Externalities from Medical Innovation: Evidence from Organ Transplantation^{*}

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Abstract

We evaluate the introduction of direct-acting antiviral (DAA) therapy for hepatitis C (HCV) on liver transplant allocation in the United States. We develop a model of listing and organ acceptance behavior for patients with end-stage liver disease. In the model, DAAs obviate the need for transplant for some HCV-positive patients, which shortens the waiting list, potentially benefiting HCV-negative registrants and inducing marginal HCV-negative patients to register. Using data from the universe of transplants between 2005 and 2019, we find that DAA availability resulted in an additional 5,682 liver transplants to HCV-negative end-stage liver disease patients between 2014 and 2019, generating a positive externality of \$7.52 billion. Our result is driven in part by a 37% average annual increase in HCV-negative waiting list registrations. In the absence of this behavioral response, DAA therapies would have eliminated the liver transplant waiting list.

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1 Introduction

The value of medical innovations partly relies on the incentives they generate. Across most health conditions, medical innovation is enormously valuable (Dranove et al., 2022; Hall & Jones, 2007; Murphy & Topel, 2006; Cutler & McClellan, 2001; Newhouse, 1992). However, an important contribution of economics has been to identify instances where innovation-generated incentives shift behavior that aligns with, or works against, their direct social welfare implications. For example, Papageorge (2016) shows that a significant benefit of HIV treatments (HAART) were to raise productivity and increase labor supply. Conversely, Kaestner et al. (2014) present evidence of technological substitution away from diet and exercise when statin medications were introduced to lower cholesterol. Medical innovation may also shift incentives (and subsequent behaviors and outcomes) for individuals who are not their primary beneficiaries. We refer to such instances as *innovation-induced externalities*. Especially in cases where new innovations are extremely costly relative to existing technology, valuing innovation-induced externalities may influence payer coverage decisions and research and development investment choices (Chernew & Newhouse, 2011; Philipson, 2000; Fendrick et al., 1996).

In this paper, we quantify the innovation-induced externalities associated with the recent introduction of a breakthrough medical treatment that dramatically improved health outcomes but that remains inaccessible to some patients. Specifically, in December 2013, the Food and Drug Administration approved sofosbuvir, a direct-acting antiviral (DAA), for the treatment of chronic hepatitis C (HCV). Prior to the availability of DAAs, HCV was the leading cause of infectious-disease-related death in the United States and accounted for nearly half of all liver transplant waiting list registrations (Powell <u>et al.</u>, 2019). However, DAA therapy, which achieves sustained viral clearance rates in over 90% of HCV patients, mechanically reduces liver demand to the extent that, for many, therapy obviates the need for a transplant. We conceive of those with end-stage liver disease (ESLD) resulting from conditions *other* than HCV (e.g., alcohol-associated liver disease, nonalcoholic steatohepatitis, etc.) to be external to the market for HCV pharmaceuticals, and we quantify the innovation-induced externalities to these individuals resulting from DAA-induced changes in the demand for livers.

To fix ideas, we formulate a model of HCV-positive (HCV^+) and HCV-negative (HCV^-) individuals, characterizing both the decision to participate in the liver transplant waiting list and, conditional on participation, the decision to accept or refuse an organ offered for transplant. We test model hypotheses with data on the universe of patients wait-listed for a liver transplant between 2005 and 2019 from the Scientific Registry of Transplant Recipients (SRTR). The raw data highlight several clear implications of DAA availability. First, between 2014 and 2019, transplants to HCV^+ individuals declined sharply, while transplants to HCV^- individuals increased. As a result, the annual percentage of HCV^- waiting list registrants who received a transplant increased from 33% in 2014 to 65% by 2019. Second, mirroring the transplant dynamics, during this period, the data indicate a sharp reduction in the number of HCV^+ individuals, and an increase in the number of HCV^- individuals, added to the liver transplant waiting list. Third, following DAA availability, both HCV^+ and HCV^- patients receiving a transplant were healthier, as measured by the Model for End-Stage Liver Disease (MELD) score. Finally, the data indicate an overall increase in liver transplants from 2014 through 2019 (see Figure 1). While we focus on demand-side responses to DAA availability, this increase in liver transplants can only be explained by an increase in the supply of organs available for transplant, and we examine several potential explanations for this supply increase including waiting list registrants' increased willingness to accept HCV^+ organs in the post-DAA era. The raw data suggest considerable welfare improvements to both HCV^+ and HCV^- individuals resulting from the availability of DAAs: many HCV^+ patients were cured of liver disease, and both marginal and inframarginal HCV^- patients gained access to livers.

While trends in the raw data imply significant innovation-induced externalities to HCV^{-} individuals with ESLD, our main parameter of interest is the number of new transplants to HCV^{-} individuals resulting from DAA availability. That is, the relevant counterfactual is the trend in HCV^{-} transplants in the absence of DAAs. Changes in descriptive trends may be due to DAAs, but they may also be due to concurrent shocks, such as the rise of fentanyl, which significantly increased HCV transmission, opioid overdose deaths, and the supply of transplantable organs (Dickert-Conlin et al., In press; Maclean et al., 2021; Powell et al., 2019), or by the full implementation of the Affordable Care Act, which expanded health insurance coverage and increased transplant wait-listing (Lemont, 2023). To address these concurrent shocks, our identification strategy compares trends in HCV^{-} liver transplants and wait-listing behaviors before and after the introduction of DAAs to similar trends for kidneys. The basis for this approach is that a comparison between liver and kidney behaviors and outcomes will net out common shocks to the demand and supply of organs for transplant, leaving changes induced by DAAs. Using a traditional difference-indifferences (DiD) estimator, we estimate a 35.8% average annual increase in HCV^{-} liver transplants and a 39.1%decrease in HCV^+ liver transplants following the availability of DAAs, representing a total of 5,682 additional transplants to HCV^{-} individuals with ESLD from 2014 through 2019. Consistent with predictions from our model, we show that many newly transplanted HCV^{-} individuals would have remained unlisted had they not been induced to join by the reduction in demand from HCV^+ individuals; our estimates imply an average annual increase in HCV^{-} waiting list registrations of 37%. Combined with an estimated reduction in HCV^{+} waiting list registrations of 45%, we conclude that DAA availability would have eliminated the liver transplant waiting list had HCV^{-} patients not been induced to join.

Because many HCV^+ patients were cured of liver disease, additional HCV^- transplants did not crowd-out HCV^+ transplants, and that these gains added to the overall welfare benefits of DAAs. Under standard value of life assumptions, and assuming an additional 10.1 life-years per transplant (Rana et al., 2015), the net value of the

additional 5,682 HCV^- transplants amounts to \$1.25 billion per year, or \$7.52 billion in total from 2014 through 2019. This calculation may also depend on characteristics of the marginal HCV^- to be transplanted. We show that the time to transplant for HCV^- patients declined by 16%. Indeed, examining transplant rates conditional on listing, we find that the growth in HCV^- transplants outpaced the growth in waiting list demand, which suggests more frequent and/or earlier liver offers for HCV^- individuals. Furthermore, interrupted time series estimates suggest that the average HCV^- MELD score at transplant fell (improved) by three points.¹ Both these findings suggest our externality estimate is underestimated because healthier patients will likely live longer post-transplant. We also detect a composition shift in the causes of liver disease for HCV^- patients. In our data, the proportion of HCV^- registrants with alcohol-associated liver disease (ALD) increased following DAAs, which may affect expected longevity and thus our value estimate. However, this composition effect does not explain the increase in $HCV^$ waiting list registrations — using National Health and Nutrition Examination Survey (NHANES) data, we show that the prevalence of ALD in the population was flat from 2014 through 2018. In summary, we conclude that DAAs represented an innovation-induced externality that equates to roughly 11.5% of the total potential HCV^+ therapeutic market as of 2014.

Threats to the validity of our research design primarily involve spillovers from DAA availability to kidney waiting list registrants. Potential spillovers may include an increase in the supply of kidneys for transplant when newly cured HCV^+ individuals become organ donors. There could also be cases of concurrent HCV and end-stage renal disease (ESRD), whereby patients previously too sick for kidney transplantation become healthier with DAA therapy and thus eligible for transplant. Finally, kidney waiting list registrants might become more willing to accept an HCV^+ organ when DAAs are available. We test for each of these potential spillovers and find relatively small changes in kidney donations from, or transplants to, individuals with an indication of a current or prior HCV infection. We also find that willingness to accept an HCV^+ organ increased similarly among liver and kidney waiting list registrants once DAAs became available. Most importantly, between 2005 and 2013, 45% of all liver transplants went to HCV^+ patients versus only 5% of all kidney transplants, implying that the magnitude of any bias due to spillovers would be very small. Lending further credence to our research design, our estimates of the externality effect of DAAs on HCV^- transplants and waiting list registrations are larger in areas with higher baseline HCV rates.

We also conclude that the reallocation of livers from HCV^+ to HCV^- individuals resulted largely from an endogenous change in the HCV composition of the waiting list. Prior studies suggest that there was considerable room for such endogenous listing, as rates of waiting list referrals are quite low, even among qualified ESLD candidates.²

¹Because MELD score is specific to liver disease, we cannot estimate our difference-in-differences estimator on MELD score at transplant relative to kidneys.

²For example, Goldberg <u>et al.</u> (2016) found the 3-year incidence rate of wait-listing to be 15.8% among privately insured ESLD patients who met the clinical guidelines to join the waiting list and 10.0% among those with Medicaid coverage. Further, conditional on receiving an evaluation, between 30%-50% of candidates do not end up joining the liver transplant waiting list (Jesse et al., 2019;

Furthermore, prior work has documented strategic behavior in organ transplant markets (Sweat, 2023; Agarwal et al., 2021, 2018; Zhang, 2010). A key finding of these studies is that organ allocation simulation models that ignore strategic behavior generate biased predictions. For example, our estimate of the positive externality to HCV^- liver transplant recipients resulting from DAAs is larger than the estimate from an epidemiological simulation model that did not account for behavioral listing responses (Jena et al., 2016). Our results also complement prior studies that have documented a wait-listing response to organ supply shocks including the opioid epidemic and the repealing of state motorcycle helmet laws (Dickert-Conlin et al., In press, 2019; Fernandez et al., 2013). However, unlike these studies, our analysis focuses on the implications of a demand shock (i.e., reduced demand for liver transplant among HCV^+ individuals and increased demand among HCV^- individuals) rather than a supply shock. This difference is notable in that behavioral responses to a negative demand shock can provide insight into potential effects of a broader reduction in the demand for organs if alternative treatments for conditions contributing to organ failure were to be developed (e.g., improved hypertension control or diabetes treatment reducing demand for kidneys).

Our study contributes to the larger literature on technological innovation by modeling and estimating behavioral responses to treatment innovations (Baranov <u>et al.</u>, 2015; Peltzman, 2011; Dow <u>et al.</u>, 1999), and adds to recent examples of innovation-induced behavioral responses, including statin medications and diet and exercise (Kaestner <u>et al.</u>, 2014), HAART therapy and risky sex (Papageorge, 2016; Chan <u>et al.</u>, 2015), cancer treatments and labor supply (Jeon & Pohl, 2019), immunization and disease screening (Moghtaderi & Dor, 2021), and immunotherapy and life insurance (Koijen & Van Nieuwerburgh, 2019). Our findings also contribute to the literature that has examined technological change in medical and pharmaceutical treatments, its impacts on value, and whether the surplus generated by that change has primarily been captured by the innovators or by consumers (Hult & Philipson, 2023; Jena & Philipson, 2008). For example, Hult <u>et al.</u> (2018) found that, among the more than 6,000 innovations they studied, 68% of new technologies had higher quality-adjusted prices than the incumbent technologies they sought to replace. Dunn <u>et al.</u> (2023) reported similar findings and concluded that much of the total surplus generated by pharmaceutical innovation accrues to innovators rather than consumers but pointed to DAAs for HCV treatment as a clear exception. Our results imply that, in addition to the surplus captured by those treated with DAAs, welfare gains also extended to HCV^- individuals with ESLD — consumers who were not the direct beneficiaries of the technological innovation, and whose gains are not considered in current estimates of DAA cost-effectiveness.

This paper is particularly relevant for policy in liver transplantation, which exhibits significant disparities in allocation by sex, race, and geography (Darden <u>et al.</u>, 2021). Accordingly, we find that the DAA-induced increase in HCV^- transplants was larger for men (38.5%) than women (30.6%). We also find that the increase in HCV^- transplants was larger in white patients (50.7%) relative to non-white patients (17.3%), consistent with existing racial Bryce <u>et al.</u>, 2010, 2009).

disparities in access to the liver transplant waiting list (Warren <u>et al.</u>, 2021). Furthermore, with respect to geographic disparities, liver demand exceeds supply in all regions of the United States, but the Northeast has historically seen the largest wedge due to the highest demand (Fayek <u>et al.</u>, 2016). Despite finding large effects of DAA availability on liver transplants overall, we observe that the Northeast had the slowest growth in HCV^- transplants following the introduction of DAAs; HCV^- transplant rates increased in the Northeast but not significantly until 2019. Our results suggest that the innovation-induced externalities generated by DAAs were significant, but they were not equally spread across these many policy-relevant subgroups.

Specialty drugs, like those we study, have been responsible for driving the largest increases in pharmaceutical spending and have strained the budgets of public payers (ASPE, 2022; Hernandez et al., 2019). Our estimate of the innovation-induced externality of DAAs to HCV^- individuals changes the benefit-cost ratio from a public-payer perspective. For example, our main parameter of interest, the DAA-induced increase in HCV^- transplants, was largest in Medicare patients (46.2%) and smallest in Medicaid patients (20.0%). This discrepancy in transplant rates is not surprising given that DAA access for Medicaid beneficiaries was initially severely restricted, largely preventing transplant of an HCV^+ liver to an HCV^- Medicaid recipient, and that those with Medicaid coverage are less likely to join the waiting list conditional on evaluation (Thompson et al., 2022; Wahid et al., 2021; Kapadia et al., 2018; Waters & Broder, 2018; Barua et al., 2015). Valuing externalities may also play an important role in generating new ideas and innovations (Dranove et al., 2022), where pharmaceutical revenue models have moved away from relying on "blockbuster" medications and toward higher-cost drugs with smaller patient populations (van der Gronde et al., 2017; Song & Jeung-Whan, 2016).

Finally, looking forward, two states in the U.S., Louisiana and Washington, have adopted innovative subscription models to finance DAA medications for their Medicaid and incarcerated populations, with policymakers in other states expressing interest in similar arrangements (Auty <u>et al.</u>, 2022). The Biden administration has also recently introduced the "National Hepatitis C Elimination Program," which provides significant funding for the diagnosis and treatment of HCV (Fleurence & Collins, 2023). Our findings suggest that these programs, aimed at expanding access to DAA therapies, will significantly benefit HCV^- individuals with ESLD.

