Supplemental Materials

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Simulation Methods

Interventions

We conducted a simulation to answer the question: From a payer's perspective, how much net savings per year would be generated were the following two interventions implemented to improve chronic kidney disease (CKD) care management?

(1) increasing the use of pre-renal replacement therapy (RRT) nephrology care to slow disease progression;[1-3] and

(2) improving care coordination for the transition to RRT.[1, 4]

Both sets of interventions have been shown in prior studies to improve intermediate outcomes that can be translated into savings,[1-4] including:

- increasing use of nephrology care prior to end-stage renal disease (ESRD) to slow disease progression;
- decreasing use of inpatient services at dialysis initiation;
- increasing adoption of permanent vascular access (an arteriovenous fistula or graft) prior to dialysis;
- increasing adoption of peritoneal dialysis; and
- increasing use of pre-emptive kidney transplant.

We did not model the use of dialysis (or comprehensive conservative management) among patients with advanced age and significant comorbidity because the population is difficult to define based on the aggregate data from the 2017 USRDS report or other published studies, for whom existing evidence suggests dialysis has limited benefits.[1]

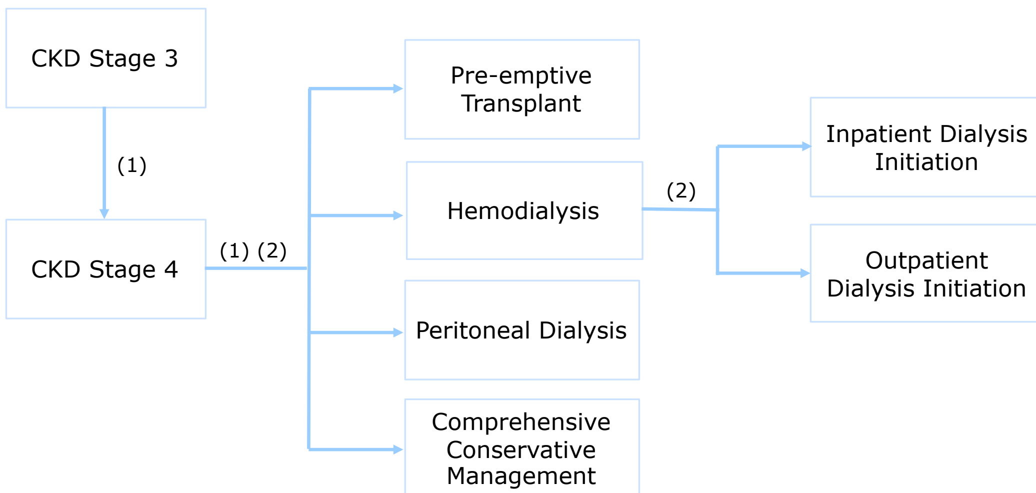
Modeling Approach

We modeled what would have happened had the interventions been implemented for the year of 2015, the most recent data available from the 2017 USRDS report.[5] As a result, we used a time horizon of one year. The savings analysis was conducted from a payer's perspective, and it is financial in nature and did not include the impact on patient mortality.

As illustrated in Figure A1, we developed a cohort-level Markov model to simulate healthcare costs. The cohort, as reported in the 2017 USRDS report for the year of 2015, was assigned to two different strategies: the status quo that represents what happened in 2015 and the intervention scenario that characterizes what would have happened, with everything else being the same across two strategies. The transitional probabilities, healthcare costs associated with each state, and intervention costs were derived from the published literature (see more details in the Data Sources and Assumptions section below). The model assumed the transition probability from Stage 4 to comprehensive conservative management to remain the same across the two strategies.

Considering the data availability, we simplified the analysis by allowing patients to move only one step either from Stage 3 to 4 or from Stage 4 to RRT in a one-year period. Increasing nephrology care was assumed to affect the transitional probabilities from Stage 3 to 4 or from Stage 4 to RRT, whereas improving care coordination for the transition to RRT was assumed to impact the use of RRT modality. Healthcare costs were computed during the process and intervention costs were taken into account in the net savings calculation.

