Cost-Utility Analysis of a Home Care Program for Peritoneal Dialysis Patients in a Tertiary Care Hospital

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KyungYi Kim

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ABSTRACT

Cost-Utility Analysis of a Home Care Program for Patients with Peritoneal Dialysis in a Tertiary Care Hospital

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Background: A wide array of digital health technologies was rapidly adopted during the coronavirus disease (COVID-19) pandemic. The Ministry of Health and Welfare of Korea has initiated a home care program to increase access to care to improve quality of life. The program includes a face-to-face educational consultation and remote patient monitoring using telephone calls or bidirectional messenger services. In this study, we focused on patients with end-stage renal disease (ESRD) on peritoneal dialysis (PD). Although PD consists of the lowest proportion (3.9%) of the ESRD population in Korea, many studies address the clinical benefits of home-based dialysis, and it is widely considered a cost-effective alternative. This new home care program should be evaluated to verify its long-term clinical and economic effectiveness.

Methods: *Clinical effectiveness analyses* A retrospective cohort study was designed as a pre-post study and conducted to analyze the clinical impact of a home care program for patients undergoing PD in a single tertiary care hospital. A total of 186 subjects on PD from June 2017 to May 2022 were the study subjects. Five-year data was used to identify the clinical changes after program implementation by analyzing the changes in peritonitis incidence and laboratory test results (hemoglobin, Hb; calcium-phosphorus product, Ca x P; potassium, K; and intact parathyroid hormone, iPTH). A chi-square (χ^2) tests, unpaired Student's t-test, and the interrupted time series (ITS) analyses with ordinary least square (OLS) linear regression were used in the analyses. *Cost-utility analysis* A Markov model was constructed to evaluate the lifetime cost-effectiveness of the PD home care program. Cohorts of 1,000 patients aged 50 years started from the PD health state and were simulated to make a state transition at each cycle (one-year in length). With the effectiveness variable as quality-adjusted life years (QALY), a cost-utility analysis was conducted with a limited societal perspective. A willingness to pay (WTP) threshold was set to KRW 40,043,036 (1 GDP) per increasing 1 QALY and the discount rate of 4.5% was applied for both QALYs and costs. A half-cycle correction was reflected, and the main outcomes were the incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (INMB). Scenario analyses, sensitivity analysis, and expected value of perfect information (EVPI) were performed to reflect the uncertainty.

Results: *Clinical effectiveness analyses* The incidence of peritonitis was reduced in the most parsimonious model. The baseline value was 8.345 cases per 1,000 patient months

(SE = 3.181, P = 0.012), and it continuously increased by 0.480 cases per 1,000 patient months (P-value for baseline trend = 0.018). After program initiation, the incidence trend significantly decreased by 0.886 cases per 1,000 patient months (P-value for trend change = 0.015). With the one-year cumulative value, it has decreased to 20.93% from 27.31% (counterfactual). The clinical laboratory test results also showed improvement. The proportion of individuals reaching the target range has increased in Hb (5.2%p, P = 0.002), maintained in Ca x P (1.1%p, P = 0.428) and K (-1.6%p, P = 0.200), while it decreased in iPTH (-11.0%p, P = 0.000). *Cost-utility analysis* In the base-case analysis, the ICER was calculated as KRW 4,571,500 per QALY, which is in the range of the WTP threshold. Regardless of the scenarios, the results of the base case analyses were in the range of the WTP threshold. A one-way sensitivity analysis was performed, and the most sensitive parameters were the costs of PD (home care) and PD (usual care) in every scenario. For the outcome of the Monte Carlo simulation (10,000 iterations), the home care group was an optimal overall strategy, with probabilities of 62.05% in Scenario 1, 59.95% in Scenario 2, 61.70% in Scenario 3, and 89.41% in Scenario 4. The WTP threshold where the probabilities of the home care group were optimal at above 50% was KRW 7,380,000. Finally, EVPI was measured, showing an additional KRW 14,818,960 per patient gained when all parameter information was obtained without uncertainty.

Conclusion: This study evaluated the clinical effectiveness and cost-effectiveness of a novel home care program for PD patients in Korea. We found that this program reduced the incidence of peritonitis, improved laboratory test results, and demonstrated cost-

effectiveness, as the ICER was under the WTP threshold. Therefore, our study suggests that conducting a home care program for PD patients is clinically effective and may be cost-effective.

Keywords: digital health, home care, peritoneal dialysis, end-stage renal disease, interrupted time series, Markov model, cost-utility analysis, COVID-19

I. Introduction

1. Background

Diverse [1] digital health solutions have emerged with the development of information and communications technologies (ICT) (1). Many digital health technologies were rapidly adopted with the outbreak of coronavirus disease (COVID-19) pandemic. Telehealth visits in the U.S. have increased to 52.7 million in 2020 from 0.84 million in 2019 (2), and the volume of claiming remote patient monitoring has increased more than four times the pre-pandemic levels (3). Just before the COVID-19 pandemic was declared, the Ministry of Health and Welfare of Korea initiated a home care program in December 2019 (4). The program includes a face-to-face educational consultation conducted by medical staff and remote patient monitoring using telephone calls or bidirectional messenger services. The multidisciplinary care team continuously monitors their patients remotely to increase access to medical support and guide self-care to improve the patients' quality of life (5). Considering that the most common purpose of digital health used during COVID-19 was clinical care (49.7%), follow-up care (15.3%),

[1] Care team email and text massages, health system disease management apps, consumer mobile apps, digital therapeutics, web-based interactive programs, telemedicine and virtual physician visits, consumer wearables, in-home connected virtual assistants, etc.

and medical education (9.9%) (6), the newly launched home care program contains the necessary digital health service content. While it is hard to set up billable digital health policy nowadays (7), the home care program in Korea is currently billable for various[2] diseases. Among diverse diseases currently available for the home care program in Korea, this study focused on end-stage renal disease (ESRD) patients undergoing peritoneal dialysis (PD) – which was the first disease adopted for the home care program. It is needed to evaluate the clinical and economic effectiveness of the program for the first time in Korea to verify whether the newly launched home care program is socially worthwhile.

The prevalence of ESRD patients in 2020 in Korea was reported to be 145,006 including hemodialysis (HD, 117,398 patients, 81.0%), renal transplantation (RTx, 21,884 patients, 15.1%) and PD (5,724 patients, 3.9%) (8). Many studies address the benefits of home-based dialysis, including flexible scheduling (9), increased effectiveness for younger patients with fewer co-morbidities (10), improved cardiovascular outcomes and risk factors (11), and reduced COVID-19 infection incidence rate compared to in-center dialysis (12). Despite these advantages, PD is rarely chosen due to some concerns regarding the dialysis procedure. While HD patients get medical support every few days when visiting the hospital for dialysis, PD patients require total self-care alone in their

[2] Peritoneal dialysis, type 1 diabetes mellitus, maternity care for high risk pregnant women, home ventilator, cardiovascular diseases, rehabilitation, colorectal cancer, tuberculosis, etc.

homes. It is difficult to notice medical problems that occur in the two-month interval between regular hospital visits. This may lead to increased patient anxiety and related complications (13). Remote monitoring by medical staff may encourage hesitant ESRD patients to change their minds. The newly implemented home care program using digital technologies should be evaluated to determine if it can fill gaps in care. Since it is known that peritonitis, the common complication of PD, is closely related to the depression and poor quality of life (14), it is needed to be verified how the home care program impacts on changing the incidence of peritonitis. Previous studies have asserted the effectiveness of home care (11), text messaging (15, 16), and patient education (17), but further clinical studies with a longer study period are needed to demonstrate the impacts of home care programs on the prevention of associated complications (peritonitis).

In Korea, total healthcare expenditure was reported to be KRW 95.5 trillion (USD 70.1 billion) in 2021, which is a 10.2% increase from the previous year (18). The burden of healthcare expenditures is rising. In U.S., total Medicare-related expenditures for ESRD have increased to USD 51.0 billion in 2019 from USD 45.0 billion in 2009 (a 13.3% of increases, or a 1.2% increase per annum with inflation-adjusted values) (19). Previous studies have examined the cost-effectiveness of diverse renal replacement therapies (RRT) – HD, RTx, and PD – for ESRD patients (20-22), and PD was considered a cost-effective alternative that requires fewer human resources than other options (leading to lower labor costs, especially in the developed countries). While PD is generally accepted to be affordable, the cost-effectiveness of the recently commenced home care program for PD

patients must be investigated to identify its societal impacts on reducing healthcare expenditures and assess program sustainability.

In this study, we aimed to demonstrate the effectiveness of a home care program for PD patients by evaluating its long-term clinical effectiveness and then establishing its lifetime cost-effectiveness. With increasing interests in adopting digital health, the results from this study would be helpful in identifying the rationale for accepting and expanding the home care program.

