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# EXTERNALITIES FROM MEDICAL INNOVATION: EVIDENCE FROM ORGAN TRANSPLANTATION

Kevin Callison Michael E. Darden Keith F. Teltser

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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 both HCV-positive and HCV-negative 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 list. 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 recipients between 2014 and 2019, driven in part by a 37% average annual increase in HCV-negative waiting list registrations. Our estimates imply that DAAs generated \$7.52 billion in positive externalities for HCV-negative patients during this period.

Kevin Callison
Department of Health Policy and Management
School of Public Health and Tropical Medicine
Murphy Institute for Political Economy
Tulane University
1440 Canal Street
New Orleans, LA 70112
kcallison@tulane.edu

Keith F. Teltser Department of Economics Andrew Young School of Policy Studies Atlanta, GA 30303 kteltser@gsu.edu

Michael E. Darden Carey School of Business Johns Hopkins University 100 International Dr. Baltimore, MD 21202 and NBER mdarden4@jhu.edu

A data appendix is available at http://www.nber.org/data-appendix/w31673

## 1 Introduction

The value of medical innovations partly rely 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 may align with or work against their direct social welfare implications. For example, Papageorge (2016) shows that a significant benefit of HIV treatments (HAART) was 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. Especially in cases in which new innovations are extremely costly relative to existing technology, valuing these behavioral effects may influence payer coverage decisions and research and development investment choices (Chernew & Newhouse, 2011; Philipson, 2000; Fendrick et al., 1996).

In this paper, we study a case where a medical innovation potentially shifted incentives, behaviors, and subsequent outcomes for a group of individuals who were not the primary beneficiaries of the innovation. We refer to these changes in welfare as innovation-induced externalities. Specifically, in December 2013, the Food and Drug Administration approved sofosbuvir, a direct-acting antiviral (DAA), for the treatment of chronic Hepatitis C (HCV). In combination with other medications, sofosbuvir achieves sustained viral clearance rates in over 90% of HCV patients. We quantify the innovation-induced externalities resulting from the introduction of DAAs for individuals with end-stage liver disease (ESLD) who tested negative for HCV. We begin by formulating 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 participating, the decision to accept or refuse an organ offered for transplant. In our model, the curative properties of DAAs preclude the need for a liver transplant for some  $HCV^+$  individuals, which both shrinks the existing number of  $HCV^+$  waiting list registrants and decreases the rate of new  $HCV^+$  waiting list additions. As a result of these changes, DAAs generate an external benefit to  $HCV^-$  individuals, both to those already on the liver transplant waiting list and to marginal  $HCV^-$  ESLD patients who are induced to list because the waiting list is shorter. In the model, DAA-induced changes to the rate of transplantation are ambiguous both because marginal  $HCV^-$  registrants change the health composition of the waiting list and because changes in the waiting list affect the optimal acceptance behavior of all registrants.

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 data contain information on liver health, including HCV status and Model for End-Stage Liver Disease (MELD) score, and other relevant outcomes of the wait-listing process, including transplantation and death. From these data, we find that the annual percentage of  $HCV^-$  waiting list registrants who received a transplant increased from 33% in 2014 to 65% by 2019. Additionally, annual  $HCV^+$  waiting list additions dropped from roughly 3,500 to 1,500, while annual  $HCV^-$  additions grew from 6,100 to more than 9,000. We detect significant improvements in the health composition of  $HCV^+$  registrants who remained on the waiting list in the post-DAA era, likely due to the steep drop in new  $HCV^+$  waiting list additions and a higher priority for transplant among those in worse health. We also find improved health among  $HCV^-$  waiting list registrants, likely due to a reduction in the average wait time from listing to transplant. In summary, the raw data suggest two clear implications of DAA availability. First, there was a reduction in the number of  $HCV^+$  individuals added to the liver transplant waiting list. Second, the beneficiaries of this change were  $HCV^-$  individuals with ESLD, both those on the waiting list and those induced to join.

While trends in the raw data imply significant welfare gains 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 before and after the introduction of DAAs to similar trends for kidney transplants. Using a traditional difference-in-differences (DiD) estimator, we find a 35.8% average annual increase in  $HCV^-$  liver transplants and a 39.1% decrease in  $HCV^+$  liver transplants following the availability of DAAs. This reallocation of organs from  $HCV^+$  to  $HCV^-$  transplant recipients resulted largely from a 45.4% decline in new  $HCV^+$  additions to the liver transplant waiting list. We estimate a total of 5,682 additional transplants to  $HCV^-$  individuals with ESLD over our six year sample period due to the availability of DAAs. Because additional  $HCV^-$  transplants did not crowd out  $HCV^+$  transplants, we conclude that the economically significant positive externalities to  $HCV^-$ 

liver transplant recipients added to the overall welfare benefits of DAAs. Under standard value of life assumptions, the net value of the positive externality to  $HCV^-$  liver transplant recipients was worth \$1.25 billion per year, or \$7.52 billion in total from 2014 to 2019.

The identification argument of the DiD estimator is that the comparison of trends in liver to kidney transplants nets out common shocks to the supply of organs for transplant, leaving changes induced by DAAs. Threats to the validity of this strategy include potential spillovers from DAA availability to kidney waiting list registrants. These spillovers may involve 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 be 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 following DAA introduction increased among liver and kidney waiting list registrants. Most importantly, between 2005 and 2013, 45% of all liver transplants went to  $HCV^+$  patients versus only 5% of all kidney transplants. 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.

Our study contributes to the larger literature on technological innovation by modeling and estimating behavioral responses to treatment innovations (Baranov et al., 2015; Peltzman, 2011; Dow et al., 1999). Even among ESLD patients who meet clinical guidelines and receive a referral, between 30% and 50% ultimately do not join the liver transplant waiting list (Jesse et al., 2019; Bryce et al., 2010, 2009), which suggests considerable capacity to adjust listing decisions. We estimate that DAAs were responsible for a 36.8% average annual increase in the number of  $HCV^-$  registrants added to the liver transplant waiting list. Therefore, we conclude that the mechanism driving our  $HCV^-$  listing result is largely behavioral, and our findings add to recent examples of innovation-induced behavioral responses, including statin medications and diet and exercise (Kaestner et al., 2014), HAART therapy and risky sex (Papageorge, 2016; Chan et al., 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 estimate of the positive externality to  $HCV^-$ 

 $<sup>^{1}</sup>$ In fact, we estimate that in the absence of DAA-induced listing by  $HCV^{-}$  patients, DAAs would have eventually eliminated the liver transplant waiting list altogether.

 $<sup>^{2}</sup>$ Of course, an alternative explanation for increased  $HCV^{-}$  listing is that the prevalence of diseases that cause

liver transplant recipients resulting from DAAs is larger than the estimate from an epidemiological simulation model that did not account for behavioral mechanisms (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) 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 were alternative treatments for conditions contributing to organ failure to be developed (e.g., improved hypertension control or diabetes treatment reducing demand for kidneys).