Figure A1. Model Structure



Note: Intervention (1) – Increasing the use of pre-RRT nephrology care; Intervention (2) – Improving care coordination for the transition to RRT.

To account for the uncertainty in estimated savings, we used the upper bound and lower bound of the range of various key parameters to create a best-case scenario and a worst-case scenario, for both of which we created a savings estimate.

All costs have been adjusted for inflation to the 2016 US dollars using the urban component of the Consumer Price Index.[6] All analysis was conducted in Microsoft Excel.

Data Sources and Assumptions

As illustrated in Table A1, key parameters were extracted from the published literature, in particular from the 2017 USRDS Report.[5] The simulation focused on Stages 3 and 4 CKD patients because the published literature does not provide sufficient evidence for the effectiveness of such interventions amongst Stages 1 and 2 CKD patients. The patient population size was derived from the total Medicare enrollment,[7] the total US population,[8] and the prevalence by disease stage from the 2017 USRDS Report. For the non-Medicare CKD population, our analysis covered only the patients who are aware of the CKD diagnosis, 10.2% and 46.9% for Stage 3 and 4 patients, respectively, because the interventions modeled do not detect more CKD patients or raise patient awareness of CKD. The annual cost of medical care by disease stage came from the 2017 USRDS Report. Since the costs from the USRDS report were not adjusted for patient-level characteristics, we included the incremental medical care costs attributed to CKD from Honeycutt et al. (2013)[9] as part of the sensitivity analysis. Cost of medical care in patients covered by commercial insurance is often higher than that of Medicare patients, but we were not able to incorporate this difference due to lack of commercial payment data. Substituting Medicare cost for commercial cost has likely biased our total savings estimate downward.

Table A1. Model Parameters, Data Sources, and Assumptions

Parameter	Value (range: the best-case scenario, the worst-case scenario)	Source	Assumption and Approach
CKD population size, n			
Medicare		2017 USRDS Report,[5] CMS[7]	To derive CKD stage-specific population, we used the total Medicare population size and the prevalence of CKD in the Medicare population by stage from the 2017 USRDS Report.
Stage 3	4,649,615		
Stage 4	755,721		
Stage 5:			
Hemodialysis	355,016		
Peritoneal dialysis	39,314		
Transplant	166,036		
All payers		2017 USRDS Report,[5] US Census Bureau[8]	To derive CKD stage-specific population, we used the total US population size and the prevalence of CKD by stage in the US population from the 2017 USRDS Report.
Stage 3	21,223,764		
Stage 4	1,384,859		
Stage 5:			
Hemodialysis	444,337		
Peritoneal dialysis	49,205		
Transplant	207,810		
Annual medical costs per patient, 2016 USD		2017 USRDS Report,[5] Honeycutt 2013[9]	Annual medical costs per CKD patient from the 2017 USRDS report are not adjusted for patient-level characteristics. We therefore used the CKD incremental cost estimates from the study by Honeycutt et al. (2013), inflation-adjusted them to the 2016 US dollars, and derived annual medical costs for Stage 3 and 4 CKD patients by adding the incremental costs to the average cost for Stage 2 patients from the 2017 USRDS report. The derived estimates were then used for the worst-case scenario because the higher the estimates, the lower the reduction in medical costs from avoiding the
Stage 3	21,922 (21,922, 23,167)		
Stage 4	29,519 (29,519, 37,145)		
Stage 5:			
Hemodialysis	89,870		

