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Mathew Padanilam March 29, 2019

An Economic Analysis of Transplanting Hepatitis C Positive Hearts in Uninfected Recipients

By

Mathew Padanilam

Dr. Ian McCarthy

Adviser

Department of Economics

Dr. Ian McCarthy

Adviser

Dr. C. Michael Hart

Committee Member

Dr. David Howard

Committee Member

Dr. Evan Saltzman

Committee Member

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Abstract

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Heart transplants are the most effective approach to treating the growing population suffering from heart failure. However, presently the demand for hearts far outpaces the supply. The previously chronic and incurable Hepatitis C (HCV) infection is now curable in a 12-week, highly-effective, and well-tolerated dose of direct-acting antivirals (DAA). Using HCV-infected hearts in uninfected patients represents an enormous potential to expand the donor pool. In the past 20 years, the prevalence of HCV positive organ donors has increased tremendously. This is in part due to unsafe practices such as needle sharing in populations at risk to overdosing as a result of the opioid epidemic. These individuals tend to be younger, healthier, and donate organs of higher quality compared to the general pool. Yet, only a small fraction of HCV positive organs is used for transplantation. Using a fixed-effects regression analysis which controlled for center-related variations, clinical factors, and changes over time, this study found multiple significant positive externalities at the hospital level in adopting the HCV strategy. By adopting the HCV strategy, the highest priority patients experience an 18.614-day reduction in wait days compared to the current 37.246 average days. This significant reduction in wait time is associated with better outcomes and reduced costs. Hospitals perform 1.849 more transplants per quarter and can more effectively serve the aging population. Heart failure is a major economic burden on the United States and using the currently wasted potential of HCV hearts has the potential to alleviate a major inefficiency in the organ market.

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Table of Contents

I. Background and Motivation:

Organ transplantations increase a patient's longevity and quality of life. Due to ethical concerns, the organ transplant market in the United States is highly regulated. Public policy prohibits organs from being bought or sold: effectively setting a price ceiling of $0 (1984). The nature of the market where altruism is a dominant factor and public policy is restricting has resulted in a severe shortage of organs for patients on waitlists. On average, 20 patients die every day due to lack of available organs (2019). Given the extreme resource constraint and number of patients in dire need, it is imperative that the usage of all available organs is maximized.

Hepatitis C (HCV) was previously an incurable chronic disease, and similar to human immunodeficiency virus (HIV), organs from HCV infected patients were never considered for transplantation. Recent advances in direct-acting antiviral (DAA) therapy have provided a curative option for those infected with HCV. This advancement has opened the opportunity to transplanting HCV naïve (non-infected) patients with infected organs. Having a highly effective curative option has been a medical breakthrough and allows for the intentional transplantation of organs from infected donors to uninfected recipients. HCV is common among individuals who inject drugs. Although treating infected individuals may reduce transmission and have an economy of scale impact on reducing HCV's comorbidity with drug overdoses, presently, many organ donors are still infected at the time of death from drug overdoses (Natasha K. Martin 2016, Hayley Bennett 2017). This is especially true for individuals currently affected by the prescription and intravenous drug abuse epidemic. Utilizing organs from such HCV infected persons and treating the recipient post transplantation could alleviate some of the dire shortage of organs for transplant, result in a potential significant expansion to the donor pool, and decrease

in transplant wait times. This, in turn, could decrease the need for expensive therapies while awaiting transplantation leading to cost savings and better clinical outcomes.

This study will retrospectively analyze national data on heart transplant donors and recipients to determine the advent of DAAs' effect on wait time and total number of transplants at the hospital level. The data is also compared with individual patient chart review of heart transplantations at St. Vincent Hospital, Indianapolis. The results will be informative of the economic efficiency of expanding the donor pool as well as the improved clinical outcomes and cost-saving mechanisms of decreasing patient wait time.

II. Introduction:

The opioid epidemic has resulted in a high prevalence of HCV infection in a subpopulation due to needle sharing and unsafe sexual practices. An unfortunate externality of the opioid epidemic has been an increase in the deaths of otherwise healthy young individuals from drug overdose. Many of these individuals are organ donors, but their organs were discarded due to an active HCV infection. The number of organ donors infected with HCV has increased substantially with the onset of the opioid epidemic. Table 1 describes the number of organ donors eligible for procurement since 2000, described by HCV antibody test result. The proportion of HCV+ donors available has significantly increased since 2000 and was as high as 7.25% of all donors with a determinant HCV antibody status in 2017. Given the comorbidity of HCV with the opioid epidemic and recent advancements in DAA therapy, the organ market is currently experiencing a positive supply shock.

Although organ supply is currently experiencing a positive shock, the demand for organs continues to far exceed the supply. It is imperative that all healthy organs are used. In order to

maximize utilization, donor organs infected with pathogens such as HIV, hepatitis B (HBV), and/or HCV were typically transplanted into recipients concurrently infected with the virus. However, the specificity of organ matching is dependent on a multitude of factors and the supply of infected organs were not always able to match with the small pool of infected recipients.

Table 1: Number of HCV positive and negative donors listed since 2000.