This paper is particularly relevant for policy in liver transplantation, which exhibits significant disparities in allocation by sex, race, and geography (Darden et al., 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 disparities in access to the liver transplant waiting list (Warren et al., 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 et al., 2016). Despite finding large effects of DAA availability on liver transplants, we observe that the Northeast had the slowest growth in  $HCV^-$  transplants following DAA availability;  $HCV^-$  transplant rates increased in the Northeast but not significantly until 2019. In summary, the results suggest that the positive externalities generated by DAAs were significant, but they were not equally spread across the 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 positive externality of DAAs to  $HCV^-$  patients 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

 $HCV^-$  patients to require a liver transplant also increased following DAAs. Indeed, in our data, the proportion of  $HCV^-$  registrants with alcoholic liver disease (ALD), the leading cause of  $HCV^-$  registration, increased following DAAs for unrelated reasons. However, using National Health and Nutrition Examination Survey (NHANES) data, we show that this increase was only a composition effect—the prevalence of ALD in the population was flat from 2014 through 2018.

 $HCV^+$  liver to an  $HCV^-$  Medicaid recipient, and that those with Medicaid coverage are less likely to join the waiting list conditional on evaluation (Thompson <u>et al.</u>, 2022; Wahid <u>et al.</u>, 2021; Kapadia <u>et al.</u>, 2018; Waters & Broder, 2018; Barua <u>et al.</u>, 2015). Valuing externalities may also play an important role in generating new ideas and innovations (Dranove <u>et al.</u>, 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).

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 et al. (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 et al. (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 suggest 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.

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 other states expressing interest in similar arrangements (Auty et al., 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 treatment, 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 et al., 2019; Zibbell et al., 2018). Traditional

treatments for HCV have had limited effectiveness and are associated with debilitating side effects (Burstow et al., 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, 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 et al., 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 et al., 2023; Chhatwal et al., 2017; He et al., 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 DAA treatment of HCV 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 et al., 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 Hepatits 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 et al., 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 et al., 2014). Prior studies have documented low rates of evaluation referrals and wait-listing among qualified ESLD candidates. For example, Goldberg et al. (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 et al., 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 frequently discarded (Levitsky et al., 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,  $HCV \in \{HCV^+, HCV^-\}$ . Higher values of h are assumed to indicate worse liver health following the MELD score, which is the relevant measure of liver health in the United Network for Organ Sharing (UNOS) liver allocation mechanism. The evolution of h is given by the state transition equation

<sup>&</sup>lt;sup>3</sup>The model extends the framework of Howard (2002), who focuses on the decision to accept an organ offer.

 $f(h_{t+1}|h_t, HCV)$ , which individuals (and physicians) must forecast. In representative period t, an individual in state  $(h_t, HCV)$  may pay  $p_l$  to be on the liver transplant list, which captures the pecuniary and non-pecuniary costs of listing and visiting with physicians (e.g., travel costs, transplant workup).<sup>4</sup> 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 longer participate, by accepting a liver for transplant, or through death, which occurs when liver health increases beyond  $H^{\omega}$ . 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 t and is decreasing in the number of individuals ahead on the waiting list t, where t is the sum of t and t and t waiting list registrants ahead. The probability is also an increasing function of the number of potential donors, t. If a liver is offered, its quality is given by t is given

The model takes the form of an optimal stopping problem conditional on being on the waiting list, where the decision to wait-list is endogenous. The following timeline provides an illustration of a representative period t in the model, showing the sequence of the events and decisions involved:

Listing Decision Liver Offer Health Evolution 
$$L_t \in \{0,1\} \qquad P(h_t,N_t,D_t) \qquad f(h_{t+1}|h_t,HCV)$$
State Vector 
$$Accept/Refuse$$

$$t-1 \qquad \{h_t,HCV\} \qquad Period t \qquad A_t \in \{0,1\} \qquad t+1$$

## 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, P(h, N, D), as 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 cash-out value is a function of pre-transplant liver health as a proxy for the potential for

<sup>&</sup>lt;sup>4</sup>Between 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).

complications from transplant. 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:

$$V^{R}(h_{t}, HCV) = U(h_{t}, I - p_{l}) + \delta EV(h_{t+1}, HCV).$$
(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  $H^{\omega}$ , 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 (paired with their physicians) 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  $\overline{q}$  as the quality of liver that leaves the individual indifferent between accepting and refusing an offer:  $V^A(h_t, \overline{q}) = V^R(h_t)$ . The associated implicit function of liver quality is a function of liver health, baseline individual-level Hepatitis C status, and the waiting list count:  $\overline{q}(h, HCV, N)$ . 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. We discuss the sign of  $\overline{q}_h(h, HCV, N)$  in our empirical work, but the number of individuals ahead of a given person negatively affects  $\overline{q}$  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, 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

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

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

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

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). The impact of such a shock on transplants and transplant outcomes is determined by the endogenous listing and organ acceptance decisions of both  $HCV^+$  and  $HCV^-$  individuals. That is, both the stock of and the flow to the wait 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. <sup>5</sup> The model is helpful in clarifying these effects, and it generates several hypotheses that we can test

<sup>&</sup>lt;sup>5</sup>In reality, a small number of transplants occur off the waiting list. We abstract from these cases here.

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  $HCV^+$  individuals, DAA availability implies that liver health  $h_{t+1}$  improves, which shifts their distribution of liver health to the left. Conditional on being on the waiting list, how this improvement in liver health affects acceptance behavior depends on  $\overline{q}_h(h, HCV, N)$ , 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,  $\overline{q}$  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,  $\overline{q}$  may be increasing in h, which says that healthier people require a healthier 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 may significantly change both the number and health composition of  $HCV^+$  waiting list registrants. Because 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. We summarize model predictions for baseline  $HCV^+$  individuals with the following testable hypotheses:

**Hypothesis 1**: The overall count of  $HCV^+$  individuals on the waiting list may go up or down depending on the relative magnitudes of  $HCV^+$  exits due to improve health, deaths, transplants, and additions.

**Hypothesis 2**: The health composition of  $HCV^+$  individuals on the list may improve or decline depending on the relative magnitudes of  $HCV^+$  individuals leaving the list because of

health improvement, the improvement in liver health for those remaining on the list, and the health of newly listed  $HCV^+$  who would have died in the absence of DAAs.

**Hypothesis 3**: The number of transplants to  $HCV^+$  individuals may increase or decrease depending on how the health composition of the  $HCV^+$  population on the waiting list changes and on the sign of  $\overline{q}_h(h, HCV^+, N)$ .

