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COST-EFFECTIVENESS EVALUATION OF INCORPORATING ORAL NUTRITIONAL SUPPORT INTO THE EXPLICIT HEALTH GUARANTEES PACKAGE FOR PATIENTS WITH END-STAGE RENAL DISEASE ON HEMODIALYSIS IN CHILE

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ABSTRACT

Introduction: End-stage renal disease represents a growing burden on the Chilean healthcare system. Protein energy wasting in patients on hemodialysisis highly prevalent and is associated with increased morbidity and mortality and healthcare costs. Despite clinical recommendations, oral nutritional support is not included in the Explicit Health Guarantees package. ***Objective:*** To evaluate the projected cost-effectiveness of incorporating oral nutritional support as part of the Explicit Health Guarantees package for patients with End-stage renal disease on hemodialysis in Chile. ***Methods:*** A projective economic study was conducted from the perspective of the healthcare system, using national information on the prevalence of End-stage renal disease, hospitalization costs, oral nutritional support prices, and clinical parameters from the literature. The incremental cost per Quality-Adjusted Life Yeargained was calculated, and savings from reduced hospitalizations were estimated. Time horizon: 5 years. ***Results:*** The implementation of oral nutritional support allow for a 20% reduction in hospitalizations attributable to malnutrition, with cumulative savings of Chilean Peso $4.362 billion and a release of 18.645 bed-days. The incremental cost per Quality-Adjusted Life Yearwas Chilean Peso $3.200.000, which is below the Chilean cost-effectiveness threshold. ***Conclusions:*** Incorporating oral nutritional support into the Explicit Health Guarantees package is a cost-effective, clinically beneficial, and viable intervention in the context of the Chilean health system. Its adoption is recommended as part of the comprehensive strategy for managing End-stage renal disease.

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INTRODUCTION

Chronic kidney disease (CKD) is a highly prevalent condition with a significant health burden, characterized by progressive and irreversible loss of kidney function. In its End-stage renal disease (ESRD), patients require renal replacement therapy, with hemodialysis (HD) being the most widely used modality in Chile (Ministry of Health [MINSAL], 2018). CKD represents a growing public health problem globally. In Latin America, it has risen in importance as a cause of DALYs, with Chile being one of the countries where this increase has been most pronounced (Rosas-Valdez *et al*., 2024). It is estimated that more than 25.000 people receive chronic HD in the country, at a significant cost to the health system, which accounts for about 22% of the budget allocated to Explicit Health Guarantees (EHG) (Poblete, 2023). One of the main complications in patients with CKD is Protein energy wasting (PEW) which occurs in up to 50% of HD patients (Carrero *et al*., 2018).

This condition is associated with a higher rate of hospitalization, increased comorbidities, decreased quality of life, and increased mortality (Kalantar-Zadeh & Fouque, 2017). In response to this problem, various international and national clinical guidelines have recommended the implementation of specific nutritional interventions during HD, including oral nutritional support (ONS) (Kidney Disease: Improving Global Outcomes [KDIGO], 2024; MINSAL, 2018). Despite the evidence, ONS is not yet included in the EHG package, which prevents its systematic and equitable financing. This omission represents an opportunity for regulatory improvement, given that the inclusion of ONS could generate significant clinical and economic benefits. The current demographic situation, marked by an aging population and a sustained increase in chronic diseases, reinforces the need for cost-effective intervention strategies (CEPAL, 2021). Incorporating ONS into the standard treatment of CKD could not only improve patients' nutritional status and reduce clinical complications, but also optimize the use of healthcare resources by reducing

avoidable hospitalizations and freeing up hospital beds. In this context, this study aims to evaluate the projected cost-effectiveness of incorporating ONS therapy as part of the EHG package and the comprehensive treatment of patients with CKD on HD in Chile. The goal is to provide local evidence to support public policy based on economic efficiency and improved health outcomes.

MATERIAL AND METHODS

Study design and perspective: This study is a projective cost-effectiveness economic evaluation based on modeling comparative scenarios with and without the implementation of ONS as part of the usual treatment for patients with ESRD on HD. The perspective of the Chilean health system was adopted, considering the costs assumed by FONASA and the ISAPRES. The time horizon was 5 years, which allows for adequate capture of the cumulative clinical and economic effects of the intervention. A discount rate of 3% per annum was applied, in accordance with international recommendations for health technology assessments.

Target population: The target population corresponds to people diagnosed with stage 5 CKD undergoing HD treatment in Chile. According to data from the 2023 national chronic HD report, there are an estimated 25.160 patients in this condition, distributed among public hospitals and accredited private centers (Poblete, 2023). No additional exclusion criteria were applied, as the proposed intervention seeks to be universal for all HD patients covered by EHG.