Parameter	Value (range: the best-case scenario, the worst-case scenario)	Source	Assumption and Approach
Peritoneal dialysis	76,088		disease progression from Stage 3 to 4 or from Stage 4 to 5. Costs of patients covered by commercial insurance are often higher but we did not incorporate this due to the lack of data. By omitting such a cost difference between commercial payers and Medicare has likely biased our total savings estimate downward.
Transplant	34,514		
Current annual CKD progression rate, %		Orlando 2007[10]	Mortality rates have been incorporated when estimating progression rates. We only included progressions from Stage 3 to 4 and Stage 4 to 5 in the analysis because the effects of nephrology care on the progressions from Stage 1 to 2 and Stage 2 to 3 are not supported by the literature (Orlando 2007).
Stage 3 to 4	5.112		
Stage 4 to 5:			
Stage 4 to Hemodialysis	6.522		
Stage 4 to Peritoneal dialysis	0.711		
Stage 4 to Transplant	0.188		
Expected annual CKD progression rate under nephrology care, % (range)			
Stage 3 to 4	4.090 (3.119, 4.601)		
Stage 4 to 5:			
Stage 4 to Hemodialysis	4.891 (2.935, 5.804)		
Stage 4 to Peritoneal dialysis	0.533 (0.320, 0.633)		
Stage 4 to Transplant	0.141 (0.085, 0.167)		
Current percent of CKD patients receiving nephrology care, %		Orlando 2007[10]	The 2017 USRDS Report has only data on the percent of ESRD patients who received nephrology care 6 or 12 months prior to dialysis initiation, which cannot be directly converted to the parameters needed for our analysis. We therefore used the data from Orlando 2007.
Stage 3	49.760		
Stage 4	67.442		
Expected percent of CKD patients receiving nephrology care under interventions, % (range)		Not available	We assumed the rate of nephrology care to increase by 30% from the current rate, with a lower and upper bound of an increase of 20% and 40%, respectively. For the non-Medicare population, our analysis covers only the patients who are aware of the CKD diagnosis, 10.2% and 46.9% for Stage 3 and 4 patients, respectively, according to the 2017 USRDS report.
Stage 3	64.688(69.663, 59.712)		
Stage 4	87.674(94.419, 80.930)		

Parameter	**Value** (range: the best-case scenario, the worst-case scenario)	**Source**	**Assumption and Approach**
Current percent of incident ESRD patients receiving a pre-emptive transplant, %	2.530	2017 USRDS Report[5]	None.
Expected percent of incident ESRD patients receiving a pre-emptive transplant, % (range)	6.000 (8.000, 4.000)	Johnson 2016[1]	Johnson (2016) estimated it to be 6% for a thorough program, which is used as the base case value. Given the limited source of kidneys, we used 8% as the upper bound.
Current percent of incident ESRD cases with a fistula or graft among hemodialysis patients, %	19.987	2017 USRDS Report[5]	None.
Expected percent of incident ESRD cases with a fistula or graft among hemodialysis patients, % (range)	42.869 (60.000, 30.000)	DCI 2016;[11] Maddux 2016[4]	Forty two percent patients in DCI's Reach Program had a fistula at dialysis initiation and its best site achieved a rate of 68%. Fresenius' Renal Care Coordinator program achieved a rate of 44.1%. For our analysis, we used the average rate of the two programs as the base case rate and 60% and 30% as the upper and lower bound, respectively.
Current percent of incident ESRD cases receiving the initial dialysis in a hospital, %	64.500	Wong 2014[15]	None.
Expected percent of incident ESRD cases receiving the initial dialysis in a hospital under interventions, % (range)	42.000 (33.000, 51.000)	Johnson 2016;[1] DCI 2016[11]	Nationwide, 42% patients in DCI's Reach Program received the initial dialysis in a hospital and 33% at its best site. We used 51% as the upper bound, 9 percentage points above the base case value.
Current percent of incident ESRD cases receiving peritoneal dialysis, %	9.559	2017 USRDS Report[5]	None.
Expected percent of incident ESRD cases receiving peritoneal dialysis under interventions, % (range)	25.600 (37.000, 14.200)	DCI 2016;[11] Maddux 2016[4]	Nationwide, 27% patients in DCI's Reach Program received peritoneal dialysis and 37% at its best site. Fresenius' Renal Care Coordinator program achieved a rate of 24.2%. We used the average rate of the two programs as the base case rate and 37% as the upper bound. The lower bound was determined to be 14.2% so that it has the same distance to the base case rate as the upper bound.
Medical cost per hospitalization due to hemodialysis catheter-related infection, 2016 USD	27,145.509	Ramanathan 2007[13]	None.