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 through the number of individuals ahead on the waiting list. If  $HCV^+$  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. We summarize model predictions for baseline  $HCV^-$  individuals with the following testable hypotheses:

**Hypothesis 4**: The overall count of  $HCV^-$  individuals on the waiting list may go up or down depending on the relative magnitudes of new  $HCV^-$  additions to the waiting list and the change in the number of transplants to  $HCV^-$  individuals.

**Hypothesis 5**: The health composition of  $HCV^-$  individuals on the waiting list may improve or decline depending on the health of  $HCV^-$  individuals induced to join the list by DAAs and the change in health composition due to the change in  $HCV^-$  acceptance behavior.

**Hypothesis 6**: DAA availability may cause the number of transplants to  $HCV^-$  individuals to increase or decrease depending on how the health composition of the  $HCV^-$  population on the waiting list changes and on the sign of  $\overline{q}_h(h, N)$ .

The theory demonstrates that changes in the number and health composition of the liver transplant waiting list will affect the transplant rates for both  $HCV^+$  and  $HCV^-$  individuals. Our data are well-suited to capture these changes. In what follows, we document raw trends in waiting list additions and exits due to improved health, death, and transplantation for both groups, and we present the change over time in the group average health on the waiting list, as measured by the MELD score. Our data also allow us to investigate an unmodeled, but potentially important, dynamic in the willingness of waiting list candidates 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 SRTR from 2005 to 2019 for our analyses.<sup>6</sup> The SRTR collects individual-level data on the universe of organ transplant waiting list registrants, donors, and transplant recipients from UNOS (Wright, 2022).<sup>7</sup> 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 DSA where each registrant wait-lists.<sup>8</sup> 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.

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

<sup>&</sup>lt;sup>6</sup>The SRTR data system includes data on all donors, wait-listed candidates, 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.

<sup>&</sup>lt;sup>7</sup>A 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.

<sup>&</sup>lt;sup>8</sup>Due 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. It is worth noting that 5 DSAs do not have a liver program. Thus, our sample includes 50 modified DSA identifiers for kidneys and 45 modified DSA identifiers for livers.

this information to infer the HCV status of waiting list registrants by examining the prevalence of diagnosis codes commonly found among  $HCV^+$  but not  $HCV^-$  liver transplant recipients, and vice versa. <sup>9,10</sup> For approximately 15% of waiting list registrants, neither the diagnosis code or the text description allow us to assign an HCV status, so we exclude these individuals from our analyses.

Table 1 presents descriptive statistics for liver transplant waiting list registrants by HCV status and over time. Waiting list registrations among  $HCV^+$  ESLD patients dropped from an average of 3,896 per year (35,068 total) during the 9 pre-DAA years 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, 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  $HCV^-$  ESLD patients, going from 5.191 to 7.803 average yearly listings, and 5.163 to 7.776 average yearly removals and transplants. For most of the  $HCV^+$  and  $HCV^-$  registrants, the most common outcome of the waiting list process is a transplant from a deceased donor, followed by removal from the waiting list due to being too sick to transplant or dying. For both  $HCV^+$  and  $HCV^-$  registrants, the probability of removal due to being too sick or dying 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.

 $<sup>^9{\</sup>rm For}$  example, 59% of  $HCV^+$  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  $HCV^+$  recipients and only 0.6% of  $HCV^-$  recipients. Conversely, "cirrhosis: fatty liver (NASH)" (SRTR code 4214) is found among 14.3% of  $HCV^-$  recipients compared to only 0.6% of  $HCV^+$  recipients. Likewise, "alcoholic cirrhosis" (SRTR code 4215) is present in 26.7% of  $HCV^-$  recipients and only 3.5% of  $HCV^+$  recipients. We identify additional  $HCV^+$  waiting list registrants by using an optionally provided text description field. The text strings in this description field include terms like "HCV," "Hepatitis C," "Hep C" as well as variations that may include periods, dashes, slashes, or minor typos.

<sup>&</sup>lt;sup>10</sup>Though we know the actual HCV status of transplant recipients, we use inferred status in all of our estimates for consistency. We have estimated transplant outcomes using actual HCV status, and our results are largely unaffected by the classification metric we use. For example, our coefficient estimate of the effect of DAA availability on transplants to  $HCV^-$  recipients is 0.31 using inferred HCV status and is 0.37 using actual HCV status. We also used 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 found little evidence of this misclassification affecting our results. For example, in 2014, 99 (3.2%) of the 3,128 liver transplant recipients that we categorized as  $HCV^-$  based on diagnosis code 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.

## 4.2 Trends in Liver Waiting List Additions/Removals and Transplant

In this section, we present a series of descriptive figures that track changes in the listing behaviors of  $HCV^+$  and  $HCV^-$  individuals. In most cases, we present these trends using a log transformation of the underlying numbers for the sake of comparability between  $HCV^+$  and  $HCV^-$  outcomes and, in the next section, with kidney waiting list registrants and transplant recipients. We quantify these changes using comparative interrupted time series (CITS) models, a more general form of the DiD design where each group is compared to its own baseline trend rather than to a counterfactual generated by an untreated group, such that there is no parallel trends assumption to satisfy. This is appropriate in our case because both  $HCV^+$  and  $HCV^-$  waiting list registrants are potentially affected by the development of DAAs. We stress that this exercise is meant to be largely descriptive in nature, and we conduct further analyses, including estimating effects using DiD models, in the following sections. A description of the CITS specification can be found in Appendix Section 1 and a full set of results in Appendix Table 1.

Figure 1a plots raw trends in the number of liver transplant waiting list registrants by HCV status. The number of  $HCV^-$  candidates on the waiting list remained largely stable between 2005 and 2009 before experiencing a gradual upward trend in 2010 that continued through 2019. In contrast, the number of  $HCV^+$  waiting list registrants exhibited a moderate decline from 2005 to 2013 before dropping dramatically after the introduction of DAAs in late 2013. In 2012, the last full year before DAAs became available, there were 6,486  $HCV^+$  liver transplant waiting list registrants; by 2019, that number had fallen by 60% to 2,576.

Figure 1b plots average MELD scores for  $HCV^+$  and  $HCV^-$  liver waiting list registrants over the sample period. Average MELD scores were rising (i.e., worsening) for both groups between 2005 and 2013, though at a slower rate for  $HCV^+$  waiting list registrants. Average MELD scores declined steeply following the availability of DAAs for  $HCV^+$  registrants, before bottoming out in 2017 and increasing modestly in 2018 and 2019. The average MELD score for  $HCV^-$  registrants appears to have been largely unaffected by the introduction of DAAs, though there is evidence of a trend break beginning in 2016. Appendix Figure 1 includes plots of initial MELD scores at the time of listing along with the last MELD score at the time of waiting list exit. Two trends in Appendix Figure 1 are worth noting. First, the average initial MELD score for  $HCV^-$  registrants increased from 2013 to 2015 before trending downward through 2017 and rising slightly in 2018 and 2019. CITS estimates

<sup>&</sup>lt;sup>11</sup>When interpreting the magnitudes of the changes implied by the coefficient estimates from our logged outcome models, we use the following calculation:  $\%\Delta = 100 \times (e^{estimate} - 1)$ .

in Appendix Table 2 confirm that the slope of the trend in average initial MELD score was lower in the post-DAA period for  $HCV^-$  registrants compared to the pre-DAA period. In other words, marginal  $HCV^-$  waiting list adds were healthier on average after the introduction of DAAs. Second, the average last recorded MELD score for  $HCV^-$  individuals receiving a transplant trended upward from 2005 through 2014 before beginning to decline once DAAs became available. This suggests that transplanted  $HCV^-$  individuals were in better health at the time of their transplant, which may have implications for post-transplant survival.

