

## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

## Supplementary Methods.

**Table S1.** Detailed report of sensitivity and specificity.**Figure S1.** Histopathological characteristics of kidney transplant recipients with low-risk score for transplant glomerulopathy.**Figure S2.** Histopathological characteristics of kidney transplant recipients with intermediate-risk score for transplant glomerulopathy.**Figure S3.** Histopathological characteristics of kidney transplant recipients with high-risk score for transplant glomerulopathy.**Figure S4.** Probability of Graft Loss by Treatment using Kaplan-Meier curves.

## Supplementary References.

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## Using Telenephrology to Improve Access to Nephrologist and Global Kidney Management of CKD Primary Care Patients



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Most chronic kidney disease (CKD) clinical guidelines recommend that patients with CKD stage 3b to 5 be referred to a nephrologist for specialized evaluations and treatment.<sup>1–3, S1–S4</sup> Unfortunately, this recommendation is difficult to follow because of a lack of specialists, a problem especially critical in developing nations, where scarcity has reached a critical

level.<sup>4,5, S5–S8</sup> The consequences include long waiting lists, lack of opportune diagnosis and/or treatment, and impaired health outcomes.

Telenephrology (TN), also known as telehealth in nephrology, is digital connectivity strategy to improve access to specialists.<sup>6–9, S9–S20</sup> It has been reported that TN facilitates distance clinical care as well

as communication and education among healthcare teams, patients, family members, and the general public. TN also provides easy access to specialists for patients with CKD in rural, remote, and hard-to-access regions.<sup>6–9, S9–S20</sup>

In Chile, the first TN program was implemented in 2012 and was restricted to 2 cities in the country (Methods in Supplementary Material and Supplementary Figure S1). The objectives of this study are to evaluate the clinical results and the waiting time required before receiving nephrologist care, before and after TN program onset, for CKD patients referred from primary health centers (PHCs).

## RESULTS

We studied 4668 teleconsultations to nephrologist in 2 Chilean cities between October 2012 and October 2018 (70.1% in Concepción and 29.9% in Talcahuano). Patient age was 69.5 years (SD, 13.2 years); 78.4% were older than 60 years; and 59.4% were women. The principal diagnosis was CKD (92.6%), and 85.1% of patients were in stage 3a to 5 (Supplementary Figure S2).

The response time ranged from 1 to 3 days; 88.2% of the teleconsultations were answered within 24 hours, and the remaining 11.8% were answered within 3 days.

In total, 2676 patients (57.3%) who did not require in-person nephrologist consultations were referred to PHCs with treatment recommendations from the specialists as follows: adjustments to hypertension and/or diabetes treatments (51.9%), confirmation of the diagnosis and preventive recommendations (32.3%), and requests for further clinical information or complementary exams (15.8%).

In addition, 1992 patients (42.7%) were sent for in-person nephrologist evaluations; these patients mainly had pre-dialysis stage 4 to 5 CKD (64.3%), glomerular syndromes (23.3%), and refractory hypertension (7.6%).

Table 1 shows the clinical and laboratory differences between the patients who were counter-referred to PHC and those sent to the hospital for in-person evaluations. The patients with stage 1, 4, and 5 CKD were referred to nephrology significantly more often than to PHC.

Opportune diagnosis and referral of patients with stage 4 to 5 CKD to the advanced renal care unit of the hospital allowed the percentage of patients undergoing peritoneal dialysis to rise from 5% to 16.3%; the proportion of patients admitted to hemodialysis with arteriovenous fistula access increased from 28.3% to 60.3%, and only 2 patients (0.9%) were admitted for

**Table 1.** General characteristics and laboratory results of the patients referred to PHC or a nephrologist

Characteristic	Total study population, n = 4668	Referral to PHC, n = 2676 (57.3%)	Referral to a nephrologist, n = 1992 (42.7%)	P value
Age, yr, mean (SD)	69.5 (13.2)	72.6 (11.9)	65.5 (13)	<0.001
Sex, female, %	59.4	63.4	54	<0.001
Diabetes, %	55.2	60.6	51.2	NS
Hypertension, %	58.7	54.7	61.6	<0.001
Dyslipidemia, %	57.9	59	57.1	<0.001
Stage 1 CKD <sup>a</sup>	193 (4.1)	91 (47.2)	102 (52.8)	<0.001
Stage 2 CKD <sup>a</sup>	503 (10.8)	265 (52.7)	238 (47.3)	<0.001
Stage 3a CKD <sup>a</sup>	1014 (21.7)	811 (80)	203 (20)	<0.001
Stage 3b CKD <sup>a</sup>	1658 (35.5)	1132 (68.3)	526 (31.7)	<0.001
Stage 4 CKD <sup>a</sup>	1068 (22.9)	326 (30.5)	742 (69.5)	<0.001
Stage 5 CKD <sup>a</sup>	232 (5)	51 (22)	181 (78)	<0.001
Creatinemia, mg/ml, mean (SD)	1.8 (1.2)	1.5 (0.8)	2.1 (2.4)	<0.001
eGFR, mean (SD)	42.2 (21.4)	44.9 (18.3)	38.4 (24.5)	<0.001
ACR, mg/g, mean (SD)	358.6 (1128)	141.6 (542)	688.2 (1606)	<0.001
PCR, mg/g, mean (SD)	846.8 (2105)	272.6 (1239)	1401.1 (2570)	<0.001
Hb, g/dl, mean (SD)	12.5 (1.9)	12.6 (1.7)	12.2 (1.9)	<0.001
Hematocrit, %, mean (SD)	37.6 (5.4)	38.0 (5)	37.0 (5.8)	<0.001
HbA1c, %, mean (SD)	7.5 (2.2)	7.3 (2.3)	7.7 (2.2)	<0.001