Year	HCV- Donors	% Change Since 2000	HCV+ Donors	% Change Since 2000
2000	5782	0	181	0
2001	5865	1.435489	197	8.839779
2002	5938	2.698028	213	17.67956
2003	6163	6.589415	252	39.22652
2004	6829	18.10792	301	66.29834
2005	7291	26.09824	285	57.45856
2006	7635	32.04773	322	77.90055
2007	7725	33.60429	352	94.47514
2008	7651	32.32446	335	85.08287
2009	7674	32.72224	348	92.26519
2010	7607	31.56347	331	82.87293
2011	7806	35.00519	320	76.79558
2012	7806	35.00519	335	85.08287
2013	7905	36.7174	361	99.44751
2014	8157	41.07575	436	140.884
2015	8542	47.73435	535	195.5801
2016	9308	60.98236	661	265.1934
2017	**9539**	**64.97752**	**746**	**312.1547**

If HCV hearts that were previously discarded nationally are added to the donor pool, then there will be a decrease in the organ market failure. Organs are an extremely limited resource with a very high value. By increasing the total number of transplants possible, an economy of

scale is demonstrated. An individual who opts to receive an HCV positive heart will experience a shorter wait time, increase in utility, and potentially improved outcomes. These savings will be passed to the entire waitlist as the individual receiving the infected heart will effectively be removed from the waitlist and allow subsequent patients to receive a transplant faster regardless of the HCV status of the heart they receive.

III. Related Literature:

Treatment and Cost Effectiveness of DAAs for Treating HCV:

There are several different DAA therapies available with prices ranging from $58,085-$115,791 for a standard treatment course to achieve sustained virologic response. Table 2 below shows five commonly used HCV therapies and their associated wholesale acquisition price and cost to obtain a sustained virologic response (SVR).

Table 2: "'Standard of care' regimens for non-cirrhotic, treatment naïve patients with HCV Genotype 1, and cost per SVR" Reproduced from (Graham 2016).

Regimen	SVR rate	WAC price	Cost per SVR
Pegasys + Ribavirin x48 weeks	41 %	$41,758	$101,849
Telaprevir + PegIFN + Ribavirin x24 weeks	75 %	$86,843	$115,791
Sofosbuvir + PegIFN + Ribavirin x12 weeks	90 %	$94,421	$104,912
Sofosbuvir + Ledipasvir x12 weeks	99 %	$94,500	$95,454
Grazoprevir + Elbasvir x12 weeks	94 %	$54,600	$58,085

Above data from package inserts for products

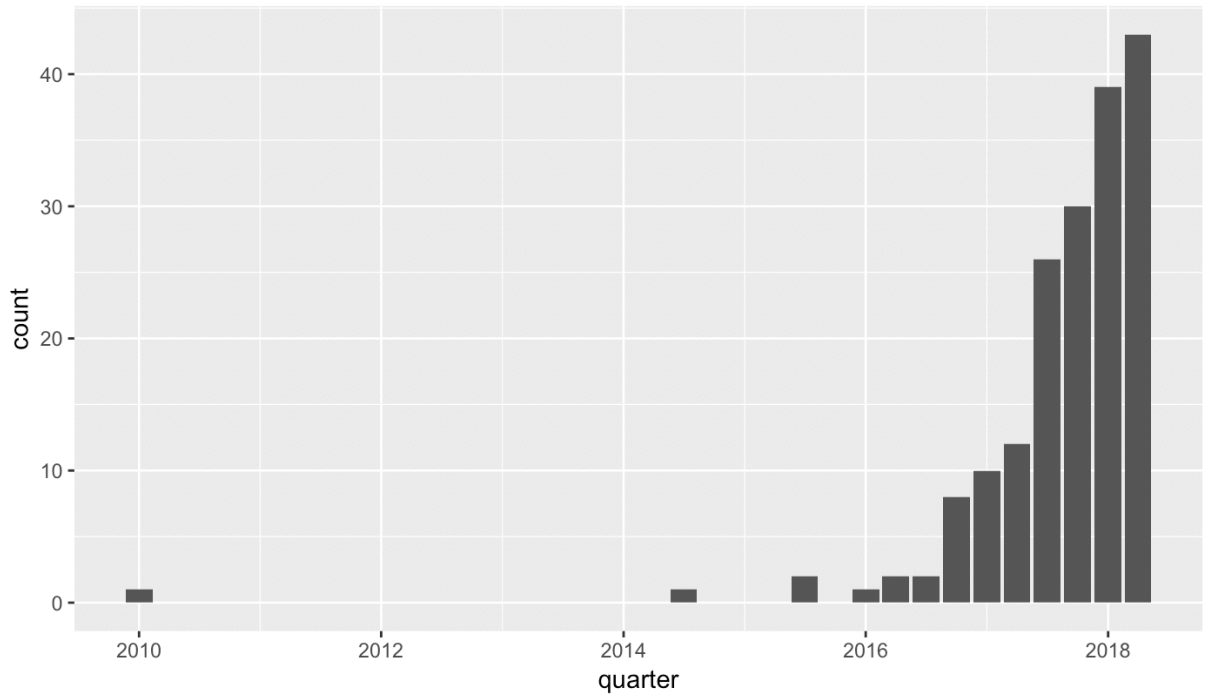
Cost Effective Analysis of HCV Positive Renal Transplants:

In 2015, an opinion piece in The New England Journal of Medicine studied the number of kidneys discarded simply due to HCV infection and no infected recipient available. The evidence suggested that approximately 4,000 additional renal transplants could have occurred between 2005 and 2014. With the advent of safe and effective DAA therapy, researchers encouraged doctors to begin considering HCV organs as a viable option (Peter P. Reese 2015). Reese et. al. found that after one year, all 20 of their patients were cured of HCV, had good quality of life, and experienced excellent renal function. A longer-term study may strengthen the findings, but the authors felt that there is no medical reason to expect worsened outcomes (Peter P. Reese 2018). As studies demonstrated positive clinical outcomes, some researchers began focusing their efforts towards the cost-effectiveness of the strategy. This analysis was straightforward for renal transplants as patients must undergo regular dialysis while waiting and costs can be easily estimated. Studies demonstrated that the reduction in wait time results in enough savings from foregone dialysis to justify the cost of DAA HCV therapy (Gaurav Gupta 2018, Mark H. Eckman 2018). Compared to studying other organs, estimating the cost of staying on the heart transplant waitlist has been more complex. For heart failure patients, usage of inotropes, mechanical circulatory assist devices, and the associated complications would contribute to the cost of longer transplant wait times.