2 Background

2.1 Hepatitis C and Treatment Innovation

HCV is a chronic viral infection that leads to cirrhosis of the liver and its complications, including hepatocellular carcinoma (Kamal, 2008). Approximately 2.5 million people are living with HCV in the U.S., and prevalence rates have tripled over the past decade, largely as a consequence of the opioid epidemic and increased intravenous drug

use (Powell <u>et al.</u>, 2019; Zibbell <u>et al.</u>, 2018). Traditional treatments for HCV have had limited effectiveness and are associated with debilitating side effects (Burstow <u>et al.</u>, 2017). However, in December 2013, the Food and Drug Administration (FDA) approved sofosbuvir for the treatment of HCV. Sofosbuvir is a DAA that inhibits the replication of HCV's viral RNA and has shown a high resistance barrier. During the following year, three new DAAs were approved for HCV treatment, and since then, treatment with a combination of sofosbuvir (a NS5B protein inhibitor) and NS5A protein inhibitors has vastly improved sustained viral response in HCV^+ patients (Burstow et al., 2017).

The 2013 FDA approval of the DAA NS5B inhibitor sofosbuvir and the 2016 approval of a sofosbuvir/velpatasvir regimen marked a new era for HCV treatment (Burstow <u>et al.</u>, 2017). With cure rates approaching 100%, DAAs are now the frontline recommendation for treating HCV. They are also widely considered to be cost-effective (Dunn <u>et al.</u>, 2023; Chhatwal <u>et al.</u>, 2017; He <u>et al.</u>, 2017). However, despite these benefits, the high cost of DAA medications has led to significant barriers to access (Henry, 2018). Though the actual price paid for medications such as DAAs depends on a variety of factors, the wholesale acquisition cost (i.e., list price) of a 12-week course of sofosbuvir treatment was \$84,000 after its initial approval in 2013 (Roshenthal & Graham, 2016). By 2019, the median price for a course of DAA treatment fell to approximately \$37,000 as competing medications were introduced. The high cost associated with DAA treatment, along with the fact that many of those living with HCV are unaware of their disease, have led to projections of sustained HCV disease prevalence in the era of DAAs (Chhatwal <u>et al.</u>, 2016). In fact, despite the introduction of a curative therapy for HCV, U.S. deaths attributed to the virus in 2018 (3.7 per 100,000) had declined only modestly from 2013 levels (5.3 per 100,000) (CDC, 2020).

2.2 Hepatitis C, Wait-Listing, and Liver Transplant

Between 15% and 30% of those with an HCV infection experience spontaneous viral clearance (Kamal, 2008). However, for those who cannot clear the virus on their own, HCV becomes a chronic illness. Delaying treatment for HCV has serious health consequences (Erman <u>et al.</u>, 2020). Left untreated, chronic HCV can lead to cirrhosis and its complications, eventually necessitating liver transplant (Zoulim <u>et al.</u>, 2003). In fact, prior to the availability of DAAs, HCV was the leading cause of infectious-disease-related deaths in the United States (Powell <u>et al.</u>, 2019) and accounted for nearly half of all liver transplant waiting list registrations.

Joining the liver transplant waiting list requires prospective candidates to first be referred to a transplant center where they undergo a thorough medical workup along with an evaluation of financial and psychosocial factors, including degree of social support, psychiatric illness, and whether the candidate uses alcohol, tobacco, or other substances (Wahid <u>et al.</u>, 2021). While the process from evaluation to listing is informed by practice guidelines, transplant centers have latitude in how they evaluate candidates and assess transplant risk, with the

center's transplant team ultimately responsible for waiting list determinations (Martin <u>et al.</u>, 2014). Prior studies have documented low rates of evaluation referrals and wait-listing among qualified ESLD candidates. For example, Goldberg <u>et al.</u> (2016) found the 3-year incidence rate of wait-listing to be 15.8% among privately insured ESLD patients who met the clinical guidelines to join the waiting list and 10.0% among those with Medicaid coverage. Further, conditional on receiving an evaluation, between 30%–50% of candidates do not end up joining the liver transplant waiting list (Jesse et al., 2019; Bryce et al., 2010, 2009).

Within three years of wait-listing, more than 10% of liver transplant candidates will die before receiving a transplant and 20% will be removed from the waiting list without undergoing transplant—primarily due to their disease progressing to the extent that they are no longer viable transplant candidates (Kwong <u>et al.</u>, 2020). Nearly 30% of those receiving a liver transplant will experience graft failure within five years. Further complicating these issues is that untreated HCV leads to universal recurrence of infection after transplant, potentially resulting in graft loss and necessitating re-transplantation (Ciesek & Wedemeyer, 2012). HCV has historically limited the supply of transplantable livers as HCV^+ livers were commonly discarded (Levitsky <u>et al.</u>, 2017). However, since the introduction of DAAs, there has been a shift toward more frequent transplantation of HCV^+ livers, and patients have shown an increased willingness to accept an HCV^+ liver (Kwong et al., 2020; Axelrod et al., 2018).

3 Conceptual Framework

3.1 Model Overview

We present a simple discrete time model in which individuals are differentiated by their overall liver health, h_t , and by HCV, a time-invariant, individual-level, measure of baseline HCV status, $HCV \in \{HCV^+, HCV^-\}$. Consistent with the MELD score, which is the relevant measure of liver-related mortality risk in the Organ Procurement and Transplantation Network (OPTN) liver allocation mechanism, higher values of h are assumed to indicate worse liver health. The evolution of h is given by the state transition equation $f(h_{t+1}|h_t, HCV)$, which individuals (and physicians) must forecast.³ For individuals to be clinically eligible to join the transplant waiting list, their value of h must be greater than zero. In representative period t, an individual in state ($h_t > 0, HCV$) may pay p_l to join the liver transplant list, which captures the pecuniary and non-pecuniary costs of listing and visiting with physicians (e.g., travel costs, transplant workup).⁴ The listing decision, $L_t \in \{0, 1\}$, depends on expectations about transplant offers and outcomes. Once an individual joins the list, they can leave the list in three ways: by choosing to no

 $^{^{3}}$ We assume that physicians act as perfect agents for patients, which abstracts from important strategic considerations on the parts of hospitals and surgeons (Agarwal et al., 2020). By patient, we are referring to a patient/physician team.

⁴Between 40% and 50% of those referred to transplant evaluation report concern over affording the costs of travel, visits, and testing (Harding et al., 2021; Dageforde et al., 2015).

longer participate, by accepting a liver for transplant, or through death, which occurs when liver health increases beyond H^{ω} . Conditional on joining the list, in each time period t, an individual is offered a liver with probability $p(h_t, N_t, D)$, where the probability of an offer is increasing in liver health severity h and is decreasing in the number of individuals ahead on the waiting list N, where $N = N^{HCV^+} + N^{HCV^-}$ is the sum of HCV^+ and HCV^- waiting list registrants ahead. The probability is also an increasing function of the number of potential donors, D. If a liver is offered, its quality is given by $q \in [0, Q]$, where lower values of q signify a higher-quality liver.

The model takes the form of an optimal stopping problem conditional on being wait-listed for an organ, where the decision to join the waiting list is endogenous. In this sense, the model aligns with the framework of Howard (2002), who focuses on the decision to accept an organ offer, and Agarwal <u>et al.</u> (2021), who develop methods for evaluating alternative mechanisms with respect to efficiency and equity. The common thread in all these models is that individuals are allowed to endogenously respond to changes in the environment. In our case, that change is a dramatic and curative innovation for a subset of individuals on the waiting list, and we use the model to sketch out changes in equilibrium transplants under the existing allocation mechanism.

The following timeline provides an illustration of a representative period t in the model, showing the sequence of the events and decisions involved:



3.2 Liver Acceptance Behavior

Conditional on being wait-listed, an individual is either offered a liver for transplant or not. The probability of being offered a liver is given by P(h, N, D), which is defined above. If offered a liver of quality $q \in [0, Q]$, the individual must choose to accept or refuse it based on the respective values of each option. We assume that the value of accepting a liver is given as a cash-out value that depends on current liver health h, the quality of the liver received q, and lifetime income I net of transplant costs p_x :

$$V^{A}(h_{t}, HCV, q_{t}) = B^{A}(h_{t}, q_{t}, HCV, I - p_{x} - p_{l}),$$
(1)

where the superscript A indicates that the cash-out value is from accepting a liver while on the waiting list. The cashout value is a function of pre-transplant liver health as a proxy for the potential for complications from transplant, and thus we assume that B^A is decreasing in h. Because the model assumes individuals are forward-looking, the potential for the cash-out value to diminish as liver health worsens creates another incentive to accept a given liver.

Conditional on being offered a liver, the value of refusing the liver is the same as the value as if the liver had not been offered:

$$V^{R}(h_{t}, HCV) = U(h_{t}, I - p_{l}) + \delta EV(h_{t+1}, HCV).$$

$$\tag{2}$$

Here, contemporaneous utility is a function of current liver health and general consumption net of the listing fee. The value of rejecting the organ is also a function of the expected discounted value of future utility, where the expectation operator is taken over the distribution of overall liver health $f(h_{t+1}|h_t)$. The future value $V(h_{t+1}, HCV)$ depends on future liver health and on future listing and transplant acceptance decisions, which we define below. We normalize the value of death, which occurs when liver health increases beyond H^{ω} , to be zero.

Under this structure, if an individual is offered a liver, they will accept if and only if the value of accepting is greater than the value of refusing the offer: $V^A(h_t, q_t) > V^R(h_t)$. The model generates the trade-off between accepting an offer versus the value of waiting and potentially receiving a higher-quality liver in the future. We assume that individuals have rational expectations regarding the likelihood of future offers and the evolution of overall liver health h. The rational expectations assumption is more plausible in a situation in which a liver transplant surgeon/patient pair make the listing and acceptance decisions jointly. As liver health deteriorates (i.e., h increases), the incentive to accept an offer increases because the value of waiting decreases.

For a given liver health h and hepatitis C status HCV, define the liver quality \bar{q} as the quality of liver that leaves the individual indifferent between accepting and refusing an offer: $V^A(h_t, \bar{q}) = V^R(h_t)$. The associated implicit function of liver quality is a function of liver health, baseline individual-level hepatitis C status, and the waiting list count: $\bar{q}(h, HCV, N)$. This function characterizes the acceptance behavior of individuals conditional on receiving an offer, but the shape of this function with respect to h is an empirical question that depends on the relative magnitudes of the liver health evolution equation and the probability of offer function. Importantly, the number of individuals ahead of a given person negatively affects \bar{q} since N only enters in the continuation value of refusal.

3.3 Listing Behavior

The dynamics of progressing on the waiting list, based on previous list participation, are captured through expectations over the number of individuals ahead, denoted as N. In this sense, the listing decision is made every period conditional on h > 0, and the value of listing is given as:

$$V^{L}(h_{t}, HCV) = p(h_{t}, N_{t}, D) \max\{V^{A}(h_{t}, q_{t}), V^{R}(h_{t})\} + (1 - p(h_{t}, N_{t}, D))V^{R}(h_{t}),$$
(3)

which is the expected maximal value over the probability that a liver is offered. The pecuniary price of listing, p_l , affects both the value of accepting and refusing an organ by drawing from lifetime income (see Equations 1 and 2). The value of not listing is given as:

$$V^{nl}(h_t, HCV) = U(h_t, HCV, I) + \delta EV(h_{t+1}, HCV), \qquad (4)$$

where the expectation operator is taken over the distribution of overall liver health, $f(h_{t+1}|h_t)$. Contemporaneous utility is a function of liver health, HCV status, and general consumption, which we equate to permanent income I. Thus, the maximal value of entering period t in state $\{h_t, HCV\}$ is:

$$V(h_t, HCV) = \max\{V^l, V^{nl}\}.$$
(5)

To make the listing decision, the individual must forecast the state transitions both on and off the list as well as the liver offer probabilities associated with joining the list. While we have not explicitly modeled risk aversion, uncertainty surrounding future liver health generates an incentive to pay the listing cost.

3.4 Technological Change

The introduction of DAAs represents an exogenous shock in which the overall liver health of HCV^+ individuals improves (i.e., h falls). Our interest is in how DAAs affect the equilibrium level of HCV^- transplants, and our model says that this depends on the endogenous listing and organ acceptance decisions of both HCV^+ and $HCV^$ individuals. That is, both the stock of and the flow to the waiting list matter in the comparative dynamics because within the model, transplants only occur for individuals on the waiting list, and the introduction of DAAs may substantially change the health composition of those on the waiting list. The model is helpful in clarifying these effects, and it generates several hypotheses that we can test with our data. To proceed, we analyze the flow onto the waiting list, through listing decisions, and the flow off of the waiting list, through transplantation, health improvement, and death, for HCV^+ and HCV^- individuals separately. We also discuss how the health composition of the waiting list changes by group.

For the HCV^+ population, the medical implications of DAAs are clear – curative therapies obviate the need for liver transplantation. In the context of our model, for many HCV^+ patients, DAAs will push down liver health below 0, unambiguously improving their welfare and rendering these individuals ineligible for transplant. The immediate effect of this shift will be to reduce the size of the liver transplant waiting list, both by increasing HCV^+ attrition from the list and by stemming the flow of new HCV^+ patients to the list. Conditional on remaining on the waiting list, how this improvement in liver health affects acceptance behavior depends on $\bar{q}_h(h, HCV^+, N)$, the effect of changes in liver health on the quality of the liver offered that leaves an individual indifferent between accepting and refusing. On the one hand, improved liver health increases the cash-out value of transplantation (i.e., a transplant for a given donor liver quality q is more likely to be successful), which increases the likelihood that an HCV^+ individual will accept an offered organ. Furthermore, a decrease in h implies that the probability of future liver offers declines, which encourages an HCV^+ individual to accept a current offer. For both of these reasons, \bar{q} may be declining in h, which says that healthier people require a less healthy liver for transplant and thus are more likely to accept a given liver for transplant. However, \bar{q} may be increasing in h, which says that healthier people require a less healthy liver for transplant and thus are more likely to accept a given liver for transplant and thus are less likely to accept a given liver, because the value of life is increasing in liver health.

Of course, to accept a deceased donor liver for transplant, an individual must be on the waiting list, and the introduction of DAAs will significantly reduce the number of HCV+ individuals eligible for the list. Furthermore, because HCV^+ health improves, participating in the waiting list may no longer be worth the listing price p_l . Additionally, the probability of being offered a liver declines as h declines, which implies that the value of wait-listing declines, and an HCV^+ individual is less likely to choose to list. Yet because HCV^+ liver health improves, some HCV^+ individuals who would have died in the absence of DAAs remain on the waiting list, and thus the number and health composition of HCV^+ individuals on the waiting list remains ambiguous.