Parameter	**Value** (range: the best-case scenario, the worst-case scenario)	Source	Assumption and Approach
Incremental hemodialysis catheter-related infection rate compared to a permanent access in a 2-month period, %	1.126	Ng 2011[12]	We assumed a catheter would be used on average for 2 months after dialysis initiation.
Medical cost per hospitalization at dialysis initiation, 2016 USD	26,068.764	Johnson 2016[1]	None.
Medical cost in the first year of transplant, 2016 USD	135,810.928	2017 USRDS Report[5]	We assumed a transplant would benefit a patient for 10 years and the initial transplant cost was therefore allocated across 10 years.
Cost of nephrology care per year, 2016 USD			
Stage 3	384.96 (275.92, 494.00)	2018 Medicare Physician Fee Schedule[14]	We assumed for a new Stage 3 patient, nephrology care would include a new patient office visit that lasts about 40 minutes and 1 (lower bound) to 3 (upper bound) follow-up office visits in a year that last about 20 minutes. The base case was assumed to have 2 follow-up visits. We used the median of non-facility payments across all Medical localities in the US from the 2018 Medicare Physician Fee Schedule and adjusted the payments to the 2016 US dollars.
Stage 4	603.03 (494.00, 821.11)	2018 Medicare Physician Fee Schedule[14]	We assumed for a new Stage 4 patient, nephrology care would include a new patient office visit that lasts about 40 minutes and 3 (lower bound) to 6 (upper bound) follow-up office visits in a year that last about 20 minutes. The base case was assumed to have 4 follow-up visits. We used the median of non-facility payments across all Medical localities in the US from the 2018 Medicare Physician Fee Schedule and adjusted the payments to the 2016 US dollars.
Cost of care coordination for RRT transition, 2016 USD	1000 (800, 1200)	Johnson 2016[1]	The base case cost estimate came from Johnson 2016, $1000 per patient per year. We assumed an upper bound of $1,200 and a lower bound of $800.

Note: CKD: Chronic Kidney Disease; ESRD: End Stage Renal Disease; USD: US Dollars; eGFR: Estimated glomerular filtration rate; RRT: Renal Replacement Therapy. All costs have been adjusted to 2016 US dollars based on the Consumer Price Index.

Pre-ESRD nephrology care has been shown effective in slowing disease progression.[2] The current disease progression rates from Stage 3 to 4 and from Stage 4 to 5 as well as the effectiveness of pre-ESRD nephrology care were extracted from Orlando et al.[10] To our knowledge, the 2017 USRDS Report does not provide information on disease progression rates. Because we were unable to find data on the rate of pre-ESRD nephrology care under interventions, we assumed that for a well-operated program, the rate would increase by 30%, with a lower and upper bound of an increase of 20% and 40%, respectively. We believe it is a reasonable assumption because it primarily involves referring patients to a nephrologist.

As of 2015, the rate of pre-emptive kidney transplant in incident ESRD cases was 2.5% according to the 2017 USRDS Report. Johnson et al. estimated it to be 6% for a thorough program, which is used as the base case value.[1] Given the limited source of kidneys, we used 8% as the upper bound for the parameter. Since kidney transplant can benefit a patient for multiple years and the transplant surgery requires a large upfront investment, we assumed a kidney to remain functional for 10 years and the upfront surgical cost was therefore allocated over 10 years.

Permanent vascular access for hemodialysis patients can reduce catheter-related infections as well as hospitalizations at dialysis initiation. Both programs by Dialysis Clinic Inc. and Fresenius Medicare Care have achieved a rate of over 40%,[4, 11] compared to the current rate of 20% according to the 2017 USRDS Report. The rate and cost of catheter-infection associated hospitalizations were from Ng et al.[12] and Ramanathan et al.,[13] respectively. The rate of hospitalization at dialysis initiation was reduced to 42% in Dialysis Clinic Inc.'s Reach program,[11] which costs over $26,000 per admission.[1] The savings were derived from the number of hospitalizations avoided and the cost per hospital admission.