Figures 1c and 1d track changes to the supply of  $HCV^+$  livers proxied through the number of deceased donors and the share of waiting list registrants willing to accept an  $HCV^+$  liver by HCV status. Figure 1c shows that the number of deceased liver donors was stable before 2014 for both  $HCV^+$  and  $HCV^-$  individuals, and remained so for  $HCV^-$  donors through 2019. The number of  $HCV^+$  donors began to rise in 2014 and continued on an upward trend through 2019, indicating an increase in the supply of  $HCV^+$  organs available for transplant. Figure 1d reflects changes in demand for  $HCV^+$  livers. While potential improvements in waiting list outcomes for  $HCV^-$  registrants are likely driven by a reallocation of livers that would have otherwise gone to  $HCV^+$  registrants, another mechanism for outcome improvements among  $HCV^-$  registrants is an increased willingness to accept a liver from an  $HCV^+$  donor. The figure indicates that  $HCV^-$  registrant willingness to accept an  $HCV^+$  liver declined from just under 40% of waiting list additions in 2005 to roughly 10% of additions by 2013, and remained stable through 2015 before beginning to increase in 2016. By 2019, nearly 60% of  $HCV^-$  registrants added to the waiting list were willing to accept a liver from an  $HCV^+$  donor.

Underlying the trends presented in Figure 1a is a dynamic process of additions and removals from the transplant waiting list. Figure 2 provides insight into this process by plotting new waiting list additions by HCV status (2a) and the share of registrants removed from the waiting list for three reasons: the registrant became too sick to transplant or died while on the waiting list (2b), they were removed from the waiting list because their condition improved (2c), or they received a liver transplant (2d). Figure 2a shows that following the introduction of DAAs in 2013, waiting list additions for  $HCV^+$  candidates sharply declined, while additions for  $HCV^-$  candidates rose. The estimates from our CITS models indicate an average annual increase in waiting list additions of 20.5% from 2014 to 2019 for  $HCV^-$  participants and an average annual decrease of 54.9% for  $HCV^+$  participants relative to each group's baseline mean (see Appendix Table 1 for a full set of CITS estimates).

Figure 2b shows waiting list removals due to deteriorated condition or death for  $HCV^-$  registrants increasing gradually in the period before DAA availability. However, once DAAs were made available, the rate of removals leveled off, resulting in an average annual reduction of 16.1% in  $HCV^-$  removals due to deteriorated condition/death compared to the pre-DAA trend.  $HCV^+$  waiting list removals for deteriorated condition or death declined by an average of 70.1% each year following the introduction of DAAs relative to the group's baseline mean.

Figure 2c shows that  $HCV^+$  registrants are consistently more likely to leave the waiting list because their conditions improved compared to  $HCV^-$  registrants. As expected, there appears to be no indication of waiting list removal due to improved health for  $HCV^-$  registrants associated with DAA availability. The trend for  $HCV^+$  waiting list registrants appears to decline beginning in 2015; however, our CITS estimate of this trend change is not statistically significant.

Finally, Figure 2d tracks changes in annual liver transplants and indicates a stark trend change for both  $HCV^+$  and  $HCV^-$  individuals beginning in 2014. From 2014 to 2019, the number of  $HCV^-$  individuals receiving a liver transplant increased by 43.4% per year relative to their baseline trend, while the number of  $HCV^+$  individuals receiving a transplant decreased by 46.8% per year, on average. 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%.

There are several key takeaways from the patterns we observe in Figures 1 and 2. Addressing hypotheses 1-3, we see a dramatic reduction in the number of  $HCV^+$  waiting list participants, an improvement in the health composition of  $HCV^+$  patients who remain on the waiting list, and a significant decline in  $HCV^+$  transplants.<sup>12</sup> The increase in the share of  $HCV^+$  registrants removed due to condition improvement is also consistent with the reduced MELD scores of newly added  $HCV^+$  registrants since DAAs became available (see Appendix Figure 1). For  $HCV^-$  individuals, the overall count on the list increased only marginally (hypothesis 4) because both waiting list additions and transplants increased dramatically (hypothesis 6). Addressing hypothesis 5, the data suggest that the health composition of  $HCV^-$  individuals on the waiting list and those newly registering improved following DAAs. Further, Figures 1 and 2 highlight the extent of the positive externalities of DAA development that have accrued to  $HCV^-$  individuals with ESLD. Namely, reduced demand for livers

<sup>&</sup>lt;sup>12</sup>Though the total number of transplants for  $HCV^+$  candidates fell after DAAs became available, transplants to  $HCV^+$  waiting list registrants as a fraction of all wait-listed  $HCV^+$  registrants increased (see Appendix Figure 2).

from  $HCV^+$  individuals has resulted in greater organ availability for  $HCV^-$  individuals. Coupled with an increased willingness on the part of  $HCV^-$  waiting list registrants to accept  $HCV^+$  livers, there has been a substantial increase in liver transplants for  $HCV^-$  individuals with ESLD following the availability of DAAs.

## 5 Estimation

CITS models allow us to compare relative changes in outcomes between  $HCV^+$  and  $HCV^-$  individuals, measured as deviations from each group's own baseline trend. While these estimates imply substantial gains for  $HCV^-$  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. Therefore, in this section, to capture the externalities generated by the availability of DAAs, we estimate a traditional DiD design that compares outcomes for liver transplant waiting list registrants and transplant recipients (both  $HCV^+$  and  $HCV^-$ ) to similar outcomes for kidney registrants/recipients before and after the introduction of DAAs.<sup>13</sup>

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  $HCV^-$  liver waiting list registrants. 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 3). 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 et al., In press). CITS models are unable to distinguish between concurrent shocks and thus estimate the combined effect of DAAs and drug overdose deaths on changes in transplant and waiting list registration. However, insofar as the magnitude of the drug overdose supply shock was similar for both  $HCV^-$  liver waiting list participants and kidney waiting list participants, our DiD models will difference out the influence of overdose deaths, allowing us to isolate the effect of DAAs.  $^{14}$ 

 $<sup>^{13}</sup>$ 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.

