

U.S. Government Accountability Office (2012, October). Medicare Part B Drug Spending. Publication No. GAO-13-46R, Retrieved from `https://www.gao.gov/assets/650/649459.pdf`.

Valderrabano, F. (2000). Quality of Life Benefits of Early Anemia Treatment. *Nephrology Dialysis Transplant 15*, 23–28.

Van der Putten, K., B. Braam, K. E. Jie, and C. A. Gaillard (2008). Mechanisms of disease: erythropoietin resistance in patients with both heart and kidney failure. *Nature clinical practice Nephrology 4*(1), 47–57.

Wang, V., C. Coffman, L. Sanders, S. Lee, R. Hirth, and M. Maciejewski (2018). Medicare's New Prospective Payment System on Facility Provision of Peritoneal Dialysis. *Clinical Journal of the American Society of Nephrology 13*, 1833–1841.

Whoriskey, P. (2012, July). Anemia Drug Made Billions, but at What Cost. *The Washington Post*.

Wilson, N. E. (2016a). For-Profit Status and Industry Evolution in Health Care Markets: Evidence from the Dialysis Industry. *International Journal of Health Economics and Management 16*(4), 297–319.

Wilson, N. E. (2016b). Market Structure as a Determinant of Patient Care Quality. *American Journal of Health Economics 2*(2), 241–271.

Winkelmayer, W. C., J. Lui, and M. A. Brookhart (2009). Altitude and All-Cause Mortality in Incident Dialysis Patients. *Journal of the American Medical Association 305*.

Zhang, Q., M. Thamer, O. Kshirsagar, and Y. Zhang (2017). Impact of the end stage renal disease prospective payment system on the use of peritoneal dialysis. *Kidney International Reports 2*(3), 350–358.

Zhang, Y., M. Thamer, K. Stefanik, J. Maukman, and D. Cotter (2004). Epoeitin Requirements Predict Mortality in Hemodialysis Patients. *American Journal of Kidney Disease 45*, 866–876.

Appendix: For Online Publication

The following appendices provide additional robustness checks, analyses, and details on our data.

Appendix A illustrates the robustness of our results to differences in the timing of PPS adoption.

Appendix B shows that neither the black box warnings nor the QIP can explain the patterns we observe for EPO doses.

Appendix C contains additional summary statistics by quintile of facility elevation.

Appendix D shows that our results are robust to a possible anticipatory response by providers.

Appendix E provides more results supporting our identifying assumptions.

Appendix F reports additional parameter estimates.

Appendix G presents additional results from the estimation of our structural model.

A. Differences in Timing of PPS Adoption

The PPS program allowed providers to gradually transition to the bundling of injectable drugs with the dialysis session such that this bundled payment comprised 25% of payments in 2011, 50% in 2012, 75% in 2013, and 100% in 2014. Alternatively, facilities could exercise a one-time option to opt in by November 2010 and immediately receive all payments under the PPS in 2011. Here, we present results showing the vast majority of providers chose to immediately transition to the new PPS and our baseline results are very similar to the results if we use only the subset of immediate-adopters.

First, we attempt to determine within our data the number of facilities that chose to immediately transition to the PPS by documenting whether a facility receives any positive payments for an injectable drug administered to a patient, which we view as a conservative measure of whether a facility has not fully adopted the PPS. We find that whereas more than 99.9% of facilities received payments for an injectable drug in each year prior to 2011, only 7.7% of facilities did afterwards, implying that over 92% of facilities immediately transitioned to the PPS based on this measure. The number increases to the point of full adoption by 2014, with independently owned facilities comprising 83.4% of those that transitioned gradually.

Next, we compare EPO use and patient outcomes by facility according to whether the facility immediately transitioned to the PPS ("Immediate") or not ("Gradual"). Table A1 shows this comparison using data from 2010. We find that patient outcomes are quite similar across these facilities, while those that opted for a gradual transition tended to use less EPO, primarily because most of the facilities that transitioned gradually were independent, which use less EPO on average. Furthermore, we do not find large elevation differences between the facilities. These facts, along with the small number of facilities that did not immediately transition, provide reassurance that selection bias does not undermine our estimates.

Nonetheless, we re-estimate our baseline results for the average treatment effects of EPO using only the sample of facilities that immediately transition to the PPS. The results, shown in Table A2, demonstrate that our baseline results are robust to focusing solely on this set of facilities.

Table A1
Summary Statistics by Immediate Transition to PPS

	PPS Without Transition?		
	Opts Out	Opts In	Total
Facility Characteristics			
Facility Elevation (ft)	644.9	639.6	641.3
Independent Ownership	0.835	0.152	0.209
EPO Use			
EPO Dose (1000 IUs)	39.13	59.09	57.02
Receives Any EPO	0.550	0.796	0.769
Health Outcomes			
Hemoglobin (g/dL)	11.26	11.33	11.32
Transfusions	0.032	0.026	0.026
Mortality	0.017	0.016	0.016
Hospitalizations			
Any Cause	0.1484	0.1412	0.1407
Cardiac Event	0.0282	0.0282	0.0280
Septicemia	0.0113	0.0092	0.0092
Patient-Months	167,827	2,282,122	2,485,214

Notes: An observation is a patient-month. Sample consists of observations from January to December 2010 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later and who are treated at a facility that does not permanently close before 2011. Facilities that opt out of PPS without transition are those for which positive payments for injectable drugs are observed in 2011 or 2012. Facilities that opt into PPS without transition are those for which no payments for injectable drugs are observed in 2011 or 2012 but which received other payments. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Facility elevation is measured in feet above sea level. Transfusion and hospitalization variables are binary indicators.

Table A2
Baseline Results Using only Facilities that Immediately Transition to PPS

	(1) HGB	(2) Transfusion	(3) Mortality	(4) Hosp., Any Cause	(5) Hosp., Cardiac Event	(6) Hosp., Septicemia
EPO	0.0285***	-0.000618**	0.000151*	0.000225	0.000211^{+}	0.0000285
	(0.00823)	(0.000190)	(0.0000757)	(0.000306)	(0.000117)	(0.0000667)
Year-Month FE	1	1	1	1	1	1
Pat/Fac Controls	1	1	1	1	1	1
Facility FE	1	1	1	1	1	1
Dep. Var. Mean	11.13	0.0279	0.0157	0.138	0.0273	0.00932
Observations	7609185	9249810	9249810	9249810	9249810	9249810
First-Stage F-statistic	20.70	34.19	34.19	34.19	34.19	34.19

Notes: IV estimates from equation (4). Dependent variable in column (1) is hemoglobin. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Dependent variables in columns (2)–(6) are binary outcomes. EPO doses are censored at the 99th percentile and measured in 1000 IUs. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later and who are treated at a facility that neither permanently closes before 2011 nor is observed to receive separate payment for injectable drugs in 2011 or later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

B. The Effect of Black Box Warnings & QIP on EPO

Although the FDA's updated black box warning for EPO and Medicare's introduction of the QIP for dialysis facilities occurred around the same time as the payment reform, we present evidence that neither contributed meaningfully to the decline in EPO doses shown in the paper. For the black box warning, four institutional details suggest that it did not cause the decrease in EPO around 2011. First, we show in Appendix E that other injectable drugs, which did not receive black box warnings, follow a pattern similar to EPO's after the PPS. Second, as we discuss in Section 2.1, the FDA has issued two black box warnings for EPO, both of which recommend providers use EPO more judiciously, but the evolution of EPO doses in Figure A1 shows that they did not change following the first black box warning in 2007, an instance when the label changed but financial incentives did not. Third, the decline in EPO begins in October 2010, eight months before the black box warning update, and it is unclear why providers would have changed their behavior in anticipation of the new black box warning even if they had been aware of the FDA's looming decision given that they did not change their behavior following the first black box warning. Finally, as shown by Figure A2 a coincidental drop in EPO use stemmed from one large chain that renegotiated its contract with drug supplier Amgen in mid-2011, as other chains and independent facilities do not exhibit the same patterns for EPO doses.

The large dialysis chains DaVita and Fresenius have at times partnered with Amgen, a leading producer of erythropoietin stimulating agents (ESAs), to make administering drugs such as EPO more profitable. In 2011, DaVita entered into a sourcing and supply agreement with Amgen, providing DaVita with discounts and rebates for Amgen's two ESAs, EPOGEN and Aranesp (DaVita Amgen Agreement 2011). In return, DaVita agreed to purchase at least 90% of its ESAs from Amgen. This 2011 contract ran through 2018 and was renewed in 2017 to extend through 2022 (DaVita Amgen Agreement 2017). Fresenius entered into a similar sourcing and supply agreement with Amgen in 2006, extending to 2011 (Fresenius Amgen Agreement 2006). Fresenius' contract lacked minimum purchase commitments, but did secure discounts for EPOGEN and Aranesp. Our understanding is that Fresenius now has year-to-year contracts with Amgen.

The distinct drop in average HGB levels in mid-2011 corresponds to the renegotiation of multiple large chains' contracts with Amgen, the monopoly supplier of EPO at the time. We see that the sharp drop in EPO and HGB levels in mid-2011 occurred only for patients at one of these large chains. This

provides further evidence that the cause of the discrete drop in EPO and HGB after the initial response to the payment reform was likely not the FDA black box warning but rather the renegotiation of this chain's supply agreement with Amgen. Because the contract renegotiation occurred at the same time as the PPS was implemented, the renegotiation likely reflected a change in this particular chain's strategy following the PPS. If this is the case, then the drop in EPO and HGB occurring in mid-2011 would be attributable to the PPS, with the delay highlighting the sticky nature of chains' supply agreements.

The other policy change around the start of the PPS was the QIP. As we explain in Section 2.2, Medicare instituted the QIP along with the PPS to provide facilities with incentives for maintaining high-quality care while still restraining health care costs. In contrast to the PPS, which focuses on cost containment, the QIP aims to promote a high standard of care by reducing payments to poorly performing facilities.

To implement the QIP, each year Medicare announces the various performance measures that will comprise a facility's Total Performance Score (TPS). Facilities whose scores fall short of the benchmark that year face a reduction of their Medicare payments of between 0.5%–2.0%, depending on the extent of the shortfall. During the sample period for our paper, Medicare used three clinical measures to construct the TPS: the percentage of patients with (i) HGB below 10 g/dL, (ii) HGB above 12g/dL, and (iii) urea reduction ratio (URR) above 0.65. For the first year of the QIP in 2012, Medicare used the facility's performance on these measures in 2010 to construct the TPS. For 2013 and 2014, only the latter two measures were used (based on facility performance in 2011 and 2012, respectively), with Medicare dropping low HGB levels as a criteria. The QIP also included a measure of vascular access in the TPS for 2014, although vascular access has no relation to EPO or other injectable drugs included in the payment reform, so we do not discuss it here.