2. Objectives

To examine the effectiveness of a home care program as a digital health, the purpose of this study is to investigate the clinical effectiveness and conduct a cost-utility analysis of a home care program for patients with peritoneal dialysis in a tertiary care hospital.

The objectives of this study are:

(1) to identify the clinical effectiveness of the home care program for PD patients using the following outcomes:

A. changes in the incidence of peritonitis; and

B. changes in clinical laboratory test results.

(2) to evaluate the cost-effectiveness of the home care program for PD patients using the following measures:

A. incremental cost effectiveness ratio (ICER); and

B. incremental net monetary benefit (INMB).

II. Literature Review

1. Home care program as a digital health

In this study, we focused on the PD home care program which uses digital health technologies in a form of remote patient monitoring (RPM). Since patients can actively communicate with their medical staffs and get feedbacks any time, the RPM technology increases the accessibility of care and improve the patient's quality of life (23). It is needed to plan detailed educational content for PD patients and the milestone for the adoption, since the remote support may lead to patient satisfaction with better health outcomes, and potentially increase the acceptance of PD (24).

In Korea, the home care program for PD patients was initiated by the Ministry of Health and Welfare to continuously manage patients who need regular care for infection prevention and to avoid potential risks that may occur due to medical gaps. The program (5) was started in December 2019, targeting PD patients with stage 5 chronic kidney disease (ICD 10 code N18.5) who agreed to participate in the program. The medical institutions should be a secondary level of care or higher for the requirement of participating in the program. According to a recent report, 3,730 PD patients from 54 hospitals participated in the first year of the home care program (25). In the second year (2021), another 29 medical institutions were included (26), resulting in a total of 83 institutions in the program. Once enrolled in the program, patients can be reimbursed for

three types of medical services (education 1, education 2, monitoring), as shown in Table 1. In this study, we excluded education 1 (claim code of IB511) cases as they do not just target PD patients but entire ESRD patients. As summarized in a previous report (25), the number of claimed cases in the first year of the program were reviewed: education 1 (1,555 cases, just including IB510), education 2 (6,236 cases, IB520), and monitoring (16,509 cases, IB530). The annual average number of claimed cases per patient by medical service type is: education 1 (0.5 times per patient), education 2 (2.0 times per patient), and monitoring (5.4 times per patient).

Table 1. Overview of the home care program

Types	Claim codes	Descriptions	Details
Education 1	IB510	− In-depth educational consultation performed by physicians when patients need additional education for better understanding of the overall management of their diseases and entire process of treatment	− Physicians[3] − Minimum of 15 minutes of education per time − Maximum of 4 times reimbursed per year
Education 1	IB511	− In-depth educational consultation for deciding the appropriate types of RRT modalities (not just for PD patients)	
Education 2	IB520	− In-depth educational consultation performed by physicians or nurses when patients need additional instructions for device use, disease/health management	− Physicians or nurses[4] − Minimum of 20 minutes of education per time − Maximum of 6 times reimbursed per year
Monitoring	IB530	− Regular remote patient monitoring conducted by physicians or nurses to check the status of patient self-care or symptoms of complications and assist any supports needed	− Physicians or nurses − Minimum of 1 bidirectional communication per month − Maximum of 12 times reimbursed per year

3 A board-certified physician in internal medicine or pediatrics is required.

4 Nurses should have longer than three-year of clinical experiences.

The same report (25) contains statistical information on the home care program based on the claims data from December 2019 to November 2020. We reviewed and reframed some of this information. The patients enrolled in the home care group were compared to the control group. Table 2 shows the direct medical costs for PD patients with detailed items described.

Table 2. Detailed items of direct medical costs for PD outpatient (no. of claims per patient)

Items (no. of cases per patient)	Tertiary care hospital			General hospital		
	All	Home care	Control	All	Home care	Control
Basic expenses	59.4	64.9	52.5	60.6	70.3	53.0
Medication	73.3	73.3	73.4	82.7	85.4	81.4
Injection	37.7	35.1	40.9	36.5	36.0	36.7
Procedures & operations	21.2	22.9	19.1	22.3	19.3	23.7
Lab tests	221.5	214.2	230.8	218.6	226.4	210.2
Imaging diagnosis / radiation	7.0	7.2	6.8	6.4	8.2	3.9
Others	5.9	5.5	6.5	46.7	67.4	34.3

The top 10 most frequently claimed sub-diagnosis for PD patients are reported in Table 3. Type 2 diabetes mellitus was the most frequent sub-diagnosis in both the home care (12.0%) and control (11.1%) groups.

Table 3. The most frequent sub-diagnosis of PD patients

Sub-diagnosis (ICD-10 code)		All		Home Care		Control	
		N	%	N	%	N	%
E11	Type 2 diabetes mellitus	534	10.0	267	12.0	267	11.1
I10	Essential (primary) hypertension	428	8.1	170	7.6	258	8.3
E78	Disorders of lipoprotein metabolism and other lipidemias	276	5.2	108	4.9	168	5.4
E14	Unspecified diabetes mellitus	166	3.1	98	4.4	68	2.2
I12	Hypertensive chronic kidney disease	130	2.4	56	2.5	74	2.4
T85	Complications of other internal prosthetic devices, implants and grafts	104	2.0	39	1.8	65	2.1
N02	Recurrent and persistent hematuria	81	1.5	54	2.3	27	0.9
E87	Other disorders of fluid, electrolyte and acid-base balance	79	1.5	28	1.3	51	1.7
I15	Secondary hypertension	71	1.3	33	1.5	38	1.2
K21	Gastro-esophageal reflux disease	71	1.3	27	1.2	44	1.4

Abbreviations: ICD-10 (International Classification of Diseases 10th Revision).

2. End-stage renal disease and peritoneal dialysis

Chronic kidney disease (CKD) is irreversible damage in the kidney structure and function, particularly an estimated glomerular filtration rate (eGFR) of <60mL/min per 1.73m^2 or markers of kidney damage[5] or both for at least 3 months duration (27-30). CKD is divided into five stages (Table 4) and is diagnosed based on the eGFR results, which indicate how damaged the kidneys are (31). End-stage renal disease (ESRD) is defined with an eGFR < 15 at stage 5, or when the kidneys cease working as they should. This is also known as end-stage kidney disease (ESKD) or kidney failure.

The incidence and prevalence of ESRD in Korea in 2020 were 18,379 and 145,006, respectively, and increasing every year (8). To survive with ESRD, long term RRT (such as HD, RTx, PD, etc.) is inevitable (32). Patients and medical staff undergo shared decision-making to choose the best treatment option. Each treatment modality has advantages and disadvantages (Table 5). PD can occur at the patient's home by themselves and does not require a hospital visit for the procedure, which may be ideal for some patients. However, since PD patients visit the hospital every one to two months for a check-up, it can be difficult for physicians to manage complications (e.g., peritonitis,

5 Markers of kidney damage (1 or more): albuminuria, urinary sediment abnormality, electrolyte or other abnormality due to tubular disorder, abnormalities on histology, structural abnormalities detected by imaging, history of kidney transplantation

exit site infections, etc.) in advance, and patients may feel anxious about managing their diseases.

Table 4. The stages of chronic kidney disease

Stage of CKD	eGFR	What it means
Stage 1	≥ 90	− Mild kidney damages − Kidneys work as well as normal
Stage 2	60-90	− Mild kidney damages − Kidneys still work well
Stage 3a	45-59	− Mild to moderate kidney damages − Kidneys don't work as well as they should
Stage 3b	30-44	− Moderate to severe damages − Kidneys don't work as well as they should
Stage 4	15-29	− Severe kidney damages − Kidneys are close to not working at all
Stage 5	< 15	− Most severe kidney damages − Kidneys are very close to not working or have stopped working (failed)

Abbreviations: CKD (chronic kidney disease); eGFR (estimated glomerular filtration rate).

Table 5. The advantages and disadvantages of renal replacement therapies

RRT	Advantages	Disadvantages	Ref
HD (In-center)	− Feel safe in hospital − Supported by trained staffs − General modality worldwide	− Time-consuming − May require dietary restrictions − Hard to work or go to school − Complications ♦ Hypotension ♦ Hypertension ♦ Muscle cramps ♦ Itching ♦ Sleep problems ♦ Anemia ♦ Bone diseases ♦ Depression	(9, 33, 34)
PD	− Possible in home − Able to work or go to school − Flexible personal schedule − Improved quality of life − Fewer dietary restrictions − Lower costs	− Every day dialysis needed − Catheter under clothing − Complications ♦ Infections (peritonitis) ♦ Weight gain ♦ Hernia ♦ Inadequate dialysis	(9, 11, 33)
RTx	− The most cost-effective − High survival rate − High quality of life − Fewer restrictions on daily activities	− Complications ♦ Blood clots and bleeding ♦ Infection ♦ Rejection from the body ♦ Nerve damage ♦ Blood vessel narrowing ♦ Recurrent kidney disease ♦ Severe heart problems ♦ Death	(35-38)

Abbreviations: RRT (renal replacement therapy); HD (hemodialysis); PD (peritoneal dialysis); RTx (renal transplantation).

