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CLINICAL RESEARCH

A Cost-Minimization Analysis of Nurse-Led Virtual Case Management in Late-Stage CKD

Thomas W. Ferguson[1,2], Drew Hager[1,2], Reid H. Whitlock[2], Michelle Di Nella[2], Navdeep Tangri[1,2], Paul Komenda[1,2] and Claudio Rigatto[1,2]

[1]Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; and [2]Seven Oaks Hospital Chronic Disease Innovation Centre, Winnipeg, Manitoba, Canada

Introduction: Interventions are needed to improve early detection of indications for dialysis before development of severe symptoms or complications. This may reduce suboptimal dialysis starts, prevent hospitalizations, and decrease costs. Our objectives were to explore assumptions around a nurse-led virtual case management intervention for patients with late-stage chronic kidney disease (CKD) with a 2-year Kidney Failure Risk Equation (KFRE) estimated risk of kidney failure ≥80% and to estimate how these assumptions affect potential cost savings.

Methods: We performed a cost-minimization analysis by developing a decision analytic microsimulation model constructed from the perspective of the health payer. Our primary outcome was the break-even point, defined as the maximum amount a health payer could spend on the intervention without incurring any net financial loss or gain. The intervention group received remote telemonitoring, including daily measurement of several health metrics (blood pressure, oxygen saturation, and weight), and a validated symptom questionnaire accompanied by nurse-led case management, whereas the comparator group received usual care. We assumed patients received the intervention for a maximum of 2 years.

Results: The break-even point was $7339 per late-stage CKD patient enrolled in the intervention. Based on the distribution of time receiving the intervention, we determined a maximum monthly intervention cost of $703.37. In probabilistic sensitivity analyses, we found that 75% of simulations produced break-even points between $3929 and $9460.

Conclusion: Nurse-led virtual home monitoring interventions in patients with CKD at high risk of kidney failure have the potential for significant cost savings from the perspective of the health payer.

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CKD is a growing epidemic affecting more than 1 in 10 individuals in North America.[1,2] CKD is a potent risk factor for death, hospitalization, and reduced quality of life.[3,4] Patients progressing to kidney failure require life-sustaining therapy in the form of dialysis or a kidney transplant to survive. Kidney transplantation is the optimal form of renal replacement therapy from a cost, quality of life, and health outcomes perspective.[5] A limited supply of organs and an aging, frail, and highly comorbid CKD population preclude this option for most patients.[6] Most patients with kidney failure are thus treated with facility-based hemodialysis, a burdensome and expensive therapy with poor health outcomes.[7]

The transition from late-stage nondialysis CKD to dialysis is challenging for both patients and health care teams. The optimal initiation of dialysis is defined as elective, outpatient implementation of a patient's chosen modality (e.g., home hemodialysis, home peritoneal dialysis, or facility-based hemodialysis) with the most suitable dialysis access in place.[8] Unfortunately, even among patients followed by a nephrologist and multidisciplinary care team, 50% or more experience a suboptimal initiation of dialysis.[9,10] Moreover, more than half of dialysis initiations involve a hospitalization or emergency department visit due to severe uremic symptoms, volume overload, or hyperkalemia.[7] Initiating dialysis earlier at a higher kidney function before patients are symptomatic and when there is less risk of suboptimal starts is not an ideal solution, as it increases health care costs without a clinical benefit.[11,12]

Correspondence: Claudio Rigatto, Seven Oaks General Hospital, 2300 McPhillips Street, 2LB10, Winnipeg, MB, Canada R2V 3M3. E-mail: crigatto@sbgh.mb.ca

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Interventions are needed to improve early detection of indications for dialysis before the development of severe symptoms and complications. This could decrease the number of suboptimal starts and may substantially decrease costs and poor outcomes associated with acute inpatient dialysis initiation. In this regard, telemonitoring and virtual ward technologies (virtual case management) have shown benefit in high-risk, specific disease states such as heart failure.[13] It is tempting to hypothesize that enhanced monitoring of patients with late-stage CKD using this technology may reduce the rate of suboptimal dialysis starts; however, the costs of any such intervention must be weighed against the potential benefits.

As a prelude to developing and testing such an intervention in CKD, and to inform decisions regarding patient selection and outcomes measures in future trials, we wished to better understand how assumptions about patient risk of progression to kidney failure, intervention effectiveness, and cost might influence the final cost-effectiveness of a putative nurse-led virtual case management intervention and in doing so, define a break-even point for such a strategy.