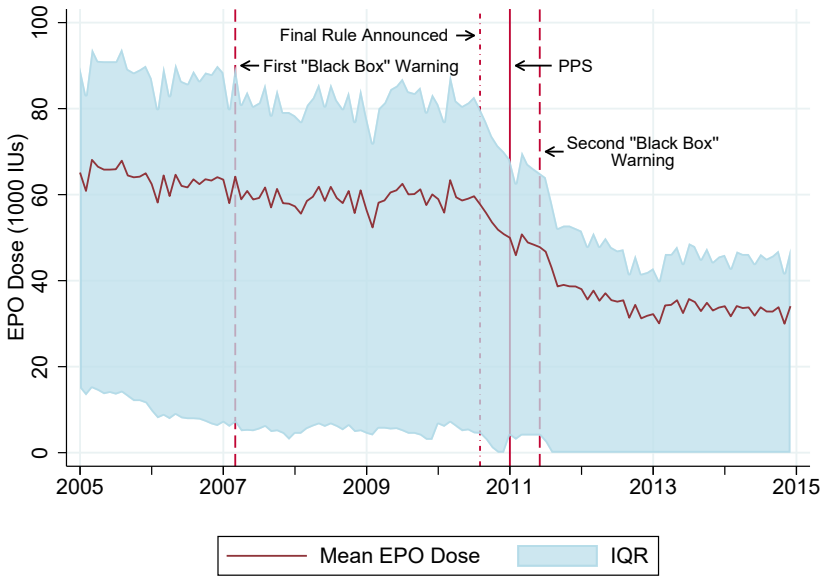
Although Medicare introduced the QIP to discipline facilities' behavior, Figure A3 shows that it did not cause the decline in EPO doses during this period—if anything, the QIP likely makes our estimate of the PPS's impact on EPO doses a conservative one. In Figure A3a, which shows the percentage of patients with HGB greater than 12 g/dL, we see no change in trend following the announcement of this performance measure in 2010. Because EPO directly affects patients' HGB levels, the fact that the trend in the proportion of patients with high HGB levels remained constant after facilities began receiving penalties suggests this standard had little impact on dosing decisions.

Figure A3b shows the percentage of patients with HGB below 10 g/dL.[26] Again, facilities did not respond to the metric's introduction, with the trend remaining constant throughout 2010, although we do see evidence consistent with facilities responding to the metric's removal in 2011. The sharp rise in patients with HGB less than 10 g/dL after Medicare removed this metric from the QIP suggests that (i) our estimates of the PPS's impact on EPO and outcomes are potentially understated, because facilities may have continued giving EPO to low-HGB patients to avoid QIP penalties, and (ii) direct financial incentives from EPO payments predominately dictate facilities' dosing decisions, as facilities cut EPO doses to reduce their drug costs immediately upon Medicare's removal of the low-HGB guardrails.

In short, although the black box warning in 2011 and the QIP performance measures applied to 2010–2012 could have potentially confounded our analysis of the payment reform's effect on EPO doses, we find little evidence that they did, and, if anything, they suggest our results may be conservative. Moreover, because Medicare introduced the QIP in conjunction with the PPS, any potential confounding from the QIP would simply add nuance to our interpretation of the reforms rather than undermine our main findings. That is, we find that the financial incentives from the payment reform had a much stronger influence on facility behavior than the penalties from the QIP did, which provides valuable insights to policymakers aiming to restrain health care costs while maintaining high standards for care. We consider the full effects of the QIP in Bertuzzi et al. (2023).

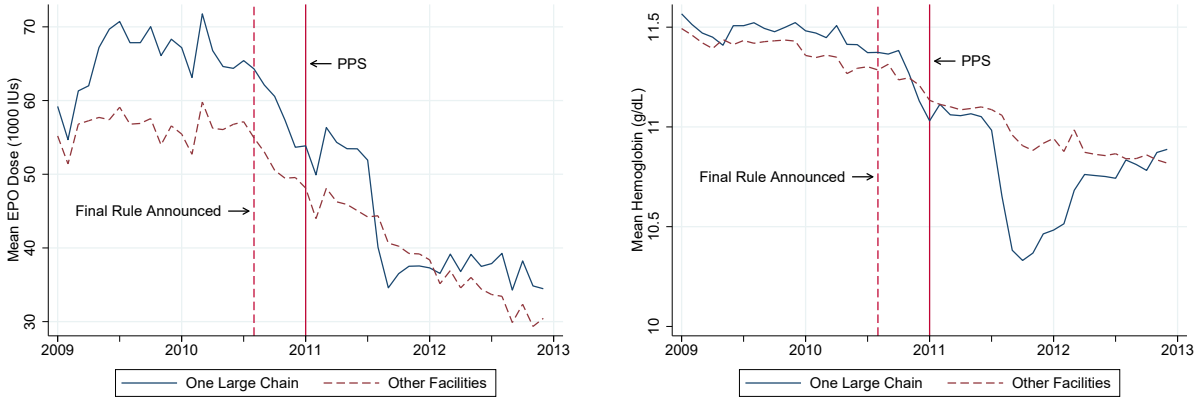
[26]The removal of the measure relating to the percentage of patients with HGB below 10 g/dL was announced in July 2011 and retroactively applied to the performance year beginning January 2011. This means that the TPS calculated using facilities' performances from January to December of 2011 did not include the percentage of patients with HGB below 10 g/dL, but facilities did not learn that this measure would not be used until midway through the year. This proposed rule change was finalized by Medicare in November 2011.

Figure A1
Monthly EPO Doses Over Time with Black Box Warnings



Notes: Figure reports the mean monthly EPO dose and shades from the first to the third quintile of monthly EPO dose. An observation is a patient-month. Sample consists of observations from January 2005 to December 2014 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Vertical long-dashed lines indicate the release of official warnings from the FDA about the safety of high EPO doses. The solid vertical line indicates the start of the PPS in January 2011, while the dot-dashed vertical line indicates the announcement of the final rule for the PPS.

Figure A2
EPO Doses and HGB by Facility Ownership

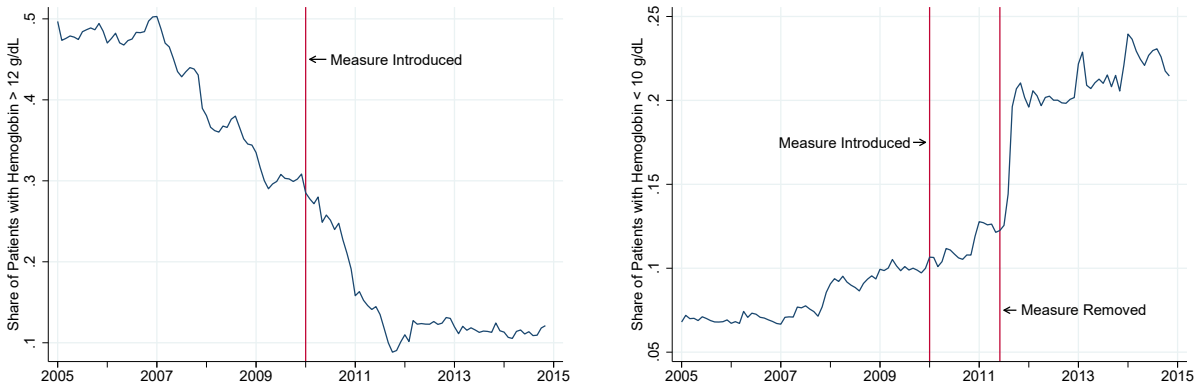


(a) Monthly EPO Dose for One Large Chain and Other Facilities' Patients

(b) Mean HGB for One Large Chain and Other Facilities' Patients

Notes: An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. The solid vertical line indicates the start of the PPS in January 2011, while the dashed vertical line indicates the announcement of the final rule for the PPS.

Figure A3
QIP HGB Performance Measures



(a) HGB > 12 g/dL Over Time

(b) HGB < 10 g/dL Over Time

Notes: Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. An observation is a patient-month. Sample consists of observations from January 2005 to December 2014 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Vertical lines indicate the introduction and removal of the QIP performance measure.

C. Summary Statistics by Elevation

We provide additional summary statistics for our data by quintile of facility elevation in three tables. The first pools patients across years from 2009 to 2012. The next two show summary statistics for 2009 and 2012 separately. Patients at higher elevations tend to be somewhat less healthy than those at lower elevations, but these differences do not change following the start of the PPS. We do, however, see EPO doses and outcomes change differentially by elevation, providing descriptive evidence that the policy had different effects depending on a patient's elevation.

Table A3
Patient Descriptive Statistics by Elevation

	Elevation Quintile					
	First	Second	Third	Fourth	Fifth	Total
Patient Characteristics						
Predicted Mortality	0.016	0.015	0.016	0.017	0.017	0.016
Age (Years)	63.41	63.60	62.91	63.53	63.57	63.40
Months with ESRD	45.59	45.35	45.72	45.49	43.22	45.08
Black	0.447	0.440	0.452	0.375	0.211	0.385
Male	0.553	0.548	0.545	0.551	0.562	0.552
Diabetic	0.526	0.534	0.536	0.544	0.560	0.540
Hypertensive	0.910	0.906	0.909	0.905	0.900	0.906
Incident Hemoglobin	9.755	9.786	9.806	9.901	10.018	9.853
Facility Characteristics						
Facility Elevation (ft)	29.4	143.7	436.1	713.5	1875.9	638.1
Independent Ownership	0.185	0.183	0.177	0.231	0.208	0.197
EPO Use						
EPO Dose (1000 IUs)	51.50	50.24	50.94	46.84	42.90	48.50
Receives Any EPO	0.791	0.784	0.779	0.725	0.694	0.755
Health Outcomes						
Hemoglobin (g/dL)	11.11	11.11	11.12	11.12	11.16	11.12
Transfusions	0.030	0.028	0.028	0.028	0.027	0.028
Mortality	0.015	0.015	0.015	0.016	0.017	0.016
Hospitalizations						
Any Cause	0.1406	0.1382	0.1355	0.1418	0.1340	0.1380
Cardiac Event	0.0280	0.0281	0.0268	0.0280	0.0248	0.0271
Septicemia	0.0097	0.0095	0.0091	0.0095	0.0090	0.0094
Unique Patients	102,897	99,507	102,182	103,307	103,770	461,477
Patient-Months	2,043,637	1,989,978	2,033,229	2,000,408	2,010,037	10,077,289

Notes: An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Predicted mortality is the predicted value for each observation using coefficients from a regression of mortality on patient controls and time fixed effects on observations from 2009 and 2010. Time fixed effects are not included in the prediction. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Facility elevation is measured in feet above sea level. The cut points between elevation quintiles are 73, 260, 599, and 870 feet above sea level.