III. Study Methods

1. Study Design

(1) Clinical effectiveness analyses

Framework of the Study Design

This retrospective cohort study was designed as a pre-post study and conducted to analyze the clinical impact of a PD home care program in a single tertiary care hospital. We measured the outcome before (pre-homecare) and after (post-homecare) program implementation. The program contains face-to-face educational consultations when PD patients visit the hospital and remote monitoring care services when they are home. The inclusion and exclusion criteria for the study are described in Figure 1. We first selected 186 PD patients who were reimbursed at least once for the home care program between June 2017 and May 2022. We then we excluded 51 cases who were reimbursed for consultation before choosing their dialysis modality (not directly related to the intervention) and 4 patients who enrolled in the program after May 2022 who had no post-homecare outcomes. The collected five-year data was used to identify the clinical changes after the home care program by analyzing the: (1) changes in the incidence of peritonitis over four years and (2) changes in clinical laboratory test results using the

proportion who achieved the target range over two years and the changes in the clinical laboratory test results over four years.

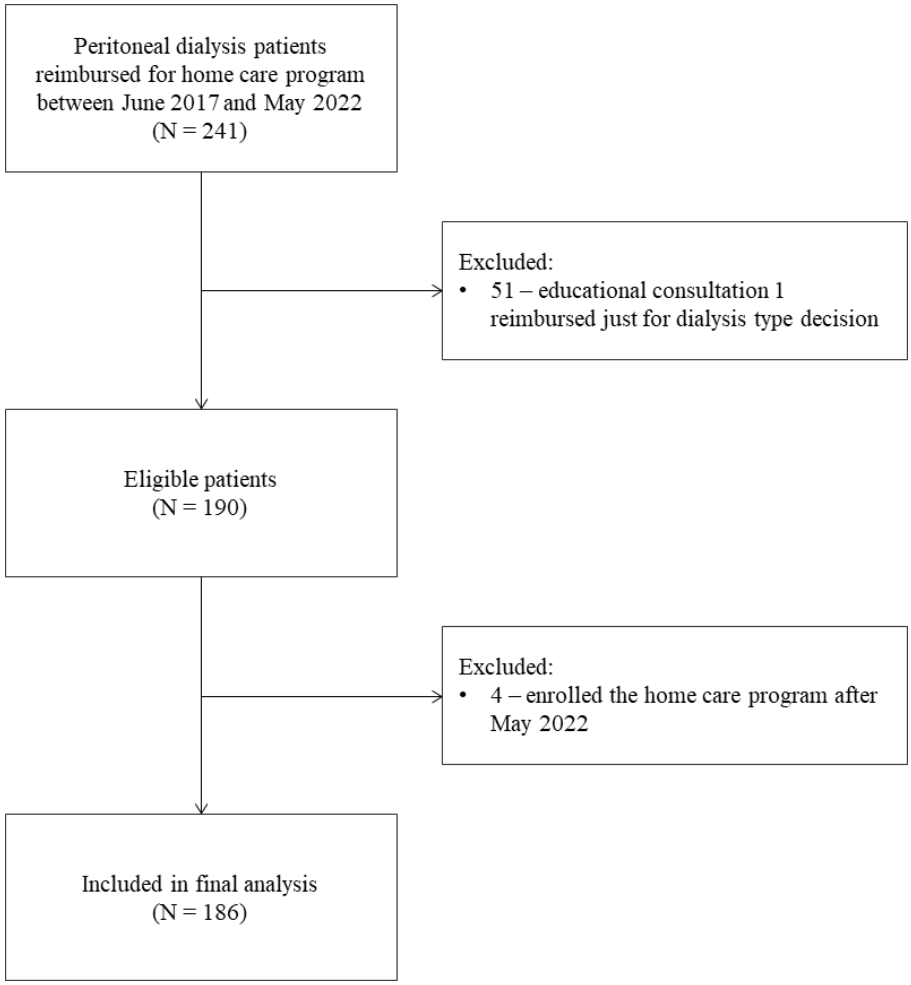

Figure 1. Flow chart of inclusion and exclusion criteria

Home care program

The home care program for PD patients was initiated by the Ministry of Health and Welfare of Korea to continuously manage patients who need regular care for infection prevention and to avoid potential risks that may occur due to medical gaps. The program (5) was started in December 2019, targeting PD patients with stage 5 chronic kidney disease (ICD 10 code N18.5) who agreed to participate in the program. Once enrolled in the program, patients can be reimbursed for three types of medical services (education 1, education 2, monitoring). The education 1 code can be reimbursed when physicians conduct face-to-face educational consultation for 15 minutes. For the education 2 code, physicians or nurses execute face-to-face educational consultation for 20 minutes. The remote monitoring code can be reimbursed when medical staff remotely monitors patient's status using bidirectional messenger services. In this study, we excluded education 1 (claim code of IB511) cases as they do not just target PD patients but entire ESRD patients.

(2) Cost-utility analysis

Study population

This study included Korean patients with ESRD undergoing PD to evaluate the cost-effectiveness of a PD home care program. A hypothetical cohort of 1,000 PD patients in a tertiary care hospital aged 50 years old was developed to perform cohort simulation.

Model structure

A Markov model was constructed to evaluate the lifetime cost-effectiveness of a PD home care program. The model (Figure 2 and Figure 3) consists of five health states (PD, peritonitis, HD RTx, and death) and we referred to previous studies (20-22, 39-41) and clinical feedbacks from our hospital to frame the structure. It was developed using TreeAge Pro 2022, R2. (TreeAge Software, Williamstown, MA). Cohorts of 1,000 patients started from the PD health state and simulated to make a state transition at each cycle. Patients can stay in the previous state or move on to other states. Background mortalities (Appendix Table 1) were reflected in all Markov cycles based on Korea nationwide statistics regarding the population (42) and number of deaths (43) in 2021. Referring to the memoryless property of Markov assumption (44), Markov chain model was executed in which the transition probability is independent of the earlier transitions. That is, the model cannot remember the previous health state.

