Physiologic Insulin Resensitization Lowers Cost in Patients With Diabetes and Kidney Disease

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ABSTRACT

OBJECTIVE: To examine the effect of physiologic insulin resensitization (PIR) on the cost of treating patients with diabetes and chronic kidney disease (CKD).

STUDY DESIGN: The mean 1-year cost of treating 66 Medicare Advantage patients with diabetes and CKD who were receiving PIR was compared with that of treating 1301 Medicare Advantage patients with diabetes and CKD not receiving PIR. Differences in disease severity were compared using mean risk adjustment factor scores.

METHODS: Cost comparisons were made for CKD stages 2, 3a, 3b, 4, and 5. The total cost of treating the PIR patients was then compared with the total costs of treating the same number of non-PIR patients to determine cost differences potentially incurred.

RESULTS: The mean annual cost of treating PIR patients with stage 2 CKD was $11,251 vs $18,058 for the non-PIR group. For patients with stage 3a CKD, the mean PIR cost was $10,974 vs $18,563 for the non-PIR group. For patients with stage 3b CKD, the mean costs were $19,520 and $18,398, respectively. The mean costs for stages 4 and 5 CKD were $14,042 vs $22,124. The costs for an equal number of non-PIR patients at each stage were $345,830 higher than the actual costs of the PIR patients. There were no significant differences in the mean risk adjustment factor scores between the 2 groups.

CONCLUSIONS: PIR is a possible method of reducing the cost of treating patients with diabetes and CKD. Given the rapidly increasing numbers of patients with diabetes and CKD who are Medicare Advantage beneficiaries, PIR should be considered for use by managed care organizations.

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According to the CDC, 38.4 million Americans have diabetes (11.3% of the US population). Of these, 8.5 million are undiagnosed and, presumably, experiencing a worsening of their untreated disease.[1] Treating those who have diabetes was estimated to consume 1 of every 4 dollars spent on health care in the US.[2] This expenditure is likely to significantly increase because the CDC estimates that 98 million Americans have prediabetes, a condition that can lead to diagnosed diabetes if interventions are not taken. Unfortunately, 80% of those with prediabetes do not know that they have this condition, so progression to diagnosed diabetes is more likely.[1] Prediabetes is prevalent in 48.8% of those 65 years or older, in 44.8% of those aged 45 to 64 years, and in 27.8% aged 18 to 44 years.[1] Data from one study showed that progressing from prediabetes to diabetes raised annual costs by 22.1% in the year following the change, by 39.1% in the second year, and by 47.6% in the third year compared with patients with prediabetes who did not transition to diabetes.[3] These data suggest that there will be a rapid escalation in the number of patients needing treatment and the costs of individuals having diabetes. This would be a continuation of a trend seen in the recent increases in costs. It has been estimated that the direct medical cost of treating diabetes increased from $227 billion in 2012 to $307 billion in 2022 (adjusted to 2022 US$).[2] Current treatments for diabetes aim to slow the progress of the disease and the conditions that accompany diabetes. The costs tend to become more expensive as diabetes progresses. Until there are therapies that reverse and/or arrest diabetes-related conditions, organizations that pay for medical care will experience rapidly increasing expenditures.

A primary driver of costs among those with type 2 diabetes (T2D) is chronic kidney disease (CKD). Among adults in the US 65 years or older with T2D, approximately 34% have CKD.[4] The natural course of diabetes-related kidney disease is that it worsens over time. Some individuals with stage 1 or 2 CKD may have an improvement in their estimated glomerular filtration rate (eGFR). However, as many as 90% of those with CKD do not receive a diagnosis until they become symptomatic, when reversal is highly unlikely.[5] Among adults in the US receiving kidney dialysis, 40% have diabetes.[5] The number