ACR, urine albumin-to-creatinine ratio; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MDRD-4, Modification of Diet in Renal Disease (ml/min per 1.73 m<sup>2</sup>); NS, non significant; PCR, urine protein-to-creatinine ratio; PHC, Primary health care.

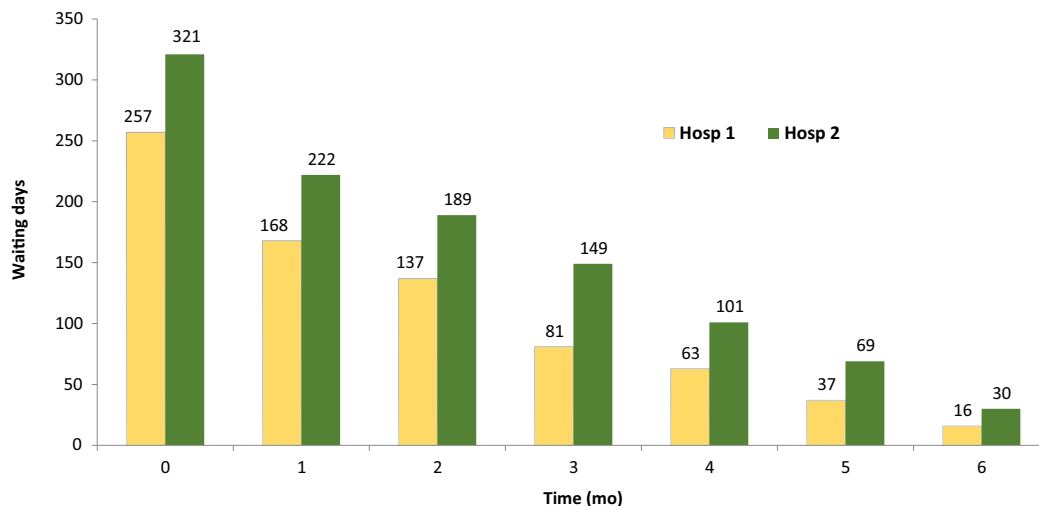
<sup>a</sup>Data are number of patients (%). CKD stages are according to the Chronic Kidney Disease (KDIGO) definition/classification.<sup>51</sup>

dialytic emergency. In total, 25.3% opted for non-dialytic conservative treatment.

Evaluating patients via TN without the need for them to visit the hospital freed up outpatient appointments in the hospital nephrology unit, which, during first 6 months, shortened the waiting times for in-person evaluations from an average between both hospitals of 289 days (range, 257–321) with the traditional method to an average of 23 days (range, 16–30) after the initiation of TN, as shown in Figure 1 (changes in the waiting time for in-person evaluations at both hospitals during first 6 months of TN). After those first 6 months (April 2013 onward), the waiting times remained relatively the same.

A multivariate logistic model analyzed the effects of age, sex, CKD stage, albumin/creatinine ratio, and hemoglobin variables on the likelihood of being referred for an in-person visit with a nephrologist. These factors were all independently associated with referral and were statistically significant (Table 2).

In total, 48 (87.3%) of the PHC doctors completed the satisfaction survey and reported an 86.7% approval rating for TN. The PHC doctors highlighted the short response times from the nephrologist, continuing education, and easy access to a specialist for collaborative patient management in their responses.



**Figure 1.** Changes in waiting time for in-person evaluations at both hospitals during the first 6 months of telenephrology. Hosp 1, Hospital Las Higueras–Talcahuano; Hosp 2, Hospital Concepción.