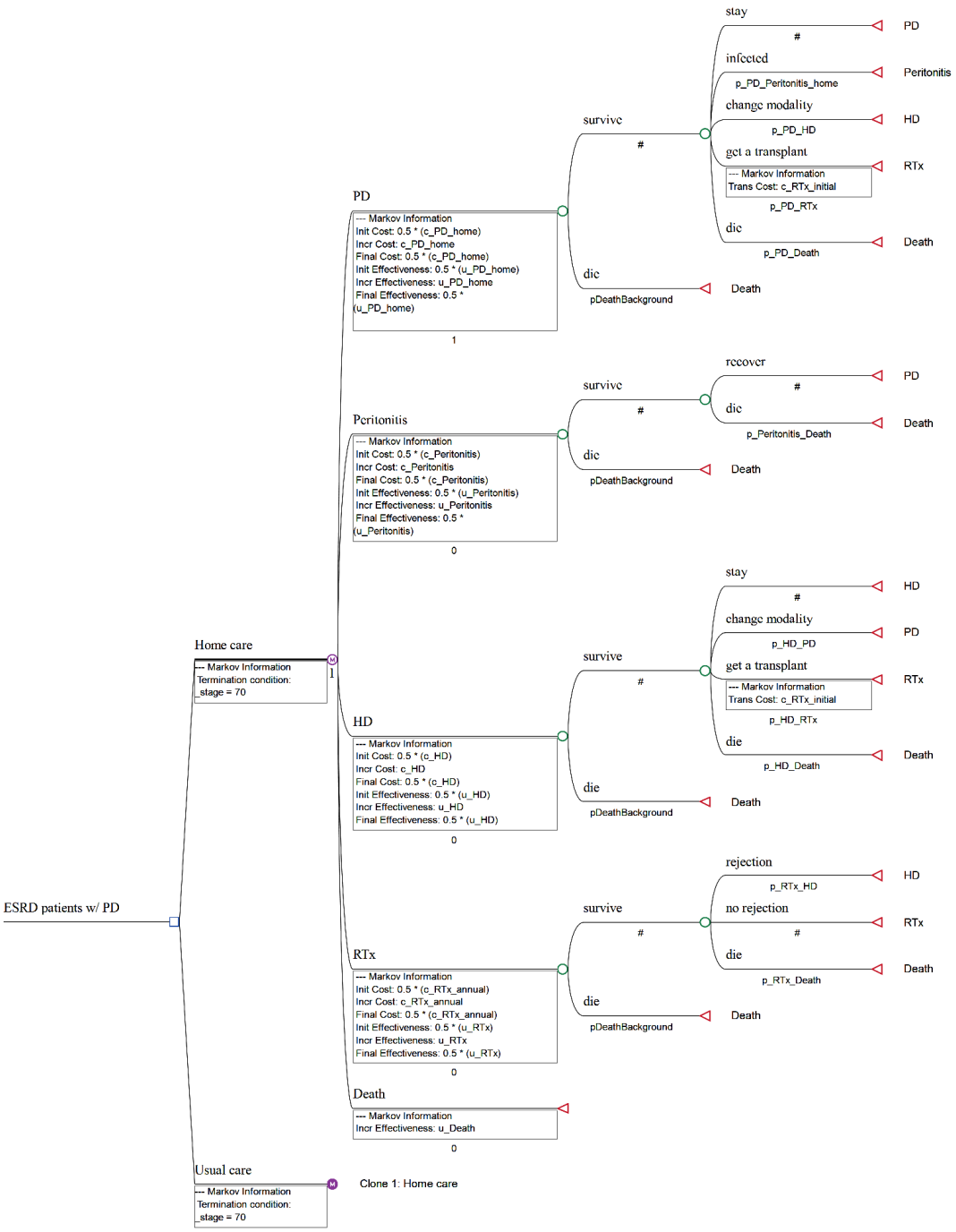

Figure 2. Structure of the Markov model

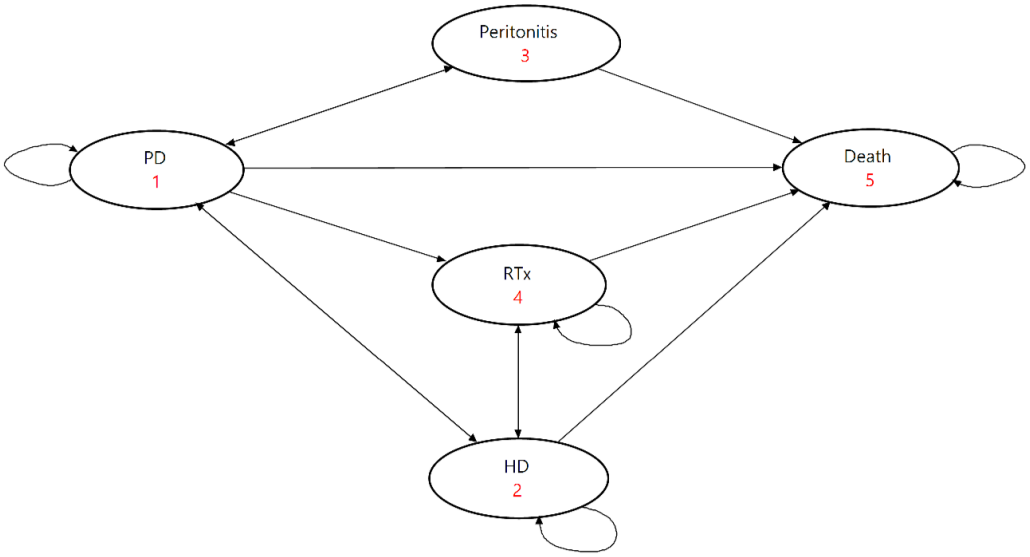

Figure 3. State transition diagram of Markov model

Intervention & Comparators

The home care intervention group (home care) was compared with the control (usual care) group. The home care group includes additional non-pharmaceutical interventions (patient care services for PD patients), while the control group sustains the usual care (Table 6).

Table 6. Description of the interventions

Intervention	Descriptions
Usual care	− Regular hospital visit (per 1-3 months) for medication − Irregular educational consultation if needed
Home care	− Regular hospital visit (per 1-3 months) for medication − Regular patient care services ♦ Regular remote monitoring care (monthly phone call) ♦ Regular educational consultation (quarterly)

Analytics & Outcomes

A cost-utility analysis was performed by determining the effectiveness variable as quality-adjusted life years (QALY). QALY ranges from 0 (death) to 1 (perfect health) and includes both quantity (life years gained) and quality (health-related quality of life, HRQOL in utility value) of life. We executed a survey to measure utility of PD patients in home care group and other outcomes were derived from previous studies (details in the Data and Variables section).

Perspective

Although the Korean government (45) recommends a healthcare system perspective, we utilized a limited societal perspective in this study that includes direct medical costs, direct non-medical costs (transportation costs and nursing care costs), and indirect costs (time costs). With the nature of dialysis patients who spend plenty of time and costs for visiting or taking care of their diseases, we decided to include time costs as the estimated costs for productivity loss.

Cost-effectiveness threshold

In this study, we referred to 2020 gross domestic product (GDP) data (46) as a willingness to pay (WTP) threshold; KRW 40,043,036 (USD 34,984) per increasing 1 QALY. We also provided a threshold at which the probability of being cost-effective is greater than 50% (47).

Scenario design

With the nature of uncertainty in conducting economic evaluation, we assumed many parameters used in this study. To verify the impact of changes in values, we performed the cost-utility analysis in four different scenarios prior to conducting sensitivity analysis. From the base scenario, we selected the most sensitive parameters in each sector and developed four scenarios: Scenario 1 (base case), Scenario 2 (changes in probability), Scenario 3 (changes in cost), and Scenario 4 (changes in utility). Details are presented in the Data and Variables section.

Discount rate

A discount rate of 4.5% was applied for both QALYs and costs according to the newly updated 2021 Korea National Guidelines for Economic Evaluation (45). Additionally, we also used sampled discount rates from 0% to 4.5% in probabilistic sensitivity analysis with the recommendations of using discount rate of 0% and 3% in the same report.

Time horizon & Cycle length

To examine the sustainability of the home care program, we analyzed the lifetime cost-effectiveness of the PD home care program with the analytic time horizon of 70 Markov cycles considering the average start age of the cohort. The model was processed until the entire cohort goes to health state “death” with a cycle length of one-year.

Half cycle correction

A half-cycle correction was reflected in both QALYs and costs to minimize the inaccuracy of transition estimates at the start or end of each cycle.

In this study, we referred to the recently updated Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 checklist including 28 items in planning and conducting the economic evaluation (Appendix Table 8).

2. Data and Variables

(1) Clinical effectiveness analysis

Clinical data recorded in the study period (from June 2017 to May 2022) were extracted from Severance Hospital's (Seoul, Korea) Severance Clinical Research Analysis Portal (SCRAP) service. The electronic medical records contained no personally identifiable information. The requirement to obtain informed consent was waived due to the retrospective nature of the study.

Demographic (sex, age) and clinical (PD durations) independent variables were categorized into two groups for the subgroup analyses. The dependent variables, clinical outcomes of (1) peritonitis and (2) clinical laboratory test results, including hemoglobin (Hb, g/dL), calcium-phosphorus product (Ca x P, mg^2/dL^2), potassium (K, mEq/L), and intact parathyroid hormone (iPTH, pg/mL) levels, were collected. Clinical laboratory test variables were gathered as categorical data of 1 (case of achieving the clinical target range) and 0 (case of not satisfying the target range) and as continuous data. The clinical target ranges for each variable were established according to the internal criteria (Table 7). Table 8 summarizes the independent and dependent variables used in this study.

Table 7. The target ranges of laboratory test results

Clinical outcomes		**Target ranges**
Hemoglobin (Hb, g/dL)	Male	10.0 – 17.4
	Female	10.0 – 16.4
Calcium-Phosphorus product (Ca x P, mg^2/dL^2)	All	< 55.0
Potassium (K, mEq/L)	All	3.5 – 5.5
Intact Parathyroid hormone (iPTH, pg/mL)	All	15 - 300

Table 8. The lists of variables

Independent variables		**Description**
Demographic	Sex	Male / Female
	Age	< 55-year / ≥ 55-year (age in 2022)
Clinical	PD duration	< 6-year / ≥ 6-year
Dependent variables		**Description**
Peritonitis		(The monthly incidence of peritonitis) = (The number of new cases of peritonitis per 1,000 patient-months)
Clinical laboratory test results	Hemoglobin	(1) categorical – 1 (in range) / 0 (out of range) (2) continuous data (g/dL)
	Calcium-Phosphorus product	(1) categorical – 1 (in range) / 0 (out of range) (2) continuous data (mg^2/dL^2)
	Potassium	(1) categorical – 1 (in range) / 0 (out of range) (2) continuous data (mEq/L)
	Intact Parathyroid hormone	(1) categorical – 1 (in range) / 0 (out of range) (2) continuous data (pg/mL)

(2) Cost-utility analysis

A. Transition probabilities

Below is a 5 x 5 transition probability matrix with P_{ij} (moving from state *i* to state *j*). The hashtag (#) in the matrix represents the complement of the sum of the other branches (48); e.g., $P_{11} + P_{12} + P_{13} + P_{14} + P_{15}$ equals 1. We determined the health states as follows: state 1 (PD), state 2 (HD), state 3 (Peritonitis), state 4 (RTx), and state 5 (Death). Once patients transitioned into the Peritonitis state, they should return to PD or move on to the Death state during the next cycle, as they cannot stay in the current state. Patients in the RTx state can stay in that state or go to the HD or Death states. However, as our hypothetical cohort starts with 1,000 PD patients, they can't return to the PD state once rejection occurs.