The primary objective of the present study, therefore, was to explore assumptions around a nurse-led virtual case management intervention for patients with late-stage CKD and to estimate how these assumptions might affect potential cost savings using a cost-minimization approach.

METHODS

We defined our hypothetical study population as adult patients with late-stage CKD receiving care from a primary care provider or nephrologist and having a KFRE estimated risk of kidney failure at 2 years of 80% or greater in the baseline model. The KFRE has been internationally validated in nearly 700,000 patients across more than 30 countries and has demonstrated excellent discrimination (C statistic > 0.90) for the prediction of kidney failure in patients with CKD stages 3 to 5.[14,15]

We constructed a cost-minimization model from the perspective of the health care payer. A decision analysis Markov Model using microsimulation ($N = 100{,}000$) was created using TreeAge Pro 2018 (Williamstown, MA) in accordance with guidelines for economic evaluations of health interventions.[16] The primary output of the model was the break-even point for the nurse-led virtual case management intervention. The break-even point is defined as the maximum amount a health payer could spend on the intervention without increasing total net costs in comparison with the usual care scenario, in which there would be no net financial loss or gain from adopting the intervention. This is equal to the cost savings calculated by assigning the intervention an incremental cost of $0 in a cost-minimization model. For example, if an intervention were expected to save the health care system $1000, an intervention cost of $1000 over the entire time horizon the patient is followed in the model would be permissible to achieve a cost neutral intervention (i.e., without incurring a net increase in total health care costs). In addition, a threshold analysis was performed in which we estimated the potential monthly cost of the intervention based on the distribution of time spent receiving the intervention observed in the model. Secondary outcomes included the number of hospitalizations and suboptimal dialysis initiations in both the intervention and comparator arms. Our model used monthly cycles, followed patients until kidney failure or death, and assumed that no patient would receive the intervention (i.e., the virtual home monitoring platform) for longer than a time horizon of 24 months, at which point we expect approximately 85% of patients to have died or progressed to kidney failure (Supplementary Figure S1). We presumed no differences in survival, time to dialysis initiation, or quality of life between the intervention and comparator in the baseline model. A half-cycle correction was applied in the model to account for the overestimation of state membership in TreeAge Pro.[17] All costs used in the model were inflated to 2017 values and then exchanged to U.S. dollars using purchasing power parities.[18–20] Costs were discounted at an annual rate of 5%. As the study contains only aggregate, previously published, or publically available data, we did not seek approval from an institutional research ethics board. An overview of the model structure is provided in Figure 1.

The hypothetical intervention considered in our analysis was composed of remote telemonitoring, including daily measurement of several health metrics that could potentially signal signs of volume overload or uremic symptoms (blood pressure, oxygen saturation, and weight), and a validated symptom questionnaire,[21] accompanied by nurse-led case management. The comparator group was assumed to receive usual care for patients with late-stage CKD with rates of hospitalization and mortality modeled after the Kaiser Permanente Renal Registry.[4]

We estimated mortality and hospitalization rates from a previously published study of patients receiving usual medical care ($n > 1.1$ million), using CKD stage 5 as a proxy for ≥80% 2-year KFRE risk.[4] Rates of kidney failure were assumed to be 80% over 2 years based on calculated KFRE risk, with a uniform distribution (i.e., equal probability of kidney failure