of patients with diabetes needing dialysis or kidney transplantation will also increase as more cases of prediabetes convert to diabetes and progress through the stages of CKD. The annual per-person spending attributable to Medicare parts A, B, and D was more than double for beneficiaries 65 years or older with CKD ($25,920) compared with those without CKD ($12,332).[6] These costs of those with diabetes and CKD account for 23.5% of Medicare's fee-for-service expenditures.[7] The cost of caring for individuals with CKD has escalated for Medicare Advantage providers since the 2021 change in federal policy that required coverage of end-stage renal disease (ESRD). Medicare Advantage enrollment in the ESRD population grew by approximately one-third in 2021, from 18.3% in 2020 to 24.5% in 2021. Medicare Advantage spending for ESRD increased by 46.4% in the year following the policy change, whereas fee-for-service costs to Medicare declined.[6] The cost implications of the impending increase in current and future patients with diabetes needing dialysis and/or kidney transplants are profound.[6] Kaplan et al reported that the cost to Medicare for kidney dialysis ranged from $91,716 to $108,656 per year.[7] Bentley and Ortner estimated that the mean charge for kidney transplants, including charges for 30-day presurgical services, organ procurement, hospitalization, and 180-day posthospitalization costs, was $442,000.[8]

TAKEAWAY POINTS

Physiologic insulin resensitization (PIR) treatment resulted in lower treatment costs for patients with diabetes and chronic kidney disease (CKD).

- Individuals 65 years or older with diabetes and CKD cost twice as much to care for as those without CKD. An estimated 36% of individuals 65 years or older have CKD.
- The mean annual cost of treating 66 patients receiving PIR who had diabetes and stage 2, 3a, 3b, 4, or 5 CKD was compared with the mean cost of treating similar patients not receiving PIR.
- Treatment costs of the 66 PIR patients were $345,830 lower than the costs of 66 matched non-PIR patients.

A new approach to treating diabetes has become available: physiologic insulin resensitization (PIR). It recognizes that, in individuals without diabetes, insulin is secreted from the pancreas every 4 to 8 minutes. This results in sharp peaks and valleys of insulin blood levels in the portal vein. As blood glucose levels and the demand for glucose rise, the threshold for insulin clearance in the liver is exceeded, causing constant elevations of insulin to be maintained in the peripheral circulation, disrupting pulses, causing insulin resistance, and leading to T2D. In patients with T2D, regular insulin secretion becomes impaired, with progressively irregular intervals and differences in insulin blood levels. As the circulating insulin level becomes more erratic, the cascade of adverse events associated with T2D occurs. The administration of PIR for a patient with T2D is intended to restore the normal circulation of insulin by providing patient-specific, physician-directed boluses of insulin every 5 to 8 minutes. Blood insulin levels are monitored and normalized by the ingestion of oral glucose as needed. Each treatment lasts for 3 to 4 hours. Treatments are given 2 to 3 times per week initially and gradually transition to weekly, biweekly, or monthly, depending on patients' concurrent conditions and response to the treatment. The treatment and the physiologic basis for it have been described in the literature.[9,10]

There are reports of improvements in patients with diabetic neuropathy and diabetic retinopathy after receiving PIR.[11,12] A 3-patient case series demonstrated that PIR could be useful in treating nephropathy in individuals with diabetes. These patients experienced increases in eGFR of 22, 12, and 20 cc/min, respectively.[13] Given the economic implications of arresting or reversing CKD, a study was conducted to examine whether PIR could have an impact on the cost of treating patients with diabetes and kidney disease.

METHODS

All patients in this study were under the care of Island Doctors, a Florida-based multispecialty medical services organization. They were all 65 years or older and enrolled in a Medicare Advantage insurance plan operated by Humana. Island Doctors is allocated funds from Humana on a per-member per-month basis related to the patients' risk scores as determined by their diagnoses. When care is provided to a patient via hospital, specialist, or other medical professional, Humana is billed, and the money it pays is deducted from the Island Doctors' allocation to pay for the product or service provided to the patient. Island Doctors receives information on the expenditures related to its patients and can analyze those expenditures directly. As a result, the dollar values analyzed in this study are the real dollars expended to provide medical care for patients who met the inclusion criteria for analysis. In addition, the direct cost of providing PIR is included in the cost figures and estimated at $200 per visit. This includes personnel and supply costs. The treatments are provided at existing buildings, so facility costs were not included. As a result, the costs reported in this study for those receiving PIR and those who did not receive PIR are the actual costs incurred by Island Doctors for the treatment of these patients.