Transition probability matrix

$$= \begin{bmatrix} P_{11} & P_{12} & P_{13} & P_{14} & P_{15} \\ P_{21} & P_{22} & P_{23} & P_{24} & P_{25} \\ P_{31} & P_{32} & P_{33} & P_{34} & P_{35} \\ P_{41} & P_{42} & P_{43} & P_{44} & P_{45} \\ P_{51} & P_{52} & P_{53} & P_{54} & P_{55} \end{bmatrix} = \begin{bmatrix} \# & 0.022 & 0.189 \; or \; 0.239 & 0.023 & 0.065 \\ 0.009 & \# & 0 & 0.023 & 0.051 \\ \# & 0 & 0 & 0 & 0.123 \\ 0 & 0.025 & 0 & \# & 0.007 \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

When using the clinical outcome as a form of transition probability, we used the following conversion formula:

$$P = 1 - \exp(-rt)$$

where *P* is the probability, *r* is rate, and *t* is time.

The transition probabilities listed in Table 9 were derived from Severance Hospital data or previous studies (49-53). In the PD state, the clinical results (parsimonious regression model) of the anticipated 1-year cumulative incidence of peritonitis were used as probabilities of the transition from PD to peritonitis: 0.239 (usual care) and 0.189 (home care). Since this is the most critical probability in the analysis, we altered these values in Scenario 2 using the clinical results from the full regression model: 0.224 (usual care) and 0.197 (home care). The probability of getting RTx was assumed to be equal for PD and HD patients. The mortalities of PD and HD patients were collected from the study on Korea's five-year cumulative survival rate. Since the peritonitis mortality was reported 95% higher than usual PD patients, we combined the mortality data of PD patients with a hazard ratio of 1.95. Our hospital did not report the transition probabilities of switching from HD to PD. A previous study found 0.009 people per year switched to PD. We used the probability of switching from PD to HD in this study (0.027) as a reference, which was similar to our hospital data (0.022 per year). For the probability

from state RTx, we referred to the 10-year survival and graft survival rate from a Korean transplantation report

Table 9. Transition probabilities

Parameters	Value	Range		Distribution	Source
PD to					
HD	0.022	0.018	0.027	beta	Hospital data
Peritonitis (home care)	0.189	0.173	0.204	beta	Hospital data
Peritonitis (usual care)	0.239	0.227	0.251	beta	Hospital data
RTx	0.023	0.018	0.027	beta	(49)
Death	0.065	0.052	0.078	beta	(50)
HD to					
PD	0.009	0.007	0.011	beta	(51)
RTx	0.023	0.018	0.027	beta	(49)
Death	0.051	0.041	0.061	beta	(50)
Peritonitis to					
Death	0.123	0.098	0.147	beta	(52)
RTx to					
HD	0.025	0.020	0.030	beta	(53)
Death	0.007	0.006	0.009	beta	(53)

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation).

For sensitivity analysis (which will be described in the Statistical analyses section in detail), all measures were assumed to have upper limits (120%) and lower limits (80%) from their mean values. Since probabilities range from 0 to 1, the distributions of all transition probabilities were beta distributions.

B. Utility inputs

To examine the utility of PD (home care), we used data from a 2020 survey using EuroQol 5-Dimension 3-Level version (EQ-5D-3L) questionnaires. Sample sizes were calculated using the following formula (54) and data was collected from 361 PD patients:

$$\text{Sample size} = \frac{\frac{Z^2 \cdot p(1-p)}{e^2}}{1 + (\frac{Z^2 \cdot p(1-p)}{e^2 N})}$$

n	sample size
N	population size (5,724 PD patients (8))
Z	z-score of 95% confidence level (1.96)
p	the observed percentage (0.5)
e	the desired level of precision (0.05)

The utilities for 402 Korean PD patients participating in the home care program were collected and calculated (55) as the mean (SD) of 0.861 (0.149). In the peritonitis state, the utilities were assumed to decrease by 30.7% compared to the PD states per a previous study (39). The utilities of HD and RTx were obtained from a previous Korean study to minimize uncertainty. The lower and upper bounds of each utility were calculated using the collected mean and SD(SE). The health utilities used in this study are summarized in Table 10.

Unlike the base analysis in Scenario 1, we changed the utility of PD (usual care) in Scenario 4 to refer to the previous study (39) rather than our calculation, and assumed that home care would increase the utility by 6.8% (56). This verified the difference in outcomes when using the published utility value.

Table 10. Utility inputs

Health states	Utility	SD	Range		N	Source
PD (home care)	0.861	0.149	0.846	0.876	402	Patient survey
PD (usual care)	0.801	0.228	0.745	0.857	64	(57)
HD	0.830	0.221	0.784	0.875	90	(58)
Peritonitis (home care)	0.597	0.216	0.544	0.649	-	(39)
Peritonitis (usual care)	0.555	0.216	0.502	0.608	-	(39)
RTx	0.947	0.088	0.931	0.962	124	(58)
Death	0.000	0.000	0.000	0.000	-	-

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation); SD (standard deviation).

C. Cost inputs

For the limited societal perspective analysis, we used direct medical costs, direct non-medical costs, and indirect costs for the input data. All costs were adjusted to 2020, and the exchange rate of KRW 1,180.01 per dollar and inflation rates shown in Appendix Table 2 were reflected.

(A) Direct medical costs

Direct medical costs for PD include the overall reimbursement and non-reimbursement costs spent annually for a single patient regardless of the purpose of the hospital visit. The costs consist of prescriptions, drugs, injections, operations, blood tests, and medical imaging costs. We extracted our hospital cost data, including outpatient, hospitalization, and emergency room visit costs, to compare the home care group and usual care group. We compared the costs history in cases of peritonitis and found 1.375-fold (P-value = 0.017) increase compared to the normal PD status. To minimize the uncertainty of gathering HD and RTx cost data, we referred to a previous study (41) that used our hospital's data. An annually changing consumer price index (healthcare sector) was adopted to reflect inflation (Appendix Table 2). The direct medical costs calculated in this study are shown in Table 11. We calculated the range of cost parameters using mean and SD (SE) in Scenario 1, but we assumed the range to be 80% - 120% from the

mean value in Scenario 3 to broadly evaluate the impact of cost parameters.

Table 11. Direct medical costs

(Units: N, KRW)	Mean	SD	Source
PD (home care)			
No. of PD patients	182		Hospital data
Total medical costs	26,452,978	14,845,787	Hospital data
Reimbursement costs	25,867,664	13,926,015	Hospital data
Non-reimbursement costs	454,681	720,689	Hospital data
PD (usual care)			
No. of PD patients	178		Hospital data
Total medical costs	26,071,418	11,958,165	Hospital data
Reimbursement costs	24,167,800	8,615,984	Hospital data
Non-reimbursement costs	339,661	544,079	Hospital data
Peritonitis			
Annual medical costs	34,605,854	37,925,440	Hospital data
HD			
Annual medical costs in 2010	26,690,961	4,322,708	(41)
Annual medical costs in 2020 (inflation adjusted)	29,125,885	4,717,053	(41)
RTx			
Operation costs in 2010	20,070,093	4,116,058	(41)
Operation costs in 2020 (inflation adjusted)	21,901,018	4,491,552	(41)
Annual medical costs in 2010	8,689,784	2,862,084	(41)
Annual medical costs in 2020 (inflation adjusted)	9,482,522	3,123,182	(41)

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation); SD (standard deviation).