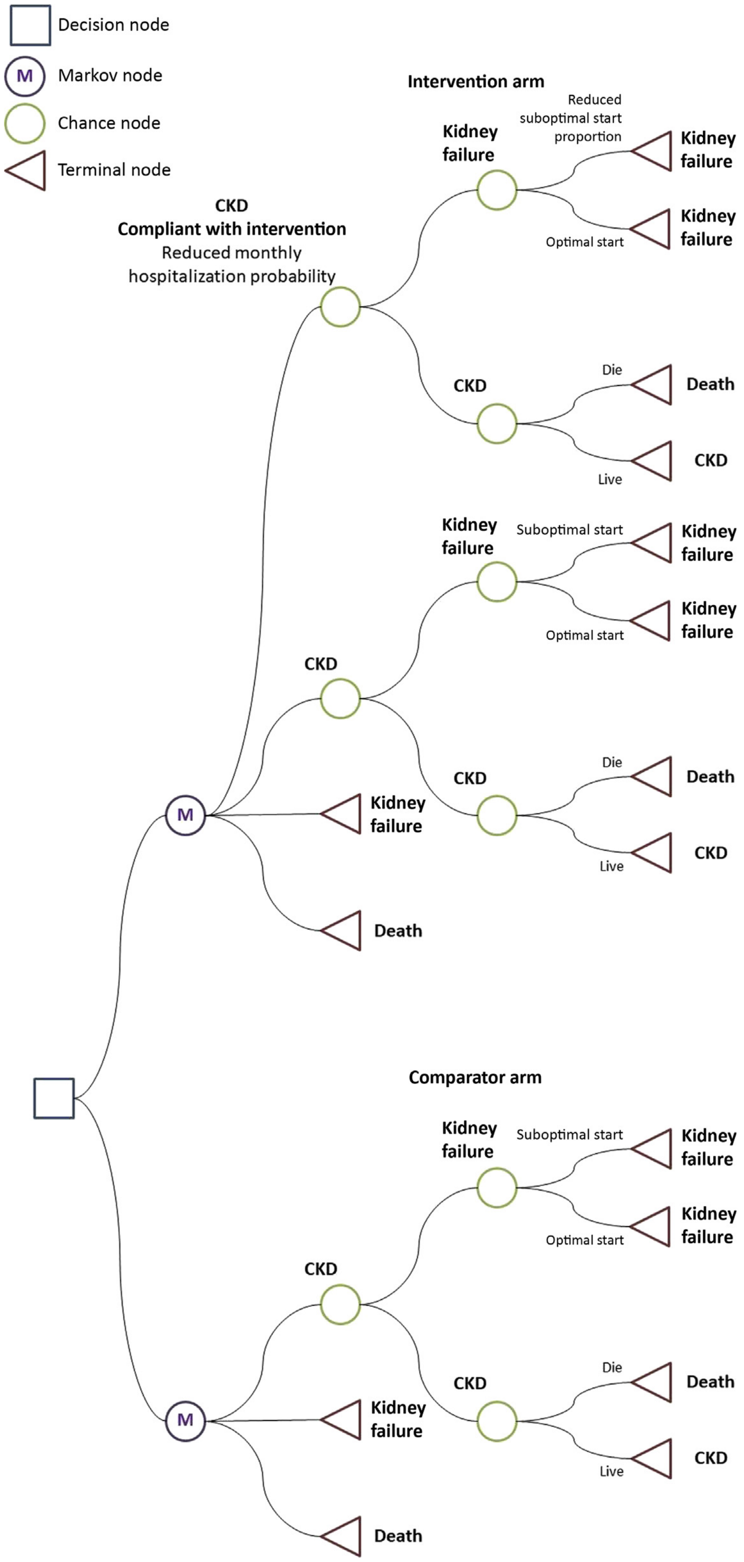


Figure 1. Overview of microsimulation model. Blue squares represent the decision node where both alternative treatments branch from and model results are calculated at its branches for each alternative. The purple circle represents a Markov process node, which runs each cycle of the model until the terminal condition is met (24 cycles or months in the baseline scenario). The green nodes represent chance nodes, where a probability event occurs. Red triangles are terminal nodes where patients are absorbed and exit the Markov process and the model (death and kidney failure). CKD, chronic kidney disease.

each month during the 2-year period) in the baseline scenario.[14] Compliance with the intervention was assumed to be 83.5% based on personal communication from virtual application developers. The baseline proportion of patients who experience a suboptimal dialysis initiation was assumed to be 0.62 (e.g., initiation

Table 1. Model inputs, data sources, ranges for sensitivity analyses, and assumed distributions

Variable	Baseline point estimate	Source	Univariate sensitivity analysis		Distribution for probabilistic sensitivity analysis[c]
			Lower limit	Upper limit	
Discount rate	0.05	Assumption	0	0.05	NA
KFRE risk cutoff for entry into cohort	0.8	Tangri *et al.* (2011)[14]	Tested in scenario analyses		NA
Monthly probability of hospitalization in patients with late-stage CKD[a]	0.1135	Go *et al.* (2004)[4]	0.0568	0.1703	Number of hospitalizations per person year – Poisson (1.4461), converted to a monthly probability
Monthly probability of mortality in patients with late-stage CKD[a]	0.0117	Go *et al.* (2004)[4]	0.0059	0.0176	Beta (1842, 11,185)
Compliance with intervention	0.835	Personal communication with virtual application developer	0.4175	1	Beta (91, 18)
Proportion of dialysis starts that are suboptimal	0.62	Piwko *et al.* (2012)[9]	0.31	0.93	Beta (200, 123)
Cost associated with suboptimal dialysis initiation[b]	$54,679	Piwko *et al.* (2012)[9]	$27,340	$82,019	Difference between optimal and suboptimal initiation cost: Gamma (63.02, 0.002629) – 2011 Canadian dollars
Cost associated with optimal dialysis initiation[b]	$33,953	Piwko *et al.* (2012)[9]	$16,977	$50,930	
Cost of a hospitalization event[b]	$11,640	Agency for Healthcare Research and Quality (AHRQ) (2015)[22]	$5820	$17,460	Log Normal (8.780, 1.047) – 2015 US dollars – sampled per model cycle
Relative risk of hospitalization afforded by intervention	0.66	Fishbane *et al.* (2017)[10]	0.33	0.99	Natural logarithm of the relative risk—normal (ln[0.66], 0.21)
Relative risk of suboptimal dialysis initiation afforded by intervention	0.5474	Fishbane *et al.* (2017)[10]	0.2737	0.8211	Natural logarithm of the relative risk—normal (ln[0.5474], 0.29)