Table A4
Patient Descriptive Statistics by Elevation, 2009

	Elevation Quintile					
	First	Second	Third	Fourth	Fifth	Total
Patient Characteristics						
Predicted Mortality	0.016	0.015	0.016	0.017	0.017	0.016
Age (Years)	63.44	63.57	62.98	63.65	63.83	63.49
Months with ESRD	42.29	42.25	42.39	42.53	40.03	41.90
Black	0.446	0.438	0.447	0.370	0.207	0.382
Male	0.550	0.546	0.543	0.549	0.559	0.549
Diabetic	0.510	0.524	0.524	0.531	0.549	0.528
Hypertensive	0.908	0.905	0.910	0.904	0.899	0.905
Incident Hemoglobin	9.836	9.855	9.866	9.975	10.094	9.925
Facility Characteristics						
Facility Elevation (ft)	29.8	143.3	437.8	714.2	1868.8	638.0
Independent Ownership	0.199	0.202	0.195	0.267	0.229	0.218
EPO Use						
EPO Dose (1000 IUs)	63.28	61.73	62.19	55.73	52.35	59.07
Receives Any EPO	0.813	0.802	0.795	0.732	0.713	0.771
Health Outcomes						
Hemoglobin (g/dL)	11.46	11.45	11.44	11.45	11.46	11.45
Transfusions	0.026	0.025	0.025	0.026	0.024	0.025
Mortality	0.016	0.016	0.017	0.018	0.017	0.017
Hospitalizations						
Any Cause	0.1471	0.1446	0.1420	0.1463	0.1391	0.1438
Cardiac Event	0.0307	0.0303	0.0289	0.0300	0.0267	0.0293
Septicemia	0.0093	0.0091	0.0088	0.0089	0.0084	0.0089
Unique Patients	54,576	52,150	54,661	53,701	54,001	256,504
Patient-Months	477,695	457,844	478,139	467,866	468,898	2,350,442

Notes: An observation is a patient-month. Sample consists of observations from January to December 2009 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Predicted mortality is the predicted value for each observation using coefficients from a regression of mortality on patient controls and time fixed effects on observations from 2009 and 2010. Time fixed effects are not included in the prediction. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Transfusion and hospitalization variables are binary indicators. Facility elevation is measured in feet above sea level. The cut points between elevation quintiles are 73, 260, 599, and 870 feet above sea level.

Table A5
Patient Descriptive Statistics by Elevation, 2012

	Elevation Quintile					
	First	Second	Third	Fourth	Fifth	Total
Patient Characteristics						
Predicted Mortality	0.016	0.016	0.016	0.017	0.017	0.016
Age (Years)	63.37	63.63	62.85	63.35	63.33	63.31
Months with ESRD	48.98	48.68	49.02	48.59	46.44	48.34
Black	0.448	0.443	0.454	0.379	0.213	0.388
Male	0.556	0.551	0.546	0.554	0.565	0.554
Diabetic	0.538	0.542	0.546	0.555	0.569	0.550
Hypertensive	0.911	0.908	0.909	0.906	0.902	0.907
Incident Hemoglobin	9.664	9.710	9.737	9.819	9.935	9.772
Facility Characteristics						
Facility Elevation (ft)	29.2	144.3	434.4	713.6	1886.7	637.2
Independent Ownership	0.172	0.161	0.150	0.197	0.184	0.173
EPO Use						
EPO Dose (1000 IUs)	36.71	36.11	36.75	34.27	30.43	34.87
Receives Any EPO	0.759	0.761	0.751	0.708	0.662	0.728
Health Outcomes						
Hemoglobin (g/dL)	10.79	10.81	10.82	10.83	10.89	10.83
Transfusions	0.033	0.030	0.0306	0.030	0.029	0.030
Mortality	0.015	0.014	0.015	0.015	0.015	0.015
Hospitalizations						
Any Cause	0.1344	0.1305	0.1283	0.1348	0.1275	0.1311
Cardiac Event	0.0257	0.0258	0.0246	0.0256	0.0227	0.0249
Septicemia	0.0103	0.0100	0.0094	0.0099	0.0094	0.0098
Unique Patients	60,055	58,219	58,652	58,026	58,970	280,751
Patient-Months	543,541	528,788	531,440	518,537	527,525	2,649,831

Notes: An observation is a patient-month. Sample consists of observations from January to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Predicted mortality is the predicted value for each observation using coefficients from a regression of mortality on patient controls and time fixed effects on observations from 2009 and 2010. Time fixed effects are not included in the prediction. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Transfusion and hospitalization variables are binary indicators. Facility elevation is measured in feet above sea level. The cut points between elevation quintiles are 73, 260, 599, and 870 feet above sea level.

D. Potential Anticipatory Responses

Due to frictions in changing clinical practices, we may expect them to change gradually and in anticipation of the PPS. Indeed, in Figure 1 we see that EPO doses began to decrease in mid-2010, prior to the PPS's start in January 2011 and shortly after the announcement of the final PPS rule in mid-August 2010. In this appendix, we both quantify these anticipatory effects and show that our results are robust to including this period of anticipatory responses by providers in the post-PPS period.

To identify and quantify this possible anticipation, we use the methods of Brot-Goldberg et al. (2017). First, we estimate

$$\bar{Y}_t = \beta_0 + \beta_1 t + X_t \Gamma + \bar{\epsilon}_t, \tag{12}$$

where $\bar{Y}_t$ is the mean EPO dose in month t and X_t is a series of month-of-year fixed effects. We estimate this equation using only data from January 2005 through December 2009 and then use the estimated coefficients to calculate the predicted level of EPO for each month in 2010 and 2011. From the predicted and observed values in Table A6, we find that the first month in which the realized mean EPO dose is below the predicted level is October 2010, and that this drop continues to grow through 2011.

We corroborate our finding that the anticipatory response began in October 2010 by using a falsification test from Baicker and Svoronos (2019). To do so, we construct a test statistic from a series of Wald tests, testing each month in our data as a potential structural break in the time series of mean monthly EPO doses. From this, October 2010 returns the highest Wald statistic, 267, suggesting it is the most likely month of a structural break in the trend in EPO doses, which would indicate an anticipation of the PPS by providers.

In light of a possible anticipatory response, we consider the robustness of our main findings to this anticipation. In particular, we recreate the tables and figures presented in the main text while treating the start date of the PPS as October 2010 rather than the actual start date of January 2011. In this way, we treat the period during which facilities were modifying their behavior in anticipation of the PPS as part of the treatment period. Tables A7–A11 and Figure A4 recreate our main results and show that they are robust to this alternative definition of the PPS period.

Table A6
Difference in EPO Relative to Trend

	Actual	Predicted	Difference
2010			
January	58.95	56.19	2.76
February	55.81	52.28	3.53
March	63.36	57.90	5.46
April	59.39	55.96	3.43
May	58.64	58.08	0.56
June	59.06	56.60	2.46
July	59.63	57.64	1.99
August	57.76	57.76	0.00
September	55.77	55.77	0.00
October	53.57	57.61	-4.04
November	51.85	55.03	-3.17
December	50.80	56.94	-6.14
2011			
January	49.98	54.64	-4.66
February	45.90	50.72	-4.82
March	50.77	56.34	-5.57
April	48.88	54.41	-5.52
May	48.36	56.52	-8.16
June	47.80	55.04	-7.25
July	46.74	56.09	-9.35
August	42.97	56.20	-13.24
September	38.66	54.21	-15.55
October	39.01	56.05	-17.03
November	38.68	53.47	-14.79
December	38.65	55.39	-16.74

Notes: Predicted values from OLS estimate of equation (12). Dependent variable is monthly EPO dose. EPO doses are censored at the 99th percentile and measured in 1000 IUs. An observation is a patient-month. Estimation sample consists of observations from January 2005 to December 2009 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Sample presented in table consist of analogous observations from January 2010 to December 2011.

Table A7
The Effect of EPO on Anemia

	HGB		Transfusion	
	(1) OLS	(2) IV	(3) OLS	(4) IV
EPO	-0.00283***	0.0161***	0.000125***	-0.000568***
	(0.0000248)	(0.00454)	(0.00000250)	(0.000146)
Year-Month FE	1	1	1	1
Pat/Fac Controls	1	1	1	1
Facility FE	1	1	1	1
Dep. Var. Mean	11.17	11.17	0.0279	0.0279
Observations	8056164	8056164	9979284	9979284
First-Stage F-statistic		37.93		55.76

Notes: OLS and IV estimates from equation (4). Dependent variable in columns (1)–(2) is hemoglobin. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Dependent variables in columns (3)–(4) is a binary outcome variable for receiving a blood transfusion. EPO doses are censored at the 99th percentile and measured in 1000 IUs. An observation is a patient-month. Sample consists of observations from October 2008 to September 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

Table A8
The Effect of EPO on Hospitalizations and Mortality

	Hosp., Any Cause		Hosp., Cardiac Event		Hosp., Septicemia		Mortality	
	(1) OLS	(2) IV	(3) OLS	(4) IV	(5) OLS	(6) IV	(7) OLS	(8) IV
EPO	0.000147***	0.0000805	0.0000146***	0.000121	-0.000000784	0.0000275	-0.000112***	0.000144*
	(0.00000343)	(0.000237)	(0.00000119)	(0.0000957)	(0.000000586)	(0.0000524)	(0.000000871)	(0.0000646)
Year-Month FE	1	1	1	1	1	1	1	1
Pat/Fac Controls	1	1	1	1	1	1	1	1
Facility FE	1	1	1	1	1	1	1	1
Dep. Var. Mean	0.139	0.139	0.0274	0.0274	0.00930	0.00930	0.0159	0.0159
Observations	9979284	9979284	9979284	9979284	9979284	9979284	9979284	9979284
First-Stage F-statistic		55.76		55.76		55.76		55.76

Notes: OLS and IV estimates from equation (4). Dependent variables are binary outcomes. EPO doses are censored at the 99th percentile and measured in 1000 IUs. An observation is a patient-month. Sample consists of observations from October 2008 to September 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