<sup>&</sup>lt;sup>14</sup>Another potential concurrent shock is ACA Medicaid expansion, which 26 states and D.C. adopted in 2014. Lemont (2023) shows that Medicaid expansion was associated with similar increases in both liver and kidney waiting

Figure 3 plots the number of deceased donor livers and kidneys recovered for transplant separately by HCV status. Figure 3a 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 et al., 2018)) and an increased willingness among waiting list registrants to accept  $HCV^+$  organs. Figure 3b shows a much smaller increase 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. Appendix Table 3 provides descriptive statistics for the kidney waiting list registrants used in our DiD analyses.

We estimate the following DiD specification separately for  $HCV^+$  and  $HCV^-$  liver transplant waiting list registrants and transplant recipients using kidney registrants and recipients as controls:

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

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

For our DiD models to produce credible causal estimates of the effect of DAA availability on  $HCV^+$  and  $HCV^-$  individuals with ESLD, baseline differences in outcomes between liver and kidney registrants/recipients must remain stable over time in the absence of DAAs. While this parallel trends assumption is not directly testable, we provide suggestive evidence that it holds by adding trends in listing and transplant outcomes for kidney transplant waiting list registrants to trends for liver transplant registrants/recipients from Figure 2. Figure 4 shows that kidney waiting list additions were largely stable over our sample period, with a slight uptick from 2017 to 2019 (Figure 4a). The patterns in kidney waiting list removals due to deteriorated condition or death and removals due to improved condition are similar to those for  $HCV^-$  liver waiting list registrants (Figures 4b and 4c). In addition, kidney transplants tracked closely with both  $HCV^+$  and  $HCV^-$  liver transplants through 2013 (Figure 4d).

list registrations (34% for livers and 38% for kidneys) and transplants (40% for livers and 50% for kidneys) for Medicaid beneficiaries. While our DiD models should address potential confounding from Medicaid expansion, we also estimated DAA effects for wait-listing and transplant restricting our sample to DSAs in states that had not yet expanded Medicaid by 2019. Estimates were similar to those from our full sample and are available upon request.

More formally, we also assess the validity of the parallel trends assumption by estimating the following 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 estimate,  $\beta_k$ , 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 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 registrants/recipients as well as the dynamics of the treatment effects across the post-treatment periods.

Another consideration of using characteristics of kidney transplant waiting list registrants and transplant recipients 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.<sup>15</sup> Third, those cured of HCV may become less likely to develop ESRD and join the kidney waiting list, <sup>16</sup> 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 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.

Figure 5b examines whether DAAs affected the supply of kidneys available for transplant in the case where those newly cured of HCV become 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

<sup>&</sup>lt;sup>15</sup>Using a simulation model and data from the U.K., 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.

<sup>&</sup>lt;sup>16</sup>This is because HCV potentially increases the risk for developing ESRD (Lee et al., 2014).

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 a small (1.2 percentage point) reduction in the share of kidney transplant recipients who are  $HCV^+$  from 2013 to 2019 in Figure 5d.

While Figure 5 demonstrates little evidence of kidney supply shocks associated with the availability of DAAs, similar to  $HCV^-$  liver registrants, DAAs do appear to influence demand for  $HCV^+$  kidneys through kidney waiting list registrants' increased willingness to accept an  $HCV^+$  organ. 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.

## 6 Results

#### 6.1 Waiting List Additions and Transplants

Table 2 contains our DiD estimates of the effect of DAA availability on liver transplant waiting list additions, transplants, and waiting list removals due to deteriorated condition/death and condition improvement. The estimates in columns 1–4 are from models where the dependent variables are measured in logs, while the estimates in columns 5–7 are from models where the dependent variable is defined as a fraction of the group-specific number of registrants on the waiting list. The estimates in column 1 indicate that DAAs resulted in a 36.8% increase in average annual  $HCV^-$  liver waiting list additions, while reducing average annual  $HCV^+$  liver waiting list additions by 45.4% compared to kidney waiting list additions.

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  $HCV^-$  waitlisting following the introduction of DAAs.<sup>17</sup> However, a competing explanation for the observed

 $<sup>^{17}</sup>$ According 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 4 plots trends in time from wait listing to transplant for  $HCV^-$  recipients and shows

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 estimated changes in waiting list additions by leading non-HCV disease indicators for wait-listing including nonalcoholic steatohepatitis (NASH) and ALD. These estimates are included in Appendix Table 5 and indicate that  $HCV^-$  waiting list additions following DAAs are being driven by individuals with ALD. Second, we used 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 5 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.

The combination of these findings leads us to 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), that physicians assign lower waiting list priority to ESLD patients who use alcohol, and that rates of liver transplant wait-listing among ALD patient are as low as 5% (Leong & Im, 2012).

Table 2, column 2 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 35.8% relative to changes in kidney transplants in the post-DAA era. The 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.

Figure 6 presents event study estimates that correspond to the DiD estimates in Table 2, columns 1 and 2. Relative to the kidney waiting list, changes in liver waiting list additions were near zero in the pre-DAA period for both  $HCV^+$  (Figure 6a) and  $HCV^-$  registrants (Figure 6b), a finding that supports the validity of our identification strategy.  $HCV^+$  liver waiting list additions began to

a steep decline following the introduction of DAAs. Estimates in Appendix Table 4 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.

<sup>&</sup>lt;sup>18</sup>An 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.

<sup>&</sup>lt;sup>19</sup>We could not include NHANES data for 2019 in our ALD prevalence rate estimates as the 2019/2020 NHANES data collection was halted due to COVID-19.

decline relative to kidney waiting list additions in 2014 and continued to decline in each year through 2019. In contrast, liver waiting list additions for  $HCV^-$  registrants began to increase shortly after DAAs became available and continued to increase through 2017, before leveling off in 2018 and 2019. We plot event study estimates for liver transplants compared to kidney transplants in Figures 6c for  $HCV^-$  liver recipients and 6d for  $HCV^+$  liver recipients. In both cases, trends in the pre-DAA period were flat, with annual estimates growing over time since 2013/2014.

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.

The estimates in Table 2, columns 3 and 4 indicate that DAAs had minimal effect on the number of liver waiting list removals among  $HCV^-$  registrants who became too sick to transplant or died, but they appreciably reduced waiting list removals for deteriorated condition/death for  $HCV^+$  registrants. We estimate a 54.6% average annual reduction in  $HCV^+$  waiting list removals for deteriorated condition/death. Both  $HCV^-$  and  $HCV^+$  waiting list participants saw similar increases in liver waiting list removals due to condition improvement. Removals for condition improvement increased by 18.9% for  $HCV^-$  and by 16.1% for  $HCV^+$  liver waiting list registrants compared to those on the kidney transplant waiting list. Figure 7 includes event study plots for liver waiting list removal due to deteriorated condition/death and condition improvement. In each case, the pre-period trends are stable, though with the exception of  $HCV^+$  liver waiting list removals due to deteriorated condition/death, the estimates are noisy and exhibit no clear pattern in the post period.  $HCV^+$  liver waiting list removals due to deteriorated condition/death follow a similar pattern to event study estimates for  $HCV^+$  liver transplants, declining monotonically after the introduction of DAAs.