CKD, chronic kidney disease; NA, not applicable; KFRE, Kidney Failure Risk Equation.

[a] An overview of methods used to convert rates to monthly transition probabilities is provided in Supplementary Figure S2.

[b] An overview of methods used to convert costs to 2017 U.S. dollars is provided in Supplementary Figure S3.

[c] An overview of methods used to determine distributional parameters for the probabilistic sensitivity analysis is provided in Supplementary Figure S4.

on a nonpreferred modality, with a nonpreferred access, or in hospital).[9] Cost estimates for optimal and suboptimal initiation of dialysis were taken from a multicenter retrospective study, and totaled $54,679 for patients who experience suboptimal dialysis initiations and $33,953 for optimally initiated patients.[9] The cost of a hospitalization event was assumed to be $11,640 based on estimates from the Agency for Healthcare Research and Quality.[22] We assumed that the intervention would afford a relative risk of 0.66 for hospitalization events and a relative risk of 0.5474 for the probability of experiencing a suboptimal dialysis initiation.[10]

Univariate sensitivity analysis was performed by varying model inputs ±50% from baseline, or until a theoretical maximum or minimum (e.g., compliance cannot exceed 100%). The annual discount rate was varied between 0% and 5%. We considered a lifetime horizon analysis in which patients could remain in the intervention for longer than 2 years. Second-order Monte Carlo simulation (probabilistic sensitivity analysis) was performed to evaluate parameter uncertainty by varying model inputs over assumed distributions across 1000 simulations. We conducted a 2-way sensitivity analysis on the primary effectiveness estimates (reduction in hospitalizations and suboptimal dialysis initiations) versus hypothetical costs of delivering the case management intervention at $400, $700, and $1000 per month. Last, we conducted a scenario analysis treating the proportion of patients compliant with the intervention as a time-dependent variable wherein compliance declined by an absolute reduction of 3% per month (e.g., month 1 compliance is the baseline value of 83.5%, month 2 compliance would have a value of 80.5%, and month 24 compliance would be 11.5%).

An overview of model inputs, data sources, ranges for sensitivity analysis, and assumed distributions is provided in Table 1.[4,9,10,14,22]

Internal model validity was evaluated by comparing output from the microsimulation to inputs used in the model. In the status quo comparator scenario, 72,656 patients in a hypothetical cohort of 100,000 are expected to initiate dialysis. In the microsimulation, we found that the status quo arm had 44,832 suboptimal dialysis initiations (61.7% vs. the assumed proportion of 62%). Mortality for patients on CKD was assumed to be a rate per person year of 0.1414. In the microsimulation a total of 12,271 patients were expected to die over a 2-year period. With a mean expected follow-up of 11.4 months, a total of approximately 94,604 patient years are observed in a hypothetical cohort of 100,000 patients, with an annual rate per person year of 0.1297; however, kidney failure is treated as an absorbing state in our model and any mortality occurring in the same cycle as a kidney failure event

Table 2. Results of microsimulation analysis ($n = 100{,}000$)

Scenario	Total expected cost per patient	Incremental cost per patient	Suboptimal dialysis initiations	Hospitalizations
Baseline	$22,751.16		44,934	127,367
Intervention	$15,411.68	−$7339.48	27,858	91,095

would not be represented in the simulation, and as such we would expect a slightly lower mortality rate in the model.