Table A9
Estimates of Production Function of Unobserved Health

	No Heterogeneity by Chain		Heterogeneity by Chain	
	(1)	(2)	(3)	(4)
	EPO	Implied Parameters	EPO	Implied Parameters
PPS	-15.72^{***}		-9.108^{***}	
	(0.420)		(0.841)	
PPS × DaVita			-9.871^{***}	
			(0.886)	
PPS × Fresenius			-6.591^{***}	
			(0.908)	
PPS × Other Chain			-8.636^{***}	
			(1.000)	
PPS × Elevation	0.00140^{***}		0.00278^{***}	
	(0.000191)		(0.000470)	
β_f		0.303^{***}		0.522^{***}
		(0.00809)		(0.0483)
δ_{DaVita}				-0.520^{***}
				(0.0435)
$\delta_{Fresenius}$				-0.420^{***}
				(0.0533)
$\delta_{OtherChain}$				-0.487^{***}
				(0.0484)
$\phi_{a,2}$		0.0000890^{***}		0.000305^{***}
		(0.0000115)		(0.0000431)
Year-Month FE	0		0	
Pat/Fac Controls	1		1	
Facility FE	1		1	
Dep. Var. Mean	50.18		50.18	
Observations	9979284		9979284	

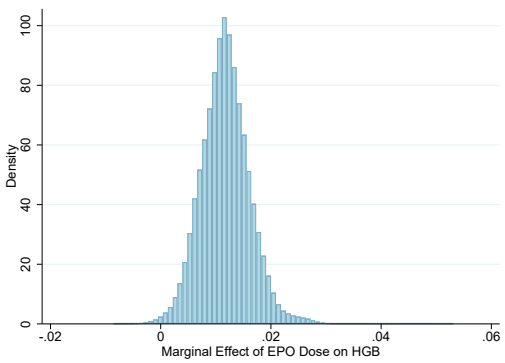
Notes: OLS estimates from equation (10) and implied parameter values. Columns (3) and (4) present results allowing for heterogeneity in altruism by chain ownership, while columns (1) and (2) do not. Dependent variable is monthly EPO dose. EPO doses are censored at the 99th percentile and measured in 1000 IUs. PPS is an indicator variable for January 2011 or later. Facility elevation is measured in feet above sea level. An observation is a patient-month. Sample consists of observations from October 2008 to September 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

Table A10
Estimates of Weights on Observable Components of Health

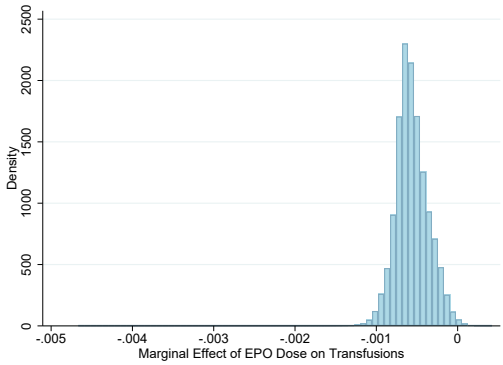
	(1) No Heterogeneity by Chain	(2) Heterogeneity by Chain
β_{HGB}	23.23^{+}	57.92*
	(13.11)	(25.33)
$\beta_{CardiacHosp.}$	-2622.8***	-4748.7***
	(440.1)	(843.3)
$\beta_{Mortality}$	-19071.2***	-36655.1***
	(906.7)	(1767.5)
$\phi_{a,1}$	0.0000171	-0.0160***
	(0.000941)	(0.00141)
Year-Month FE	0	0
Facility Controls	1	1
Facility FE	0	0
Dep. Var. Mean	27.36	53.73
Observations	9979315	9979315

Notes: OLS estimates from equation (11). Column (2) presents results allowing for heterogeneity in altruism by chain ownership, while column (1) does not. An observation is a patient-month. Sample consists of observations from October 2008 to September 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility to freestanding or hospital-based, and chain ownership status, as well as geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

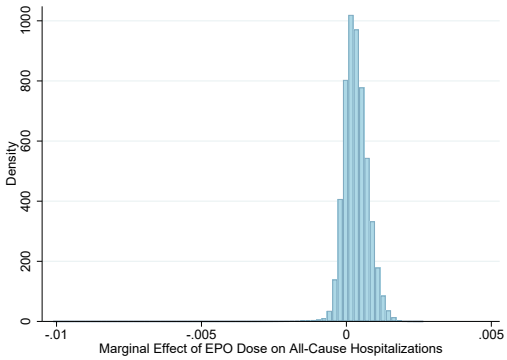
Figure A4
Histogram of Estimated Marginal Effects of EPO



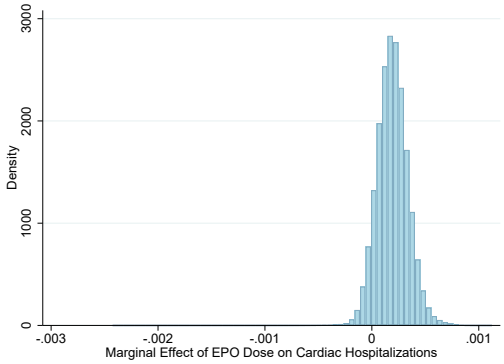
(a) HGB



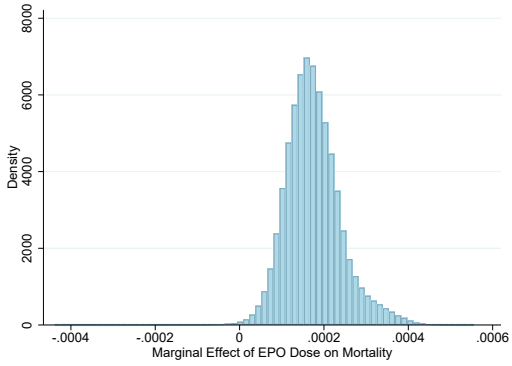
(b) Transfusions



(c) All-Cause Hospitalization



(d) Cardiac Hospitalization



(e) Mortality

Notes: Estimated marginal effects come from IV estimates of equation (7). An observation is a patient-month. Sample consists of observations from October 2008 to September 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter.

Table A11
Counterfactual Outcomes

	(1) Health-Maximizing EPO Dose	(2) Uniform EPO Dose	(3) Minimum HGB Target	(4) Chain Altruism Equal to Independent Altruism	(5) Lower Acquisition Cost of EPO
EPO Dose (%)	22.25	22.25	19.86	9.083	1.391
Hemoglobin (%)	1.114	0.310	0.975	0.480	0.0731
Transfusion Rate (%)	-18.58	-18.82	-15.34	-7.589	-1.164
All-Cause Hospitalizations (%)	2.411	2.964	2.152	0.987	0.149
Cardiac Hospitalization (%)	7.426	8.491	6.116	2.994	0.460
Mortality (%)	11.87	13.01	10.66	4.837	0.736
Unobserved Health ($)	177.0	-2376.2	-651.4	87.38	12.25
Total Health ($)	110.0	-2651.7	-882.7	63.25	8.317

Notes: Change under counterfactual scenarios. Rows related to observable health outcomes (EPO dose to mortality) report percentage change relative to baseline while unobserved and total health report the level change in dollars per patient month relative to baseline. The baseline for all columns is the PPS regime. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. An observation is a patient-month. Sample consists of observations from October 2008 to September 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later.

E. Investigating Identifying Assumptions

E.1. Other Drugs

In addition to EPO, intravenous iron and vitamin D are common classes of injectable drugs administered to dialysis patients. Like EPO, these were separately billable prior to 2011, but were then bundled together with dialysis in the payment reform. Unlike EPO, these drugs were not the subject of any changes in clinical guidelines, such as the black box warning for EPO issued by the FDA in mid-2011.

Any change in providers' use of these drugs in response to the payment reform may violate the exclusion restriction for identifying the marginal effect of EPO on health outcomes. To address this, we present an alternative approach in which we account for intravenous iron in addition to EPO, although we exclude vitamin D because it was not used to treat anemia. Table A12 presents the summary statistics with information on the use of these other injectable drugs, which are used much less often than EPO.

Table A12
Summary Statistics including the Use of Other Drugs

	Mean	Std. Dev.
Resource Use		
EPO Dose (1000 IUs)	48.50	64.11
Receives Any EPO	0.755	0.430
IV Iron Dose (1000 IUs)	0.20	0.26
Receives Any Iron	0.571	0.495
Vitamin D Dose (1000 IUs)	0.03	0.06
Receives Any Vitamin D	0.659	0.474
Receives Any Cinacalcet	0.099	0.299
Dialysis Sessions	12.08	9.90
Unique Patients	461,477	
Patient-Months	10,077,289	

Notes: An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Injectable iron drugs include Ferrlecit, Venofer, Ferumoxytol, and Iron Dextran. Injectable vitamin D drugs include Calcitriol, Doxercalciferol, and Paricalcitol.

We re-estimate our main specification from Section 5.1 using a combined measure of intravenous iron and EPO as our instrumented variable. Specifically, in each month we calculate each patient's Z-score for EPO based on the mean and standard deviation of EPO in our entire sample as well as a Z-score for intravenous iron. We sum those together for a combined total anemia drug dose Z-score, which captures each patient's position in the distribution of total anemia drug use. The results are presented in Table A13 and are very similar to our baseline results, demonstrating their robustness.

Table A13
Combined Injectable Anemia Drugs and Outcomes

	(1) HGB	(2) Transfusion	(3) Mortality	(4) Hosp., Any Cause	(5) Hosp., Cardiac Event	(6) Hosp., Septicemia
Combined Injectibles Z-score	1.584***	-0.0471***	0.0103+	0.0165	0.0148+	0.00288
	(0.384)	(0.0126)	(0.00533)	(0.0206)	(0.00795)	(0.00441)
Year-Month FE	1	1	1	1	1	1
Pat/Fac Controls	1	1	1	1	1	1
Facility FE	1	1	1	1	1	1
Dep. Var. Mean	11.12	0.0282	0.0157	0.138	0.0271	0.00939
Observations	8181736	10077264	10077264	10077264	10077264	10077264
First-Stage F-statistic	33.56	38.35	38.35	38.35	38.35	38.35

Notes: IV estimates from equation (4). Dependent variable in column (1) is hemoglobin. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Dependent variables in columns (2)–(6) are binary outcomes. Combined injectables Z-score is the mean of the patient-month's Z-scores for EPO use and IV iron use. Injectable iron drugs include Ferrlecit, Venofer, Ferumoxytol, and Iron Dextran. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. +, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

E.2. Dialysis Modality

As discussed by (Zhang et al., 2017), a change in relative profitability after the PPS that favored peritoneal dialysis may have led providers to shift patients away from in-center hemodialysis. Like the use of other anemia drugs, this change may violate the exclusion restriction for identifying the marginal effect of EPO on health outcomes. In Table A14, we show that neither the share of patients receiving in-center hemodialysis nor the share receiving peritoneal dialysis changed differentially by elevation after the PPS, further supporting our identification strategy.