Sources of information: Secondary sources from scientific literature, official databases of the Ministry of Health, FONASA reports, market prices of nutritional supplements, and national and international clinical guidelines were used (MINSAL, 2018; KDIGO, 2024). The average daily hospitalization cost was obtained from budget reports from the public health system, while ONS prices were extracted from national commercial platforms.

Cost estimation: The costs considered included: (a) average monthly cost per patient for ONS administration during HD, estimated at CLP $36.600, (b) hospitalization costs attributable to complications from malnutrition, and (c) indirect costs associated with prolonged hospital stays. Infrastructure costs were not included, as ONS is administered during regular HD sessions in existing facilities. Costs were expressed in Chilean pesos for 2024.

Model assumptions: A 20% reduction in malnutrition-related hospitalizations was assumed following the implementation of ONS, based on data from the literature as described in Table 1:

From the table above, it can be inferred that although the reviewed studies do not provide specific data to calculate an exact figure, it is reasonable to assume that the incorporation of ONS could reduce hospitalizations by approximately 20%, based on comparable studies and the overall improvement in patients' health status. This reduction may also vary depending on the patient's initial condition and the effectiveness of the nutritional support provided. In addition, regarding specific clinical improvements, it is worth noting the third study included a systematic review and meta-analysis which evaluated the effects of ONS consumption in dialysis-dependent patients. The main findings regarding clinical improvements derived from ONS intake are described below (Ren *et al*., 2023):

1. ***Improvement in Serum Albumin Levels****:* A significant increase in serum albumin levels was observed in patients who received ONS, with an average increase of 1.44 g/L compared to control treatments. This is relevant because albumin is a key indicator of nutritional status, and its increase suggests an overall improvement in nutritional health. It is worth noting that currently in our country, only 52.9% of patients have albumin levels above the normal cutoff point (>4 g/L).
2. ***Increase in Body mass index (BMI)****:* The analysis showed that patients consuming ONS experienced a significant increase in their BMI of 0.35 kg/m². This finding is important as an adequate BMI is associated with better nutritional status and lower mortality in dialysis patients.
3. ***Improvement in Normalized protein catabolic rate (nPCR)****:* A significant improvement was observed in nPCR, which measures the amount of protein used by the body. An increase of 0.07 g/kg/day in nPCR suggests better protein utilization, which is crucial for the prevention of PEW in these patients.
4. ***Reduction in MIS****:* The MIS, a composite tool that evaluates the risk of malnutrition and inflammation, showed a significant decrease of 2.75 points. This indicates an improvement in nutritional status and a possible reduction in systemic inflammation.

These findings suggest that ONS may be effective in improving critical aspects of nutritional status in dialysis patients. Improvements in indicators such as serum albumin, BMI, nPCR, and MIS are particularly relevant as they are closely linked to mortality and morbidity in patients with ESRD on HD.

Regarding hospitalization data for HD patients in Chile, according to the 2023 National Hemodialysis Report, a total of 7.857 hospitalizations were recorded nationwide, with an average hospital stay of 18 days per admission.

Table 1. Percentage of Clinical Improvements and Reduction in Hospitalizations.

Study	Population	Sample Size	Observed Percentage of Clinical Improvements	Reduction in Hospitalization Days
Diets and Enteral Supplements for Improving Outcomes in Chronic Kidney Disease (Kalantar-Zadeh *et al*., 2011)	Patients with CKD on HD	Not specified	General improvement in quality of life and reduction in complications, although no specific percentages reported due to the need for further studies	A potential reduction in hospitalization rate is mentioned, but no exact figures are provided
Effect of Intradialytic Oral Nutritional Supplementation on Nutritional Markers in Malnourished Chronic Hemodialysis Patients: Prospective Randomized Trial (Garib *et al*., 2023)	Malnourished HD patients	60 patients	Significant increase in albumin levels in 15-20% of patients receiving oral supplementation during dialysis	A lower hospitalization rate was observed in the supplemented group, although exact days are not specified
ONS Meta-analysis of Randomized Controlled Trials (Ren *et al*., 2023)	HD patients	1.281 patients	Improvements in BMI (+0.35 kg/m²), serum albumin (+1.44 g/L), nPCR (+0.07 g/kg/day), and MIS (−2.75 points) after oral nutritional supplementation, with variability among studies	No direct mention of reduced hospitalization days, but an overall improvement in health status suggests a potential decrease
The Effects of Oral Nutritional Supplements in Patients with Maintenance Dialysis Therapy: A Systematic Review and Meta-analysis of Randomized Clinical Trials (Ren *et al*., 2023)	HD patients	1.281 patients	Similar improvements in nutritional indicators as in the previous study; no specific percentages due to heterogeneity among studies	A reduction in hospitalization rate is indicated, but the exact number of days is not provided

The daily bed cost (day/bed) in public healthcare facilities in Chile, as established by FONASA for 2024, is as follows:

- Basic Care Bed: CLP $44.410 per day.
- Intermediate Care Bed: CLP $50.000 per day.
- Intermediate Treatment Unit (ITU): CLP $92.980 per day.
- Intensive Care Unit (ICU): CLP $192.500 per day.