RESULTS

In our hypothetical cohort of 100,000 patients with CKD with a KFRE risk ≥80%, 44,934 would have a suboptimal dialysis initiation in the status quo comparator, reduced to 27,858 with the virtual case management intervention. In our baseline model, we would expect the intervention to prevent approximately 36,000 hospitalization events across 100,000 patients (127,367 hospitalizations in the comparator arm versus 91,095 hospitalizations in the treatment arm) (Table 2). The median cost of hospitalizations and suboptimal dialysis initiations was $14,405.86 (interquartile range, $4780.86–$23,571.63) in the intervention arm in comparison with $23,505.62 (interquartile range, $11,780.80–$31,199.66) in the comparator arm, The expected value associated with the cost of hospitalizations and suboptimal dialysis initiations was $15,411.68 in the intervention arm versus $22,751.16 among patients receiving usual care, providing a break-even cost of $7339 per patient with late-stage CKD enrolled in the intervention (amount that the health payer could spend on the intervention per-patient to result in no net financial loss or gain). Patients were expected to remain in the CKD state receiving the intervention for a median time of 9 months (interquartile range, 4 to 18 months), with an expected value of 11.4 months, following a bi-modal distribution (Supplementary Figure S5), providing a potential monthly intervention cost of $703.37 in threshold analyses.

In univariate sensitivity analysis, we found that the maximum break-even point for the virtual case management intervention ranged from approximately $3500 to $11,500 per patient with late-stage CKD enrolled. Evaluating the model with a lifetime horizon did not have an impact on our results, producing a total break-even spending of $8481.95, and based on the distributions of time spent receiving the intervention produced a potential monthly intervention cost that was approximately the same as the base model ($702.72). The model was most sensitive to assumptions surrounding the effectiveness of the intervention (e.g., the relative risk of hospitalization and relative risk of suboptimal dialysis initiation) and patient compliance (Figure 2). In the probabilistic sensitivity analysis, we found that more than 99% of simulations produced break-even points greater than $0 for the virtual case management intervention, with a median break-even point of $6124 per patient with CKD enrolled in the intervention (interquartile range, $3930–$9013) (Figure 3). Our 2-way sensitivity analysis of both effectiveness estimates (reduction in all-cause hospitalizations and reduction in suboptimal dialysis initiations) found that at the baseline assumed relative risk of suboptimal dialysis initiation (0.5474) and a putative

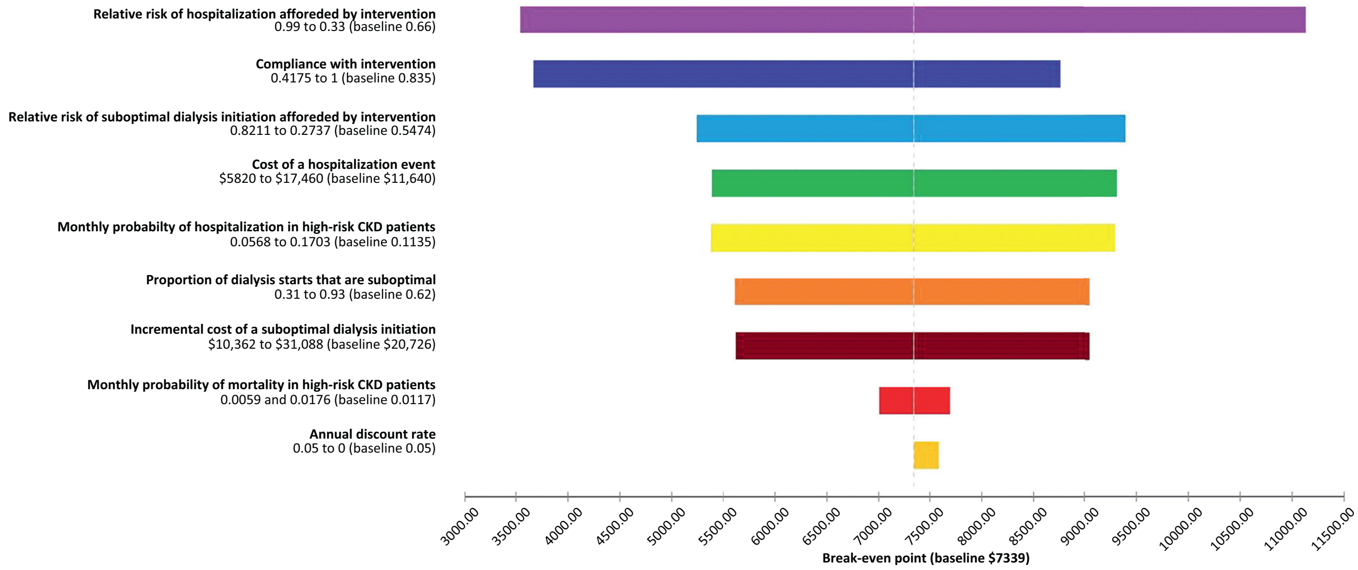


Figure 2. Univariate sensitivity analysis of break-even points associated with the virtual case management intervention. CKD, chronic kidney disease.