Table 2, columns 5–7 provide estimates of the effect of DAAs on transplant and waiting list outcomes scaled by the number of waiting list registrants by HCV status. Thus, these estimates effectively remove the influence of DAA-induced changes to waiting list inflows and outflows and provide an indication of how DAAs impacted existing waiting list registrants (i.e., effects conditional on wait-listing). We continue to find large increases in transplants to  $HCV^-$  recipients (16.0 percentage points), though the effect on transplants for  $HCV^+$  recipients is now small and not statistically significant. We interpret this finding as evidence that the large transplant reductions to  $HCV^+$  recipients we identified in Table 2, column 2 is driven by  $HCV^+$  individuals who are cured through

DAA treatment and avoid listing altogether.

The estimates in columns 6 and 7 indicate small increases in  $HCV^-$  waiting list removals due to deteriorated condition/death (2.7pp) and condition improvement (1.9pp). Again, the estimates in column 6 suggest that the large effect estimate on  $HCV^+$  waiting list removals due to deteriorated condition/death in column 3 is driven by fewer  $HCV^+$  registrants. Waiting list removals due to condition improvement for existing  $HCV^+$  registrants increased by 4.7pp, likely due to receiving treatment for HCV once DAAs became available. Event studies for scaled outcomes in columns 5–7 are plotted in Appendix Figures 6 and 7.

Finally, our model suggests that DAA availability could increase the supply of donors, and the descriptive evidence we presented in 1d showing trends in the willingness of registrants to accept an  $HCV^+$  liver is consistent with this prediction. While those with ESLD might be more likely to accept an  $HCV^+$  liver when DAAs become available, our model indicates that they will also 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 6.<sup>20</sup> 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 share of poor quality discards increased by 2.4 percentage points (column 2). Alternatively, estimates in column 3 of Appendix Table 6 show that there was no relative increase in the share of  $HCV^+$  livers discarded due to poor quality in the DAA era. 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 quality.

## 6.2 Reconciling CITS and DiD Estimates

In Section 4.2, we discussed 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 used a CITS procedure, which is detailed in Appendix Section 1. We then presented DiD estimates that assessed the effect of DAAs on transplant and liver waiting list

<sup>&</sup>lt;sup>20</sup>We 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.

outcomes, using kidney transplant waiting list registrants and transplant recipients as a control group. In this section, we compare the estimates generated by these two different techniques and briefly describe the relevance of this exercise to our preferred identification strategy of comparing liver to kidney transplant waiting list registrants and transplant recipients.

Table 3 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 2013. 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, 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 3 merit particular attention. 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 waiting list registrants and transplant recipients to approximate the counterfactual in our DiD model.

## 6.3 Heterogeneity in HCV<sup>-</sup> Transplant Gains

Table 4 presents estimates of the effect of DAA availability on liver transplants for  $HCV^-$  recipients 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.<sup>21</sup> 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.<sup>22</sup> 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 4, 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 annual gain in  $HCV^-$  transplants for those between the ages of 18 and 39, a 21.6% average annual gain for those ages 40 to 64, and a 43.0% average annual gain for those ages 64 and older.

Panel B, columns 4 and 5 show that  $HCV^-$  transplants to white recipients increased by 50.7%,

<sup>&</sup>lt;sup>21</sup>These 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).

<sup>&</sup>lt;sup>22</sup>In 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).

on average, compared to a relative increase of only 17.3% for non-white recipients. Despite a higher burden of chronic 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 et al., 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 et al., 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 et al., 2015; Yeh et al., 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 conducted a heterogeneity analysis that allowed the effect of DAAs on wait-listing and transplants for  $HCV^-$  recipients to vary by baseline DSA HCV prevalence.<sup>23</sup> 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 up 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 model specification indicate a strong doseresponse relationship between HCV prevalence and both  $HCV^-$  wait-listing and transplants to

<sup>&</sup>lt;sup>23</sup>The model specification is akin to a triple difference model where we compared liver waiting list registrants/transplant recipients to kidney registrants/recipients and allowed that comparison to vary by the baseline share of DSA transplant recipients testing positive for HCV.

 $HCV^-$  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.

## 7 Value of Externalities

Our DiD event study estimates from Table 3 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 vear, in value to  $HCV^-$  transplant recipients between 2014 and 2019. 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, we found evidence that  $HCV^-$  transplant recipients are in slightly 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. For context, Chhatwal et al. (2015) estimate that providing DAAs for all  $HCV^+$  patients in 2015 at market prices would have cost roughly \$65 billion. Recognizing that providing all patients with DAAs would have generated further externalities, our estimated externality is roughly 11.5% of the total potential market for DAAs in 2015.

The heterogeneity in the mechanisms driving the transplant results highlighted above generates uncertainty regarding the life-years gained from a liver transplant. Rana et al. (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 et al. (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  $HCV^-$  ESLD patients are large. For example, Jena et al. (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 et al. (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 et al., 2019), 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  $2019.^{24}$  That same year, there were 6,182 liver transplants performed on  $HCV^-$  recipients and, as Figure 2d indicates, this number was maintaining an upward trend in the post-DAA period. As a result, our estimates suggest that the development of DAAs would have effectively eliminated the liver transplant waiting list with no DAA-induced  $HCV^-$  wait-listing. Instead the gap between the number of  $HCV^-$  waiting list adds and transplants to  $HCV^-$  recipients was actually larger in  $2019\$ than in 2012, prior to the development of DAAs.  $^{25}$ 

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 indicate that Medicare beneficiaries accounted for 22.5% and Medicaid beneficiaries accounted for 8.1% of DAA-induced transplants to

 $<sup>^{24}</sup>$ The actual number of  $HCV^-$  liver transplant waiting list adds in 2019 was 9,399.

<sup>&</sup>lt;sup>25</sup>There 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).

 $HCV^-$  recipients from 2014 through 2019. Combined, these results imply that \$389 million per year of the innovation-induced externality generated by DAAs accrued to publicly-insured patients.