(B) Direct non-medical costs

a. Transportation costs

Transportation costs were defined as the annual round-trip transportation costs per patient for either outpatient hospital visits or hospitalization. Using the data in Table 12 and Table 13, transportation costs can be calculated as follows:

Annual transportation costs per patient

= {(the average number of outpatient visits per year)
x (round-trip transportation costs for outpatient)}
+ {(the average number of hospitalizations per year)
x (round-trip transportation costs for hospitalization)}

For PD data, we could compare the differences in healthcare utilization between the home care and usual care group from the previous study (25). For HD patients data, the number of outpatient visits was assumed to be 156 days since HD patients generally visit the hospital three-times a week for dialysis, and the hospitalization was calculated to be 0.667 times that of PD patients as reported previously (8). The utilization for peritonitis was derived from our hospital data (1.437 times higher for the number of outpatient visits and 1.577 times higher for hospitalization), while the length of hospitalization for RTx (first year) was assumed to be take two more weeks than PD for

transplantation.

Table 12. Parameters for direct non-medical costs (1)

Healthcare utilization per patients	Mean	SD	Source
Annual no. of outpatient			
PD home care	12.6	8.1	(25)
PD usual care	10.7	6.0	(25)
HD	156.0	-	Assumed
Peritonitis	16.7	-	Hospital data
RTx (1st year)	14.7	-	Assumed
RTx (after 1st year)	6.0	-	Assumed
Annual no. of hospitalizations			
PD home care	0.52	0.96	(25)
PD usual care	0.54	0.97	(25)
HD	0.53	-	Assumed
Peritonitis	0.83	-	Hospital data
RTx (1st year)	1.53	-	Assumed
RTx (after 1st year)	0.53	-	Assumed
Hospitalization rate of HD to PD	0.667		(8)
Average length of hospitalization days			
PD home care	15.8	13.0	(25)
PD usual care	18.5	16.4	(25)
HD	17.2	-	Assumed
Peritonitis	17.2	-	Assumed
RTx (1st year)	31.2	-	Assumed
RTx (after 1st year)	17.2	-	Assumed

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation); SD (standard deviation).

The average transportation cost per hospital visit was based on the national health and nutrition survey conducted in 2005. The data was adjusted to 2020 monetary values based on the consumer price index of the transportation sector (Appendix Table 2).

Table 13. Parameters for direct non-medical costs (2)

Parameters	Mean	SD	Source
One-way transportation cost per patient (KRW)			
Costs for outpatient in 2005	8,607	2,129	(59)
Costs for outpatient in 2020 (inflation adjusted)	10,231	2,531	(59)
Costs for hospitalization in 2005	10,667	657	(59)
Costs for hospitalization in 2020 (inflation adjusted)	12,679	781	(59)
Average salary per day (KRW)			
30s	114,667		(60)
40s	131,000		(60)
50s	123,667		(60)
60s +	72,333		(60)
Employment rate (%)	65.9		(61)
Nursing care fee per day (KRW)	85,579	75,281, 98,303*	(62)

* Lower and upper bound
Abbreviations: SD (standard deviation).

b. Nursing care costs

Nursing care costs are the amount paid for caregivers when patients are admitted to the hospital. The costs were calculated using collected parameters (Table 12 and Table 13) and defined as follows:

Annual nursing care costs per patient

= {(the number of hospitalizations per year)
x (length of stay per hospitalization)}
x (the average nursing care fee per day)

(C) Indirect costs (Productivity costs)

Indirect costs should be considered in the analysis of the societal perspective (47). As it is difficult to measure all productivity loss, we included patients' time costs (leading to a 'limited' societal perspective) to reflect the time spent on hospital visits annually, leading to productivity loss. This is defined as follows:

Annual time costs per patient

= [{(the average number of outpatient visits per year) ÷ 2}
+ {(the number of hospitalizations per year)
x (length of stay per hospitalization)}]
x (the average salary per day)
x (employment rate)

Without calculating the exact outpatient time spent per hospital visit, we assumed that a one-day outpatient visit is equivalent to the loss of a half-day of economic activities (full-day loss in Scenario 3). Since the hypothetical cohort of this study was 50 years old, we referred to the average salary data for individuals in their 50-60s (KRW 98,000 per day). All data for the above parameters are shown in Table 12 and Table 13.

D. Parameters summarized

(A) Scenario 1: Base case analysis

Table 14. Transition probabilities and utilities in Scenario 1

Parameters	Value	Range		Distribution
Transition probabilities				
PD to				
HD	0.022	0.018	0.027	beta
Peritonitis (home care)	0.189	0.173	0.204	beta
Peritonitis (usual care)	0.239	0.227	0.251	beta
RTx	0.023	0.018	0.027	beta
Death	0.065	0.052	0.078	beta
HD to				
PD	0.009	0.007	0.011	beta
RTx	0.023	0.018	0.027	beta
Death	0.051	0.041	0.061	beta
Peritonitis to				
Death	0.123	0.098	0.147	beta
RTX to				
HD	0.025	0.020	0.030	beta
Death	0.007	0.006	0.009	beta
Utilities				
PD (home care)	0.861	0.846	0.876	beta
PD (usual care)	0.801	0.745	0.857	beta
HD	0.830	0.784	0.875	beta
Peritonitis (home care)	0.597	0.544	0.649	beta
Peritonitis (usual care)	0.555	0.502	0.608	beta
RTx	0.947	0.931	0.962	beta
Death	0.000	0.000	0.000	uniform

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation); SD (standard deviation).

Table 15. Cost input data in Scenario 1

(Unit: KRW)	Value	Range		Distribution
Direct medical costs				
PD (home care)	26,452,978	24,296,110	28,609,846	gamma
PD (usual care)	26,071,418	24,314,665	27,828,170	gamma
HD	29,125,885	27,818,385	30,433,385	gamma
Peritonitis	34,605,854	25,591,549	43,620,159	gamma
RTx (1st year)	21,901,018	20,656,023	23,146,013	gamma
RTx (after 1st year)	9,482,522	8,616,820	10,348,224	gamma
Direct non-medical costs				
Annual transportation costs				
PD (home care)	270,925	263,651	278,198	gamma
PD (usual care)	232,631	227,522	237,740	gamma
HD	3,200,918	2,410,809	3,991,028	gamma
Peritonitis	363,730	290,984	436,475	gamma
RTx (1st year)	338,521	270,817	406,225	gamma
RTx (after 1st year)	136,171	108,937	163,405	gamma
Annual nursing care costs				
PD (home care)	699,062	614,942	802,997	gamma
PD (usual care)	854,936	752,059	982,046	gamma
HD	517,114	454,888	593,997	gamma
Peritonitis	1,223,338	1,076,130	1,405,221	gamma
RTx (1st year)	4,074,663	3,584,347	4,680,474	gamma
RTx (after 1st year)	775,671	682,332	890,995	gamma
Indirect (Productivity) costs				
PD (home care)	934,411	747,529	1,121,293	gamma
PD (usual care)	990,688	792,550	1,188,825	gamma
HD	5,427,634	4,342,107	6,513,161	gamma
Peritonitis	1,463,847	1,171,077	1,756,616	gamma
RTx (1st year)	3,547,991	2,838,393	4,257,590	gamma
RTx (after 1st year)	779,103	623,282	934,923	gamma
Total costs for PD (home care)	**28,357,376**	**25,922,232**	**30,812,334**	gamma
Total costs for PD (usual care)	**28,149,673**	**26,086,796**	**30,236,782**	gamma
Total costs for HD	**38,271,551**	**35,026,189**	**41,531,571**	gamma
Total costs for Peritonitis	**37,656,768**	**28,129,741**	**47,218,472**	gamma
Total costs for RTx (1st year)	**29,862,193**	**27,349,580**	**32,490,301**	gamma
Total costs for RTx (after 1st year)	**11,173,466**	**10,031,371**	**12,337,548**	gamma

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation).

(B) Scenario 2: Changes in transition probabilities

Parameters for utilities and costs are equivalent to those in Scenario 1.

Table 16. Transition probabilities in Scenario 2

Parameters	Value	Range		Distribution
Transition probabilities				
PD to				
HD	0.022	0.018	0.027	beta
Peritonitis (home care)	0.197	0.172	0.221	beta
Peritonitis (usual care)	0.224	0.210	0.238	beta
RTx	0.023	0.018	0.027	beta
Death	0.065	0.052	0.078	beta
HD to				
PD	0.009	0.007	0.011	beta
RTx	0.023	0.018	0.027	beta
Death	0.051	0.041	0.061	beta
Peritonitis to				
Death	0.123	0.098	0.147	beta
RTX to				
HD	0.025	0.020	0.030	beta
Death	0.007	0.006	0.009	beta

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation); SD (standard deviation).

(C) Scenario 3: Changes in costs

Parameters for transition probabilities and costs are equivalent to those in Scenario 1.