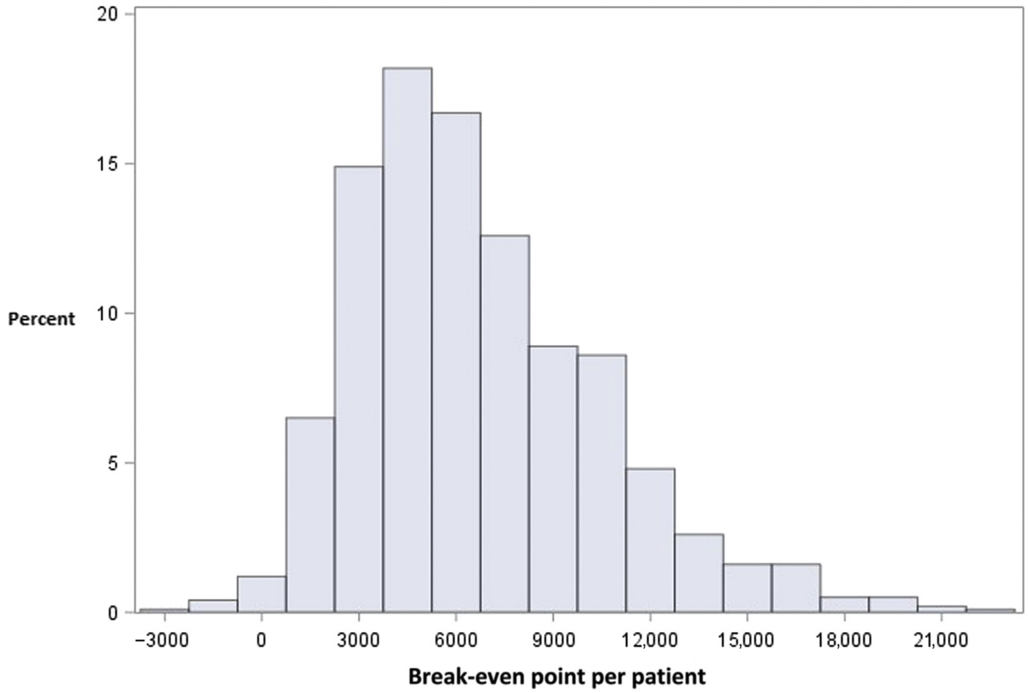
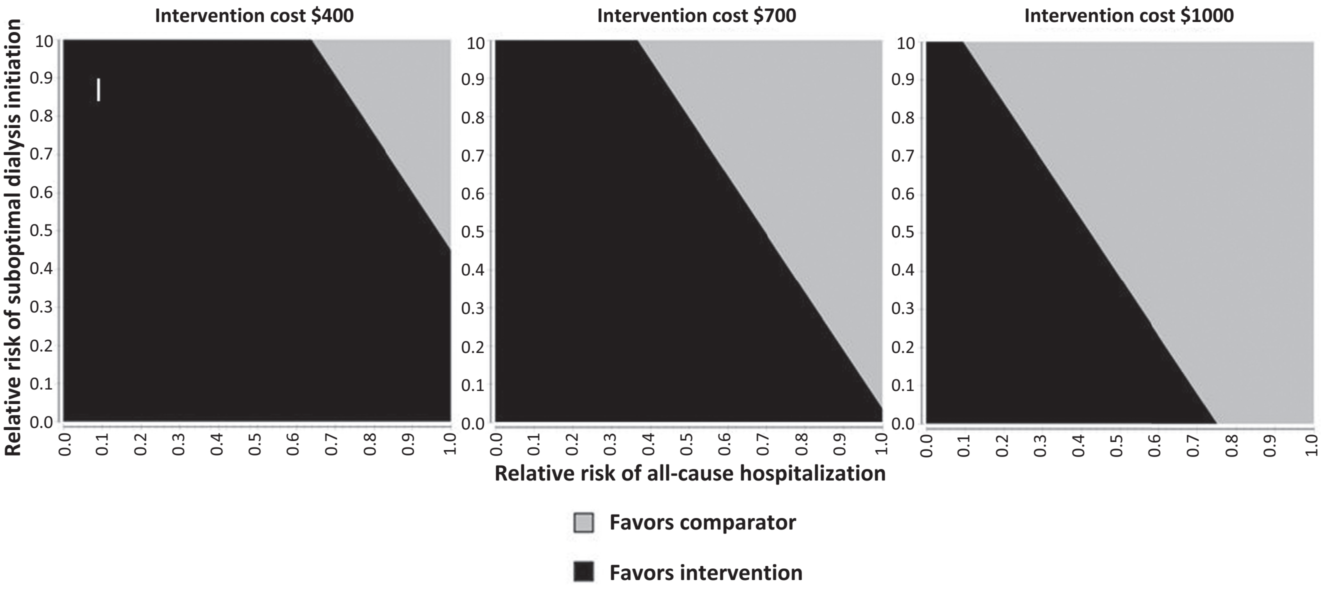