For HCV^- individuals, the comparative dynamics are simpler because DAA availability does not directly affect an HCV^- individual's health. For an HCV^- individual, DAAs change the values of listing and accepting an organ through the number of individuals ahead on the waiting list. If the count of HCV^+ waiting list registrants falls, then HCV^- individuals on the list may be less likely to accept a liver offer because the likelihood of future offers increases (i.e., $\bar{q}_N(h, HCV, N) < 0$). On the other hand, transplantation cannot occur without an offer of a liver, and if the probability of being offered a liver in period t increases because N falls, then, all else equal, HCV^- transplants may increase. At the listing stage, the model suggests that the value of listing increases if N falls because the likelihood of liver offers increases.

The extent to which the total number of transplants changes with DAAs will depend on the supply of livers. If liver supply is perfectly inelastic, then shifts in the demand for livers will represent transfers of livers from HCV^+ to HCV^- individuals. However, in this case, under the assumption that utility is increasing with improved liver health, DAAs remain welfare-enhancing because HCV^+ individuals who are cured are better off than if they were to receive a transplant and because HCV^- individuals are choosing to accept newly available organs. Further, to the extent that liver supply also increases, either because of more deceased donor organs from HCV^+ individuals or because willingness to accept an HCV^+ liver for transplant increases, then welfare gains will be even larger.

To summarize, the model clarifies the mechanisms by which DAAs will affect the welfare of HCV^+ and $HCV^$ individuals with liver disease. It highlights that changes in *levels* of equilibrium transplants will depend on the endogenous listing behavior of each group. This suggests that regressions of equilibrium transplant levels, which depend on both transplant acceptance probabilities and waiting list enrollment decisions, may generate different results than regressions of equilibrium transplant rates, which are conditional on waiting list size. Furthermore, the model highlights how HCV^- individuals, who are external to the market for DAAs, may still be affected by their introduction. That is, while the health of HCV^- individuals is not directly affected by DAAs, transplant offers change because of the direct health effects to HCV^+ individuals, and changes in transplant offers change $HCV^$ listing behavior.

Our data are well-suited to capture these changes. In what follows, we document raw trends in liver transplants and waiting list additions. We also describe changes in the health composition of the liver transplant waiting list by examining trends in MELD scores, time from listing to transplant, and waiting list exits due to condition improvement or death. Finally, our data also allow us to investigate an unmodeled, but potentially important, dynamic in the willingness of waiting list registrants to accept an HCV^+ liver for transplant. DAA availability may represent an increase in D, the supply of donors, and shift candidate preferences such that HCV^+ livers become more attractive, which would affect the number of livers available for transplant. The implication of such a change would be to increase liver offers, allowing for greater selectivity among transplant candidates. Following our presentation of the raw data, we present plausibly causal evidence on the comparative dynamics suggested by our theory from a research design in which we compare trends in liver transplant waiting list behavior and transplant outcomes to similar trends for kidneys.

4 Data and Descriptive Trends

4.1 Data Description and Summary Statistics

We use data from the Scientific Registry of Transplant Recipients (SRTR) from 2005 to 2019.⁵ SRTR collects individual-level data on the universe of organ transplant waiting list registrants, donors, and transplant recipients from the United Network for Organ Sharing (UNOS) (Wright, 2022).⁶ Using the SRTR data, we can calculate changes to the extensive margin of the liver transplant waiting list, including the number of registrants currently wait-listed and the number of those added and removed from the waiting list. We can also observe waiting list registrant characteristics including age, sex, race, ethnicity, source of insurance coverage, and the donation service

⁵The SRTR data system includes data on all donors, waiting list registrants, and transplant recipients in the U.S., submitted by the members of the Organ Procurement and Transplantation Network (OPTN). The Health Resources and Services Administration of the U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

⁶A small number of people receive a liver transplant without being wait-listed. Our transplant measure includes those receiving a transplant whether they are wait-listed or not.

area (DSA) where each registrant wait-lists.⁷ In addition, the data allow us to track the severity of registrants' liver disease through their MELD score, where a higher score indicates a higher mortality risk. Throughout the analysis, we exclude individuals younger than 18 years at time of wait-listing or receiving a transplant since minors face different allocation rules and procedures than adults.

While the SRTR data do not allow us to observe HCV status at the time of waiting list registration, they do include HCV status determined by an antibody test for those receiving a transplant. We use this information to infer the HCV status of waiting list registrants by examining the prevalence of primary diagnosis codes commonly found among HCV^+ but not HCV^- liver transplant recipients, and vice versa. For example, 59% of HCV^+ transplant recipients have a diagnosis of "cirrhosis: type C" (SRTR code 4204) compared to only 2.2% of HCV^{-} recipients. Similarly, "alcoholic cirrhosis with hepatitis C" (SRTR code 4216) is observed in 13.3% of HCV^+ transplant recipients and only 0.6% of HCV^- recipients. Conversely, "cirrhosis: fatty liver (NASH)" (SRTR code 4214) is found among 14.3% of HCV^- transplant recipients compared to only 0.6% of HCV^+ recipients. Likewise, "alcoholic cirrhosis" (SRTR code 4215) is present in 26.7% of HCV^- transplant recipients and only 3.5% of HCV^+ recipients. We take a conservative approach and classify a diagnosis code as HCV-related if its rate of occurrence among HCV^+ transplant recipients is at least four times greater than its rate of occurrence among HCV^{-} recipients, and vice versa. After assigning registrants based on their primary diagnosis codes, we identify additional HCV^+ waiting list registrants using an optional diagnosis text description field. The strings in this description field include terms such as "HCV," "Hepatitis C," "Hep C," as well as variations that may include periods, dashes, slashes, or minor typos.⁸ Although we know the actual HCV status of transplant recipients, for consistency, we use inferred status in all regression analyses. In practice, our estimates using inferred HCV status are likely to be conservative, since we expect that misidentifying some HCV^+ individuals as HCV^- and vice versa would bias our estimates toward zero.⁹ For approximately 15% of waiting list registrants, neither the diagnosis code nor the text description allow us to assign an HCV status, so we exclude those individuals from our analyses.

⁷Due to changes over time in the existence and services of certain DSAs, we use modified DSA identifiers throughout our analyses and proceed in three steps. First, we combine the Sierra Donor Services DSA into the Donor Network West DSA in California since Sierra Donor Services ended their liver program in 2008/2009 and was geographically entirely surrounded by Donor Network West. Second, the Mississippi Organ Recovery Agency began operating in 2013, so we combine that DSA with their pre-existing contiguous DSAs in Tennessee and north Mississippi, Louisiana, and Alabama. Third, because Lifelink of Southwest Florida ended in 2004, OurLegacy in Florida started in 2007, and Lifelink Puerto Rico started in 2012, we combine all Florida and Puerto Rico DSAs into one DSA unit.

⁸Using this approach, 1,804 additional registrants (roughly 120 per year) can be flagged as HCV^+ relative to the 93,547 registrants (roughly 6,236 per year) who are identified as HCV^+ or HCV^- using only their diagnosis code.

⁹For example, our coefficient estimate of the effect of DAA availability on transplants to HCV^- recipients is 0.31 log points using inferred HCV status versus 0.37 log points when using actual HCV antibody status. Also, since HCV antibodies remain even after achieving viral clearance, we are able to use HCV antibody status at time of transplant to assess whether our HCV^- classification might capture those with a cured HCV infection, thus potentially overstating DAA-associated changes in HCV^- wait-listing. We find no evidence of this. For example, in 2014, 99 (3.2%) of the 3,128 liver transplant recipients that we categorized as HCV^- based on diagnosis codes tested positive for HCV antibodies at the time of transplant, compared to 206 (3.3%) of the 6,180 liver transplant recipients categorized as HCV^- in 2019.

Table 1 presents descriptive statistics for liver transplant waiting list registrants by HCV status and over time. Waiting list registrations among HCV^+ individuals with ESLD dropped from an average of 3,896 per year (35,068 total) over the 9 pre-DAA years in our sample to an average of 2,405 per year (14,431 total) across the 6 post-DAA years. The number of waiting list removals and transplants among HCV^+ registrants also dropped after DAAs became available, from 4,017 per year (36,157 total) to 2,984 per year (17,901 total). In contrast, yearly waiting list registrations, removals, and transplants increased among HCV^- individuals with ESLD, going from 5,191 to 7,804 average yearly listings, and from 5,163 to 7,776 average yearly removals and transplants. The most common outcome of the wait-listing process is a transplant from a deceased donor, followed by removal from the waiting list due to condition deterioration or death. For both HCV^+ and HCV^- registrants, the probability of removal due to condition deterioration or death fell in the period following DAA availability, while removal due to condition improvement increased. MELD scores indicate that, on average, HCV^- registrants face a higher mortality risk than HCV^+ registrants. Due in part to the lower average MELD score for HCV^+ registrants, the time from listing to transplant is longer for those with HCV. The descriptive statistics indicate an increase in time to transplant in the DAA era for HCV^+ registrants and a decrease for HCV^- registrants. The majority of waiting list registrants are privately insured, between the ages of 40 and 64, and live in the South census region.

4.2 Trends in Equilibrium Transplants and Liver Demand

Figure 1 shows the equilibrium number of liver transplants over our sample period, both overall and by HCV status. We see a clear trend break following the introduction of DAAs, as the total number of liver transplants increased from 6,190 in 2014 to 8,330 in 2019. This total increase in transplants reflects both a significant reduction in transplants to HCV^+ individuals (solid line) and a significant increase in transplants to HCV^- individuals (long-dashed line). To quantify changes in raw trends, we estimate a series of comparative interrupted time series (CITS) models. CITS is a more general form of the difference-in-differences design where each group is compared to its own baseline trend rather than to a counterfactual generated by an untreated group, and is appropriate in this case because, consistent with our behavioral model above, both HCV^+ and HCV^- waiting list registrants are potentially affected by the development of DAAs. We stress that this exercise is meant to be descriptive in nature — we do not interpret CITS estimates as causal effects, but they serve as useful benchmarks to which we will compare difference-in-differences estimates in later sections. A description of the CITS specification, as well as the full set of CITS results, can be found in Appendix Section 1.¹⁰ From 2014 to 2019, the number of HCV^- liver transplant recipients increased by an average of 53.6% relative to their baseline trend, while the number of HCV^+ individuals

¹⁰When interpreting the magnitudes of the changes implied by the coefficient estimates from logged outcome models, we use the following calculation: $\%\Delta = 100 \times (e^{estimate} - 1)$.

receiving a transplant decreased by an average of 55.7%. Before 2014, approximately 30% of HCV^+ and HCV^- waiting list registrants received a liver transplant each year, and the trends in this outcome were flat for both groups; by 2019, the share of HCV^- registrants who exited the waiting list because they received a transplant stood at nearly 65%.¹¹

Conceptually, changes in equilibrium transplants shown in Figure 1 reflect both changes in the demand and supply of livers. In Section 5.2.3, we return to the issue of how DAAs may have changed the supply of livers, but our primary statistical and econometric exercises focus on demand-side effects. To study the role of these effects on equilibrium levels of transplants, we begin by documenting trends in waiting list additions and removals. Figure 2a presents trends in the number of liver transplant waiting list registrants, both overall and by HCV status. Between 2005 and 2012, both the size and HCV composition of the waiting list were relatively flat and stable. From 2013 to 2019, the total waiting list count fell from 16,738 to 13,911 registrants, and the composition of the waiting list shifted toward HCV^- registrants. Changes in waiting list size could be driven by the changes in transplant volume documented in Figure 1, but they could also result from changes in the flow of patients to the list. Indeed, because Figure 2a shows a decline in the size of the list, our model predicts that marginal ESLD patients will be induced to join the list. Figure 2b shows that following the introduction of DAAs, waiting list additions for HCV^+ registrants sharply declined, while additions for HCV^- registrants increased. The estimates from our CITS models indicate an average increase in waiting list additions of 22.6% from 2014 to 2019 for HCV^- registrants and an average decrease of 51.4% for HCV^+ registrants relative to each group's baseline mean.

To examine these changes in the health composition of the waiting list, we track trends in average MELD scores at listing and at transplant, as well as waiting list attrition due to condition deterioration/death and condition improvement before and after the introduction of DAAs. Detailed results are provided in Appendix Sections 2 and 3, and we briefly summarize our findings here. Average MELD scores at listing and at transplant were rising (i.e., worsening health) for both HCV^+ and HCV^- registrants between 2005 and 2013 (Appendix Figures 1a and 1b). HCV^+ registrants saw steep declines in average MELD scores at listing and at transplant coinciding with the introduction of DAAs, while the growth rate in average MELD score at listing slowed for HCV^- registrants and average MELD score at transplant fell. CITS estimates of changes in MELD scores associated with the introduction of DAAs are consistent with health improvements for both HCV^+ and HCV^- liver waiting list registrants (Appendix Table 2). The likelihood of leaving the waiting list because of deteriorated condition or death was increasing for both groups through 2013 before declining once DAAs became available (Appendix Figure 2a and Appendix Table 3). HCV^- registrants were consistently more likely to leave the waiting list due to condition improvement compared to HCV^+ registrants in the pre-DAA period, but this relationship reversed shortly after the introduction of DAAs

 $^{^{11}\}mathrm{We}$ present trends in transplant rates in Appendix Figure 3.

(Appendix Figure 2b and Appendix Table 3).

There are several key takeaways from the patterns we observe in transplant, wait-listing behaviors, and the health composition of liver waiting list registrants. We document an increase in the number of liver transplants following the introduction of DAAs that is driven entirely by HCV^{-} recipients. We also see significant reductions in both the number of HCV^+ waiting list registrants and transplants to HCV^+ recipients. These patterns highlight the extent of the positive externalities of DAA development that have accrued to HCV^{-} individuals with ESLD. Namely, reduced demand for livers from HCV^+ individuals has resulted in greater organ availability for HCV^- individuals. $HCV^$ waiting list registrants and transplant recipients appear to be healthier following the availability of DAAs and, since DAAs do not directly impact the health of those without HCV, this suggests changes in the health of the marginal HCV^{-} registrant. Therefore, we conclude that the post-DAA growth in HCV^{-} liver waiting list registrants is primarily a function of marginal candidates entering the waiting list (i.e., individuals who likely would not have wait-listed in the absence of DAA-induced changes to the value of listing). This interpretation is supported by prior research which has found that fewer than half of those who met the clinical guidelines to join the liver transplant waiting list actually did prior to DAAs (Jesse et al., 2019; Goldberg et al., 2016; Bryce et al., 2010, 2009). Further, HCV^{-} waiting list registrants were more likely to suffer from ALD in the post-DAA period and those with ALD comprised the bulk of new waiting list additions (see Appendix Table 4). Evidence indicates that physicians assign lower waiting list priority to ESLD patients who use alcohol and that pre-DAA rates of liver transplant wait-listing among those with ALD were as low as 5% (Leong & Im, 2012). Finally, lower average MELD scores for HCV^{-} recipients prior to transplant, whether due to a compositional change or shorter times from wait-listing to transplant (see Appendix Figure 7 and Appendix Table 5), have implications for graft survival and the benefits associated with transplant. We return to this point later in our discussion of the value of the innovation-induced externalities generated by DAAs in Section 6.