Table A14
Differential Change by Elevation for Dialysis Modality

	(1) Dialysis Sessions	(2) In-Center Hemodialysis	(3) Peritoneal Dialysis	(4) Good URR
Facility Elevation	-0.0000138	-0.00000705	0.00000779	-0.0000117**
	(0.0000343)	(0.00000843)	(0.00000779)	(0.00000377)
Elevation × PPS	-0.00000472	-0.000000661	0.000000426	0.000000987
	(0.00000560)	(0.000000854)	(0.000000802)	(0.000000696)
Year-Month FE	1	1	1	1
Pat/Fac Controls	1	1	1	1
Facility FE	1	1	1	1
R-squared	0.00617	0.281	0.264	0.0923
Dep. Var. Mean	12.08	0.909	0.0702	0.933
Observations	8869420	10267613	10267613	8560825

Notes: OLS estimates from equation (5). Dependent variable in column (1) is monthly number of dialysis sessions, in column (2) is an indicator for receiving in-center hemodialysis treatment, in column (3) is an indicator for receiving peritoneal dialysis treatment, and in column (4) is an indicator for having a urea reduction ratio above 0.85. PPS is an indicator variable for January 2011 or later. Facility elevation is measured in feet above sea level. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for ESRD patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

E.3. Exclusion of Elevation

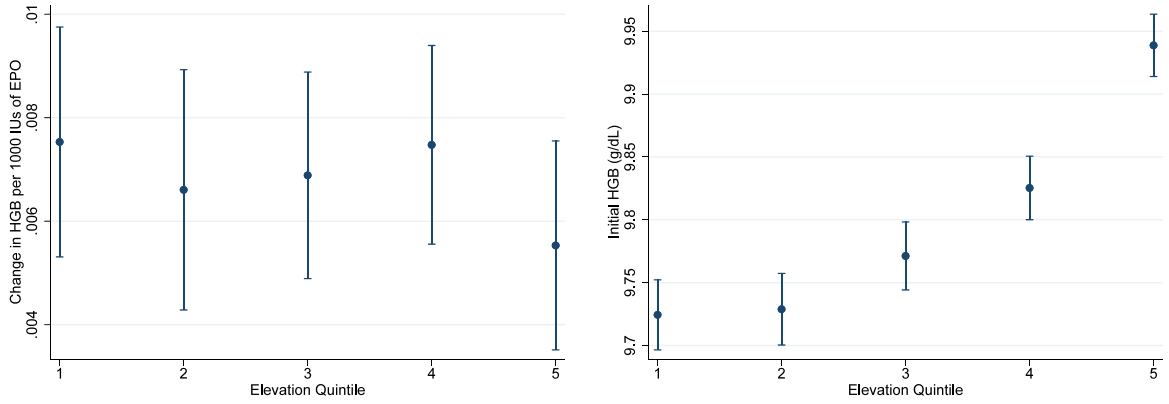
We allow the baseline observable health outcomes that patients would attain without EPO to differ by elevation, but we assume that the causal effect of EPO on observable health outcomes does not. These assumptions are consistent with the medical literature on EPO and elevation, which documents that patients at higher elevations achieve higher HGB levels while using lower EPO doses (Brookhart et al., 2008, 2011a). That literature, however, abstracts away from whether the differences across elevation arise from differing returns from EPO or from differences in the baseline health outcomes patients would attain without EPO. Given a lack of clear guidance from the medical literature, we provide empirical evidence that supports our assumptions.

First, we present suggestive evidence that the effect of EPO on HGB does not differ by elevation. To do so, we consider the first month that a patient receives dialysis and assess how the patient's HGB level changes over the course of that month depending on the amount of EPO the patient receives. Because many of these patients are receiving EPO for the first time, any changes in their HGB level can plausibly be attributed to the amount of EPO they receive in that month. Although it remains possible that patients whose health is deteriorating more quickly may receive larger doses of EPO, as long as the correlation between the counterfactual change in HGB and the amount of EPO received does not vary by elevation, a lack of correlation between elevation and the estimated effect of EPO would be strong suggestive evidence that the true causal effect of EPO does not differ by elevation.

Panel (a) of Figure A5 reports the average change in HGB per 1000 IUs of EPO received in the patient's first month on dialysis by elevation quintile. We find no clear relationship between this estimated effect of EPO and elevation, lending support to our assumption that the true causal effect of EPO on observable health outcomes does not differ by elevation. Providing further support, we find no correlation between elevation and the change in HGB per EPO dose, even conditional on patient and facility characteristics and time fixed effects, as shown in Table A15.

By contrast, we find that patients' initial HGB levels differ considerably by elevation. In both panel (b) of Figure A5 and Table A15, we see a clear positive relationship between pre-EPO HGB levels and elevation. This indicates the importance of allowing baseline levels of observable health outcomes to differ by elevation.

Figure A5
HGB Differences by Elevation



(a) HGB Change Per EPO Dose

(b) Initial HGB

Notes: An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. The sample is further limited to the first month the patient recieves dialysis. Panel (a) gives the average change in HGB from the beginning to end of the month divided by the amount of EPO given in the month by elevation quintile. Change in HGB per dose is winsorized to the first and 99th percentiles. Panel (b) gives the average HGB at the beginning of the month by elevation quintile. Facility elevation is measured in feet above sea level. The cut points between elevation quintiles are 73, 260, 599, and 870 feet above sea level. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. 95% confidence intervals are shown. Standard errors are clustered by facility.

Table A15
HGB Differences by Elevation

	(1) HGB Change per Dose	(2) HGB Change per Dose	(3) HGB Change per Dose	(4) Initial HGB	(5) Initial HGB	(6) Initial HGB
Elevation (1000 ft.)	0.000553	0.000805	0.000805	0.0909***	0.0111**	0.0115**
	(0.000750)	(0.000820)	(0.000821)	(0.00760)	(0.00357)	(0.00354)
Year-Month FE	0	0	1	0	0	1
Pat/Fac Controls	0	1	1	0	1	1
Facility FE	0	0	0	0	0	0
Dep. Var. Mean	0.00682	0.00682	0.00682	9.801	9.801	9.801
Observations	64973	64973	64973	149363	149363	149363

Notes: Estimates from a regression of the dependent variable listed in each column on elevation. Dependent variable in columns (1)–(3) is change in HGB from the beginning to end of the month divided by the amount of EPO given in the month. Change in HGB per dose is winsorized to the first and 99th percentiles. Dependent variable in column (4)–(6) is HGB at the beginning of the month. Facility elevation is measured in thousands of feet above sea level. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. The sample is further limited to the first month the patient recieves dialysis. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility to freestanding or hospital-based, and chain ownership status, as well as geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses. $^{+}$, *, **, and *** indicate significance at the 10%, 5%, 1%, and 0.1% level, respectively.

E.4. Unobserved Heterogeneity

In Section 6, we assume there is no unobserved heterogeneity in the effect of EPO on observed health outcomes, resulting in the health production function given by equation (8). Strictly speaking, we actually only need to assume that if there is unobserved heterogeneity in the effect of EPO on observed health outcomes, that it does not enter providers' dosing decisions and that it is independent of other patient and facility characteristics. In this appendix section, we first show that the parameters of the model are identified even under the weaker assumption that there exists unobserved heterogeneity but providers do not use it in dosing decisions. Next, we provide empirical evidence supporting this assumption. Finally, we discuss the bias that would result if this assumption were incorrect.

To see how the existence of unobserved heterogeneity that is omitted from dosing decisions does not affect identification of the parameters of interest, suppose providers make dosing decisions as if equation (8) gives the production function for observed health outcomes while the true production function is actually given by

$$\alpha_c(epo, X, \nu) = \left(\alpha_{c,1} + \sum_{x \in X} \alpha_{c,x} x + \nu\right) epo, \tag{8'}$$

where ν captures the unobservable mean-zero heterogeneity in the effect of EPO on health component c and $\nu \perp (X, a, F, \varepsilon)$. Note that $\alpha_{c,1}$ and $\alpha_{c,x}$ continue to be identified using our instrumental variables strategy. Furthermore, β_f, $\phi_{a,2}$, and δ_j continue to be identified by equation (10) because it relies only on the production function of unobserved health and the relationship p and a have with the level of EPO chosen by providers, epo^*, which is unchanged since ν does not enter equations (2) or (3). Finally, for the same reason, the first-order condition given by equation (11) does not depend on ν. Thus, under this weaker assumption that there exists unobserved heterogeneity but providers do not use it in dosing decisions, our model parameters remain identified.

However, making this weaker assumption does change the interpretation of two of our counterfactual scenarios. Rather than interpreting the counterfactual outcomes presented in columns (1) and (3) of Table 10 as representing the outcomes under the *true* health-maximizing EPO doses and amount of EPO necessary to achieve the minimum HGB target, respectively, they must be interpreted as representing the outcomes under *what providers believe* these scenarios to be. That is, as long as we

restrict providers to use no more information in the counterfactual scenarios than they are using at baseline, the counterfactuals accurately capture what would occur.

To provide empirical evidence in support of the assumption that there is no unobserved heterogeneity, we attempt to test for the presence of what Heckman and Vytlacil (2005) call *essential heterogeneity* using methods from the econometrics literature on characterizing average treatment effects in terms of marginal treatment effects. Essential heterogeneity is present if any unobserved heterogeneity in the treatment effect of EPO on observable health outcomes is correlated with treatment (Heckman et al., 2006). Under our assumption that providers do not factor any unobserved heterogeneity in the treatment effect of EPO into their dosing decisions, this correlation will be zero; in other words, there will be no essential heterogeneity. This test has an additional benefit of establishing whether we can interpret our IV estimators as being policy relevant. In particular, if there is no essential heterogeneity, then the weighted average comprising our IV estimands (LATE) will be the same as the weighted average of a treatment effect resulting from a policy intervention (Heckman and Vytlacil, 2005).

We follow Heckman et al. (2006) to test for essential heterogeneity. We first convert our continuous measure of EPO to a binary measure indicating whether the patient received an above- or below-median amount of EPO in the month. This greatly simplifies estimation of the marginal treatment effects and represents the case most commonly considered and developed by the literature (Angrist and Pischke, 2009). We estimate the marginal treatment effects on the observable health outcomes we consider, instrumenting treatment with the instrumental variable presented in Section 4.2: the interaction of the payment reform with elevation. We allow the effect of treatment to vary by patient and facility characteristics and allow for jointly normal errors in the effect of treatment and the unobserved resistance to treatment. For tractability, we estimate the level of essential heterogeneity using a random 10% sample of patient-months and omitting facility fixed effects from the model.