## 8 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, individuals with marginal  $HCV^-$  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 still highlight the presence of these externalities. Additionally, it is likely we underestimate the number  $HCV^-$  liver transplant waiting list registrants, and our results show larger effects when HCV status is measured at transplant rather than at listing. In sum, we provide the first retrospective evidence on these effects for the U.S. population, and 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 et al. (2016), Chhatwal et al. (2023) simulates 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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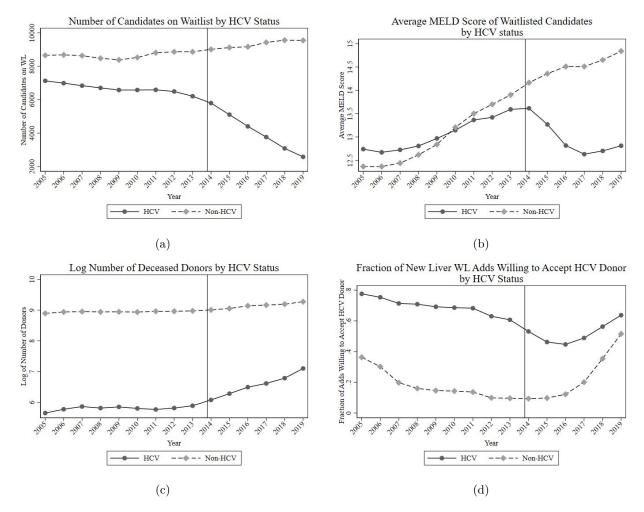
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## Figures and Tables

Figure 1: Liver Waiting List Characteristics and Supply of Deceased Donors



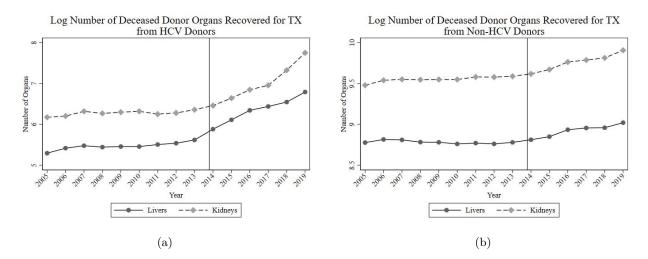
Notes: Authors' calculations of yearly national log counts, fractions, and means using SRTR data.

Log Waitlist Additions by HCV Status Log Waitlist Removals b/c Too Sick or Died by HCV Status Log of Number of Additions 8.5 9 Log Number of Removals 6.5 HCV ----- Non-HCV ----- Non-HCV (a) (b) Log Transplants by HCV Status Log Waitlist Removals b/c Improved Condition by HCV Status Log Number of Removals Log Number of Transplants 7.5 8 8.5 Year HCV ----- Non-HCV HCV ----- Non-HCV (d) (c)

Figure 2: Liver Waiting List Inflows and Outflows

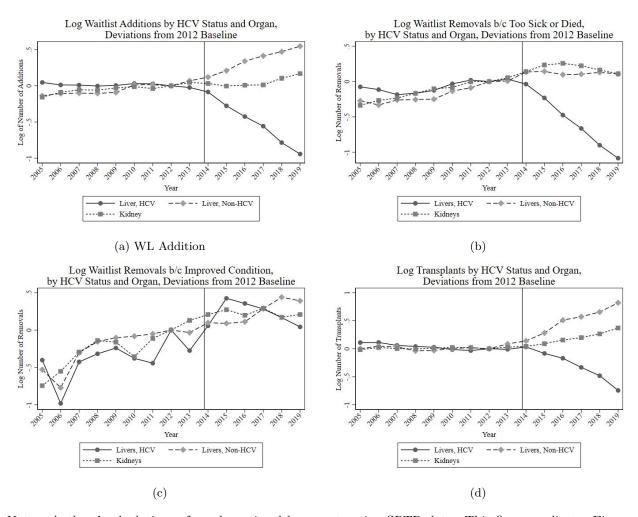
Notes: Authors' calculations of yearly national log counts using SRTR data.

Figure 3: Supply of  $HCV^+$  and  $HCV^-$  Donor Organs



Notes: Authors' calculations of yearly national log counts using SRTR data. Includes all livers and kidneys 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. he 2005-2013 average number of  $HCV^+$  kidneys recovered is 531; the corresponding average for livers is 237.

Figure 4



Notes: Authors' calculations of yearly national log counts using SRTR data. This figure replicates Figure 2, adding the kidney candidate comparison group and recalculating the trends in terms of deviations from the baseline period, which we set as the year 2012. We exclude kidney candidates who are known to have an HCV-related diagnosis using the optional diagnosis text field in the data.

Log Number of Living Donor Kidney Transplants by Donor Anti-HCV Status Fraction of New WL Adds Willing to Accept HCV Donor 10 Fraction Willing to Accept HCV Donor Log Number of Transplants ------ Non-HCV Liver Registrants - HCV+ Donors Kidney Registrants (b) (a) Log Number of HCV+ Transplant Recipients by Organ Share of HCV+ Transplant Recipients by Organ Log Number of TX Recipients Fraction of TX Recipients Livers ----- Kidneys Livers ----- Kidneys (d) (c)

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

Notes: Authors' calculations of yearly national log counts and fractions using SRTR data. In panel (a), we exclude kidney candidates 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 candidates from 2005 to 2019. Panels (c) and (d) use known HCV antibody test results, which are only observable for those who receive a transplant at the time of transplant, to identify  $HCV^+$  transplant recipients.

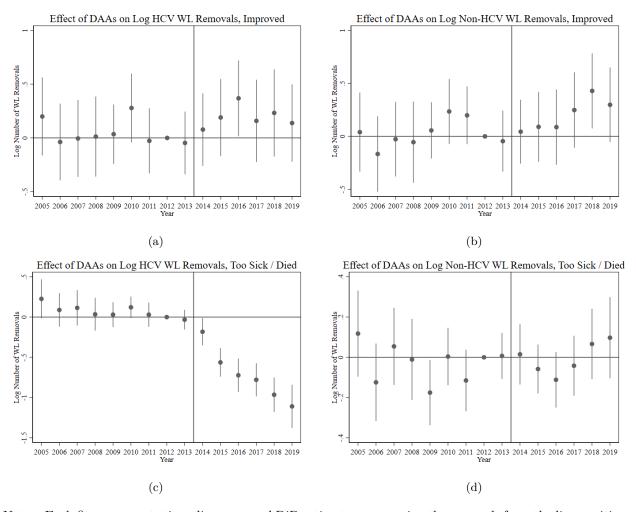
Figure 6: Liver vs. Kidney Waiting List Additions and Transplants, Log Counts

Notes: Each panel presents time-disaggregated DiD estimates, comparing  $HCV^+$  and  $HCV^-$  liver waiting list additions and transplants to kidney waiting list additions and transplants. 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  $100 \times (e^{\beta_k} - 1)$ . The bars around each coefficient reflect the 95% confidence interval using standard errors clustered at the DSA-by-organ level.

(d)

(c)

Figure 7: Liver vs. Kidney Waiting List Removals Due to Improved/Deteriorated Condition, Log Counts



Notes: Each figure presents time-disaggregated DiD estimates, comparing the removals from the liver waiting list for both  $HCV^+$  and  $HCV^-$  patients due to improved and deteriorated conditions, with the corresponding removals from the kidney waiting list. 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.