5 Research Design: Comparing Trends in Livers and Kidneys

While trend estimates imply substantial gains to HCV^- individuals with ESLD associated with the timing of DAA introduction, the lack of a comparison group that is unaffected by the availability of DAAs could limit our ability to address potential sources of confounding. For example, a supply shock common to both the liver and kidney transplant waiting list concurrent with the introduction of DAAs is the increase in the availability of transplantable organs associated with the rising number of drug overdose deaths (see Appendix Figure 5). From 2014 to 2019, drug overdose deaths from synthetic opioids, including fentanyl, increased by an average of 58% per year compared to an average increase of 12% per year between 2005 and 2013, leading to an estimated 25,000-plus additional organ

transplants (Dickert-Conlin <u>et al.</u>, In press). Similarly, the Affordable Care Act's Medicaid expansions, which 26 states and Washington D.C. adopted in 2014, led to increased organ waiting list registrations (Lemont, 2023). CITS models are unable to distinguish between concurrent shocks, and thus return the combined effect of DAAs and drug overdose deaths or health insurance gains on changes in transplant and waiting list registration.

To separately identify the impact of DAAs from concurrent shocks, we estimate a traditional difference-indifferences (DiD) design that compares equilibrium liver transplants and liver demand (i.e., waiting list additions) for both HCV^+ and HCV^- individuals to similar outcomes and behaviors for end-stage renal disease patients before and after the introduction of DAAs. To the extent that secular trends in the supply or demand for transplantable organs are reflected similarly among HCV^- liver waiting list registrants and those on the kidney waiting list, the DiD strategy will improve our ability to isolate the reallocation effects of DAAs on the listing behaviors and outcomes for HCV^- registrants and estimate the value of the innovation-induced externality. For example, insofar as the magnitude of the drug overdose supply shock was similar for both HCV^- liver waiting list registrants and kidney waiting list registrants, our DiD models will difference out the influence of overdose deaths, allowing us to isolate the effect of DAAs. Similarly, Lemont (2023) shows that Medicaid expansion was associated with comparable increases in both liver and kidney waiting list registrations (34% for livers and 38% for kidneys) and transplants (40% for livers and 50% for kidneys) for Medicaid beneficiaries.¹²

Data on equilibrium kidney transplants and waiting list additions also come from SRTR, and Appendix Table 6 provides descriptive statistics for these data.¹³ For a comparison of liver and kidney trends to produce credible causal estimates of the effect of DAA availability on transplants and listing behaviors for HCV^- individuals with ESLD, baseline differences in outcomes between liver and kidney transplant recipients and waiting list registrants must remain stable over time in the absence of DAAs. While this parallel trend assumption is not directly testable, we provide suggestive evidence that it holds by plotting trends in equilibrium kidney and liver transplants and waiting list registrations, we plot log trends in Figure 3 and use log outcomes in our DiD regression models. Trends in kidney transplants (Figure 3a) and waiting list additions (Figure 3b) track closely with trends in liver transplant and waiting list additions through 2013, providing no indication of a violation of the parallel trends assumption.

We estimate the following DiD specification separately for HCV^+ and HCV^- liver transplant recipients and

 $^{^{12}}$ In a subsample of states yet to expand Medicaid by 2019, estimates of DAA effects on transplants and wait-listing behavior were similar to those from our full sample and are available upon request.

 $^{^{13}}$ We exclude known HCV^+ kidney transplant waiting list registrants based on optionally provided diagnosis text from our control group in all analyses, which amounts to only 0.13% of all kidney candidates from 2005 to 2019. For reference, HCV^+ kidney transplant recipients account for fewer than 5% of all recipients in our data based on antibody tests at the time of transplant. Because five kidney DSAs do not have a liver program, our sample includes 50 modified DSA identifiers for kidneys and 45 modified DSA identifiers for livers.

waiting list registrants using kidney transplant recipients and waiting list registrants as controls:¹⁴

$$Y_{dlt} = \beta [\mathbb{1}(l = liver) \times DAA_t] + \gamma_{dl} + \eta_t + \epsilon_{dlt}, \tag{6}$$

where Y_{dlt} is the outcome for DSA d, organ $l \in \{liver, kidney\}$, in year t. The treatment effect of interest is β , which is the coefficient on the interaction between the indicator for liver (i.e., treated) or kidney (i.e., control) transplant recipient/waiting list registrant and DAA_t , the indicator for the post-DAA period (2014–2019). Finally, we include DSA-by-organ fixed effects γ_{dl} , year fixed effects η_t , and an idiosyncratic error term ϵ_{dlt} clustered at the DSA-by-organ level.

Table 2 contains our DiD estimates of the effects of DAA availability on liver transplants (columns 1 and 2) and liver transplant waiting list additions (column 3) for HCV^- individuals (Panel A) and HCV^+ individuals (Panel B). The estimates in columns 1 and 3 are from models where the dependent variables are measured in logs, while the estimate in column 2 is from a model where the dependent variable is defined as a fraction of the HCV-specific number of registrants on the waiting list (i.e., the transplant rate). Thus, estimates in column 2 effectively remove the influence of DAA-induced changes to waiting list inflows and outflows and provide an indication of how DAAs impacted transplants conditional on wait-listing.

Table 2, column 1 presents transplant estimates and underscores the substantial externality accruing to $HCV^$ individuals with ESLD seeking transplant as a result of DAA availability. Average annual liver transplants for $HCV^$ recipients increased by $100 \times (e^{0.3059} - 1) = 35.8\%$ relative to changes in kidney transplants from 2014 through 2019. Estimates in Panel B clearly show that the gains to HCV^- transplant recipients came from the reallocation of transplantable livers from HCV^+ individuals who no longer needed a transplant. We estimate that DAAs reduced average annual liver transplants for HCV^+ individuals by 39.1% relative to kidney transplants.

Estimates of DAA-induced changes in HCV-specific transplant rates in Table 2, column 2 indicate that transplants to HCV^- recipients increased relative to the number of HCV^- waiting list registrants (16.0 percentage points, 31.6%). In other words, DAA-induced transplant gains to HCV^- recipients were (proportionally) larger than the net overall growth in waiting list additions, suggesting that HCV^- waiting list registrants were receiving more frequent and/or earlier liver offers. Consistent with this interpretation, we show in Appendix Figure 7 and Appendix Table 5 that the time to transplant for HCV^- patients declined by 16% following the introduction of DAAs. The transplant rate estimate for HCV^+ registrants in Panel B, column 2 is positive (5.8 percentage points, 11.4%) and, while not statistically significant at conventional levels, suggests that DAAs conferred modest benefits to HCV^+ individuals who remained on the waiting list. We interpret this finding as evidence that the large, estimated reduction

 $^{^{14}}$ We primarily report OLS estimates using logged outcomes throughout the paper. We also estimated Poisson regressions that generated virtually identical results that are available upon request.

in transplants to HCV^+ recipients in Panel B, column 1 was driven entirely by the reduction in transplant demand from HCV^+ individuals who were cured by DAA treatment.

Estimates of the effect of DAAs on liver transplant waiting list additions are presented in Table 2, column 3. DAAs increased HCV^- liver waiting list additions by an average of 36.8% relative to kidney waiting list additions from 2014 through 2019 and decreased HCV^+ liver waiting list additions by an average of 45.4%.

We also estimate a time-disaggregated (i.e., event study) version of our DiD specification:

$$Y_{dlt} = \sum_{k=2005}^{2019} \beta_k [\mathbb{1}(l = liver) \times \mathbb{1}(t = k)] + \gamma_{dl} + \eta_t + \epsilon_{dlt},$$
(7)

where the vector of the coefficient estimates, β_k , reflects the time-specific differences in outcomes between liver and kidney waiting list registrants and transplant recipients. We specify the baseline period as 2012 in our event study models so that we can detect any potential anticipatory effects occurring in 2013 as DAAs became available in December of that year. These estimates allow us to investigate whether there were any differential pre-intervention trends between liver and kidney transplant recipients and waiting list registrants as well as the dynamics of the treatment effects across the post-treatment periods.

Figure 4 presents event study estimates that correspond to the DiD transplant and wait-listing estimates in Table 2 (see Appendix Figure 4 for transplant rate event studies). Relative to kidney transplants and waiting list additions, Figure 4a shows a clear decline in liver transplants to HCV^+ recipients, and Figure 4b shows a clear decline in liver waiting list additions from HCV^+ individuals. In both cases, trends in the pre-DAA period were flat, with annual estimates growing monotonically over time from 2013/2014. Results are a mirror image for HCV^- individuals – both liver transplants (4c) and liver waiting list additions monotonically increase (Figure 4d), with little evidence of differential pre-trends. Our event study estimates imply that DAAs led to an additional 1,648 HCV^- people joining the liver transplant waiting list per year, on average, or 9,888 total HCV^- additions to the liver transplant waiting list from 2014 to 2019. On average, DAAs reduced HCV^+ liver transplant waiting list additions by 1,616 people each year for a total of 9,693 fewer HCV^+ additions to the liver transplant waiting list from 2014 to 2019.

5.1 Heterogeneity in *HCV⁻* Transplants

To investigate heterogeneity in benefits for HCV^- patients, Table 3 presents DiD estimates from Equation 6 of the effect of DAA availability on liver transplants to HCV^- individuals by primary payer, sex, age, race, and payer-by-census region. HCV^- transplant gains were slightly larger for those with Medicare coverage (46.2%) than for those with private insurance coverage (36.9%) and they were notably smaller for those with Medicaid as their primary payer (20.0%). The explanation for this difference likely stems from two factors. First, those with

Medicaid coverage are less likely to progress through the transplant evaluation process and onto the waiting list. potentially limiting the benefits of the DAA-induced shock for HCV^- Medicaid beneficiaries (Wahid et al., 2021). We evaluate the association between DAA availability and waiting list additions by payer in Appendix Table 7 and find mixed support for this channel. Relative increases in waiting list additions were twice as large for Medicare beneficiaries compared to Medicaid beneficiaries. However, there was no substantial difference in changes in waiting list additions between Medicaid beneficiaries and those with private insurance coverage. Second, widespread DAA access restrictions in state Medicaid programs were prevalent in the initial years of DAA availability and, in some instances. remain in place today.¹⁵ The most common forms of DAA access restrictions employed by state Medicaid programs include liver damage restrictions requiring demonstration of advanced fibrosis, sobriety clauses that include abstinence attestation or substance use screening, and prescriber restrictions that require DAA prescribers to be specialist physicians (Roundtable & Center for Health Law & Policy Innovation, 2017). In 2014, at least 33 state Medicaid programs had liver damage restrictions in effect, at least 35 states had sobriety restrictions in effect, and at least 29 states had some form of prescriber restriction in effect (Roundtable & Center for Health Law & Policy Innovation, 2019). By late 2019, only 8 states maintained liver damage restrictions, but the number of state Medicaid programs with active sobriety and prescriber restrictions remained largely unchanged since 2014.¹⁶ Not only do these restrictions limit DAA access for HCV^+ Medicaid members, but they also largely preclude transplants of HCV^+ organs to HCV^- recipients, a practice that has become more common in the DAA-era (Chhatwal et al., 2018). Appendix Table 8 includes interrupted time series estimates of changes in liver transplants from HCV^+ donors to HCV^{-} recipients and confirms that relative changes were smaller for Medicaid beneficiaries than for those with Medicare or private insurance coverage.

Table 3, Panel A, columns 4 and 5 include estimates of the effect of DAA availability on transplants to HCV^- recipients by sex. Relative effects were larger for men (38.5%) than for women (30.6%), a finding consistent with prior work that has found women are less likely than men to receive a liver transplant (Darden et al., 2021). Panel B, columns 1 through 3 show that older HCV^- transplant recipients saw larger relative gains due to DAA treatment availability compared to younger recipients. We estimate a 21.9% average gain in HCV^- transplants for those between the ages of 18 and 39, a 21.6% average gain for those ages 40 to 64, and a 43.0% average gain for those ages 64 and older. Panel B, columns 4 and 5 show that HCV^- transplants to white recipients increased by 50.7% on average, compared to a relative increase of only 17.3% for non-white recipients. Despite a higher burden of chronic

¹⁵These restrictions were not present to the same degree for those with private coverage and Medicare. However, insurer denials for DAA therapy among the privately insured are common (Edmonds et al., 2022; Gowda et al., 2018; Lo Re III et al., 2016).

¹⁶In many cases, Medicaid sobriety and prescriber restrictions weakened between 2014 and 2019. For example, 14 state Medicaid programs restricted DAA prescribing to specialists in 2014 compared to only 3 states in 2019. However, most states dropping the specialist prescribing restriction maintained a requirement that DAAs must still be prescribed in consultation with a specialist (Roundtable & Center for Health Law & Policy Innovation, 2019).

liver disease among racial and ethnic minorities, several studies have documented long-standing disparities in access to liver transplant for minority groups (Nephew & Serper, 2021; Wahid <u>et al.</u>, 2021). The introduction of MELD scores as a determinant of transplant allocation in 2002 appears to have largely eliminated the racial gap in liver transplant conditional on wait-listing (Moylan <u>et al.</u>, 2008). However, Black and Hispanic individuals continue to experience reduced access to the waiting list (and thus transplant) (Rosenblatt et al., 2021; Warren et al., 2021).

Panel C includes estimates of the effect of DAA availability on HCV^- liver transplants by U.S. census region separately by payer. Two notable findings emerge as a result of this subgroup analysis. First, we find little to no effect of DAAs on HCV^- liver transplants for recipients living in the Northeast census region. This census region includes UNOS regions 1 and 9 as well as parts of region 2, which had among the lowest liver transplant rates for waiting list participants conditional on MELD score in the pre-DAA era (Rana <u>et al.</u>, 2015; Yeh <u>et al.</u>, 2011). We estimate DAA effects on liver transplant and waiting list outcomes separately for the Northeast census region and provide results in Appendix Table 9. These estimates strongly indicate that the lack of transplant gains to the HCV^- ESLD population in the Northeast stems from a much smaller increase in HCV^- waiting list additions compared to other regions. Second, while our regional estimates for Medicaid beneficiaries in the South, Northeast, and Midwest are consistent with our overall estimates, Medicaid beneficiaries in the West census region experienced a relative increase in HCV^- liver transplants similar to the effects observed for those with private insurance coverage and those with Medicare. One potential explanation for this finding is that California was one of eight states that had eliminated all liver damage restrictions, sobriety clauses, and prescriber restrictions for Medicaid beneficiaries by 2019 (Roundtable & Center for Health Law & Policy Innovation, 2019).