Hepatitis C Heart Transplants—Proof of Concept:

Beginning in Sept. 2017, heart failure specialists from Vanderbilt University began transplanting HCV naïve patients with HCV positive organs. They report preliminary outcomes including a nearly 100% seroconversion rate. This was groundbreaking in the field as it inspired other centers to also begin accepting HCV positive organs (Kelly H. Schlendorf 2018). A paper published from Stanford University discussed the clinical outcomes of two patients in more economic detail and introduced the concept of cost-effectiveness analysis in this scenario (Yasbanoo Moayedi 2018). My study will logically expand on the Stanford study by applying more advanced models to understand the impact on the wider supply of organs. Finally, a previous study I conducted at St. Vincent Hospital, Indianapolis evaluated the feasibility and clinical success of transplanting HCV viremic hearts in 10 patients beginning Feb. 2018 (Morris 2018). Figure 1 below shows the number of HCV positive to HCV naïve transplants nationally since 2010. As of Sept. 2018, 26 out of 138 heart transplant centers in the country had performed an HCV transplant. The data are obtained from the Organ Procurement and Transplant Network (OPTN). There is a clearly increasing trend as centers across the United States become aware of this opportunity. As such, the start date for this treatment lies between late 2016 and late 2017.

Figure 1: Count of HCV Adult Heart Transplants per Quarter



IV. Data:

Organ Procurement and Transplant Network (OPTN) (2018):

My primary dataset originates from the Organ Procurement and Transplant Network (OPTN). The United Network for Organ Sharing (UNOS) is a private, non-profit organization contracted by the United States federal government to manage the OPTN. The Standard Transplant Analysis and Research (STAR) file provides data on transplants dating back to Oct. 1, 1987. The data include heart, lung, liver, kidney, pancreas, and intestine transplants. Not all variables were recorded since the database's inception; in fact, nucleic acid testing (NAT) for HCV serostatus only began on April 20, 2016 for hearts and lungs. Before NAT, HCV antibody testing was used which is less accurate because individuals who were previously infected with

the disease will continue to present antibodies. These data provide a large amount of national data on wait time, utilization, and clinical indicators. Arbitrary hospital and patient identifiers exist for tracking within the database, but they cannot be associated with actual patients or hospitals.

The data contains an entry for every waitlist, transplant, and deceased donor event that occurs. The data is therefore distilled to include only the organs, transplants, clinical indicators, etc. that are relevant for the analysis. I limited the waitlist study to the highest priority patients (status 1A) in order to show the potential benefit HCV transplants will have on the patients most in need. Lower priority patients are expected to wait longer on the waitlist and would confound the wait times. For the regression analyses, the entries are merged by hospital ID in order to see a hospital-level change in number of transplants and wait time. Although this dataset provides very rich data going back over 30 years, the transplant market has changed significantly over time. Wait time has become increasingly long since transplants first began and therefore would introduce a confounding variable if all data is used. The primary data frame used for analyses contains only adult heart transplants in the United States on or after the arbitrarily selected date of Jan. 1, 2010. Nonetheless, dummy variables will be introduced quarterly to account for changes over the time.

Descriptive Statistics:

Analysis of the dataset shows that 177 HCV positive donor hearts have been transplanted to an uninfected patient since 2010. Comparatively, over 19,000 HCV negative donor heart transplants have occurred in the same time frame. The two tables below summarize the statistics

for the major data frames used in the analysis. Each observation is a heart transplant event. Table 3 summarizes all heart transplants since 2010. Table 4 includes only transplants from an HCV positive donor to a naïve patient. Height, weight, and BMI are included in the analysis because they are the most important clinical indicators for heart matching.

Table 3: Summary Statistics of Variables Affecting Transplant Wait Time (all transplants) (STAR 2018).

Statistic	N	Mean	St. Dev.	Min	Max
Age	19,660	53.33	12.785	18	79
Weight (kg)	19,648	82.777	18.003	12	177.5
Height (cm)	19,618	173.72	10.041	66	221
BMI	19,651	27.396	4.938	15.1	52.8
1A Days	19,660	37.246	64.81	0	1,515
Total Days	19,660	239.335	370.792	0	6,412

Table 4: Summary Statistics of Variables Affecting Transplant Wait Time (HCV transplants) (STAR 2018).

Statistic	N	Mean	St. Dev.	Min	Max
Age	177	54.898	11.738	19	76
Weight (kg)	177	83.364	18.267	47.2	138.6
Height (cm)	177	174.994	10.656	150	213
BMI	177	27.484	4.877	17.3	37.7
1A Days	177	24.028	43.7	0	402
Total Days	177	233.056	396.979	2	2,400

Literature suggests that height, weight, and BMI are the characteristics that are most important in heart transplant matching (Bergenfeldt H 2017). However, HCV+ regression results

are not consistent with the literature or HCV- results. Height and weight alone appear to have a slight negative effect on 1A days waited but these are not significant by the t-test. Therefore, the coefficients may actually equal zero. This is an interesting result and may be explained by the fact that the supply of these HCV hearts is so much greater than HCV- hearts. Because the supply is so much greater, the height, weight, BMI characteristics do not significantly effect wait time. Anyone willing to receive the HCV heart may receive it in a similar amount of time. However, once the sample size grows, it may also result in increased waiting times due to increased demand for a constant supply. Thus, sample size may introduce an endogeneity problem. The regression results are summarized in Tables 5 and 6.