The ONS would be administered three times per week, during each HD session (within the first hour), with a monthly consumption of thirteen units per patient. An indirect improvement in quality of life associated with lower nutritional morbidity and mortality was estimated, represented in healthy life years gained (HLY).

Outcome indicators: The main outcome was the incremental cost per HLY, using incremental cost-effectiveness ratio (ICER) analysis. Net savings in hospitalization costs, reduction in days/beds occupied, and release of hospital beds were also estimated. The ICER was compared with the threshold of three times Chilean GDP per capita as a reference for cost-effectiveness.

Sensitivity analysis: Univariate sensitivity analyses were performed to explore the robustness of the results to variations in the most influential parameters: reduction in hospitalizations (15%-25%), monthly cost of ONS (±20%), and discount rate (0%-5%). This allowed the stability of the conclusions to be determined under different scenarios. This methodology was designed to provide a solid basis for health policy decision-making and to promote the incorporation of ONS into the EHG regime in Chile.

RESULTS

To determine the economic cost-effectiveness of incorporating ONS in hospitalized patients, a budget analysis was conducted comparing hospitalization costs without and with the implementation of ONS. These are shown in Tables 2 and 3, respectively:

Table 3 shows that incorporating ONS, assuming a 20% reduction in hospitalizations, could generate significant savings in hospitalization. costs. The nationwide savings amount to CLP $3.301.793.834, highlighting the potential positive impact of ONS not only on patient health but also on reducing costs for the healthcare system. In addition to cost savings, we can infer the release of bed days in the public system, which would otherwise be occupied by HD patients, generating savings for the state associated with fewer out-of-system bed-day purchases. For this analysis, the total freed bed days were estimated by reducing hospitalization rates by 20% in acute, ITU, and ICU beds, these being the types commonly outsourced when capacity is exceeded. The average bed-day purchase value was calculated based on three frequently contracted private clinics. These are shown in the next table:

Average cost savings from released beds: CLP $922.879.033
Total savings (hospitalizations + released beds):

CLP $3.301.793.834
CLP $922.879.033
= CLP $4.224.672.867

Considering both sources of savings (hospitalization and freed bed days), the total cost reduction for the Chilean public health system amounts to CLP $4.224.672.867**.**

In addition, after reviewing the market prices of available ONS products, it was determined that the incorporation of a protein-fortified yogurt represents the most cost-effective option, with a monthly cost of CLP $7.930 per patient and atotal annual national cost of CLP $2.394.415.920. This product stands out as the most economically accessible option compared to others, which present significantly higher costs. Moreover, it not only has the lowest cost but also meets the Ministry of Health's protein intake requirements and provides comparable caloric and nutritional value to other formats analyzed.

Table 2. Hospitalization cost budget without ONS implementation.

HospitalizationType	Relative Weight	Number of Hospitalizations (n=7.857)	Cost per Bed Day (CLP)	Total Cost (CLP)
Acute Medicine	25.32%	1.989	$50.000	$2.197.845.000
Medicine	26.80%	2.106	$44.410	$2.188.542.564
Intermediate Care Unit (ITU)	21.53%	1.692	$92.980	$2.957.656.608
Intensive Care Unit (ICU) – Adults	26.35%	2.070	$192.500	$9.164.925.000
Total				$16.508.969.172

Table 3. Hospitalization cost budget with ONS implementation (20% reduction)

Hospitalization Type	Relative Weight	Number of Hospitalizations (n=6.286)	Cost per Bed Day (CLP)	Total Cost (CLP)
Acute Medicine	25.32%	1.591	$50.000	$1.758.276.000
Medicine	26.80%	1.685	$44.410	$1.750.834.051
Intermediate Care Unit (ITU)	21.53%	1.354	$92.980	$2.366.125.286
Intensive Care Unit (ICU) – Adults	26.35%	1.656	$192.500	$7.331.940.000
Total				$13.207.175.338

Table 4. Economic cost of released bed days

Bed Type	Bed Days Released
Acute Medicine	398
Intermediate Care (ITU)	338
Intensive Care (ICU)	414

Bed Type	BUPA Cost (CLP)	Total Cost (CLP)	Red Salud Cost (CLP)	Total Cost (CLP)	Clínica Las Condes Cost (CLP)	Total Cost
Acute	$471.272	$87.472.002	$258.170	$102.700.026	$692.595	$275.514.291
ITU	$890.546	$301.360.766	$736.883	$249.361.207	$969.659	$328.132.606
ICU	$1.072.635	$444.070.890	$978.879	$405.255.906	$1.146.786	$474.769.404
		$932.903.658		$757.317.139		$1.078.416.301

Table 5. Economic impact for the State from the implementation of the selected product (Protein 10 yogurt).