Figure 3. Distribution of break-even points based on 1000 second-order Monte Carlo simulations (probabilistic sensitivity analysis).

monthly intervention cost of $400, the relative risk of hospitalization would need to be 0.93 to reach a break-even point, decreasing to 0.39 at a monthly intervention cost of $1000. At the baseline assumed relative risk of all-cause hospitalization (0.66) and a monthly intervention cost of $400, the relative risk of suboptimal dialysis initiation would need to be 0.97 to reach a break-even point, decreasing to 0.14 at a monthly intervention cost of $1000 (Figure 4). In our scenario analysis considering a declining compliance over time



Relative risk of suboptimal dialysis initiation required to break-even by monthly intervention cost at baseline relative risk of all-cause hospitalization (RR = 0.66)		
0.97	0.55	0.14
Relative risk of hospitalization required to break-even by monthly intervention cost at baseline relative risk of suboptimal dialysis initiation (RR = 0.5474)		
0.93	0.66	0.39

Figure 4. Scenario analyses of intervention effectiveness estimates by putative monthly cost of intervention. RR, relative risk.

of 3% absolutely per month, we arrived at a monthly intervention cost of $499.43 to reach a break-even point.

DISCUSSION

In our cost-minimization analysis we found that a nurse-led home virtual monitoring intervention for patients with late-stage CKD at high risk of progression to kidney failure could reach a monthly cost of $703.37 to reach a break-even point in comparison with usual care. Based on the distribution of time spent receiving the intervention, this permits the health care payer to spend up to $7399 per patient with high-risk CKD enrolled in the intervention without experiencing net financial loss or gain. In our multivariate sensitivity analyses, we found that more than 75% of simulations found break-even points above $3930 per patient.

As expected, our Markov simulation was influenced by changes to the input assumptions. Our model was most sensitive to assumptions about the efficacy of the intervention, specifically the presumed relative risk reductions in hospitalizations and suboptimal dialysis initiations. This is not surprising, as both these events are extremely costly when they occur. We drew our estimates from the only published data directly in the CKD population.[10] Although additional data in CKD would be ideal to strengthen the evidence, it is important to note that similar estimates have been observed in home-monitoring interventions in heart failure populations. Drawing a parallel between CKD at high risk of kidney failure and heart failure is not unreasonable: both conditions, for example, are single-organ diseases with systemic consequences, both share a propensity to fluid retention and pulmonary edema, and as a consequence volume management and monitoring is a large component of ongoing care in both. In addition, drawing an analogy between telemonitoring and nurse-led case management is also reasonable, because most telemonitoring interventions apply principles or components of case management delivered remotely.[13]

Our model has several important implications for the future development of home monitoring technologies in CKD. First, the economics appear to be very favorable, as even a small effect could allow for a reasonable intervention cost to generate substantial cost savings for the health care payer. Innovation in this area should be prioritized by health care providers and insurers, particularly those who assume global risk for their subscribers, such as Accountable Care Organizations.[23] Second, we have defined reasonable minimum efficacy thresholds for a monitoring intervention to result in cost savings. Interventions must offer a combined effectiveness across a reduction in hospitalizations and suboptimal dialysis initiations that will permit a cost savings to be achieved based on reasonable putative intervention costs, or offer additional benefits such as increasing the time it takes to reach dialysis, a reduction in emergency department utilization, or an increase in home modality uptake. These data can inform the design of implementation RCTs of home monitoring in CKD. Understandably, integration of these types of interventions into existing patient management may impact the burden of workflow on staff or may require hiring new staff to accommodate these additional tasks. Augmented care interventions have shown to be feasible with nursing ratios of 100 patients:1 nurse,[10] and it is possible that avoided hospitalizations or suboptimal dialysis initiations may lessen the burden on hospital nursing resources. Further research evaluating the human resources implications of these interventions is warranted.