Both programs by Dialysis Clinic Inc. and Fresenius Medicare Care have achieved a rate of peritoneal dialysis of over 20% among incident ESRD cases,[4, 11] compared to the current national rate of 9.6% according to the 2017 USRDS Report. And the savings would come from the lower cost of peritoneal dialysis in comparison to that of hemodialysis.

The costs of nephrology care were based on the 2018 Medicare Physician Fee Schedule.[14] For Stage 3 CKD patients, we assumed an initial visit to a nephrologist and 1 to 3 follow-up visits. For Stage 4 CKD patients, we assumed an initial visit and 3 to 6 follow-up visits. An initial visit was assumed to last about 40 minutes, and a follow-up visit 20 minutes. We use the median of non-facility payments across all Medicare localities in the US to approximate the cost of nephrology visits. The cost of care coordination for the RRT transition was based on the experience of Dialysis Clinic Inc.[4]

Limitations

There are several limitations of the simulation analysis. First, it was based on observational studies due to a lack of randomized clinical trials on CKD progression by stage or care coordination for the RRT transition. Observational studies may be biased due to inadequate controls of confounders or due to unobserved and omitted variables in the analysis. Nonetheless, two major studies used in the simulation were well conducted and applied a propensity score weighting or matching approach.[4, 10] The study by Johnson et al.[1] is descriptive in nature and did not use a formal analysis, whose results, however, are very similar to what was found by Maddux et al.[4] Second, the populations examined in the referenced studies are not necessarily the same as the Medicare population or privately insured patients. For example, the study by Orlando et al.[10] focuses on a Department of Veterans Affairs population, and the results may not be generalizable to other populations. Third, due to the data available from the published literature, the model allowed patients to move only one step either from Stage 3 to 4 or from Stage 4 to RRT in a one-year period. It is possible that a patient's condition may deteriorate quickly and move from Stage 3 to RRT within one year, which we did not consider in the model. Also, the economic benefits of interventions may sustain more than one year, and our model does not capture the benefits beyond one year and could potentially under-estimate the savings. Finally, our savings estimates did not include the impact of interventions on mortality benefits as we focused on the financial analysis from a payer's perspective, which has likely biased our savings estimates downward.

Simulation Results

Table A2. Healthcare Cost Changes, Intervention Costs, and Net Savings

Costs or Savings in Millions (2016 US Dollars)	Increase Nephrology Care - Stage 3	Increase Nephrology Care - Stage 4	Improve Coordination for RRT Transition	Increase Nephrology Care - Stage 4 & Improve Coordination for RRT Transition	All Interventions
Medicare					
Healthcare Cost Changes					
Base Case	(54)	(163)	(718)	(882)	(936)
Best Case	(140)	(480)	(1,037)	(1,517)	(1,657)
Worst Case	(33)	(42)	(361)	(402)	(435)
Intervention Costs					
Base Case	267	92	61	153	420
Best Case	255	101	49	149	405
Worst Case	229	84	73	157	385
Net Savings					
Base Case	213	(71)	(657)	(729)	(515)
Best Case	115	(379)	(989)	(1,367)	(1,252)
Worst Case	196	42	(288)	(246)	(50)
All Payers					
Healthcare Cost Changes					
Base Case	(74)	(227)	(1,381)	(1,609)	(1,682)
Best Case	(191)	(667)	(2,031)	(2,698)	(2,889)
Worst Case	(45)	(58)	(653)	(710)	(755)
Intervention Costs					
Base Case	364	128	124	252	617
Best Case	348	140	99	239	588
Worst Case	312	116	149	265	577
Net Savings					
Base Case	291	(99)	(1,257)	(1,356)	(1,065)
Best Case	157	(527)	(1,932)	(2,459)	(2,302)
Worst Case	267	59	(504)	(445)	(178)

Note: Negative numbers represent savings, and positive numbers cost increases.

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