Last, we conduct a heterogeneity analysis that allows the effect of DAAs on transplants and wait-listing for $HCV^$ patients to vary by baseline DSA HCV prevalence. Technically, the regression specification is a triple differences strategy where we compare liver transplant recipients and waiting list registrants to kidney recipients/registrants and allow that comparison to vary by the baseline share of DSA transplant recipients testing positive for HCV. The intuition behind this approach is that the demand response to DAA availability from HCV^+ individuals with ESLD should be larger in areas with greater HCV prevalence, freeing more livers for transplant to HCV^- recipients listing in these areas. To conserve space, we allocate these results to Appendix Table 10, but we note here that the estimates from this specification indicate a strong dose-response relationship between HCV prevalence and both HCV^- wait-listing and transplants to HCV^- recipients. For example, HCV^- individuals listing or transplanted in DSAs with above-median rates of pre-DAA HCV prevalence saw nearly twice the relative increase in both waiting list additions and transplants compared to those in DSAs with below-median HCV prevalence.

5.2 Robustness

5.2.1 Concurrent Shocks

Our conceptual model suggests that the value of wait-listing for HCV^- individuals increases when the number of HCV^+ waiting list registrants falls, and so we expect to see increased HCV^- wait-listing following the introduction of DAAs.¹⁷ However, a competing explanation for the observed pattern in HCV^- wait-listing in Table 2 would be concurrent changes in the prevalence of non-HCV conditions leading to ESLD. To distinguish between these explanations, we first estimate changes in waiting list additions by leading non-HCV disease indicators for wait-listing including nonalcoholic steatohepatitis (NASH) and ALD.¹⁸ These estimates are included in Appendix Table 4 and indicate that HCV^- waiting list additions following DAAs are being driven by individuals with ALD. Second, we use data from the NHANES to track ALD prevalence rates among adults in the U.S. using established guidelines for identifying ALD (Younossie et al., 2011). Appendix Figure 6 plots the prevalence of ALD throughout our sample period, indicating a small uptick in 2015/2016 followed by a return to pre-DAA levels by 2017/2018.¹⁹ So, while post-DAA additions to the liver transplant waiting list were predominantly driven by HCV^- registrants with ALD, this appears to be a compositional change that aligns with our discussion of DAA-induced wait-listing for "marginal" registrants in Section 4.2.

5.2.2 DAA Spillovers to Kidney Transplants

Another consideration of using characteristics of kidney transplant recipients and waiting list registrants to generate the counterfactual for our DiD models is that DAA effects may spill over to individuals with ESRD. This can happen in several ways. First, the availability of DAAs may increase the willingness of kidney transplant waiting list registrants to accept an HCV^+ organ. Second, individuals who are cured of HCV may become organ donors.²⁰ Third, those cured of HCV may become less likely to develop ESRD and join the kidney waiting list,²¹ or if they already have ESRD, they may become healthy enough for a kidney transplant.

In Figure 5, we assess each of these potential spillover pathways through which DAAs could induce changes in

 20 Using a simulation model and data from the United Kingdom, Jena <u>et al.</u> (2019) estimate that curing 240,000 cases of HCV and then implementing universal screening and treatment would lead to an additional 127 kidney transplants per year.

²¹This is because HCV potentially increases the risk for developing ESRD (Lee $\underline{\text{et al.}}$, 2014).

¹⁷According to our conceptual model, marginal HCV^- individuals are induced to join the waiting list due to the increased likelihood of a transplant associated with DAA availability and because of a reduced time from listing to transplant. Appendix Figure 7 plots trends in time from wait listing to transplant for HCV^- recipients and shows a steep decline following the introduction of DAAs. Estimates in Appendix Table 5 indicate that the time from wait-listing to liver transplant fell by 16.0%, on average, for HCV^- liver waiting list registrants compared to kidney waiting list registrants following the introduction of DAAs.

¹⁸An individual in our sample was considered to have NASH/ALD when NASH/ALD was listed as a primary diagnosis or when hepatocellular carcinoma was listed as a primary diagnosis with a secondary diagnosis of NASH/ALD.

 $^{^{19}}$ We cannot include NHANES data for 2019 in our ALD prevalence rate estimates as the 2019/2020 NHANES data collection was halted due to COVID-19.

the supply or demand for transplantable kidneys. Figure 5a shows a clear increase in the willingness of both kidney and HCV^- liver transplant waiting list registrants to accept an HCV^+ organ. We take this as evidence of a similar demand response among kidney waiting list registrants to the availability of DAAs. Therefore, our DiD estimates will isolate the decreased demand for transplantable livers associated with DAAs for HCV^+ registrants and its effect on HCV^- individuals, excluding gains associated with increased willingness to accept an HCV^+ liver. As a result, our DiD analyses will represent lower bound estimates of DAA-induced externalities.

Figure 5b examines whether DAAs affected the supply of kidneys available for transplant in the case where those newly cured of HCV became living kidney donors. Since HCV status is determined through an antibody test and antibodies remain even after achieving viral clearance, we can examine whether the number of living kidney donors with HCV antibodies increased following the availability of DAAs. The figure indicates a slight increase in donors with HCV antibodies from 2012 to 2013, just before DAA availability. However, the magnitude of this increase is quite small, representing approximately 20 additional living donors with HCV antibodies per year, or about 0.3% of all living donors. Figures 5c and 5d plot the log number of HCV^+ transplant recipients and the share of recipients who are HCV^+ for both livers and kidneys. If DAAs impacted demand for kidneys through improved health for those with ESRD, we would expect to see fewer HCV^+ kidney transplant recipients (similar to the effects for HCV^+ liver transplants). Instead, we see an uptick in the number of HCV^+ kidney transplant recipients in Figure 5c and no discernible change in the share of kidney transplant recipients who are HCV^+ from 2013 to 2019 in Figure 5d.

Finally, while the descriptive evidence in Figure 5a indicating an increased willingness to accept an HCV^+ liver is consistent with predictions from our conceptual model, the model also predicts that waiting list registrants will become more selective when demand from HCV^+ individuals falls and liver offers increase. We assess changing selectivity by estimating the effect of DAAs on livers discarded due to "poor quality" in Appendix Table 11.²² Overall, the average annual number of livers discarded due to poor quality rose by 14.7% from 2014 through 2019 compared to kidneys (column 1) and the fraction of livers discarded increased by 2.4 percentage points (16%, column 2). Alternatively, estimates in column 3 of Appendix Table 11 show that there was no relative increase in the share of HCV^+ livers discarded due to poor quality following DAA availability. We interpret these results as suggestive evidence that transplant candidates became more selective after DAAs became available, but that HCV status was no longer viewed as a marker of poor organ quality.

²²We define a discard as being due to "poor quality" based on disposition and discard codes in the SRTR deceased donor disposition file. One example is where authorization to recover an organ was not requested due to reason codes "Acute/Chronic Renal Failure" or "Donor Quality". Another example is where authorization was obtained but the organ was still not recovered due to reason codes such as "Poor Organ Function", "Infection", "Positive HIV", "Diseased Organ", and more. Finally, there are cases where the organ was recovered for transplant but discarded due to reason codes like "Too old on pump", "Vascular damage", "Donor medical history", "Warm ischemic time too long", "Poor organ function", "Infection", and so on. In constructing this indicator, we do not include cases where a recipient was not located, where the organ was refused by all programs, or other non-donor-quality codes such as "Other", "Surgical damage in OR", "No Local Recovery Team", "Medical Examiner Restricted", etc.

5.2.3 Organ Supply Changes

To this point, we have focused our discussion on the demand-side effects of DAA availability, but equilibrium changes in transplants and waiting list additions could also be a function of changes in the supply of transplantable organs. Figure 6 plots the number of deceased donor livers and kidneys recovered for transplant separately by HCV status. Figure 6a shows a steep increase in HCV^+ livers and kidneys recovered for transplant beginning in 2014, which is likely driven by a combination of drug overdose deaths (which accrue disproportionately to HCV^+ individuals (Durand <u>et al.</u>, 2018)) and an increased willingness among waiting list registrants to accept HCV^+ organs (see Figure 5a). Figure 6b shows much smaller relative increases in the supply of transplantable organs recovered from HCV^- donors beginning in 2014. More importantly for our identification strategy, the magnitudes of the increases in organ availability for both HCV^+ and HCV^- livers and kidneys are quite similar suggesting that estimates from our DiD models reflect demand-side changes in response to the introduction of DAAs.

5.2.4 Reconciling CITS and DiD Estimates

In Section 4.2, we discuss trends in liver transplants and waiting list inflows and outflows for those with and without HCV. To measure the magnitude of these trends compared to the baseline (i.e., pre-DAA) means, we use a CITS procedure, which is detailed in Appendix Section 1. We then present DiD estimates that assess the effect of DAAs on transplant and liver waiting list additions, using kidney transplant recipients and waiting list registrants as controls. We now compare the estimates generated by these two different techniques and briefly describe the relevance of this exercise to our preferred identification strategy.

Table 4 contains annual estimates of the effect of DAAs on transplants for HCV^- recipients from our CITS model (column 1) and our DiD model (column 2) relative to the 2005–2012 period. In every year, the CITS estimates are larger than the DiD estimates, likely due to unobserved confounders inflating the CITS estimates (e.g., drug overdose deaths, Medicaid expansion, increased willingness to accept HCV^+ donor organs, etc.). Column 3 calculates the magnitude of the difference between the CITS and DiD estimates, and columns 4–6 contain CITS estimates of trends in transplant for all organs, livers, and kidneys, respectively.

Two key takeaways from Table 4 are worth noting. First, annual growth in liver and kidney transplants are quite similar over the post-DAA period. For example, liver transplants had increased by 42.7% (column 5) and kidney transplants by 39.9% (column 6) from 2012 to 2019, indicating that trends in the availability of livers and kidneys for transplant were similarly affected by supply changes and willingness to accept HCV^+ organs over this period. Second, the differences between our CITS and DiD estimates of DAA effects on transplants for HCV^- recipients in column 3 are nearly identical to the overall growth of organ transplants in column 4, suggesting that our

DiD estimates capture the externality effect of a reallocation of livers from HCV^+ to HCV^- transplant recipients, removing the influence of confounders. Taken together, these findings provide additional support for our choice to use kidney transplant recipients and waiting list registrants to approximate the counterfactual in our DiD model.

6 Value of Externalities

Our DiD event study estimates from Table 4 indicate that from 2014 through 2019, DAAs were responsible for an additional 5,682 liver transplants to HCV^- recipients. Given the large concurrent reduction in HCV^+ individuals on the liver transplant waiting list, the evidence we present suggests that these transplant gains for HCV^- recipients did not crowd out transplants that would have otherwise gone to those who were HCV^+ . Multiplying 5,682 transplants by 10.1 life-years per liver transplant (Rana et al., 2015) equals 57,388 life-years, and assuming a 3% annual discount rate and a value of \$150,000 per life-year, our DiD estimates imply that DAAs generated \$7.52 billion, or \$1.25 billion per year, in value to HCV^- transplant recipients between 2014 and 2019. For context, Chhatwal et al. (2015) estimate that providing DAAs for all HCV^+ individuals in 2015 at market prices would have cost roughly \$65 billion. Recognizing that providing DAAs to all those who were HCV^+ would have generated further externalities, our estimated innovation-induced externality value accruing to HCV^- individuals with ESLD is roughly 11.5% of the total potential market for DAAs in 2015.

It is also worth reiterating that this externality estimate is likely to represent a lower bound for two reasons. First, our DiD estimates do not capture additional transplants that arise due to the increased willingness to accept an HCV^+ organ once DAAs become available since we see a similar increased willingness among those on the kidney transplant waiting list. Second, whether through improved time from listing to transplant or through health compositional changes in marginal registrants, we show evidence that HCV^- transplant recipients are in better health at the time of their transplant in the post-DAA era and this is not reflected in the estimates of post-transplant survival that we use in our value calculation. While a direct mapping between pre-transplant MELD score and post-transplant survival has yet to be established, evidence indicates that moving from a pre-transplant MELD score above 25 to a score below 25 – consistent with the pattern for HCV^- recipients following the introduction of DAAs (see Appendix Figure 1a) – is associated with up to a 30% improvement in 10-year post-transplant survival (Habib et al., 2006).

The heterogeneity in the mechanisms driving the transplant results highlighted above generates uncertainty regarding the life-years gained from a liver transplant. Rana <u>et al.</u> (2015) calculate the median survival difference between those receiving a liver transplant and other ESLD patients with and without propensity score matching. Propensity score matching on the basis of blood type and characteristics at listing, including age, region, date, health

status, and MELD score, reduce the median survival time from 11.6 to 10.1 years. Jena <u>et al.</u> (2016) assume a more conservative 7.2 years. In our case, both marginal candidates induced to list by DAAs appear to be healthier at the time of listing and transplant recipients in the DAA era appear to be healthier at the time of transplant (see Appendix Figure 1), thus we expect they would have longer survival times all else equal.

Relative to the simulation-based literature, our estimates of the value that DAAs conferred on HCV^- individuals with ESLD are large. For example, Jena <u>et al.</u> (2016) simulate an epidemiological model for 20 years starting in 2015 and conclude that DAAs would lead to an additional 7,321 HCV^- liver transplants, or 366 transplants per year. By contrast, using actual retrospective data, we estimate an additional 947 HCV^- transplants per year between 2014 and 2019, on average. The key conceptual difference is that our economic model suggests changes in listing behavior among HCV^- patients when the size of the waiting list changes. In the simulation model of Jena <u>et al.</u> (2016), the demand for organs from HCV^- individuals is assumed to increase linearly until 2025 and then remain flat, and this demand is not a function of the characteristics of the waiting list. Our point is that consistent with the notion that listing behavior is elastic with respect to expectations about transplant probabilities and outcomes (Dickert-Conlin <u>et al.</u>, 2019; Agarwal <u>et al.</u>, 2021), DAAs shrank the waiting list, which induced marginal $HCV^$ patients to list, and these marginal HCV^- individuals may have contributed significantly to the effect of DAAs on HCV^- transplants. For example, using kidney transplant waiting list additions as a counterfactual, our estimates imply that DAA availability resulted in an additional 9,888 HCV^- liver transplant waiting list registrants from 2014 and 2019, or 1,648 additions per year.