Table 5: HCV+ Clinical Characteristics Effect on 1A Wait Time

	Regression Models for HCV+ Donors			
	Number of Days Waited			
	Simple	Simple	Simple	Additive
	(1)	(2)	(3)	(4)
Height	-0.090			0.043
	(0.462)			(0.594)
Weight		-0.097		-0.110
		(0.241)		(0.310)
BMI			0.648	
			(0.926)	
Constant	42.574	35.177	8.555	28.869
	(81.709)	(21.440)	(26.401)	(90.657)
Observations	97	97	97	97
R^2	0.0004	0.002	0.005	0.002
Adjusted R^2	-0.010	-0.009	-0.005	-0.019
Residual Std. Error	42.964 (df = 95)	42.936 (df = 95)	42.862 (df = 95)	43.163 (df = 94)
F Statistic	0.038 (df = 1; 95)	0.161 (df = 1; 95)	0.489 (df = 1; 95)	0.082 (df = 2; 94)
Note:				*p<0.1;* ***p<0.05;*** p<0.01

Table 6: HCV- Clinical Characteristics Effect on 1A Wait Time

	Regression Models for HCV- Donors			
	Number of Days Waited			
	Simple	Simple	Simple	Additive
	(1)	(2)	(3)	(4)
Height	0.892***			0.375**
	(0.139)			(0.173)
Weight		0.601***		0.479***
		(0.077)		(0.096)
BMI			1.521***	
			(0.287)	
Constant	-112.181***	-7.918	0.230	-62.656**
	(24.176)	(6.629)	(8.119)	(26.061)
Observations	2,277	2,282	2,283	2,273
R^2	0.018	0.026	0.012	0.028
Adjusted R^2	0.017	0.026	0.012	0.027
Residual Std. Error	67.811 (df = 2275)	67.461 (df = 2280)	67.926 (df = 2281)	67.517 (df = 2270)
F Statistic	41.130*** (df = 1; 2275)	60.780*** (df = 1; 2280)	28.056*** (df = 1; 2281)	32.807*** (df = 2; 2270)
Note:				*p<0.1;* ***p<0.05;*** p<0.01

V. Methodology:

Hospital-Level Wait Time Regression:

The first goal of this paper is to assess how using HCV hearts will impact transplant wait times at the hospital-level. The analysis will begin by first illustrating trends in the raw data. Figure 2 shows the number of status 1A days waiting vs. time. The shaded region is the time period where the HCV method begins to be adopted. A difference-in-difference calculation in Table 7 quantifies the impact of this treatment. The "before" column is the average 1A waiting days for the year prior to the treatment start date of Oct. 1, 2016 and the "after" column is the average for a year following the treatment start date. As illustrated in Table 7, there is a -10.25-day difference-in-difference in the number of status 1A days waited between the HCV-adopters and non-adopters during the pre vs. post treatment periods. The average 1A wait time across all

transplant recipients is 37.246 days. After observing this dramatic decrease across the treatment adoption period (shaded in gray), a regression analysis was pursued to control for additional variables and quantify the effect.

Figure 2: Average 1A Wait Time for Adult Heart Transplants by Adopter Type

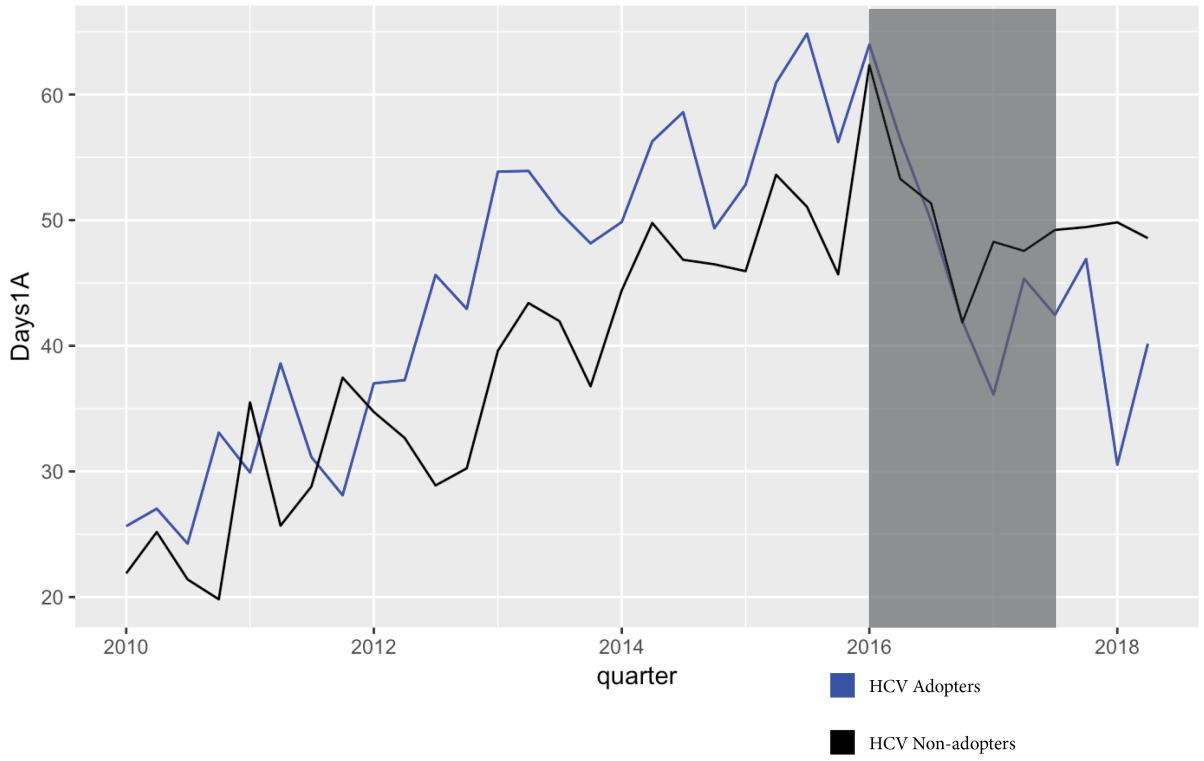


Table 7: Average 1A Wait Time Separated by Treatment – Difference-in-Difference

	Before	After	Difference
Treatment	58.280456	42.554378	-15.726078
Control	52.742642	47.271054	-5.471588
Difference			-10.25449