Approximately 200 of Island Doctors' Medicare Advantage patients are currently receiving PIR. All PIR patients with CKD who met the inclusion criteria were included in the study. Study inclusion criteria were that patients were 65 years or older; had Medicare Advantage; had stage 2, 3a, 3b, 4, or 5 CKD; and had been receiving PIR for 21 months continuously as of November 5, 2023. The PIR patients also had to have been receiving PIR for at least 6 months prior to November 1, 2022, to allow any effects of PIR to have occurred, and to have been consistently on the treatment plan since starting PIR. All the Humana Medicare Advantage patients with CKD who were not receiving PIR were used as the comparison group. These patients had to be 65 years or older; have been diagnosed with CKD in stages 2, 3a, 3b, 4, or 5; and had to be under the care of Island

TABLE 1. Cost Comparison Between Patients With Diabetes and CKD Receiving PIR and Those Not Receiving PIR, November 1, 2022-October 31, 2023

CKD stage	No. of PIR patients	PIR mean cost	No. of non-PIR patients	Non-PIR mean cost	Mean cost difference
2	27	$11,251	121	$18,058	–$6807
3a	12	$10,974	413	$18,563	–$7589
3b	16	$19,520	434	$18,398	$1122
4 and 5	11	$14,042	333	$22,124	–$9812
Total	66		1301		

CKD, chronic kidney disease; PIR, physiologic insulin resensitization.

Doctors between November 1, 2022, and October 31, 2023. The cost of treating the PIR patients was compared with the cost of treating all other Island Doctors Medicare Advantage patients with CKD who were not receiving PIR. Patient costs for both groups were compared for patients with CKD stages 2, 3a, 3b, 4, or 5 who met the inclusion criteria. The costs for both the PIR and the non-PIR groups were for the period between November 1, 2022, and October 31, 2023.

The frequency of the treatment varied by the CKD stage of the patient. Patients with stage 2 CKD were treated every 3 to 4 weeks depending on response. In calculating costs for stage 2 patients, a treatment frequency of every 3.5 weeks was used. Patients with stages 3a and 3b were treated with PIR biweekly. Those with stages 4 and 5 were treated with PIR weekly.

The mean costs during the study period for the PIR patients and the non-PIR patients were compared to determine PIR's effect on costs. In addition, the total cost of treating the PIR patients for 1 year was compared with the total cost of an equal number of non-PIR patients for each of the stages of CKD. This was done by multiplying the mean difference per patient in each of the CKD stages by the number of patients in that stage. These were summed to provide the total cost differences between these 2 groups for the study year.

Recognizing that there may have been a selection bias in who might have received PIR vs those who had not, it was considered necessary to examine whether the severity of the patients' conditions was similar. This is a complex task when dealing with older patients with diabetes because they may have multiple medical conditions that make matching them difficult. However, the risk adjustment factor (RAF) is regularly used to determine Medicare reimbursements and is designed to be a global measure of overall medical condition. A Medicare Advantage beneficiary's RAF score is based on their clinical conditions, Medicaid and disability status, sex, age, and residence in the community or an institution such as a skilled nursing facility. The mean RAF scores were calculated for both the PIR and the non-PIR groups. These were compared to determine whether medical severity was an explanation for any cost differences between the 2 groups.

RESULTS

Of the 66 patients in the PIR group who met the inclusion criteria, 27 had stage 2, 12 had stage 3a, 16 had stage 3b, 10 had stage 4, and 1 had stage 5 CKD. Because there was only a single patient with stage 5 CKD, this patient was included with the stage 4 patients for analysis purposes. Of the 1301 patients in the non-PIR group, 121 had stage 2, 413 had stage 3a, 434 had stage 3b, 333 had stage 4, and 5 had stage 5 CKD.