The first row of Table A16 reports estimates of the p-values of joint tests of the coefficients of the essential heterogeneity function.[27] We find no statistically significant evidence of essential heterogeneity for any outcome. Furthermore, it is important to note that these p-values are likely too low because they do not account for the necessary pre-estimation of treatment propensity. Thus, the generally high p-values found in Table A16 represent evidence that providers do not provide more (or less) EPO to patients for whom EPO has a larger unobserved effect on observable health outcomes. This is consistent

[27]Details on this function and test can be found in Andresen (2018).

with providers disregarding or not being aware of treatment effect heterogeneity beyond that which can be projected onto our rich set of observable characteristics and would also be implied by there being no such unobserved heterogeneity at all. In short, our assumption of a lack of essential heterogeneity is supported by the data.

While there is little evidence of essential heterogeneity, we continue to find strong evidence of heterogeneity in the effect of treatment by observable characteristics. The second row of Table A16 reports p-values of joint tests of the coefficients capturing heterogeneity in the treatment effect along observable dimensions. In contrast to the high p-values presented in Table A16, here we can reject the null hypothesis of no heterogeneity using a significance threshold of at least 0.01 for all models. This result not only highlights the importance of estimating heterogeneity in the effect of EPO along observable dimensions, it also demonstrates that our inability to detect essential heterogeneity is unlikely attributable to issues related to low power.

Table A16
P-Values of Test for Essential and Observable Heterogeneity

	(1) HGB	(2) Transfusion	(3) Hosp., Any Cause	(4) Hosp., Cardiac Event	(5) Mortality
Essential Heterogeneity	0.712	0.589	0.281	0.250	0.363
Observable Heterogeneity	0.000	0.000	0.000	0.000	0.007

Notes: Estimated p-values of joint tests of the coefficients of the essential and observable heterogeneity functions from estimates of equation (4) with an indicator for whether the patient received an above-median amount of EPO in the month as the endogenous variable, allowing for heterogeneity in the marginal treatment effects along observable dimensions and unobservable dimensions according to Heckman selection. Dependent variable in column (1) is hemoglobin. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Dependent variables in columns (2)–(5) are binary outcomes. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. The sample is further limited to a 10% random sample of patient-months. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility to freestanding or hospital-based, and chain ownership status, as well as geographic information about the patient's residence, including state and average income in the ZIP code. Standard errors clustered by facility are in parentheses.

Finally, despite the evidence supporting our assumption of no essential heterogeneity, we consider how our estimates would be biased if this assumption were incorrect. In this case, $\alpha_{c,1}$, $\alpha_{c,x}$, β_f, $\phi_{a,2}$, and δ_j would continue to be identified for the reasons outlined above. However, equation (11) would

now be given by

$$(11') \quad Y_{ijt} = \eta_1 + \eta_j^{Chain} Chain_{jt} + \sum_c \beta_c \left(\hat{\alpha}_{c,1} + \sum_{x \in X} \hat{\alpha}_{c,x} x_{it} + \nu_{it} \right) + \phi_{a,1} WtElev_{ijt} - F_{jt}\xi + \varepsilon_{ijt}.$$

The inclusion of ν introduces an error-in-variables problem whereby we would be estimating β_c using only a proxy for the true effect of EPO on observable health component c. In the bivariate case, error-in-variables results in an attenuated coefficient estimate, although in the multivariate case, the bias is less clear. Thus, if there is unobservable heterogeneity in the effect of EPO on observed health outcomes that providers consider when making dosing decisions, contrary to the empirical evidence provided in Table A16, then our estimates of the weights providers place on these outcomes will be biased due to mismeasurement of the true causal effect of EPO.

E.5. Characterizing Compliers

In the previous section of this appendix, we presented evidence against unobserved heterogeneity in the treatment effect of EPO on observed health outcomes, particularly heterogeneity that is correlated with EPO doses. While a lack of unobserved heterogeneity implies that the local average treatment effect from an instrument is equal to the average treatment effect, in this appendix we present evidence that the compliers with our instrument span the support of EPO doses.

Following Angrist and Pischke (2009), we can conceptualize our 2SLS estimates as the weighted average of the potentially nonlinear causal effects of EPO on the outcome, where the weighting comes from the number of compliers at each level of EPO, which relies on the usual assumptions about the validity of the instrument (exclusion/independence, existence of the first stage, and monotonicity). Given those assumptions hold, the size of the complier group can be written as

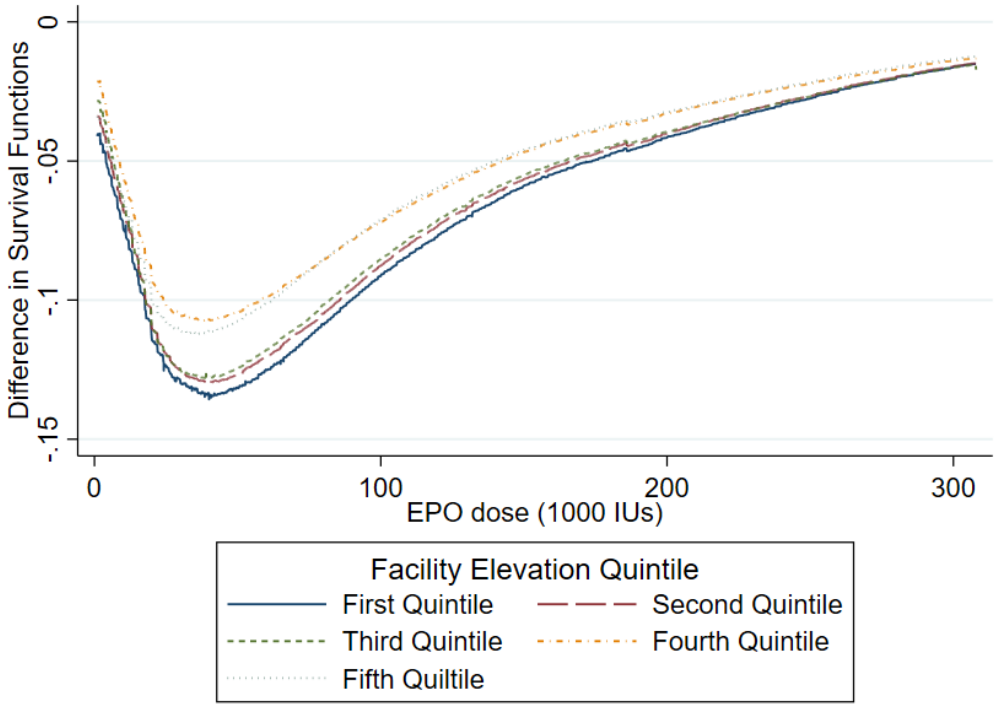
$$P[e_{1i} \leq e < e_{0i}] = P[e_{1i} \leq e] - P[e_{0i} < e],$$

where e_{1i} is the EPO given to patient i when the instrument is "switched on" and e_{0i} is the amount given when the instrument is "switched off." Thus, the measure of compliers at some EPO level e is the measure of patients who are induced to receive a dose larger than e by the instrument and would not otherwise. In other words, the weighting function compares the CDFs of the endogenous variable across different values of the instrument.

Because our instrument is continuous, it is difficult to analytically recover the exact weights placed on observations with different characteristics. However, Figure A6 gives a sense of how these weights are distributed. The figure plots the differences in the CDF for EPO doses in the pre-PPS period and the post-PPS period for the five elevation quintiles, where the reference groups are the pre-PPS quintiles. In other words, each line is the difference for a given elevation quintile between the probability that a patient receives or exceeds the dose indicated on the x-axis *before* the policy change and the probability that the patient receives or exceeds that dose *after* the policy change.

Figure A6 provides a number of insights. First, compliance is near universal. Across the entire range of EPO doses and for all elevations, patients tend to receive lower doses after the policy change, with larger differences for the low elevations (quintiles 1-3) than the high elevations (quintiles 4-5). Second,

Figure A6
Difference in EPO Survival Function by Elevation



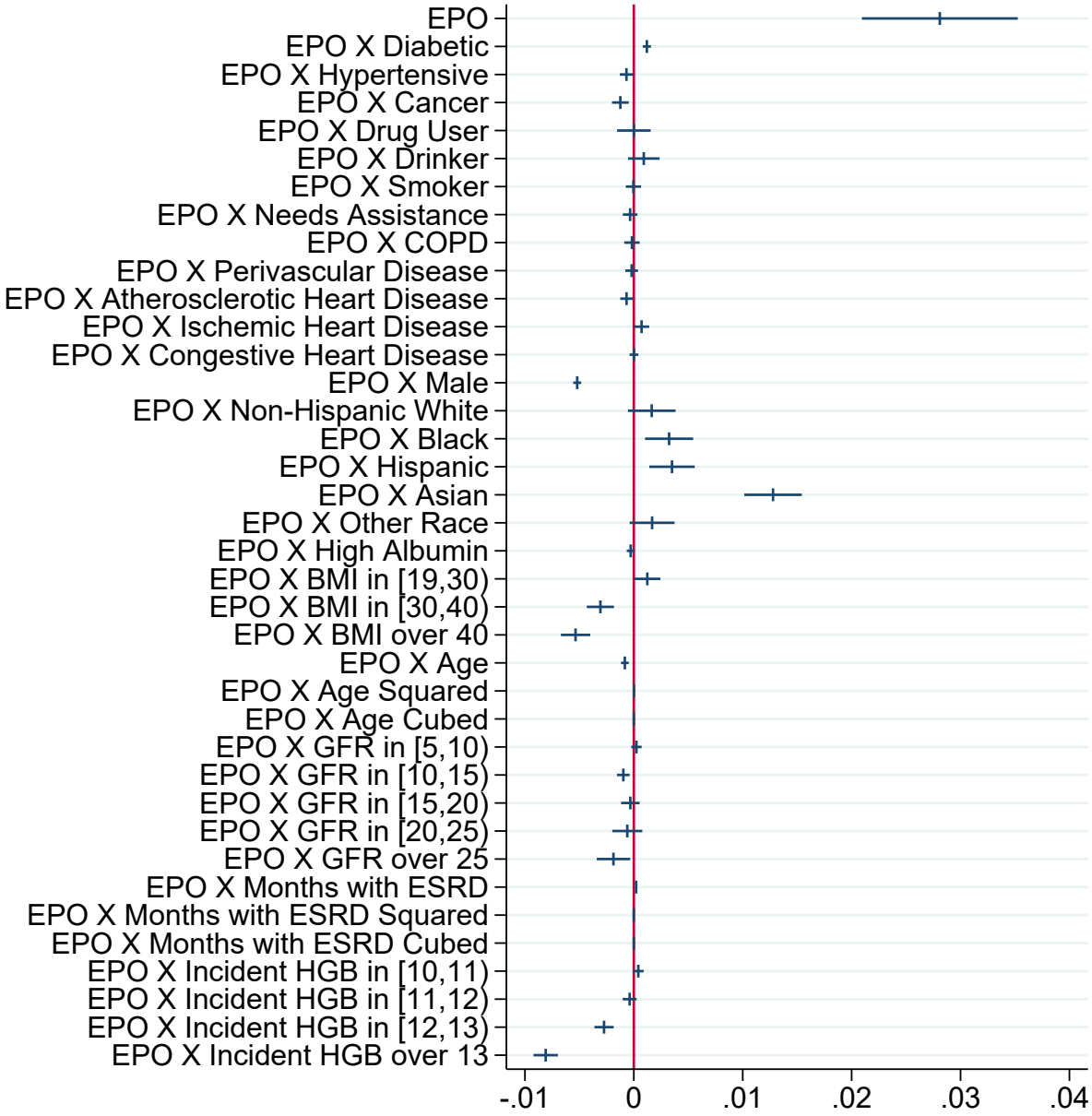
Notes: Figure plots the difference in the survival function for EPO doses between observations from 2009–2010 and 2011–2012. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Facility elevation is measured in feet above sea level. The cut points between elevation quintiles are 73, 260, 599, and 870 feet above sea level. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter.