The regression will attempt to estimate the following equation from a data frame containing observations per hospital per quarter:

$$Y_{it} = \beta_1 X_{it} + \gamma_{center} + \gamma_{time} + \lambda X_i + \varepsilon_{it}$$

Y_{it} represents the number of status 1A days waited. β_1 is the coefficient of most interest and determines the magnitude of the dependent variable. X_{it} is equal to "1" if a given hospital adopts the HCV method and is on or after Oct. 1, 2017. This date was chosen to correspond with the quarter following the first major report of HCV heart transplants from Vanderbilt University. All other centers/quarters are indicated by a "0". The coefficient on this variable will represent the effect that adopting the HCV strategy has on transplant wait time at an average hospital. γ_{center} and γ_{time} represent the fixed-effects of each transplant center and changes over time. A within-estimator model will be used to account for variation across transplant centers. Dummy variables representing the year and quarter will account for any changes in wait time in the recent past. There are several clinical variables that are controlled for in the λX_i term. The average heights, weights, and BMIs of each hospital's patient population will control for the clinical indicators most important in organ matching. Finally, ε_{it} is the error term to account for random noise.

The regression analysis will quantify the effect of adopting the HCV transplant strategy on the expected wait time at a given hospital. Although most patients at a given hospital are not receiving HCV viremic hearts, the HCV treatment option can be expected to reduce the overall wait time for all patients at a center. By accessing the previously untapped resources, at least some patients are removed from the wait list and no longer competing for organs. Therefore, individuals who do not receive an HCV infected heart, but are listed for a transplant at a center that provides this option, are effectively higher on the wait list and can expect a shorter wait time.

Hospital-Level Average Number of Transplants Regression:

The second goal of this paper is to estimate the increase in transplants done as a result of using HCV hearts. Descriptive statistics of the raw data are presented below which motivate the regression analysis. Figure 3 illustrates the average number of transplants vs. quarter. The shaded black region is the time period where the HCV method begins to be adopted. A difference-in-difference calculation in Table 8 quantifies the impact of this treatment. The "before" column is the average number of transplants for the year prior to the treatment start date of Oct. 1, 2016 and the "after" column is the average for a year following the treatment start date. As illustrated in Table 8, there is a 1.24-unit difference-in-difference in the number of transplants between the HCV-adopters and non-adopters during the pre vs. post treatment periods. After observing this increase across the treatment adoption period (shaded in gray), a regression analysis was pursued to control for additional variables and quantify the effect.