When the 12-month costs of treating the patients with stage 2 CKD were compared, the mean cost for the PIR group was $6807 lower than that for the non-PIR group. The mean cost for the PIR group was lower than for the non-PIR group by $7589 for the patients with stage 3a CKD. The mean cost for PIR patients was $1122 higher than for the non-PIR patients with stage 3b CKD. The mean cost for PIR patients was lower than that for the non-PIR patients by $9812 for patients with stage 4 and 5 CKD (**Table 1**).

When the total costs for the 27 PIR patients with stage 2 CKD were compared with the costs of 27 non-PIR patients with stage 2 CKD, the PIR group's costs were $183,796 lower. The total costs for the 12 PIR patients with stage 3a CKD were lower than the costs of 12 non-PIR patients by $91,075. The 16 PIR patients with stage 3b CKD had costs $17,953 higher than those of the 16 non-PIR patients. The total costs for the 11 PIR patients with stage 4 and 5 CKD were lower than those of 11 non-PIR patients by $88,912. Overall, the 66 PIR patients had costs that were $345,830 lower than those of the non-PIR patients who had been matched by stage of CKD. This was a difference of $5240 less per patient (**Table 2**).

When the RAF scores between the PIR group and the non-PIR group were compared, there were no differences of any importance (**Table 3**).

DISCUSSION

This study's results show the potential cost savings that can be realized by having patients with diabetes and CKD receive PIR. This study has several strengths. The study's cost figures are the actual costs incurred by Island Doctors. This is different from most other health care cost studies that do not have exact measures of provider cost and instead rely on averages or imputed costs. This study also had complete, computer-accessible data on CKD stages and RAF scores that allowed the researchers to ensure the cost comparisons were between patients with similar levels of both CKD and global measures of disease severity. It also presented the cost comparisons over 12 months so that the effects of anomalous events could be averaged out over a significant period.

The study's findings should be considered to offer indications of potential cost reduction and not be thought of as definitive. The

TABLE 2. Cost Comparison Between 66 Patients With Diabetes and CKD Receiving PIR and Expected Costs of Equal Number of Patients Using Mean Cost of Those Not Receiving PIR, November 1, 2022-October 31, 2023

CKD stage	No. of PIR patients	Mean cost per PIR patient	Total cost for PIR patients	No. of non-PIR patients	Mean cost per non-PIR patient	Total cost for non-PIR patients	Difference
2	27	$11,251	$303,782	27	$18,058	$487,578	–$183,796
3a	12	$10,974	$131,691	12	$18,563	$222,767	–$91,075
3b	16	$19,520	$312,331	16	$18,398	$294,378	$17,953
4 and 5	11	$14,042	$154,472	11	$22,124	$243,384	–$88,912
Total	66			66			–$345,830[a]

CKD, chronic kidney disease; PIR, physiologic insulin resensitization.

[a]The mean difference was $5204 less per PIR patient.

TABLE 3. Comparison of Mean RAF Scores Between Patients Receiving PIR and Patients Not Receiving PIR by CKD Stage

CKD score	No. of PIR patients	Mean RAF score	No. of non-PIR patients	Mean RAF score
2	27	1.97	121	1.97
3a	12	2.10	413	2.19
3b	16	2.39	434	2.37
4 and 5	11	2.39	333	2.40
Total	66		1301	

CKD, chronic kidney disease; PIR, physiologic insulin resensitization; RAF, risk adjustment factor.

66 PIR patients represent a small sample with small numbers in stages 2, 3a, 3b, and 4/5 of CKD. It covered only a 12-month period, so it is not known whether its results can be sustained. The reasons that the patients were referred to PIR or the motivations for patient willingness to receive PIR are not known. Becoming a PIR recipient requires significantly more office visits than traditional diabetes care. This may exclude those with jobs, transportation problems, caregiving responsibilities, etc. It is expected that some of these issues can be resolved in future studies.

CONCLUSIONS

PIR could reduce the high costs of the treatments that make CKD such an expensive disease. It has the prospect of alleviating some of the tsunami of oncoming expenses that will occur as millions of individuals with prediabetes and diagnosed diabetes develop CKD and move on to dialysis and/or transplantation. ■

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