## DISCUSSION

In this report, we present the first Latin American study on the use of TN in real practice. We showed an average response time of 2.5 days and the identification of 57.3% of patients who did not require in-person consultations, who were able to continue treatment at the original PHC center according to the specialist's recommendations. This outcome allows patients to avoid incurring transportation costs, as well as unnecessary consultations, unnecessary examinations and delays in treatments, among others. Although we described the outcomes of the intervention without a control, which can be viewed as an important limitation of this study, we cannot identify any other intervention observed in the Chilean health system over the last 6 months that could explain a difference of this magnitude (289 days vs. 2 days for TN evaluations and, if required, 23 days for in-person evaluations).

In addition, the analysis showed that waiting times for specialty consultations decreased continuously over a 6-month period, and that the designated 10-minute time frame (50% less than the time assigned for in-person consultations) was sufficient to adequately

respond to the teleconsultations, in accordance with previous reports.<sup>7</sup> This time frame saves time, allows more outpatient appointment opportunities in the nephrology unit at hospitals, and reduces the waiting times for patients who require in-person evaluations by a nephrologist to a maximum of 30 days.

Most patients (85.1%) referred to our TN platform had CKD between stages 3a and 5, a point at which early evaluation and treatment by a nephrologist has a greater impact on progression to advanced stages, preventing complications, improving survival, and decreasing hospitalizations.<sup>1,2,S2–S4,S21–S24</sup>

Telenephrology programs have been proposed as a strategy to address and to solve the health challenge presented by the growing proportion of CKD patients referred from PHC<sup>S25–S28</sup> and the lack of nephrologists.<sup>4,5,S5–S8</sup> Our program would confirm this proposal and provide data that could be very valuable for health systems around the world like that in Chile that face similar constraints.<sup>6–9,S9–S20</sup> As a result, the Ministry of Health of Chile decided in 2019 to extend the TN strategy throughout the country's health network.

The variables of young age, male sex, advanced-stage CKD, elevated albuminuria, and low levels of hemoglobin were independent factors, and patients with these factors were sent to the hospital significantly more frequently than patients without these factors. Future studies should verify the clinical value of these associations among variables and morbidity and mortality, the number of hospitalizations, complications, and dialysis use.

An added value of our TN program was that it facilitated faster and more opportune access to the advanced renal care unit for stage 4 to 5 CKD patients. This benefit allowed for informed and consensus-

**Table 2.** Multivariate analysis variables associated with a referral to a nephrologist at the hospital

	OR	SE	z	P >  z	95% CI
Age	0.9319714	0.0035734	-18.37	0.000	0.9249938–0.9390016
Sex	0.514891	0.0457828	-7.47	0.000	0.4325424–0.6129173
CKD stage	1.938131	0.0861569	14.89	0.000	1.776413–2.11457
ACR	1.001039	0.0000968	10.74	0.000	1.000849–1.001228
Hemoglobin	0.9014331	0.0231739	-4.04	0.000	0.8571383–0.9480169
Intercept	31.77198	15.64604	7.02	0.000	12.10242–83.4097

ACR, urine albumin-to-creatinine ratio; CKD, chronic kidney disease; CI, confidence interval; OR, odds ratio.

based decisions regarding treatment options, including dialysis/transplantation (74.7%) and conservative treatment (25.3%). In addition, the number of patients with arteriovenous fistula doubled, those who chose peritoneal dialysis tripled, and the number of admissions for dialytic emergencies was minimized.

One of this study's limitations is that the patients' level of satisfaction and the feasibility of following the recommended treatments through the TN method were not evaluated. Furthermore, we did not evaluate whether the specialist's recommendations had an impact on disease progression and cardiovascular morbidity and mortality.

Another aspect that was not evaluated in our study was the costs associated with the TN strategy, opportune access, and the treatment recommended by the specialist. Use of TN could potentially reduce costs by enabling online patient care through referrals from PHC.<sup>7,S14,S20,S29–S31</sup>

In summary, the TN is a feasible intervention that can be implemented in a healthcare system like the Chilean public system. Use of TN is very likely to be responsible for a decrease in the demand for nephrologist consultations at the hospital level, a transference of resolution capacities to primary care, and a decrease in waiting times for specialist in-person evaluation. The opportune diagnosis and referral of stage 4 to 5 CKD patients allowed time for a consensus regarding the choice of elective renal replacement therapy or conservative treatment. Although further research should be undertaken to confirm these findings, we argue that the magnitude of the outcomes observed as well as the absence of other explanatory factors indicate that TN explains most of the observed effect.

## DISCLOSURE

CZ has received speaker honoraria from Fresenius Kabi, AstraZeneca, and Grunenthal. ME has received honoraria from Novartis, Pfizer, Roche, Grunenthal, MSD, Merck, Boehringer Ingelheim, and Bayer. All the other authors declared no competing interests.

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## SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

**Supplementary Methods.**

**Figure S1.** Telenephrology workflow. Study protocol.

**Figure S2.** Teleconsultations according to stages of CKD and sex.

**Supplementary References.**

**STROBE Statement.**

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