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

	Liver Candidates, $HCV^+$				Liver Candidates, $HCV^-$				
	2005-19		2005 - 13	2014-19		2005-19		2005 - 13	2014-19
	Mean	SD	Mean	Mean	Me	ean	SD	Mean	Mean
Too Sick / Died	0.257	0.437	0.269	0.235	0.2	226	0.418	0.240	0.213
Improved	0.048	0.213	0.032	0.079	0.0	067	0.251	0.066	0.069
Dec. Don. TX	0.511	0.500	0.511	0.511	0.5	535	0.499	0.510	0.559
Liv. Don. TX	0.014	0.119	0.015	0.014	0.0	)27	0.163	0.024	0.031
Days to TX	316.7	548.8	302.1	346.1	22	8.1	473.4	241.5	215.9
Initial MELD	16.47	8.13	16.60	16.15	19	.67	9.17	19.18	20.15
High School or Less	0.582	0.493	0.576	0.593	0.4	148	0.497	0.470	0.429
White Pct.	0.680	0.466	0.691	0.654	0.7	731	0.444	0.736	0.725
Primary Payer: Private	0.549	0.498	0.584	0.464	0.6	609	0.488	0.642	0.576
Primary Payer: Medicare	0.251	0.433	0.226	0.311	0.2	236	0.424	0.217	0.255
Primary Payer: Medicaid	0.200	0.400	0.190	0.225	0.1	155	0.362	0.141	0.170
Listing Age 18 to 39	0.022	0.147	0.024	0.019	0.1	135	0.341	0.139	0.131
Listing Age 40 to 64	0.873	0.333	0.906	0.792	0.6	694	0.461	0.713	0.675
Listing Age Over 64	0.105	0.307	0.070	0.189	0.1	171	0.377	0.148	0.194
South Census Region	0.372	0.483	0.359	0.405	0.3	379	0.485	0.361	0.397
NE Census Region	0.220	0.414	0.228	0.199	0.1	186	0.389	0.195	0.177
MW Census Region	0.170	0.375	0.170	0.170	0.2	231	0.422	0.236	0.226
West Census Region	0.238	0.426	0.243	0.226	0.2	204	0.403	0.208	0.201
N of Listings	49,499		35,068	$14,\!431$	93,	542		46,719	$46,\!823$
N of WL Removals & TXs	54,058		$36,\!157$	17,901	93,	123		46,470	46,653

Notes: Authors' calculations of fraction of liver candidates 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 candidates 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 candidates, or 24,847 of 167,888 total liver candidates who listed between 2005 to 2019.

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

		Log Oı	itcomes	Outcome/WL Size			
	WL Additions (1)	Transplant (2)	Too Sick / Died (3)	Improved (4)	Transplant (5)	Too Sick / Died (6)	Improved (7)
Panel A: $HCV^-$							
DAA	0.3134*** (0.0545)	0.3059*** (0.0514)	0.0215 $(0.0665)$	0.1733* (0.0889)	0.1604*** (0.0407)	0.0274*** (0.0095)	0.0194*** (0.0049)
Baseline Mean Observations Number of Clusters	115.36 1,425 95	61.27 1,425 95	27.52 1,425 95	7.60 1,425 95	0.507 $1,425$ $95$	0.161 $1,425$ $95$	0.046 $1,425$ $95$
Panel B: $HCV^+$							
DAA	-0.6044*** (0.0601)	-0.4965*** (0.0578)	-0.7886*** (0.0717)	0.1490* (0.0822)	0.0576 $(0.0392)$	-0.0144 (0.0121)	0.0473*** (0.0055)
Baseline Mean Observations Number of Clusters	86.59 1,425 95	46.89 1,425 95	23.99 1,425 95	2.88 1,425 95	0.506 $1,425$ $95$	0.181 $1,425$ $95$	0.026 $1,425$ $95$

Notes: The outcome variable in column 1 is the log number of new waiting list additions per DSA-year. In columns 2–4, the outcome variables are defined as log counts of waiting list/transplant outcomes. Note that these first four columns of coefficients represent log point changes, which can be transformed into percentages using the formula  $100 \times (e^{\hat{\beta}} - 1)$ . In columns 5–7, the outcome variables are defined as waiting list/transplant outcome counts divided by the organ-specific number of candidates on the waiting list. Baseline means reflect the pre-treatment period (2005–2013) means for liver candidates only. In columns 1–4, 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 8) 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

Table 3: CITS vs. DiD Estimates of  $HCV^-$  Candidate Transplants

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

Notes: The outcome variables in columns 1 and 2 are log number of transplants received by  $HCV^-$  candidates, 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 candidates (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 8) 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

Table 4: Heterogeneity in Log Transplants to  $HCV^-$  Candidates, Subsample Regressions

	(1)	(2)	(3)	(4)	(5)
Panel A: Primary Payer, Sex	Private	Medicare	Medicaid	Male	Female
DAA	0.3138*** (0.0539)	0.3797*** (0.0616)	0.1825** (0.0835)	0.3257*** (0.0522)	0.2672*** (0.0557)
Baseline Mean	39.02	11.66	7.85	36.62	24.65
Observations Number of Clusters	$     \begin{array}{r}       1,425 \\       95     \end{array} $	$1{,}425$ $95$	1,425 $95$	1,425 $95$	1,425 $95$
Panel B: Age, Race	18 to 39	40 to 64	Over 64	White	Non-White
DAA	0.1977*** (0.0574)	0.1955*** (0.0550)	0.3579*** (0.0685)	0.4098*** (0.0535)	0.1593*** (0.0554)
Baseline Mean	9.15	43.91	8.20	45.60	15.67
Observations	$1,\!425$	$1,\!425$	$1,\!425$	1,425	1,425
Number of Clusters	95	95	95	95	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)	0.3758*** (0.0580)	
Baseline Mean	39.08	14.10	6.35	62.91	
DAA x Northeast	-0.0007 (0.1630)	0.1441 (0.1448)	0.1833 (0.2113)	0.0451 $(0.1539)$	
Baseline Mean	49.11	14.37	11.24	78.98	
DAA x Midwest	0.3209*** (0.1000)	0.4105*** (0.1081)	0.1251 (0.1498)	0.3113*** (0.1049)	
Baseline Mean	36.76	10.45	7.16	56.15	
DAA x West	0.3201*** (0.0930)	0.3626*** (0.0796)	0.3864*** (0.0873)	0.3398*** (0.0692)	
Baseline Mean	35.44	6.98	9.43	53.78	
Observations Number of Clusters	$1{,}425$ $95$	$1{,}425$ $95$	$1{,}425$ $95$	$1{,}425$ $95$	

Notes: Each coefficient in Panels A and B come from separate DiD regressions of log transplants received by  $HCV^-$  candidates 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) means for  $HCV^-$  liver recipients only. While there are 57 DSAs in the U.S., we use modified DSA identifiers (see footnote 8) 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