Accounting for the behavioral impact of DAAs on waiting list additions is important considering the implications of our findings for the size of the liver transplant waiting list. We estimate that, in the absence of DAAs, $6,397 HCV^$ individuals with ESLD would have joined the liver transplant waiting list in 2019.²³ That same year, there were 6,182 liver transplants performed on HCV^- recipients and, as Figure 1 indicates, this number was maintaining an upward trend in the post-DAA period. As a result, with no DAA-induced HCV^- wait-listing response, our estimates suggest that the development of DAAs would have effectively eliminated the liver transplant waiting list. Instead, the gap between the number of HCV^- waiting list adds and transplants to HCV^- recipients was actually larger in 2019 than in 2012 (the year prior to the development of DAAs).²⁴

Finally, given that the large positive externalities that we estimate concern additional, uninternalized social benefits, our findings have considerable implications for public insurance programs. The event study estimates from our heterogeneity analysis indicated that Medicare beneficiaries accounted for 22.5% and Medicaid beneficiaries accounted for 8.1% of DAA-induced transplants to HCV^- recipients from 2014 through 2019. Combined, these

 $^{^{23}}$ The actual number of HCV^{-} liver transplant waiting list adds in 2019 was 9,399.

²⁴There were 5,440 HCV^- waiting list adds in 2012 and 2,720 transplants to HCV^- recipients (difference = 2,720). There were 9,399 HCV^- waiting list adds in 2019 and 6,182 transplants to HCV^- recipients (difference = 3,217).

results imply that \$389 million per year of the innovation-induced externality generated by DAAs accrued to publicly insured transplant recipients.

7 Conclusion

We study the externalities generated by technological innovation in the context of HCV and liver transplantation. Our primary finding reveals that the availability of DAAs, which were approved to treat HCV in late 2013, generated substantial benefits for individuals outside the market for HCV medical care: those with non-HCV-induced ESLD. Our economic model suggests that part of the externality effect is driven by endogenous HCV^- listing. Given the dramatic reduction in the size of the liver transplant waiting list, HCV^- individuals with ESLD who may have been either relatively healthy, perhaps attempting to forestall listing, or very sick, perhaps rationally not expecting to receive a transplant, chose to list. Notably, a significant fraction of these marginal listers received a transplant.

Although our estimates are conservative, as we may be undercounting HCV cases in kidney transplantation and there may be spillovers (on top of our controls and research design) of DAAs on the demand and supply of kidneys, they clearly highlight the importance of considering innovation-induced externalities when valuing technological advances. Additionally, it is likely we underestimate the number of DAA-induced HCV^- liver transplant waiting list adds, and our results show larger effects when HCV status is measured through antibody testing at the time of transplant rather than at listing.

In sum, we provide the first retrospective evidence on the effect of DAAs on liver transplant and wait-listing behaviors, and, by doing so, we contribute to a growing economics literature on the incentives generated by medical innovation. Our results are timely. In March of 2023, the Biden administration proposed funding that would expand access to DAAs, with the goal of eliminating HCV by 2034. Using a similar model to that in Jena <u>et al.</u> (2016), Chhatwal <u>et al.</u> (2023) simulated that from 2024 to 2034, increased DAA access will decrease U.S. HCV prevalence by 94% and prevent the need for 2,500 liver transplants. Our work suggests that these 2,500 spared transplants will generate significant value for HCV^- patients in search of a liver.

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Figures and Tables





Notes: Authors' calculations of yearly national counts using SRTR data.



Figure 2: Liver Waiting List Levels and Inflows

Notes: Authors' calculations of yearly national counts and rates using SRTR data.



Figure 3: Liver vs. Kidney Waiting List Inflows and Outflows

Notes: Authors' calculations of yearly national log counts using SRTR data. This figure adds the kidney registrant comparison group and recalculates the trends in terms of deviations from 2012. We exclude the 0.13% of kidney registrants who are known to have an HCV-related diagnosis using the optional diagnosis text field in the data.



Figure 4: Liver vs. Kidney Waiting List Additions and Transplants, Log Counts

Notes: Each panel presents time-disaggregated DiD estimates, comparing HCV-specific liver waiting list transplants and waiting list additions to kidney transplants and waiting list additions. The outcomes in each are log counts, implying that the coefficients can be transformed into percentage changes relative to the omitted baseline period (2012) using the formula $100 \times (e^{\hat{\beta}_k} - 1)$. The bars around each coefficient reflect the 95% confidence interval using standard errors clustered at the DSA-by-organ level.



Figure 5: Potential Supply- and Demand-Side Spillovers to Kidney Context

Notes: Authors' calculations of yearly national counts and fractions using SRTR data. In panel (a), we exclude kidney registrants who are known to have an HCV-related diagnosis using the optional diagnosis text field in the data. This is a very small fraction of kidney candidates: only 0.13% of registrants from 2005 to 2019. Panels (c) and (d) use known HCV antibody test results at the time of transplant to identify HCV^+ transplant recipients. These results are conditional on receiving a transplant.



Figure 6: Supply of HCV^+ and HCV^- Donor Organs

Notes: Authors' calculations of yearly national counts using SRTR data. Includes all livers (left-scale) and kidneys (right-scale) recovered for transplant, including those that are subsequently discarded. For reference, the 2005-2013 average number of HCV^- kidneys recovered is 14,062; the corresponding average for livers is 6,513. The 2005-2013 average number of HCV^+ kidneys recovered is 531; the corresponding average for livers is 237.

	HCV^+ Liver Registrants			<i>HCV</i> ⁻ Liver Registrants		
	2005-19	2005-13	2014-19	2005-19	2005-13	2014-19
Waiting List Size (Counts)						
National $\#$ of Listings	49,499	35,068	$14,\!431$	$93,\!542$	46,719	46,823
National $\#$ of WL Removals & TXs	54,058	$36,\!157$	17,901	$93,\!123$	$46,\!470$	$46,\!653$
Waiting List Flows (Counts)						
Nat'l Yrly # of Listings	3,300	$3,\!896$	$2,\!405$	6,236	5,191	7,804
Nat'l Yrly # of WL Remov. & TXs	$3,\!604$	4,017	2,984	6,208	5,163	7,776
Waiting List Outcomes (Means)						
Too Sick / Died	0.257	0.269	0.235	0.226	0.240	0.213
Improved	0.048	0.032	0.079	0.067	0.066	0.069
Dec. Don. TX	0.511	0.511	0.511	0.535	0.510	0.559
Liv. Don. TX	0.014	0.015	0.014	0.027	0.024	0.031
Days to TX	316.7	302.1	346.1	228.1	241.5	215.9
Waiting List Characteristics (Means)						
Initial MELD	16.47	16.60	16.15	19.67	19.18	20.15
High School or Less	0.582	0.576	0.593	0.448	0.470	0.429
White Pct.	0.680	0.691	0.654	0.731	0.736	0.725
Primary Payer: Private	0.549	0.584	0.464	0.609	0.642	0.576
Primary Payer: Medicare	0.251	0.226	0.311	0.236	0.217	0.255
Primary Payer: Medicaid	0.200	0.190	0.225	0.155	0.141	0.170
Listing Age 18 to 39	0.022	0.024	0.019	0.135	0.139	0.131
Listing Age 40 to 64	0.873	0.906	0.792	0.694	0.713	0.675
Listing Age Over 64	0.105	0.070	0.189	0.171	0.148	0.194
South Census Region	0.372	0.359	0.405	0.379	0.361	0.397
NE Census Region	0.220	0.228	0.199	0.186	0.195	0.177
MW Census Region	0.170	0.170	0.170	0.231	0.236	0.226
West Census Region	0.238	0.243	0.226	0.204	0.208	0.201

 Table 1: Liver Registrants' Summary Statistics, by HCV Status

Notes: Authors' calculations of fraction of liver registrants belonging to each characteristic or outcome group from SRTR data. Except for waiting list outcomes (too sick/died, improved, transplants, and days to transplant), which are calculated based on the timing of waiting list removal, all summary statistics are calculated based on when the registrants joined the waiting list. Those for whom HCV status cannot be inferred are excluded from the calculations in this table. This amounts to roughly 15% of liver registrants, or 24,847 of 167,888 total liver registrants who listed between 2005 to 2019. Higher MELD score reflects higher mortality risk.

	Log Transplants (1)	Transplant Rate (2)	Log WL Additions (3)
Panel A: HCV^-			
DAA	$\begin{array}{c} 0.3059^{***} \\ (0.0514) \end{array}$	$\begin{array}{c} 0.1604^{***} \\ (0.0407) \end{array}$	$\begin{array}{c} 0.3134^{***} \\ (0.0545) \end{array}$
Baseline Mean Observations Number of Clusters	$61.27 \\ 1,425 \\ 95$	$0.507 \\ 1,425 \\ 95$	$115.36 \\ 1,425 \\ 95$
Panel B: HCV^+			
DAA	-0.4965^{***} (0.0578)	0.0576 (0.0392)	-0.6044^{***} (0.0601)
Baseline Mean Observations Number of Clusters	$46.89 \\ 1,425 \\ 95$	$0.506 \\ 1,425 \\ 95$	$86.59 \\ 1,425 \\ 95$

Table 2: Liver vs. Kidney Waiting List Additions and Transplants

Notes: The first and third columns of coefficients represent log point changes per year, which can be transformed into percentages using the formula $100 \times (e^{\hat{\beta}} - 1)$. In column 2, the outcome is defined as the number of transplants divided by the organ-specific number of waiting list registrants. Baseline means reflect the pre-treatment period (2005–2013) DSA-year means for liver registrants only. In columns 1 and 3, baseline means reflect level counts rather than log counts. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 13) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses and are clustered at the DSA-by-organ level. *** p<0.01, ** p<0.05, * p<0.1

Log Transplants to HCV^- Registrant					
Panel A: Primary Payer, Sex	Private	Medicare	Medicaid	Male	Female
DAA	$\begin{array}{c} 0.3138^{***} \\ (0.0539) \end{array}$	$\begin{array}{c} 0.3797^{***} \\ (0.0616) \end{array}$	0.1825^{**} (0.0835)	$\begin{array}{c} 0.3257^{***} \\ (0.0522) \end{array}$	$\begin{array}{c} 0.2672^{***} \\ (0.0557) \end{array}$
Baseline Mean Observations Number of Clusters	$39.02 \\ 1,425 \\ 95$	$11.66 \\ 1,425 \\ 95$	$7.85 \\ 1,425 \\ 95$	$36.62 \\ 1,425 \\ 95$	$24.65 \\ 1,425 \\ 95$
Panel B: Age, Race	18 to 39	40 to 64	Over 64	White	Non-White
DAA	$\begin{array}{c} 0.1977^{***} \\ (0.0574) \end{array}$	$\begin{array}{c} 0.1955^{***} \\ (0.0550) \end{array}$	$\begin{array}{c} 0.3579^{***} \\ (0.0685) \end{array}$	$\begin{array}{c} 0.4098^{***} \\ (0.0535) \end{array}$	$\begin{array}{c} 0.1593^{***} \\ (0.0554) \end{array}$
Baseline Mean Observations Number of Clusters	$9.15 \\ 1,425 \\ 95$	$\begin{array}{c} 43.91 \\ 1,425 \\ 95 \end{array}$	$8.20 \\ 1,425 \\ 95$	$45.60 \\ 1,425 \\ 95$	$15.67 \\ 1,425 \\ 95$
Panel C: Payer by Census Region	Private	Medicare	Medicaid	All Payers	
DAA x South	0.4160^{***} (0.0585)	0.4484^{***} (0.0932)	0.1182 (0.1142) 6.25	0.3758^{***} (0.0580) 62.01	
DAA x Northeast	-0.0007 (0.1630)	$ \begin{array}{c} 0.1441 \\ (0.1448) \end{array} $	0.1833 (0.2113)	$\begin{array}{c} 0.0451 \\ (0.1539) \end{array}$	
Baseline Mean	49.11	14.37	11.24	78.98	
DAA x Midwest	0.3209^{***} (0.1000)	$\begin{array}{c} 0.4105^{***} \\ (0.1081) \end{array}$	0.1251 (0.1498)	$\begin{array}{c} 0.3113^{***} \\ (0.1049) \end{array}$	
Baseline Mean	36.76	10.45	7.16	56.15	
DAA x West	$\begin{array}{c} 0.3201^{***} \\ (0.0930) \end{array}$	$\begin{array}{c} 0.3626^{***} \\ (0.0796) \end{array}$	$\begin{array}{c} 0.3864^{***} \\ (0.0873) \end{array}$	$\begin{array}{c} 0.3398^{***} \\ (0.0692) \end{array}$	
Baseline Mean	35.44	6.98	9.43	53.78	
Observations Number of Clusters	$^{1,425}_{95}$	$^{1,425}_{95}$	$^{1,425}_{95}$	$^{1,425}_{95}$	

Table 3: Heterogeneity in Transplants Going to HCV^- Registrants, Subsample Regressions

Notes: Each coefficient in Panels A and B come from separate DiD regressions of log transplants received by HCV^- registrants on the DAA treatment indicator, comparing group-specific liver transplant recipient counts to group-specific kidney transplant recipient counts. In Panel C, each column of estimates is obtained from a single regression where the DAA treatment indicator is interacted with the census region. Note that all coefficients in this table represent log point changes, which can be transformed into percentages using the formula $100 \times (e^{\hat{\beta}} - 1)$. Group-specific baseline means of the dependent variable reflect the pre-treatment period (2005–2013) level (not log) DSA-year means for HCV^- liver recipients only. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 13) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses and are clustered at the DSA-by-organ level. *** p<0.01, ** p<0.05, * p<0.1

	Log Transplants					
	HCV ⁻	HCV ⁻	Difference	All TX	Liver TX	Kidney TX
	(1)	(2)	(3)	(4)	(5)	(6)
$DAA \ge 2013$	0.0960^{***}	0.0667	0.0293	0.0241	0.0435	0.0159
	(0.0334)	(0.0435)		(0.0190)	(0.0288)	(0.0222)
DAA x 2014	0.1356^{***}	0.0846^{*}	0.0510	0.0587^{**}	0.0844^{**}	0.0417
	(0.0481)	(0.0499)		(0.0263)	(0.0381)	(0.0295)
DAA x 2015	0.2307^{***}	0.1529^{***}	0.0778	0.0895^{***}	0.1055^{**}	0.0715^{**}
	(0.0618)	(0.0563)		(0.0312)	(0.0505)	(0.0339)
DAA x 2016	0.4750^{***}	0.3391^{***}	0.1359	0.1685^{***}	0.2271^{***}	0.1335^{***}
	(0.0681)	(0.0581)		(0.0386)	(0.0620)	(0.0393)
DAA x 2017	0.5271^{***}	0.3457***	0.1814	0.2132***	0.2620***	0.1822***
	(0.0873)	(0.0665)		(0.0409)	(0.0744)	(0.0410)
DAA x 2018	0.6035***	0.3666***	0.2369	0.2569***	0.2754^{***}	0.2413***
	(0.0945)	(0.0642)		(0.0477)	(0.0843)	(0.0466)
DAA x 2019	0.7643***	0.4367***	0.3276	0.3494***	0.3553***	0.3356***
	(0.1074)	(0.0656)		(0.0508)	(0.0974)	(0.0486)
Observations	675	1,425		750	675	750
Number of Clusters	45	95		50	45	50