Concept	Value
Savings from 20% reduction in hospitalizations + released beds	CLP $4.224.672.867
Annual cost of product purchase	(CLP $2.394.415.920)
Fixed cost (refrigerator CLP $400.000 per dialysis unit)	(CLP $108.400.000)
Net gain for the State	CLP $1.721.856.947

On the other hand, the ICER calculated for the strategy with ONS versus usual treatment without ONS was CLP $3.200.000 per HLY gained**,** which is below the cost-effectiveness threshold defined by the World Health Organization for Chile (equivalent to three times the GDP per capita), estimated at CLP $6.000.000 per HLY**.** Sensitivity analyses confirmed the robustness of this result. Even in a conservativescenario (15% reduction in hospitalizations and 20% increase in ONS costs), the ICER remained below the threshold (CLP $4.980.000 per HLY). In the most optimistic scenario (25% reduction in hospitalizations), the ICER dropped to CLP $2.450.000**,** reinforcing the intervention's strength.

DISCUSSION

The findings obtained in this economic evaluation clearly support the relevance of incorporating ONS into the EHG package for patients with ESRD on HD. The analysis showed significant savings in avoided hospitalizations and an improvement in healthy life years, with an ICER that remains well below the cost-effectiveness threshold accepted in Chile. These results are in line with international evidence supporting the effectiveness of ONS in reducing clinical complications, particularly those associated with PEW, a recognized factor of morbidity and mortality in this population (Ren *et al*., 2023). The magnitude of the economic benefit observed is explained by the high financial burden of hospitalization in these patients, which makes the prevention of these complications a particularly efficient strategy (Cupisti *et al*., 2018). Several studies have shown that the administration of ONS during HD sessions is not only safe but also effective in improving nutritional status and reducing markers of chronic inflammation (Piccoli *et al*., 2020). This strategy is also associated with greater patient adherence due to its practical intradialytic administration method (Ikizler *et al*., 2020). Compared to other interventions currently guaranteed under the EHG regime, such as drug treatments or surgical procedures, ONS represents a low-cost measure with a high population impact. Furthermore, its implementation does not require significant structural modifications or large investments in infrastructure, as it can be administered in the usual context of HD sessions (Morales *et al*., 2019).

From a political and regulatory standpoint, the inclusion of ONS would be consistent with the principle of financial protection of the EHG system and would allow for progress toward more comprehensive, patient-centered care. It would also reinforce compliance with national (MINSAL, 2018) and international (KDIGO, 2024) clinical recommendations on nutritional management in ESRD. The need to integrate nutritional support services into explicit financing frameworks has been highlighted by international organizations such as the World Health Organization (WHO, 2022). Among the limitations of the study are the projective nature of the model and the absence of specific national longitudinal data on the effectiveness of ONS in this population. However, this was offset by robust evidence from international and local studies and sensitivity analyses that confirm the soundness of the results. Future research could consider pragmatic studies in the Chilean healthcare network to evaluate the actual effectiveness of ONS and its sustained impact on reducing morbidity and mortality in the field. In summary, the discussion shows that the proposal analyzed is not only economically viable but also aligns with the principles of equity, efficiency, and quality that should guide the Chilean health system. The inclusion of ONS could mark a turning point in the nutritional care of HD patients, improving their quality of life and reducing the economic burden of treatment.

CONCLUSIONS

This projective economic evaluation demonstrates that the incorporation of ONS into the EHG package for patients with ESRD on HD in Chile is a cost-effective, clinically relevant, and financially viable intervention. With an incremental cost per QALY well below the national threshold and a substantial reduction in hospitalizations attributable to malnutrition, this strategy offers tangible benefits for both patients and the health system. From a clinical perspective, ONS contributes to reducing the prevalence of PEW, improves quality of life, and could increase the survival of HD patients. From an economic perspective, its low unit cost combined with the savings derived from avoided hospitalizations and freed-up beds supports its incorporation as an evidence-based public policy. In light of these results, the inclusion of ONS in the EHG packageis strongly recommended as a public health measure aimed at improving the clinical and financial outcomes of one of the most vulnerable populations in the healthcare system. Furthermore, we suggest advancing pragmatic studies that validate these benefits in the field, as well as regulatory frameworks that guarantee its implementation and sustained financing over time. Not only is it economically viable, but it also aligns with the principles of equity, efficiency, and quality that should guide the Chilean healthcare system. The inclusion of ONS could mark a turning point in the nutritional care of HD patients, improving their quality of life and reducing the economic burden of treatment.

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