Figure 3: Average Count of Adult Heart Transplants per Center per Quarter

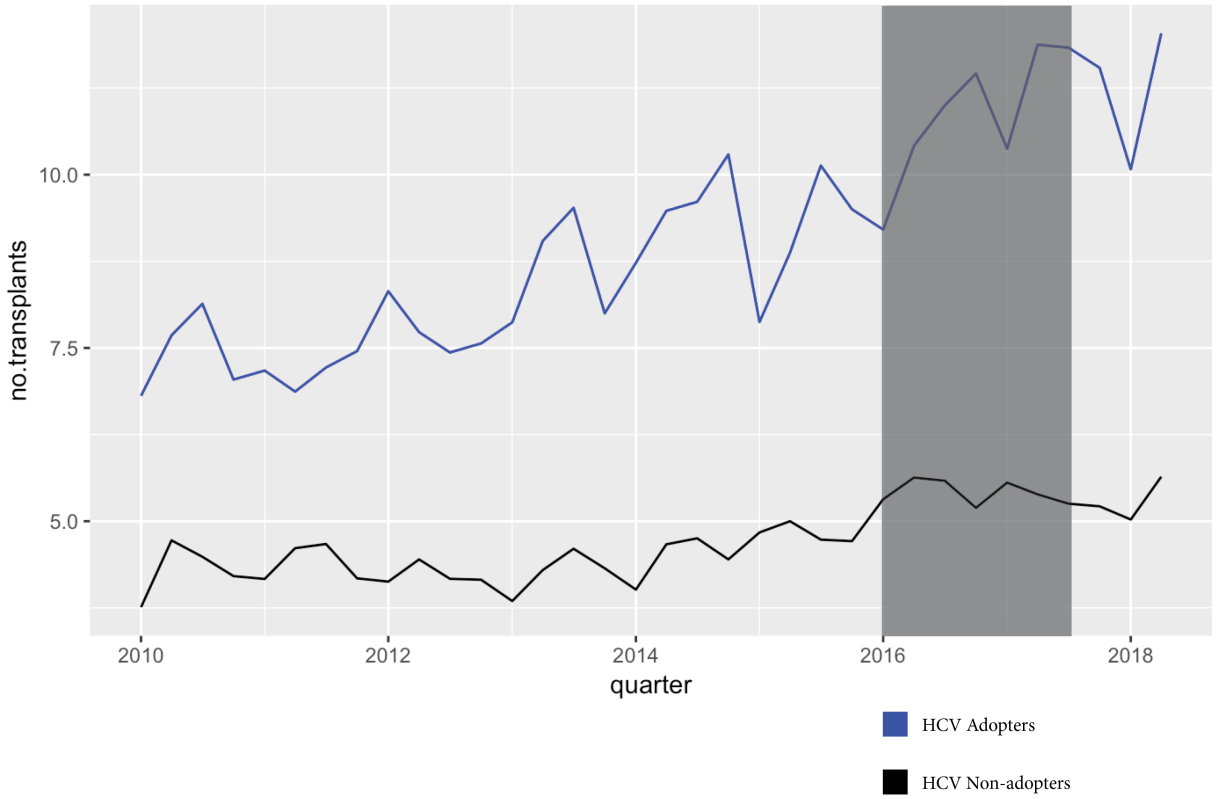


Table 8: Count of Adult Transplants Separated by Treatment—Difference-in-Difference

	Before	**After**	**Difference**
Treatment	10.051087	11.41667	1.365579
Control	5.1954358	5.321087	0.1256512
Difference			**1.2399278**

Table 9: Hospital-Level Regressions

	1A Days (1)	Number of Transplants (2)
HCV Adopter	-18.614***	1.849***
	(6.762)	(0.484)
Weight	0.629***	0.008
	(0.151)	(0.011)
Height	0.308*	-0.007
	(0.175)	(0.013)
BMI	-0.695	0.011
	(0.446)	(0.032)
"2011"	8.925***	-0.010
	(2.718)	(0.194)
"2012"	10.681***	0.003
	(2.694)	(0.193)
"2013"	19.925***	0.231
	(2.705)	(0.194)
"2014"	24.100***	0.574***
	(2.722)	(0.195)
"2015"	27.185***	0.794***
	(2.709)	(0.194)
"2016"	28.753***	1.634***
	(2.707)	(0.194)
"2017"	24.450***	1.702***
	(2.705)	(0.193)
"2018"	25.785***	1.429***
	(3.678)	(0.263)
Q2	1.008	0.499***
	(1.787)	(0.128)
Q3	-0.708	0.564***
	(1.868)	(0.134)
Q4	-2.108	0.311**
	(1.869)	(0.134)
Observations	3,385	3,385
R2	0.089	0.075
Adjusted R2	0.046	0.032
F Statistic (df = 15; 3232)	20.982***	17.582***
Note:	*p<0.1; **p<0.05; ***p<0.01	

The regression equation and variables are the same as the previous model, except that Y_{it} now represents the average number of transplants done at a center per quarter. Once again, the HCV treatment option can be expected to have a spillover effect to centers not adopting the strategy. By accessing the previously untapped resources, more organs are available for the centers and patients that did not adopt the strategy. Therefore, centers that do not transplant HCV infected hearts are able to be offered more organs from the original pool comparatively had the other centers not opted to transplant HCV organs.

VI. Results:

The results of the two regressions are shown in Table 9. The results are consistent with literature describing HCV organs' potential to expand the market (Peter P. Reese 2015). The values presented adjacent to "HCV Adopter" in the table are the coefficients β_1. When a given center is an HCV center in the era of these transplants, X_{it}=1 and the full value of β_1 is felt by the dependent variable. The

results indicate that patients at a hospital that conducts HCV heart transplants can expect to wait 18.614 fewer 1A days than at a hospital that does not conduct these transplants. Hospitals that adopt the HCV method can also expect to perform 1.849 more transplants per quarter (7.396 annually) than a hospital that does not perform these transplants. A fixed-effects estimator accounts for variations between transplant centers. Therefore, the values strictly represent the effect of being an HCV-transplant center and not any attribute of the center itself. Both values are statistically significant at the 99% confidence interval. The clinical variables are included to ensure that any variation in patient characteristics between hospitals are being considered. As expected, weight and height have a statistically significant positive effect on wait time. The effects on average number of transplants performed is less clear. Finally, year and quarter dummy variables are included to assess any changes over time. As expected, the number of transplants as well as the wait time has increased over time. Some seasonality is also observed as quarters 2, 3, and 4 display a statistically significant positive coefficient when regressing on the average number of transplants.

VII. Discussion:

This study quantified an expansion to the organ market's effects on health systems and patients. The results of this study suggest that patients at participating hospitals will wait a mean 18.6 days less than patients at non-participating institutions. Further, participating hospitals will conduct 1.849 more transplants every quarter. These results have multiple positive externalities. Considering the dire shortage of organs relative to the great demand of candidates, maximizing the use of available HCV organs has the potential to alleviate the shortage crisis. Additionally, considering the critical nature time plays in caring for patients with advanced heart failure, any

strategy that can shorten the wait for a transplant will have a profound impact on health care expenditure and patient outcomes (Elisa F. Long 2014).

Effects of a Lower Wait Time:

The time-saving element of using HCV viremic hearts suggests better outcomes for patients. The OPTN data suggest a mean 18.6 day decrease in 1A wait time which is nearly half of the average 1A wait time for all patients. This in turn will have the potential for improved outcomes in terms of QALY and ICER. Table 10 was reproduced from (Elisa F. Long 2014). The study by Long et. al. showed the cost-effectiveness of the most common advanced heart failure therapies. There is a clear inverse relationship between wait time and survival, life expectancy, QALYs, and ICER for heart transplants. Patients that are able to receive a heart transplant quickly through the HCV method may avoid highly invasive bridge to transplant therapies including ventricular assist devices (VAD), save money, and reap better outcomes (Elisa F. Long 2014).