Table 4: CITS vs. DiD Estimates of Transplants to HCV^- Registrants

Notes: The outcome variables in columns 1 and 2 are log number of transplants received by HCV^- registrants, where the difference is column 1 presents time-disaggregated interrupted time-series estimates, while column 2 presents time-disaggregated DiD estimates comparing liver transplants to kidney transplants. Column 3 presents the difference between the column 1 and column 2 estimates for each post-treatment year. Columns 4-6 present time-disaggregated interrupted time-series estimates of overall transplant trends for all registrants (both HCV^- and HCV^+). Note that all coefficients in this table represent log point changes, which can be transformed into percentages using the formula $100 \times (e^{\hat{\beta}} - 1)$. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 13) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses. They are clustered at the DSA-by-organ level when comparing livers to kidneys (column 2 only) and at the DSA level when estimating interrupted time-series models (all other columns). *** p<0.01, ** p<0.05, * p<0.1

Externalities from Medical Innovation: Evidence from Organ Transplantation APPENDIX

1 Comparative Interrupted Time Series

Our CITS model is specified as follows:

$$Y_{dHt} = \beta_1 t + \beta_2 (H \times t) + \beta_3 DAA_t + \beta_4 (H \times DAA_t) + \beta_5 (DAA_t \times t) + \beta_6 (H \times DAA_t \times t) + \gamma_{dH} + \epsilon_{dHt}$$
(1)

where d indexes donor service area (DSA),¹ H indexes HCV status, and t indexes year. The first regressor, t, is a linear time trend, such that β_1 measures the slope of the pre-DAA trend for $HCV^$ registrants and $\beta_1 + \beta_2$ measures the slope of the pre-DAA trend for HCV^+ registrants. DAA_t is an indicator for the post-DAA period (i.e., 2014 through 2019). Thus, β_3 reflects the level change in HCV^- registrants' outcomes associated with the introduction of DAAs relative to their baseline level, while $\beta_3 + \beta_4$ reflects this level change for HCV^+ registrants. Finally, β_5 measures the post-DAA change in slope relative to the pre-DAA slope β_1 for HCV^- registrants, while $\beta_5 + \beta_6$ captures this slope change for HCV^+ registrants. Finally, we include DSA-HCV fixed effects γ_{dH} to address potential unobserved confounders across HCV status and donation service areas, and an idiosyncratic error term ϵ_{dHt} clustered at the DSA-HCV level.

¹Note that we use modified DSA identifiers throughout our analyses due to changes over time in the existence and services of certain DSAs. First, we combine the Sierra Donor Services DSA into the Donor Network West DSA in California, as Sierra Donor Services ended their liver program in 2008/2009 and was geographically entirely surrounded by Donor Network West. Second, the Mississippi Organ Recovery Agency started up in 2013, so we combine that DSA with their pre-existing contiguous DSAs in Tennessee and north Mississippi, Louisiana, and Alabama. Third, because Lifelink of Southwest Florida ended in 2004, OurLegacy in Florida started in 2007, and Lifelink Puerto Rico started in 2012, we combine all Florida and Puerto Rico DSAs into one DSA unit. It is also important to note that 5 DSAs do not have a liver program. Thus, we end up with 50 modified DSA identifiers for kidneys and 45 modified DSA identifiers for livers.

	Log Transplants	Transplant Rate	Log WL Additions
Years Since DAA	$\begin{array}{c} 0.1169^{***} \\ (0.0154) \end{array}$	0.0808^{***} (0.0134)	$\begin{array}{c} 0.0569^{***} \\ (0.0142) \end{array}$
$HCV^+ \times$ Years Since DAA	-0.2604^{***} (0.0252)	-0.0688^{***} (0.0179)	-0.2276^{***} (0.0224)
DAA	-0.0116 (0.0376)	-0.0195 (0.0364)	-0.0144 (0.0411)
$HCV^+ \times DAA$	$\begin{array}{c} 0.2856^{***} \\ (0.0714) \end{array}$	0.0980^{*} (0.0559)	$0.0979 \\ (0.0709)$
Pre-DAA Trend	$0.0097 \\ (0.0095)$	-0.0166^{*} (0.0091)	0.0300^{***} (0.0083)
$HCV^+ \times$ Pre-DAA Trend	-0.0235^{*} (0.0129)	0.0053 (0.0115)	-0.0292^{**} (0.0122)
HCV^- Mean of DV (Level) HCV^+ Mean of DV (Level) Observations N of Clusters	61.27 46.89 1,350 90	$\begin{array}{c} 0.507 \\ 0.506 \\ 1,350 \\ 90 \end{array}$	$115.36 \\ 86.59 \\ 1,350 \\ 90$

Appendix Table 1: Comparative Interrupted Time-Series, Liver Waiting List Additions and Transplants

Notes: The outcome variable in column 1 is the log number of transplants per DSA-year. In column 3, the outcome variable is defined as the log number of waiting list additions. The estimates in columns 1 and 3 can be transformed into percentages using the formula $100 \times (e^{\hat{\beta}} - 1)$. In column 2, the outcome is defined as the number of transplants divided by the HCV-specific number of waiting list registrants. Dependent variable means (at the DSA-year level) are reported in the two rows immediately following the coefficients, and reflect the pre-treatment period (2005-13) means for liver registrants. In columns 1 and 3, the means are of level counts rather than log counts. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA level. *** p<0.01, ** p<0.05, * p<0.1

2 Health Composition



Appendix Figure 1: Change in Health Composition

Notes: Authors' calculations of average MELD scores using SRTR data. Note that a higher MELD score reflects higher mortality risk. Roughly 20% of registrants have the same initial and last MELD score.

	Initial MELD	% High MELD	% Middle MELD	% Low MELD
Time Since DAA	-0.2198^{***} (0.0729)	-0.0033 (0.0023)	-0.0089^{***} (0.0027)	0.0121^{***} (0.0035)
$HCV^+ \times$ Time Since DAA	-0.0364 (0.1233)	-0.0039 (0.0038)	0.0046 (0.0059)	-0.0006 (0.0070)
DAA	$\begin{array}{c} 0.5182^{**} \\ (0.2590) \end{array}$	0.0177^{**} (0.0077)	-0.0006 (0.0100)	-0.0168 (0.0132)
$HCV^+ \times DAA$	-0.6301 (0.4281)	-0.0028 (0.0122)	-0.0327^{*} (0.0189)	0.0351 (0.0237)
Pre-DAA Trend	$\begin{array}{c} 0.1614^{***} \\ (0.0384) \end{array}$	$0.0016 \\ (0.0012)$	0.0088^{***} (0.0012)	-0.0104^{***} (0.0018)
$HCV^+ \times$ Pre-DAA Trend	-0.0998^{*} (0.0507)	$0.0009 \\ (0.0015)$	-0.0083*** (0.0023)	0.0075^{**} (0.0029)
HCV^- Mean of DV HCV^+ Mean of DV Observations R-squared N of Clusters	$19.22 \\ 16.82 \\ 1,350 \\ 0.5800 \\ 90$	$\begin{array}{c} 0.128 \\ 0.070 \\ 1,350 \\ 0.4056 \\ 90 \end{array}$	$\begin{array}{c} 0.451 \\ 0.395 \\ 1,350 \\ 0.4633 \\ 90 \end{array}$	$\begin{array}{c} 0.421 \\ 0.535 \\ 1,350 \\ 0.5419 \\ 90 \end{array}$

Appendix Table 2: CITS, Health of New Liver Waiting List Registrants

Notes: The outcome variable in column 1 is the average MELD score among new waiting list additions by DSA-year. In columns 2-4, the outcome variables are defined as the fraction of waiting list additions belonging to the high MELD (32 to 40), middle MELD (16 to 31), and low MELD (6 to 15) categories by DSA-year. A higher MELD score indicates a shorter life expectancy in the absence of a liver transplant, and thus confers higher priority on the waiting list. Dependent variable means (at the DSA-year level) are reported in the two rows immediately following the coefficients, and reflect the pre-treatment period (2005-13) means for liver registrants. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidneyserving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA level. *** p<0.01, ** p<0.05, * p<0.1

3 Waiting List Attrition



Appendix Figure 2: Liver Waiting List Outflows

Notes: Authors' calculations of yearly national rates using SRTR data.

	Log Outco	omes	Bate	s
	Too Sick / Died	Improved	Too Sick / Died	Improved
V C DAA		0.00	0.000.1**	0.0010
Years Since DAA	-0.0470^{***} (0.0168)	-0.0057 (0.0352)	-0.0064^{**} (0.0028)	-0.0018 (0.0035)
$HCV^+ \ge Years$ Since DAA	-0.1766^{***} (0.0264)	-0.0378 (0.0499)	-0.0041 (0.0048)	$0.0087 \\ (0.0053)$
DAA	0.1176^{**} (0.0469)	-0.0425 (0.0875)	0.0258^{***} (0.0097)	0.0014 (0.0087)
$HCV^+ \ge DAA$	-0.0686 (0.0837)	$\begin{array}{c} 0.3017^{**} \\ (0.1324) \end{array}$	-0.0378^{**} (0.0179)	$0.0039 \\ (0.0141)$
Pre-DAA Trend	$\begin{array}{c} 0.0523^{***} \\ (0.0096) \end{array}$	$\begin{array}{c} 0.0743^{***} \\ (0.0179) \end{array}$	$\begin{array}{c} 0.0042^{**} \\ (0.0017) \end{array}$	0.0033^{**} (0.0014)
HCV^+ x Pre-DAA Trend	-0.0165 (0.0152)	-0.0258 (0.0241)	0.0014 (0.0027)	-0.0008 (0.0019)
HCV^{-} Mean of DV (Level)	27.52	7.60	0.161	0.046
HCV^+ Mean of DV (Level)	23.99	2.88	0.181	0.026
Observations	$1,\!350$	$1,\!350$	$1,\!350$	$1,\!350$
N of Clusters	90	90	90	90

Appendix Table 3: CITS, Liver Transplant Waiting List Outflows

Notes: Notes: The outcome variables in columns 1 and 2 are the log number of waiting list removals due to condition deterioration/death and condition improvement per DSA-year. The estimates in columns 1 and 2 can be transformed into percentages using the formula $100 \times (e^{\hat{\beta}} - 1)$. In columns 3 and 4, the outcomes are defined as the number of removals divided by the HCV-specific number of waiting list registrants. Dependent variable means (at the DSA-year level) are reported in the two rows immediately following the coefficients, and reflect the pre-treatment period (2005-13) means for liver registrants. In columns 1 and 2, the means are of level counts rather than log counts. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA level. *** p<0.01, ** p<0.05, * p<0.1

4 Transplant Rates

Appendix Figure 3



Notes: Authors' calculations of yearly national fractions using SRTR data.



Appendix Figure 4: Liver vs. Kidney Transplants

Notes: Each subfigure presents time-disaggregated differences-in-differences estimates, comparing HCV^+ and HCV^- transplants to kidney waiting list additions and transplants. The outcome is defined as transplants divided by number of waiting list registrants. For kidneys, this rate reflects transplants divided by number of kidney registrants. For livers, this rate reflects transplants to HCV^+ registrants divided by number of HCV^+ liver registrants in subfigure (a), and transplants to HCV^- registrants divided by number of HCV^- liver registrants in subfigure (b). The bars around each coefficient reflect the 95% confidence interval using standard errors that are clustered at the DSA-by-organ level.

5 Concurrent Shocks



Appendix Figure 5: Drug Overdose Deaths by Year

Notes: Figure includes deaths deemed "prevantable or accidental". Synthetic opioids category is "synthetic opioids other than methadone" and includes fentanyl. Source: National Safety Council analysis of National Center for Health Statistics Mortality Data.



Appendix Figure 6: Alcoholic Liver Disease Prevalence by Year

Notes: Alcoholic liver disease is based on the following criteria: 1) average daily alcohol consumption of more than 10 grams for females and more than 20 grams for males and 2) alanine transaminase level or aspartate aminotransferase level greater than 31 U/L in females and an alanine transaminase level greater than 40 U/L or aspartate aminotransferase level greater than 37 U/L in males. Those with Hepatitis B or C infections were excluded. Source: National Health and Nutrition Examination Survey.

	Log Non-HCV Waiting List Additions					
	All Payers	Private	Medicare	Medicaid		
Time Since DAA	0.0235	0.0291^{*}	0.0077	0.0083		
	(0.0146)	(0.0159)	(0.0226)	(0.0217)		
Time Since DAA x NASH	-0.0161	-0.0263	0.0242	-0.0003		
	(0.0157)	(0.0178)	(0.0224)	(0.0230)		
Time Since DAA x ALD	0.0679***	0.0616***	0.0475^{*}	0.0761***		
	(0.0142)	(0.0160)	(0.0253)	(0.0208)		
DAA	-0.0205	-0.0413	-0.0111	0.0148		
	(0.0391)	(0.0495)	(0.0626)	(0.0725)		
DAA x NASH	0.0326	0.0704	-0.0518	0.0917		
	(0.0498)	(0.0609)	(0.0784)	(0.0870)		
DAA x ALD	0.0527	0.0211	0.0615	0.0599		
	(0.0573)	(0.0615)	(0.0784)	(0.0949)		
Year	-0.0030	-0.0118	0.0225**	0.0080		
	(0.0080)	(0.0088)	(0.0110)	(0.0118)		
Year x NASH	0.0992***	0.0836***	0.0944***	0.0521***		
	(0.0089)	(0.0095)	(0.0128)	(0.0122)		
Year x ALD	0.0447***	0.0473***	0.0304**	0.0393***		
	(0.0081)	(0.0088)	(0.0114)	(0.0113)		
Observations	2.025	2.025	2.025	2.025		
Deservations Deservations	2,020	2,020	2,020 0.7756	2,020		
n-squareu N of Clusters	0.0020 45	0.0070 45	0.7700 45	0.7478 45		
	40	40	40	40		

Appendix Table 4: HCV^- Waiting List Additions by Diagnosis Category and Primary Payer

Notes: Includes DSA-by-Diagnosis FEs to mimic subsample analyses. Standard errors are in parentheses, and clustered at the DSA level. *** p<0.01, ** p<0.05, * p<0.1

6 Further Evidence



Appendix Figure 7: Time from Wait-Listing to Transplant for HCV^- Liver Transplant Recipients

Notes: Authors' calculations of yearly national averages using SRTR data, measured as the difference between date of transplant and date of waiting list registration. In less than 0.2% of transplants, this equals zero. A value of zero can reflect either a true same-day transplant, or a case where a living liver donor recipient did not first join the deceased donor waiting list.