we can observe where the weighting from our instrument comes from: the differences between the high and low elevation differences plotted. There are compliers at nearly all levels of EPO, particularly at moderate levels of EPO common among patients. This indicates that rather than exploiting variation only for very specific amounts of EPO, our analysis uses variation across the distribution. Furthermore, even if the essential heterogeneity we find no evidence of in Appendix E.4 is actually present, this analysis suggests that the local average treatment effect we recover is indeed informative of the broader, policy-relevant effect.

F. Additional Parameter Estimates

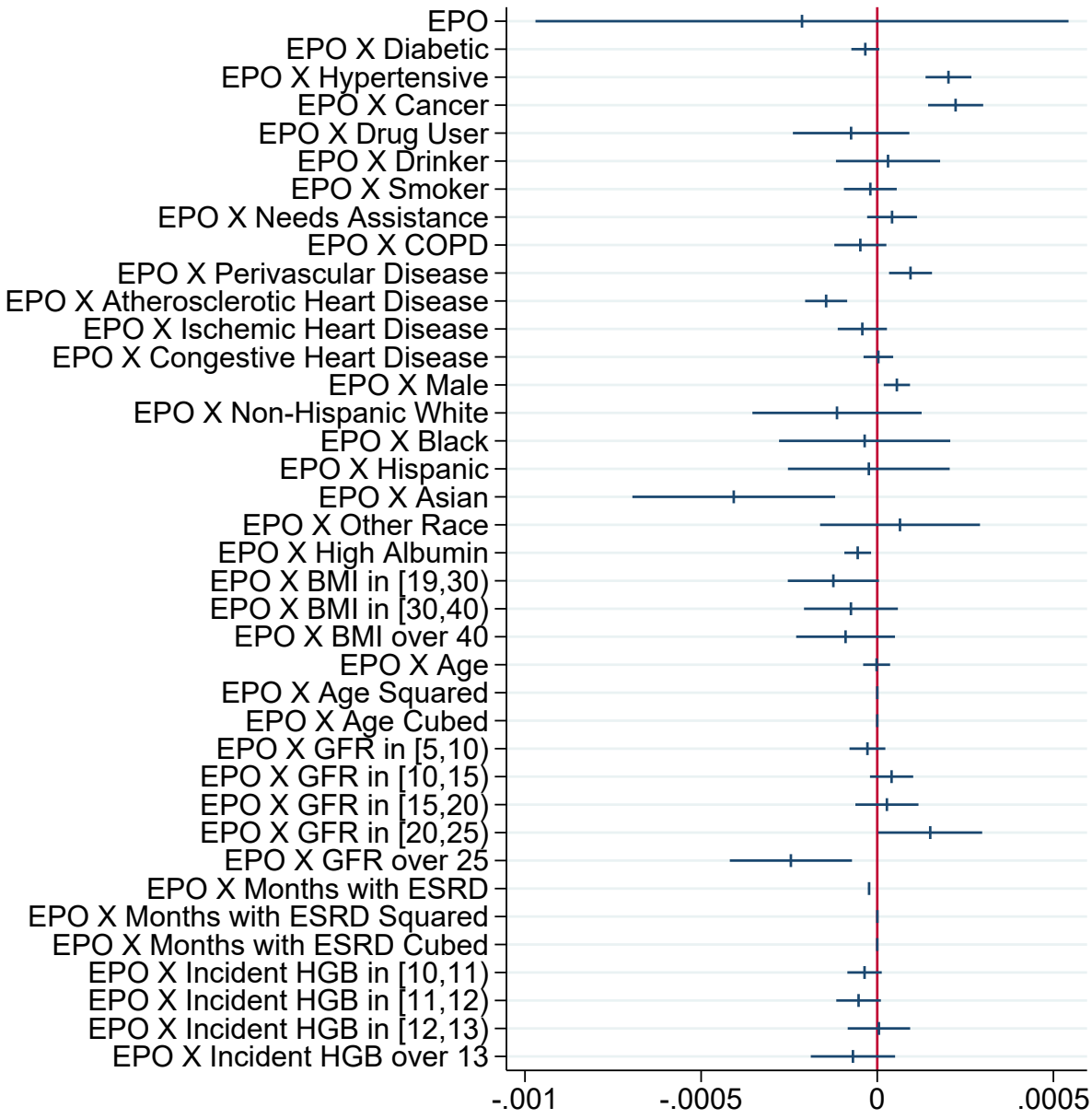
In this appendix, we report estimates of parameter values not reported in the main text. Figures A7–A11 report estimates of $\alpha^{IV}_{c,X}$, which are also $\alpha_{c,x}$ in structural model equation (8).

Figure A7
Coefficient Estimates of Heterogeneity in Responsiveness of HGB to EPO



Notes: IV estimates from (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. Horizontal bands give 95% confidence intervals. Standard errors are clustered at the facility level.

Figure A8
Coefficient Estimates of Heterogeneity in Responsiveness of Transfusions to EPO

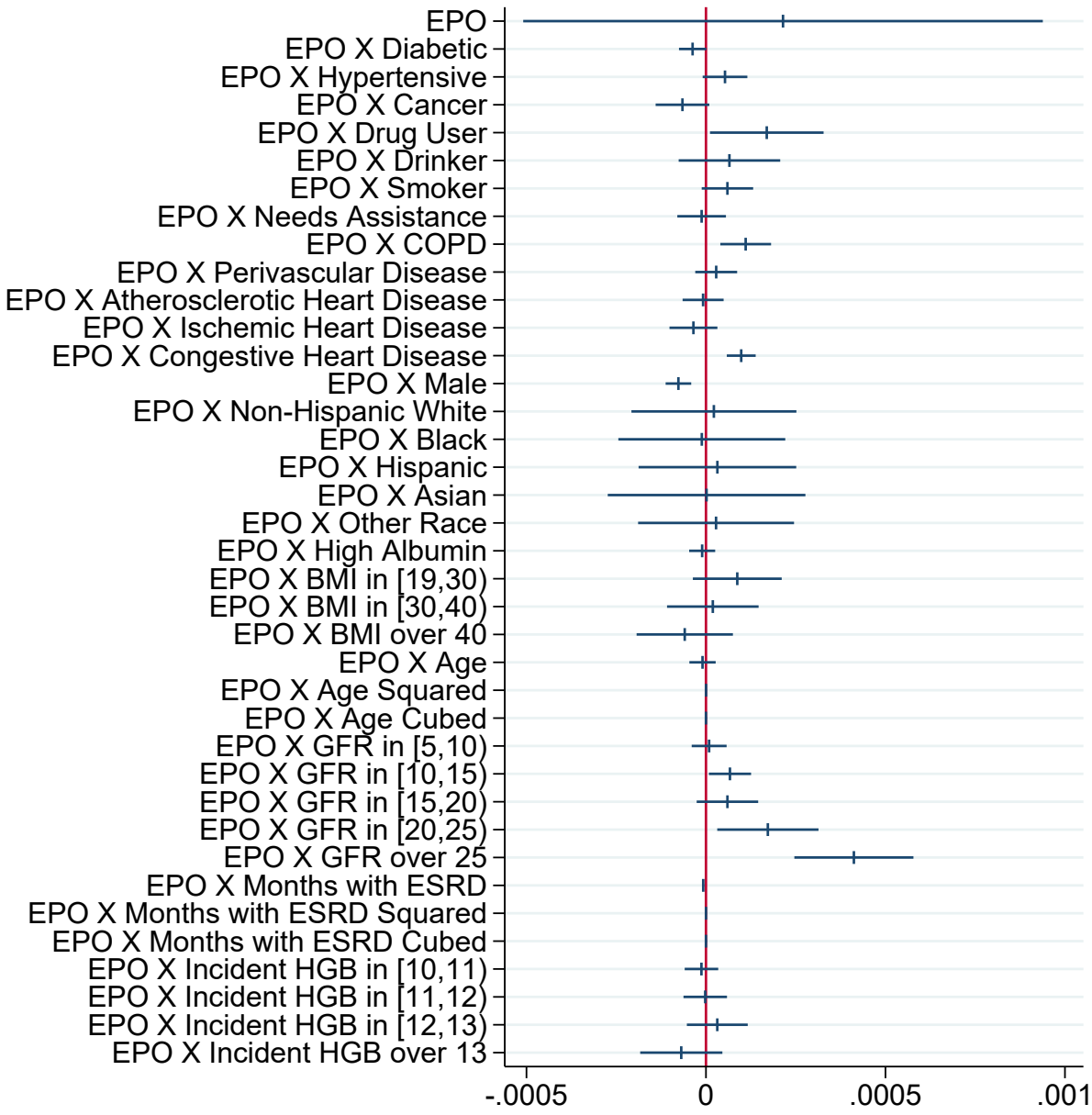


Notes: IV estimates from (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Horizontal bands give 95% confidence intervals. Standard errors are clustered at the facility level.