Table 17. Cost input data in Scenario 3

(Unit: KRW)	Value	Range		Distribution
Direct medical costs				
PD (home care)	26,452,978	21,162,382	31,743,574	gamma
PD (usual care)	26,071,418	20,857,134	31,285,701	gamma
HD	29,125,885	23,300,708	34,951,062	gamma
Peritonitis	34,605,854	27,684,683	41,527,025	gamma
RTx (1st year)	21,901,018	17,520,814	26,281,222	gamma
RTx (after 1st year)	9,482,522	7,586,018	11,379,027	gamma
Direct non-medical costs				
Annual transportation costs				
PD (home care)	270,925	216,740	325,109	gamma
PD (usual care)	232,631	186,105	279,157	gamma
HD	3,200,918	2,560,735	3,841,102	gamma
Peritonitis	363,730	290,984	436,475	gamma
RTx (1st year)	338,521	270,817	406,225	gamma
RTx (after 1st year)	136,171	108,937	163,405	gamma
Annual nursing care costs				
PD (home care)	699,062	559,250	838,875	gamma
PD (usual care)	854,936	683,949	1,025,923	gamma
HD	517,114	413,691	620,536	gamma
Peritonitis	1,223,338	978,671	1,468,006	gamma
RTx (1st year)	4,074,663	3,259,730	4,889,595	gamma
RTx (after 1st year)	775,671	620,536	930,805	gamma
Indirect (Productivity) costs				
PD (home care)	1,341,278	1,073,022	1,609,533	gamma
PD (usual care)	1,336,202	1,068,961	1,603,442	gamma
HD	10,465,030	8,372,024	12,558,036	gamma
Peritonitis	2,004,506	1,603,604	2,405,407	gamma
RTx (1st year)	4,021,055	3,216,844	4,825,265	gamma
RTx (after 1st year)	972,849	778,279	1,167,418	gamma
Total costs for PD (home care)	**28,764,242**	**23,011,394**	**34,517,091**	gamma
Total costs for PD (usual care)	**28,495,186**	**22,796,149**	**34,194,224**	gamma
Total costs for HD	**43,308,947**	**34,647,158**	**51,970,736**	gamma
Total costs for Peritonitis	**38,197,428**	**30,557,942**	**45,836,913**	gamma
Total costs for RTx (1st year)	**30,335,256**	**24,268,205**	**36,402,307**	gamma
Total costs for RTx (after 1st year)	**11,367,212**	**9,093,770**	**13,640,655**	gamma

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation).

(D) Scenario 4: Changes in utilities

Parameters for transition probabilities and costs are equivalent to those in Scenario 1.

Table 18. Utilities in Scenario 4

Parameters	Value	Range		Distribution
Utilities				
PD (home care)	0.869	0.788	0.951	beta
PD (usual care)	0.814	0.738	0.890	beta
HD	0.830	0.784	0.875	beta
Peritonitis (home care)	0.602	0.546	0.659	beta
Peritonitis (usual care)	0.564	0.511	0.617	beta
RTx	0.947	0.931	0.962	beta
Death	0.000	0.000	0.000	uniform

Abbreviations: PD (peritoneal dialysis); HD (hemodialysis); RTx (renal transplantation); SD (standard deviation).

3. Statistical Analyses

(1) Clinical effectiveness analyses

Data were presented as mean ± standard deviation for continuous variables and a number with percentage (%) for categorical parameters. To examine the proportion of those achieving the clinical target range, chi-square (χ^2) tests were conducted for the in-range and out-of-range groups. We compared one-year of data before and one-year of data after the home care program. The clinical laboratory test results of pre-homecare and post-homecare were analyzed using an unpaired Student's t-test to identify the overall changes after the intervention; the analysis included the entire cases of testing differed by patients (results in the Appendix). The interrupted time series (ITS) analyses (63, 64) using an ordinary least square (OLS) linear regression model were structured as final models. Data was aggregated by time intervals for both peritonitis and clinical laboratory test result measures to evaluate the long-term clinical effectiveness of the home care interventions. We adjusted the time point of the intervention per patients, as the study subjects enrolled in the home care program on different dates. Thus, the baseline period (pre-homecare) includes two-years of data before adopting the intervention and the post-homecare period includes two-years of data after the program in one-month intervals. The full linear regression ITS models were conducted and the parsimonious model was then adjusted for peritonitis analyses. The ITS models used in this study were described by the

following formula:

Results of the full regression model

$$Y_t = \beta_0 + (\beta_1 * T) + (\beta_2 * D_t) + (\beta_3 * TD_t) + \varepsilon_t$$

Results of the parsimonious model

$$Y_t' = \beta_0 + (\beta_1 * T) + (\beta_3 * TD_t) + \varepsilon_t$$

where

Y_t	the results of the full regression model at time *t*
Y_t'	the results of parsimonious model at time *t*
β_0	the baseline level at $T = 0$
β_1	the changes in outcome per time unit increase (pre-homecare trend)
β_2	the level of change after the home care intervention
β_3	the changed trend (slope) after the intervention
T	one-month interval since the start of the study
D_t	a dummy variable (0 for pre-homecare, 1 for post-homecare) at time *t*
TD_t	a time interval of one-month after the intervention at time *t*

For the ITS analyses on peritonitis, integration was added to identify the area under the parsimonious regression model and compare the observed value with the counterfactual scenario. The integration between the limits of t = 24 (the start of home care intervention) and t = 36 (after one-year) – representing a one-year cumulative incidence of peritonitis – was performed using the following formula:

1-year incidence (with home care intervention, where $D_t = 1$)

$$= \int_{24}^{36} Y_t' \, dt = \int_{24}^{36} \{\beta_0 + (\beta_1 * T) + (\beta_3 * T) + \varepsilon_t\} \, dt$$

1-year incidence (counterfactual; without intervention, where $D_t = 0$)

$$= \int_{24}^{36} Y_t' \, dt = \int_{24}^{36} \{\beta_0 + (\beta_1 * T) + \varepsilon_t\} \, dt$$

All analyses were performed using R Statistical Software (v4.2.1; R Core Team 2022, Vienna, Austria), RStudio Software (v2022.07.1; RStudio Team 2022, Boston, MA) and SPSS Statistics for Windows version 26.0 (IBM Corp., Armonk, NY, USA). The statistical significance level was determined as $p < 0.05$.

(2) Cost-utility analysis

A. Base-case analysis

The main outcome measures in this study are the incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (INMB), which were calculated as follows:

Incremental cost-effectiveness ratio (ICER)

= ΔCost / ΔEffectiveness

= {(Costs of home care) – (Costs of usual care)} /

{(Effectiveness of home care) – (Effectiveness of usual care)}

with cost-effective when "*ICER* < *WTP*"

Incremental net monetary benefit (INMB)

= {(Willingness-to-pay) x (incremental effectiveness)}

- (incremental costs)

with cost-effective when "*INMB* > *0*"

The annual discount rate of 4.5% was adjusted for the base-case analysis.

B. Sensitivity analysis

It is difficult to avoid uncertainty since the input data contains various assumptions. To indicate the effect of parameters, a sensitivity analysis should be conducted, such as deterministic sensitivity analysis (DSA) or probabilistic sensitivity analysis (PSA) (44).

(A) Deterministic sensitivity analysis (DSA)

DSA was conducted to identify when parameter values changed in the given range. We used one-way and two-way sensitivity analyses in our study to examine the impact of all parameters on cost-effectiveness. We first performed a one-way sensitivity analysis. The 95% confidential interval (CI) of each parameter was calculated as the range with the mean and SD (SE) of the variables. Where we did not have the variation values, we used a range of 80% - 120% from the base-case value (data summarized in Table 14 and Table 15). A one-way sensitivity analysis assesses the impact of a certain parameter at a time, enabling us to identify the relative impacts of each variable on the results. The results of the analysis were presented in the form of a tornado diagram, which visualizes the changes in ICER and INMB according to the changes in the parameters in the given range. After executing a one-way sensitivity analysis, we could select the two most sensitive variables and conduct a two-way sensitivity analysis, to identify the changes in the cost-effectiveness outcome when those values vary simultaneously in the given range and the correlation between the two. The analyses were performed in all four scenarios.