There are some additional considerations that need to be taken into account with home monitoring interventions in the CKD population. First, interventions similar to that proposed in this study have not been shown to be efficacious in patients with CKD who are at low risk of progression to kidney failure, whereas we hypothesize that targeting patients with a substantial risk of progression would be ideal. A randomized controlled trial of patients with an estimated glomerular filtration rate <60 ml/min per 1.73 m^2 found no improvement in mortality, hospitalization, or emergency department visits. The population in this study, however, had a mean estimated glomerular filtration rate of 37 ml/min per 1.73 m^2 and a mean urine albumin-to-creatinine ratio of 296 mg/g.[24] This would, on average, produce a 2-year KFRE risk of only approximately 3%, and as such, the risk of hospitalization or transition to dialysis would likely be very low even over an extended period. Second, there is uncertainty with regard to the timing of dialysis initiation in the context of the proposed intervention, where it may be possible that patients initiate dialysis earlier if indicated by interaction with the health care team or by metrics measured with home monitoring devices; conversely, there also may be a delay in the time to dialysis initiation if timely care can be offered in a situation that may have been overlooked in the usual care setting. Last, considering the effects of increasing home modality uptake as a result in reduced suboptimal dialysis, initiations may be warranted. The clinical trial used to inform effectiveness estimates in our study found that 23% of patients initiated with home PD in the intervention arm versus only 3% in the control arm, but was not statistically significant within the size of their study.[10] In the context of kidney failure populations where home modalities are currently prescribed in greater numbers than the United States (e.g., Canada, Australia, and New Zealand),[25,26] there may be an additional hypothetical benefit and subsequent cost savings.

Our model has several limitations. First, our model used rates of mortality and hospitalization taken from a study of patients with CKD stage 5 as a proxy for patients with a KFRE risk $\geq$80%, and as such, are likely an underestimation of the true rate of hospitalization and an overestimation of the true rate of mortality in our population; however, this would be a difference that is unlikely to alter the conclusion of our model, as it was robust to changes in the rate of mortality and the estimated maximum break-even point would increase with a higher baseline rate of hospitalization. Second, the data on the effectiveness of a virtual case management intervention with the outcome of an optimal start (elective outpatient initiation on hemodialysis with an arteriovenous access, on home dialysis, or with a preemptive transplant) was unavailable, and as such we took a conservative approach and estimated the effectiveness of the intervention based solely on a reduction in hospitalization at dialysis initiation, therefore possibly underestimating the true effectiveness of the intervention. Third, our perspective took that of the health payer, and we did not take into account other costs and benefits that may be associated with the intervention, such as changes to productivity, caregiver burden, or disability and social security payments. A final caveat of our model is that it applied average estimates for many variables (e.g., compliance, hospitalization risk), which may not be independent of a patient's history. For example, patients with low compliance may have a higher risk of kidney failure, death, or hospitalization, and conversely, patients with high compliance may have a higher than average treatment effectiveness. Further research to explore these relationships is warranted.

In conclusion, nurse-led virtual home monitoring interventions in patients with CKD at high risk of kidney failure have the potential for significant cost savings from the perspective of the health payer. We believe we have defined the necessary factors required for a successful virtual monitoring program trial and encourage innovators throughout the world to design, develop, and implement programs that meet these specifications to reduce suboptimal dialysis initiations and related hospital admissions, evaluating them with formally conducted, randomized control trials to develop the stronger evidence to support these interventions.

DISCLOSURE

All the authors declared no competing interests.

AUTHOR CONTRIBUTIONS

DH, PK, CR, TWF, and NT researched the idea and designed the study; PK, CR, and TWF acquired data; DH, MD, PK, CR, TWF, RHW, and NT analyzed and interpreted data; TWF and RHW analyzed statistics; and PK, CR, and NT supervised and mentored. Each author contributed important intellectual content during manuscript drafting or revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy or integrity of any portion of the work are appropriate investigated and resolved.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Proportion of patients remaining in CKD state over time.

Figure S2. Overview of methods used to convert rates to monthly transition probabilities.

Figure S3. Overview of methods used to convert costs to 2017 U.S. dollars.

Figure S4. Overview of methods used to determine distributional parameters for the probabilistic sensitivity analysis.

Figure S5. Distribution of time spent receiving the intervention in months.

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