Table 10: "Model Results and Cost-Effectiveness Analysis" of Heart Failure Strategies. Reproduced from (Long 2014).

Strategy	Lifetime Costs, ($)*	5-Year Survival, %†	Life Expectancy, y	QALYs*	Incremental Cost-Effectiveness Ratio,‡ $/life-year	Incremental Cost-Effectiveness Ratio,‡ $/QALY
Heart transplant ineligible						
Inotrope-dependent medical therapy	112 600	0	0.78	0.41	…	…
LVAD destination therapy	593 000	32	4.42	2.79	131 800	201 600
Heart transplant eligible						
Inotrope-dependent medical therapy	130 300	1	1.13	0.58	…	…
Heart transplant						
Immediate	802 200	74	13.76	7.67	53 200	94 800
Wait-list 5.6 mo	529 000	44	8.48	4.70	54 300	96 900
Wait-list 12 mo	405 700	31	6.18	3.41	54 500	97 300
LVAD bridge to transplant						
Immediate	1 025 500	71	13.12	7.32	Dominated	Dominated
Wait-list 5.6 mo	1 011 900	65	12.29	6.83	126 700	226 300
Wait-list 12 mo	978 000	59	11.41	6.40	109 400	191 400

LVAD indicates left ventricular assist device; and QALY, quality-adjusted life-year.
*Lifetime costs and QALYs are discounted at a 3% annual rate.
†Results are based on a simulation of 20 000 hypothetical patients aged 50 years.
‡Incremental cost-effectiveness ratios for LVAD destination therapy and heart transplant are relative to inotrope-dependent medical therapy, and LVAD bridge to transplant is relative to heart transplant.

Treatments of varying invasiveness are used in patients suffering organ failure while they await a transplant match. In heart failure, intravenous inotropes can be used to increase the contractility of the heart. Such treatments are quite expensive, and there is a high mortality rate among patients with severe heart failure awaiting heart transplantation. Many patients will need a VAD due to intractable heart failure before receiving a transplant. While effective in prolonging quality and longevity of life, these devices require open-heart surgery with its antecedent risks, have high costs, and require close monitoring. They are associated with frequent complications such as infections, strokes, and mechanical failure of the pump due to blood clots. Such complications lead to high morbidity and mortality and are associated with high health care expenditure. For example, infections often require prolonged intravenous antibiotic therapy and mechanical failures require new VAD placement via open-heart surgery. Minimizing the number

of patients who must receive VADs, repeat surgeries for VAD exchanges, and/or the amount of time that patients have a VAD will improve clinical outcomes and reduce costs.

The economic burden of heart failure on the American healthcare system was described by Lee et. al. in 2004. $20 billion was estimated as the medical cost of treating heart failure with an additional $2 billion in indirect costs and loss of productivity. This societal loss is particularly relevant in the United States as heart failure related costs are most frequent in Medicare patients. More Medicare funds are spent on heart failure than any other diagnosis (Won Chan Lee 2004). Hospitalization and repeat hospitalizations are the main source of the cost and the most common cause of hospitalization for Medicare-covered patients (Meredith Kilgore 2017). Given the widespread prevalence and high associated costs, any intervention that is able to reduce costs may have a substantial positive societal impact (Won Chan Lee 2004). Singh et. al. describe the mortality pre and post-transplant for patients awaiting heart transplant. They find a wide variability in mortality based on 10 risk groups identified. The findings of Singh's paper suggest that the increase in transplants may have a wide impact on utility as not all recipients benefit equally (Tajinder P. Singh 2014). Clinicians treating the sickest patients that could most benefit from an immediate transplant should consider the HCV option as an expedited way to receive a transplant.

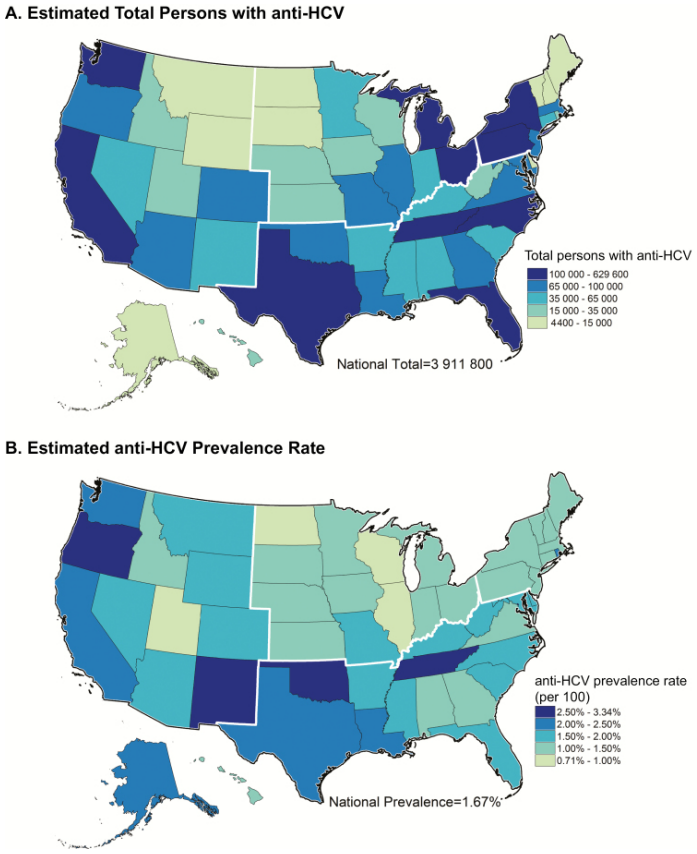
The wait time aspect of my study is limited to 1A patients only. This decision was made because the majority (over 64%) of transplants conducted are on status 1A patients and they are the highest priority patients (2018). Lower priority patients would be expected to have longer wait times with a greater range. As of Oct. 18, 2018, UNOS has changed the heart allocation system and no longer uses the same priority listings. Status 1A patients will still be broadly representative of the higher priority patients in the new priority system. Previously, only three

status levels existed. Now, there are six status levels that are meant to better serve the patients who are in greatest need of a transplant.