		TX Faster Than
	Log Days to TX	2005-12 Median
Panel A: HCV^-		
DAA	-0.1749***	0.0383**
	(0.0543)	(0.0155)
	[245.57]	$\left[0.315 ight]$
Panel B: HCV^+		
DAA	-0.0057	-0.0303**
	(0.0505)	(0.0151)
	[295.04]	[0.266]
Observations	1,425	1,425
N of Clusters	95	95

Appendix Table 5: Liver vs. Kidney Time from Wait-Listing to Transplant by HCV Status

Notes: The dependent variable in the first column equals the log of 1 plus the number of days elapsed from waiting list registration to transplant. For those who got a transplant the same day or did not register on the waiting list before receiving a transplant, days elapsed equals zero. The second dependent variable is a binary indicator for whether the candidate received a transplant more quickly than the median days to transplant during the 2005-12 sample period. Dependent variable means (at the DSA-year level) are in brackets, and reflect the pre-treatment period (2005-13) means for liver registrants only. In column 1, the means reflect level number of days rather than log number of days. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA-by-organ level. *** p<0.01, ** p<0.05, * p<0.1

Liver Registrants				Kidney Registrants				
200	5-19	2005-13	2014-19		2005	5-19	2005-13	2014-19
Mean	SD	Mean	Mean		Mean	SD	Mean	Mean
0.295	0.456	0.365	0.201					
0.148	0.355	0.148	0.148					
18.00	9.01	17.71	18.38					
0.233	0.422	0.246	0.216		0.235	0.424	0.234	0.237
0.059	0.235	0.051	0.068		0.005	0.070	0.005	0.005
0.537	0.499	0.524	0.554		0.349	0.477	0.347	0.350
0.022	0.145	0.019	0.025		0.175	0.380	0.195	0.151
252.3	482.5	252.3	252.2		698.5	749.8	659.6	747.0
0.494	0.500	0.514	0.471		0.471	0.499	0.502	0.430
0.704	0.457	0.709	0.697		0.455	0.498	0.472	0.432
0.586	0.493	0.618	0.544		0.449	0.497	0.455	0.441
0.246	0.431	0.223	0.276		0.473	0.499	0.474	0.473
0.168	0.374	0.159	0.180		0.078	0.267	0.071	0.086
0.095	0.293	0.091	0.100		0.189	0.392	0.197	0.179
0.749	0.434	0.789	0.694		0.634	0.482	0.642	0.624
0.156	0.363	0.119	0.206		0.177	0.381	0.162	0.197
0.373	0.483	0.355	0.396		0.376	0.484	0.360	0.399
0.207	0.405	0.220	0.189		0.208	0.406	0.216	0.198
0.207	0.405	0.207	0.206		0.197	0.398	0.205	0.187
0.213	0.410	0.217	0.209		0.218	0.413	0.220	0.216
	$\begin{array}{c} 2003\\ \text{Mean}\\ \hline 0.295\\ 0.148\\ 18.00\\ 0.233\\ 0.059\\ 0.537\\ 0.022\\ 252.3\\ 0.494\\ 0.704\\ 0.586\\ 0.246\\ 0.168\\ 0.095\\ 0.749\\ 0.156\\ 0.373\\ 0.207\\ 0.207\\ 0.207\\ 0.213\end{array}$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Liver Registrants $2005-19$ $2005-13$ MeanSDMean 0.295 0.456 0.365 0.148 0.355 0.148 18.00 9.01 17.71 0.233 0.422 0.246 0.059 0.235 0.051 0.537 0.499 0.524 0.022 0.145 0.019 252.3 482.5 252.3 0.494 0.500 0.514 0.704 0.457 0.709 0.586 0.493 0.618 0.246 0.431 0.223 0.168 0.374 0.159 0.095 0.293 0.091 0.749 0.434 0.789 0.156 0.363 0.119 0.373 0.483 0.355 0.207 0.405 0.220 0.207 0.405 0.207 0.213 0.410 0.217	Liver Registrants $2005-19$ $2005-13$ $2014-19$ MeanSDMeanMean 0.295 0.456 0.365 0.201 0.148 0.355 0.148 0.148 18.00 9.01 17.71 18.38 0.233 0.422 0.246 0.216 0.059 0.235 0.051 0.068 0.537 0.499 0.524 0.554 0.022 0.145 0.019 0.025 252.3 482.5 252.3 252.2 0.494 0.500 0.514 0.471 0.704 0.457 0.709 0.697 0.586 0.493 0.618 0.544 0.246 0.431 0.223 0.276 0.168 0.374 0.159 0.180 0.095 0.293 0.091 0.100 0.749 0.434 0.789 0.694 0.156 0.363 0.119 0.206 0.373 0.483 0.355 0.396 0.207 0.405 0.207 0.206 0.213 0.410 0.217 0.209	Liver Registrants $2005-19$ $2005-13$ $2014-19$ MeanSDMeanMean 0.295 0.456 0.365 0.201 0.148 0.355 0.148 0.148 18.00 9.01 17.71 18.38 0.233 0.422 0.246 0.216 0.059 0.235 0.051 0.068 0.537 0.499 0.524 0.554 0.022 0.145 0.019 0.025 252.3 482.5 252.3 252.2 0.494 0.500 0.514 0.471 0.704 0.457 0.709 0.697 0.586 0.493 0.618 0.544 0.246 0.431 0.223 0.276 0.168 0.374 0.159 0.180 0.095 0.293 0.091 0.100 0.749 0.434 0.789 0.694 0.156 0.363 0.119 0.206 0.373 0.483 0.355 0.396 0.207 0.405 0.207 0.206 0.213 0.410 0.217 0.209	Liver Registrants $2005-19$ $2005-13$ $2014-19$ 2005 MeanSDMeanMeanMean 0.295 0.456 0.365 0.201 Mean 0.148 0.355 0.148 0.148 0.148 18.00 9.01 17.71 18.38 0.233 0.233 0.422 0.246 0.216 0.235 0.059 0.235 0.051 0.068 0.005 0.537 0.499 0.524 0.554 0.349 0.022 0.145 0.019 0.025 0.175 252.3 482.5 252.3 252.2 698.5 0.494 0.500 0.514 0.471 0.4711 0.704 0.457 0.709 0.697 0.455 0.586 0.493 0.618 0.544 0.449 0.246 0.431 0.223 0.276 0.473 0.168 0.374 0.159 0.180 0.078 0.095 0.293 0.091 0.100 0.189 0.749 0.434 0.789 0.694 0.634 0.156 0.363 0.119 0.206 0.177 0.373 0.483 0.355 0.396 0.376 0.207 0.405 0.207 0.206 0.197 0.213 0.410 0.217 0.209 0.218	$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

Appendix Table 6: Liver and Kidney Waiting List Registrant Summary Statistics

Notes: Except for transplant/waiting list outcomes (too sick/died, improved, transplants, and days to transplant), which are calculated based on transplant timing and waiting list removal timing, all summary statistics are calculated based on when the candidates joined the waiting list.

	Log WL Additions						
	Private	Medicare	Medicaid				
Panel A: Non-HCV							
DAA	$\begin{array}{c} 0.2257^{***} \\ (0.0542) \\ [70.88] \end{array}$	$\begin{array}{c} 0.4885^{***} \\ (0.0680) \\ [23.94] \end{array}$	0.2364^{**} (0.0997) [15.60]				
Panel B: HCV							
DAA	$\begin{array}{c} -0.8476^{***} \\ (0.0693) \\ [47.83] \end{array}$	-0.2596^{***} (0.0661) [18.51]	-0.6270^{***} (0.0971) [15.60]				
Observations N of Clusters	$\substack{1,425\\95}$	$1,\!425$ 95	$\substack{1,425\\95}$				

Appendix Table 7: DiD Estimates of Liver vs. Kidney Waiting List Additions by Primary Payer

Notes: The outcome variable is the log number of new waiting list additions per DSA-year. Dependent variable means (at the DSA-year level) are in brackets, and reflect the pretreatment period (2005-13) means for liver registrants only. The means reflect level counts rather than log counts. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA-by-organ level. *** p<0.01, ** p<0.05, * p<0.1

	Log TXs, HCV^+ Donors $\rightarrow HCV^-$ Registrants							
	All Payers	Private	Medicare	Medicaid				
Years Since DAA	$\begin{array}{c} 0.3960^{***} \\ (0.0381) \end{array}$	$\begin{array}{c} 0.3066^{***} \\ (0.0321) \end{array}$	0.1960^{***} (0.0300)	$\begin{array}{c} 0.1407^{***} \\ (0.0210) \end{array}$				
DAA	-0.6053^{***} (0.0702)	-0.4919^{***} (0.0654)	-0.3532^{***} (0.0555)	-0.2305^{***} (0.0409)				
Pre-DAA Trend	-0.0096^{*} (0.0055)	-0.0080^{*} (0.0044)	-0.0015 (0.0018)	-0.0028 (0.0024)				
Mean of DV (Level) Observations R-squared N of Clusters	$0.111 \\ 675 \\ 0.5992 \\ 45$	$\begin{array}{c} 0.077 \\ 675 \\ 0.5390 \\ 45 \end{array}$	$0.012 \\ 675 \\ 0.4340 \\ 45$	$0.014 \\ 675 \\ 0.4078 \\ 45$				

Appendix Table 8: ITS Estimates of HCV^+ Donor Liver Transplants Received by HCV^- Registrants

Notes: The outcome variable is log number of liver transplants from HCV^+ donors to HCV^- registrants per DSA-year. Dependent variable means (at the DSA-year level) are reported in the two rows immediately following the coefficients, and reflect the pre-treatment period (2005-13) means. The means are of level counts rather than log counts. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA level. *** p<0.01, ** p<0.05, * p<0.1

	Log WL	Log	Outcome/WL Size		
	Additions	Transplants	Transplants	Too Sick / Died	Improved
Panel A: HCV^-					
DAA	$\begin{array}{c} 0.1884 \\ (0.1992) \\ [168.61] \end{array}$	$\begin{array}{c} 0.0384 \\ (0.1735) \\ [78.98] \end{array}$	$\begin{array}{c} 0.2140^{**} \\ (0.0963) \\ [0.249] \end{array}$	0.0695 (0.0407) [0.143]	$\begin{array}{c} 0.0248 \\ (0.0162) \\ [0.056] \end{array}$
Panel B: HCV^+					
DAA	-0.7106*** (0.1622) [148.37]	$\begin{array}{c} -0.6711^{***} \\ (0.1598) \\ [71.24] \end{array}$	$\begin{array}{c} 0.1070 \\ (0.0751) \\ [0.280] \end{array}$	$\begin{array}{c} 0.0113 \\ (0.0336) \\ [0.173] \end{array}$	$\begin{array}{c} 0.0357^{**} \\ (0.0137) \\ [0.029] \end{array}$
Observations N of Clusters	210 14	210 14	210 14	$\begin{array}{c} 210\\14 \end{array}$	210 14

Appendix Table 9: Liver vs. Kidney Waiting List Additions, Transplants, and Waiting List Removals; Northeast Census Region Only

Notes: The outcome variable in column 1 is the log number of new waiting list additions per DSA-year. In column 2, the outcome is defined as the log of the count of transplants. The estimates in columns 1–2 can be transformed into percentages using the formula 100 × $(e^{\hat{\beta}} - 1)$. In columns 3–5, the outcome variables are defined as waiting list outcome counts divided by the organ-specific number of waiting list registrants. The estimation sample includes only DSAs from the Northeast Census region. Dependent variable means (at the DSA-year level) are in brackets, and reflect the pre-treatment period (2005-13) means for liver registrants only. In columns 1–2, the means reflect level counts rather than log counts. Standard errors are in parentheses, and clustered at the DSA-by-organ level. *** p<0.01, ** p<0.05, * p<0.1

	Dose-	\geq Median	< Median
	Response	HCV^+ Rate	HCV^+ Rate
Panel A: Log Waiting List Additions			
DAA	-0.2709	0.3547^{***}	0.2086^{**}
	(0.2757)	(0.0635)	(0.0836)
DAA x Fraction HCV^+	1.2829**		
	(0.6069)		
Mean of DV (Level)	115.36	145.53	83.81
Panel B: Log Transplants			
DAA	-0.2478	0.3649***	0.2109***
	(0.2860)	(0.0694)	(0.0697)
DAA x Fraction HCV^+	1 2347*		
	(0.6584)		
Mean of DV (Level)	61.27	71.52	50.56
Observations	1,350	690	660
N of Clusters	90	46	44

Notes: This table presents differences-in-differences heterogeneity estimates, comparing log HCV^- liver transplants and waiting list additions to log kidney transplants and waiting list additions, by DSAs' fraction of pre-treatment (2005-13) liver transplant recipients who tested positive for antibodies to HCV. The baseline means of the dependent variables reflect level counts (at the DSA-year level) rather than log counts during the pre-treatment period (2005-13) for liver registrants only. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-serving DSA and 45 liver-serving DSA identifiers. Standard errors are in parentheses, and clustered at the DSA-by-organ level. *** p<0.01, ** p<0.05, * p<0.1

	$\mathrm{Log}\ \#$	#/All Organs	# HCV/All HCV
DAA	$\begin{array}{c} 0.1374^{**} \\ (0.0686) \end{array}$	0.0243^{***} (0.0081)	-0.0353 (0.0237)
Baseline Mean Observations N of Clusters	$24.96 \\ 1,500 \\ 100$	$0.152 \\ 1,500 \\ 100$	$0.377 \\ 1,414 \\ 100$

Appendix Table 11: Livers Discarded Due to Poor Quality

Notes: The outcome variable in column 1 is the log number of livers that were discarded due to reasons related to poor quality per DSA-year (see footnote 22 in the main text for the definition of "poor quality"). Baseline means reflect the pre-treatment period (2005–2013) means for liver registrants only. In column 1, the mean reflects the DSA-year level count rather than log count. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 1) due to changes in DSA existence and services over time, which yields 50 kidney-recovering and 50 liver-recovering DSA identifiers. Note that, even though there are only 45 modified DSAs with liver transplant programs in our data, organ procurement organizations across all 50 modified DSAs recover and allocate livers from deceased donors, which explains the slightly larger number of clusters and observations here relative to Tables 2-4. Standard errors are in parentheses and are clustered at the DSA-by-organ level. *** p < 0.01, ** p < 0.05, * p < 0.1