Figure A9
Coefficient Estimates of Heterogeneity in Responsiveness of All-Cause Hospitalizations to EPO

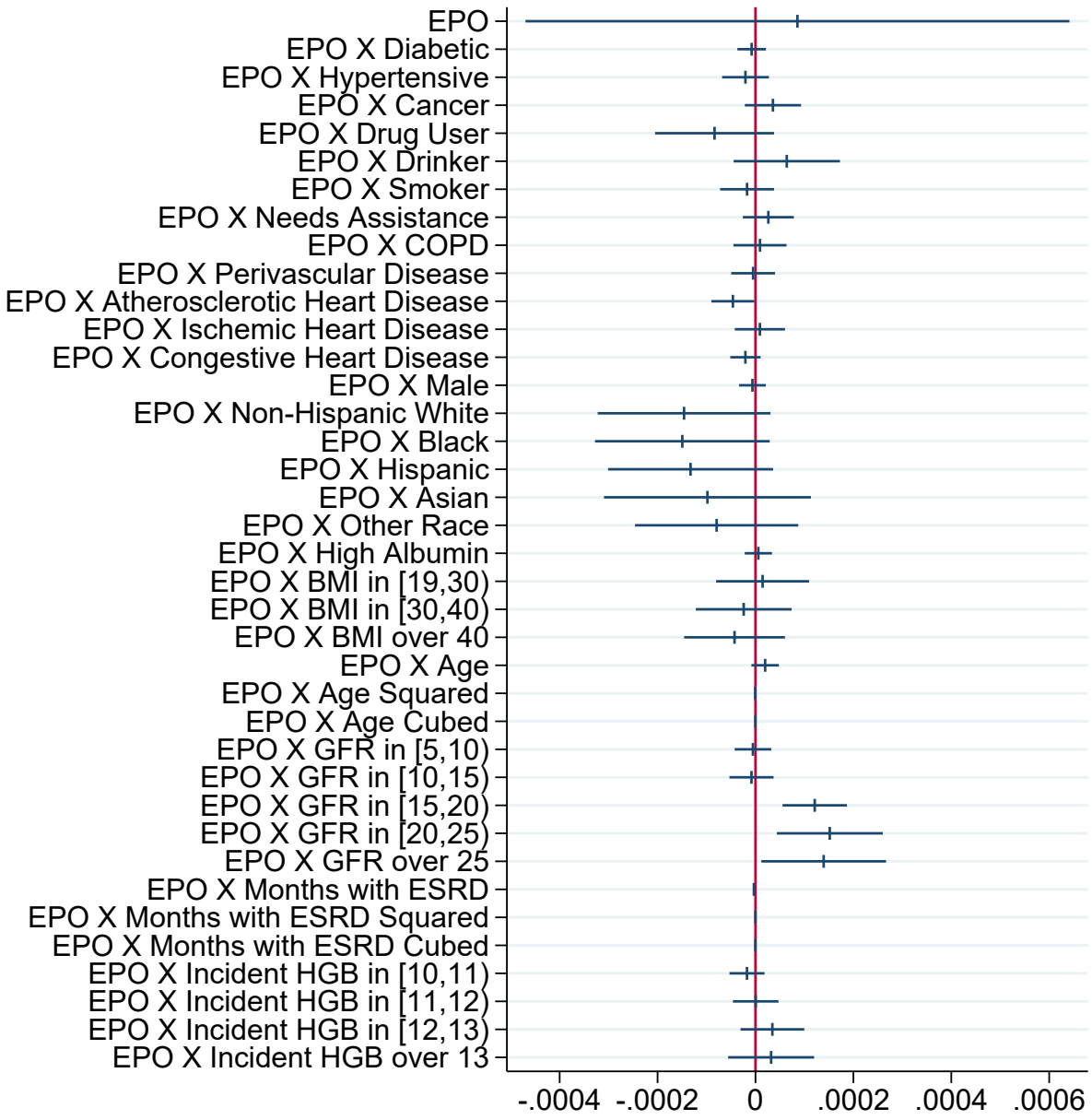
Notes: IV estimates from (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Horizontal bands give 95% confidence intervals. Standard errors are clustered at the facility level.

Figure A10
Coefficient Estimates of Heterogeneity in Responsiveness of Cardiac Hospitalizations to EPO



Notes: IV estimates from (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Horizontal bands give 95% confidence intervals. Standard errors are clustered at the facility level.

Figure A11
Coefficient Estimates of Heterogeneity in Responsiveness of Mortality to EPO



Notes: IV estimates from (7). An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. Patient controls include dummy variables for incident comorbidities and characteristics reported on medical evidence forms, including diabetes, hypertension, BMI bin, GFR bin, HGB bin, high albumin, cancer, drug use, alcoholism, smoking behavior, necessity of assistance, COPD, ASHD, PVD, ischemic heart disease, and congestive heart disease, along with patient race, gender, and cubic functions of age and dialysis tenure. Facility controls include facility elevation, whether the facility is freestanding or hospital-based, and chain ownership, as well as facility fixed effects and geographic information about the patient's residence, including state and average income in the ZIP code. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Horizontal bands give 95% confidence intervals. Standard errors are clustered at the facility level.

G. Additional Structural Model results

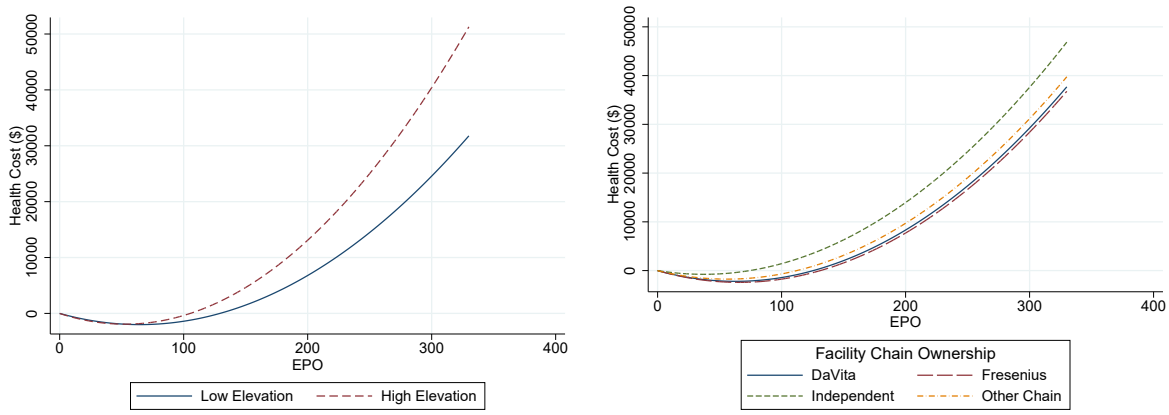
This appendix, we report additional results from estimation of our structural model that we reference in the main text. Table A17 reports the estimated mean and standard deviation of costs by chain ownership. Note that the mean costs for each chain are calibrated to match the mean EPO acquisition costs reported in the 2010 cost report data. Figure A12 reports the estimated unobserved health cost function by elevation and chain ownership, the observable dimensions along which this function is allowed to vary. We see that at high levels of EPO use, health costs are increasing rapidly, with this increase being greater at higher elevations and for patients at independent facilities. Table A18 reports the counterfactual values of EPO use and observed health outcomes. These results underlie the percentage change results reported in Table 10. Note that we do not report the level of unobserved or total health because, while we are able to estimate level changes in these variables, we do not observe the baseline levels. Finally, Table A19 reports counterfactual changes using our estimates that do not allow for heterogeneity in altruism by chain ownership. The results are broadly similar to those reported in the main text.

Table A17
Estimated EPO Acquisition Costs by Chain

	Mean	Standard Deviation	Obs.
DaVita	7.92	3.19	3192294
Fresenius	7.33	3.85	3471080
Independents	8.54	16.9	1980611
Other Chains	8.36	3.35	1433304
Overall	7.90	8.13	10077289

Notes: Estimated EPO acquisition costs by chain. Mean acquisition costs are calibrated to match 2010 cost report data. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later.

Figure A12
Health Cost Function



(a) By Elevation (b) By Chain

Notes: Estimated average unobserved health cost of EPO without unobserved heterogeneity $(\phi_j + \phi_{a,1}a)epo + (1 + \phi_{a,2}a)epo^2$ by level of EPO. Unobserved health cost is measured in dollars per patient month. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later. EPO doses are censored at the 99th percentile and measured in 1000 IUs. In panel (a), estimated health costs are reported for patients at high and low elevation facilities. High (low) elevation denotes facility elevation in the fifth (first) quintile. This corresponds to being above 870 (below 73) feet above sea level. Facility elevation is measured in feet above sea level. In panel (b), estimated health costs are reported for patients at facilities owned by DaVita, Fresenius, or another chain and for patients at independent facilities.

Table A18
Counterfactual Outcomes in Levels

	(1) Baseline	(2) Health-Maximizing EPO Dose	(3) Uniform EPO Dose	(4) Minimum HGB Target	(5) Chain Altruism Equal to Independent Altruism	(6) Lower Acquisition Cost of EPO
EPO Dose (1000 IUs)	42.97	54.35	54.35	50.49	47.95	43.66
Hemoglobin (g/dL)	11.02	11.21	11.10	11.14	11.11	11.03
Transfusion Rate	0.0313	0.0248	0.0247	0.0274	0.0284	0.0309
All-Cause Hospitalizations	0.135	0.141	0.141	0.139	0.138	0.136
Cardiac Hospitalization	0.0258	0.0285	0.0288	0.0275	0.0270	0.0260
Mortality	0.0148	0.0167	0.0169	0.0161	0.0156	0.0149

Notes: Outcomes under counterfactual scenarios. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later.

Table A19
Counterfactual Outcomes without Chain Heterogeneity

	(1) Health-Maximizing EPO Dose	(2) Uniform EPO Dose	(3) Minimum HGB Target	(4) Lower Acquisition Cost of EPO
EPO Dose (%)	28.54	28.54	17.62	1.890
Hemoglobin (%)	1.854	0.830	1.124	0.126
Transfusion Rate (%)	-22.09	-22.37	-12.49	-1.464
All-Cause Hospitalizations (%)	4.292	4.820	2.645	0.284
Cardiac Hospitalization (%)	11.44	12.53	6.503	0.758
Mortality (%)	13.50	14.56	8.311	0.891
Unobserved Health ($)	86.56	-1014.9	-184.7	7.978
Total Health ($)	57.38	-1135.0	-250.1	6.114

Notes: Change under counterfactual scenarios. Rows related to observable health outcomes (EPO dose to mortality) report percentage change relative to baseline while unoberved and total health report the level change in dollars per patient month relative to baseline. The baseline for all columns is the simulated outcome under PPS. EPO doses are censored at the 99th percentile and measured in 1000 IUs. Counterfactual EPO doses are restricted to the observed support of doses. Hemoglobin is winsorized from below to 5 and from above to 20 and is measured in grams per deciliter. An observation is a patient-month. Sample consists of observations from January 2009 to December 2012 for in-center hemodialysis patients between the ages of 18 and 100 with Medicare as their primary payer for whom we observe all patient and facility controls used in the analyses in Section 4.2 and later.