Geographic Considerations:

Geographic considerations are important when interpreting the results of this study. With the advent of better technology that can allow organs to exist outside the body for longer periods of time, higher priority patients (status 1 and 2) are now considered for donors within a 500-mile radius (2019). The reported figures are representative for the entire country, but HCV prevalence varies across the United States. Figure 4 was reproduced from (Eli S. Rosenberg 2017) and describes the distribution of people with HCV antibodies across states in the United States. The states most heavily hit by the opioid epidemic may be more likely to see an excess supply of HCV donor hearts. A future study may attempt to control for geography in estimating the effects of the HCV method. However, controlling for this presents multiple challenges as organ matching occurs radially beginning at the donor site ignoring any state or regional boundaries. Thus, it is difficult to generalize the United States regionally as a 500-mile radius from a donor center will in most cases cross at least one state or regional boundary. While these considerations may impact the economics of transplanting HCV positive hearts, the current study did not factor it for the above reasons.

Figure 4: State-level HCV Distribution and Prevalence. Reproduced from (Eli S. Rosenberg 2017)



Cost of DAA Therapy:

Although the life-saving potential of this option is enormous, there has been some resistance by insurers to cover the heavy cost of DAA therapy. I personally reviewed patients from St. Vincent Hospital, Indianapolis, Vanderbilt University, and Stanford University and found that all patients responded successfully to the DAA therapy within the standard 12-week regimen (Kelly H. Schlendorf 2018, Morris 2018, Yasbanoo Moayedi 2018). A more general study of these drugs outside of transplant patients found a greater than 90% success rate (Tarik Asselah 2016). Experience at St. Vincent Hospital and literature has reported insurance

companies denying treatment until a viral load is detected (Graham 2016). Strict price rationing particularly for people who use alcohol and drugs has resulted in some insurance companies denying coverage until or after cirrhosis of the liver is confirmed (Jason Grebely 2015). This ethical blight has been passed on to transplant patients who are also met with insurance companies delaying coverage (Vincent Lo Re III 2016). 52.4% of privately insured patients, 32.4% of Medicaid patients, and 14.7% of Medicare patients prescribed DAA were denied treatment (Charitha Gowda 2018). Denying perioperative coverage of the drug results in an economic inefficiency as early treatment can be cost-saving and the data strongly suggests a nearly 100% transmission rate for seropositive donors (Kelly H. Schlendorf 2018, Morris 2018, Yasbanoo Moayedi 2018). The likelihood of a patient not getting infected after being transplanted with a seropositive heart is extremely low. In the St. Vincent experience, all patients were infected and the mean time to seroconversion was seven days (Morris 2018). Studies on HCV positive liver transplants have shown that perioperative commencement of DAA therapy reduced the time to sustained virologic response to just four weeks in 14 out of 15 patients (Josh Levitsky 2016). Reducing the treatment period by 67% could be vastly cost saving further justifying the HCV method. Regardless, given the highly successful and curative nature of this therapy for a chronic disease, it is ethically difficult to deny coverage to patients post-transplant.

Utilization of Available Resources:

It is unclear how many of the 746 HCV positive deceased donors in 2017 were suitable for transplant. However, the recent spike in HCV positive organs are in no small part a result of the drug over dosage resulting from the opioid epidemic. Compared to the average organ donor

population, these donors typically provide younger and healthier organs (M. Bowring 2016). The life-saving impact is enormous.

Study Limitations:

An important limitation of this study is that the data source is primarily a retrospective analysis of a national database. Consistency and reliability are questionable in such data sources. However, the data is gathered by medical professionals and submitted to UNOS at donor/recipient listing and transplantation. The data are used to determine heart matchings and are therefore audited and checked by UNOS staff and medical staff at both the donor and recipient centers. Therefore, although national databases edited by thousands of individuals may have some concerns, there are some quality assurance mechanisms in place. Use of data from St. Vincent Hospital records and matching with multiple sources correlated with data from the national database giving credence to the source.

A future study may consider the expansions to healthcare labor and capital in order to accommodate for the increasing number of transplants.

VIII. Conclusion:

This paper intended to quantify the effects that a novel exploitation of resources would have on the transplant market. The advent of DAAs made the utilization of the rapidly increasing number of HCV infected hearts a reality. Specifically, I studied the effect adopting this strategy had on an average hospital's wait time and number of transplants using a national database and validated it with an individual hospital's experience. The linear regression model which

controlled for clinical characteristics, fixed-effects of the center, and time indicated that adopting this strategy would present multiple advantages to a hospital and its patients. The model indicates that there is a statistically significant reduction in wait time and statistically significant increase in the number of transplants done per center per quarter. Although this generalization may vary depending on supply and demand across regions in the United States, modern medicine's ability to procure donors from up to 500 miles away from the recipient has reduced the effect of this limitation.

The development of DAAs has been a significant advancement in medicine that has major downstream effects for patients suffering from organ failure. This strategy is notably new and only a fraction of transplant centers across the country perform these transplants. As the adoption of this strategy becomes more widespread, the positive effects may be more widely embraced. Over time, further adoption of the strategy will result in more transplants, and a future study may evaluate this expansion's impact on the national management of heart failure. As additional data become available, follow up research is needed to understand the true effect DAAs and HCV transplants will have.

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