(B) Probabilistic sensitivity analysis (PSA)

PSA considers the uncertainty of every variable simultaneously by randomly sampling the value of the parameters in the given distribution and computes the percentage of certain alternatives being more optimal. A Monte Carlo simulation with 10,000 iterations was performed using pre-defined distributions (gamma distribution for cost data and beta for utilities and transition probabilities, ranging from 0 to 1) as summarized in Table 14 and Table 15. Discount rates from 0% to 4.5% were randomly sampled as well. Then, the results of the PSA were presented as an incremental cost-effectiveness (ICE) scatter plot and a cost-effectiveness acceptability curve (CEAC). The ICE scatter plot plots the outputs (incremental costs and incremental effectiveness) from the Monte Carlo simulation for comparison with the incremental cost-effectiveness ratio (ICER) threshold line to examine the probability of certain alternatives being more cost-effective. Although our study compares a home care group and a control group, it is difficult to interpret ICE scatter plot with three or more groupings. In this case, a cost-effectiveness acceptability curve (CEAC) can be used to anticipate which alternative is cost-effective at a certain threshold. In the CEAC graph, we demonstrated the probability of being cost-effective in the WTP threshold (KRW 40,043,036), but also the threshold where the probability of the home care group being cost-effective is greater than 50%. Caution should be used when interpreting the graph, as the highest probability of being cost-effective does not always mean that the alternative is cost-effective.

C. Value of information analysis – The expected value of perfect information (EVPI)

Lastly, we measured the EVPI, which is defined as 'an estimate of the net health (or monetary) benefits that could potentially be gained per patient if the uncertainty surrounding their treatment choice could be resolved' (44). EVPI means the expected gains of the outcome when perfect information is given without any uncertainty. The EVPI can be calculated by extracting the expected net benefits with current information from the expected net benefits with perfect information as follows:

$$EVPI = E_\theta max_j NB(j,\theta) - max_j E_\theta NB(j,\theta)$$

j	alternative interventions
θ	a range of possible values
E_θ	the average value
NB	net benefit

4. Ethics Statement

This study's procedures were reviewed and approved by the Institutional Review Board at Severance Hospital, Yonsei University (IRB number: 4-2022-0552).

IV. Results

1. General Characteristics

Table 19 shows the general characteristics of the 186 PD patients enrolled in the home care program at a single center. The mean age of the population was 54.7 years with a standard deviation (SD) of 13.6 years. The average duration since the PD start date was 6.6 ± 4.4 years. We divided the population into subgroups of sex (male vs. female), age (<55 vs. ≥55 years) and PD durations (<6 vs. ≥6 years) for detailed analyses. In general, PD patients were enrolled in the home care program in June 2020. To identify patients' exposure to the home care program, we identified the number of reimbursement cases. The average number of reimbursed cases was 0.42 ± 0.47 times for educational consultation 1 (conducted by physicians), 3.54 ± 1.31 times for educational consultation 2 (executed by other medical staffs), and 7.15 ± 2.45 times for remote monitoring care (phone calls by medical staffs). The baseline clinical outcomes at home care program enrollment were reviewed: Hb (10.20 g/dL), Ca x P (46.5 mg^2/dL^2), K (4.45 mEq/L), and iPTH (243.0 pg/mL).

Table 19. General characteristics of the study subjects (N = 186)

Variables	N	%
Total	186	100.0%
Sex		
Male	94	50.5%
Female	92	49.5%
Age (years)		
<55	84	45.2%
≥55	102	54.8%
Mean±SD	54.7 ± 13.6	
PD duration (years)		
<6	93	50.0%
≥6	93	50.0%
Mean±SD	6.56 ± 4.42	
No. of homecare reimbursed annually (Mean±SD)		
Educational consultation 1	0.42 ± 0.47	
Educational consultation 2	3.54 ± 1.31	
Remote monitoring (phone call)	7.15 ± 2.45	
Date enrolled in the program (Median)	2020-06-10	
Baseline lab test results		
Hb (g/dL)	10.20 ± 1.56	
Ca x P (mg^2/dL^2)	46.5 ± 14.3	
K (mEq/L)	4.45 ± 0.76	
iPTH (pg/mL)	243.0 ± 190.0	

Abbreviations: SD (standard deviation); Hb (hemoglobin); Ca x P (calcium-phosphorus product); K (potassium); iPTH (parathyroid hormone).

2. Clinical effectiveness analyses

(1) Changes in the incidence of peritonitis over the four years

Table 20 shows the overall results of ITS analyses representing the changes in the monthly peritonitis incidence. The baseline value was 8.892 cases per 1,000 patient-months (SE = 3.383, P = 0.012), which continuously increased by 0.409 cases per 1,000 patient-months (P-value for baseline trend = 0.097). After starting the home care program, the incidence increased by 2.538 per 1,000 patient-months, without significance (P-value for level change = 0.614). Rather, the incidence trend significantly decreased by 0.898 cases per 1,000 patient-months (P-value for trend change = 0.014).

Table 20. Results of ITS analyses on the incidence of peritonitis (all)

	Coefficient	SE	P-value
Full regression model			
Constant (β_0)	8.892	3.383	0.012
Time (β_1)	0.409	0.242	0.097
Prepost (β_2)	2.538	4.992	0.614
TimeSince (β_3)	-0.898	0.353	0.014
Parsimonious model			
Constant (β_0)	8.345	3.181	0.012
Time (β_1)	0.480	0.195	0.018
TimeSince (β_3)	-0.886	0.349	0.015

(Unit: cases per 1,000 patient-months)
Abbreviations: SE (standard error).

After elimination of the non-significant variable ("Prepost(β_2)" in this case), the most parsimonious regression model included Constant(β_0), Time(β_1), and Timesince(β_3) variables (Table 20). When the home care intervention was sustained for one-year in this parsimonious model, the anticipated incidence of peritonitis became 15.01 cases per 1,000 patient-months at Time = 36 (months) while the counterfactual value increased to 25.64 (Figure 4). Thus, we can integrate the parsimonious model and its counterfactual between the limits of Time = 24 and 36 months to identify the one-year cumulative incidence of peritonitis. This incidence decreased to 20.93% after the home care intervention from 27.31% in counterfactual (P < .001).

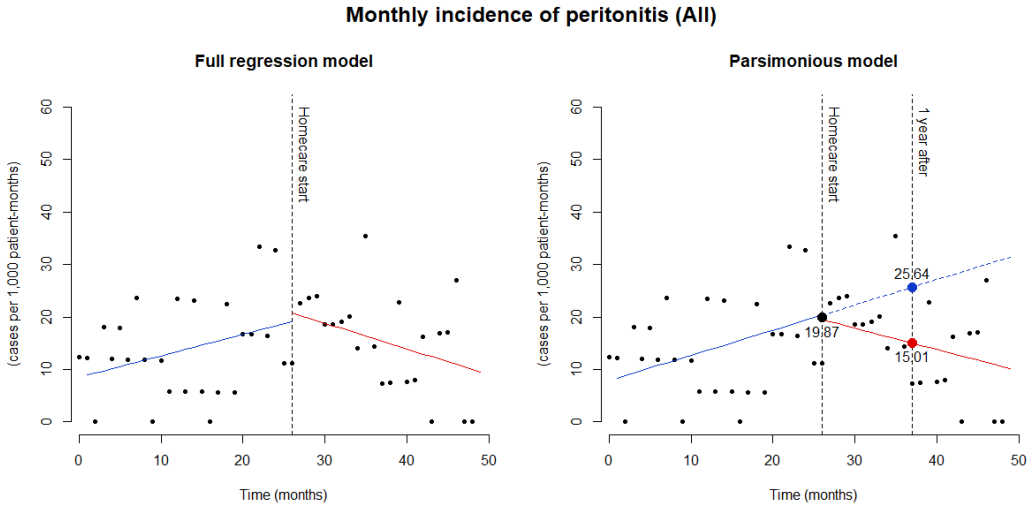

Figure 4. Impact of the home care program on peritonitis: ITS analyses (all)

The results of the subgroup (sex) analyses are represented in Table 21. While the male group showed no significant changes, the incidence trend in the female group significantly decreased by 1.251 cases per 1,000 patient-months after starting the home care program (P-value for trend change = 0.021). After eliminating the most non-significant Prepost(β_2) variable, the significance in the parsimonious model improved in both the Time(β_1) and TimeSince(β_3) variables. In this model, the incidence of peritonitis after one-year (at Time = 36) decreased to 18.30 cases per 1,000 patient-months in the male group and 11.61 in the female group (Figure 5). The one-year cumulative incidence in each subgroup was calculated for both males (decrease from 27.14% to 23.10%, P < .001), and females (decrease from 27.49% to 18.71%, P < .001).

Table 21. Results of ITS analyses on the incidence of peritonitis (sex)

	Male			**Female**		
	Coefficient	SE	P-value	Coefficient	SE	P-value
Full regression model						
Constant (β_0)	10.275	5.470	0.067	7.617	5.024	0.136
Time (β_1)	0.435	0.391	0.272	0.376	0.359	0.300
Prepost (β_2)	-1.102	8.072	0.892	6.376	7.414	0.394
TimeSince (β_3)	-0.556	0.570	0.335	-1.251	0.524	0.021
Parsimonious model						
Constant (β_0)	10.512	5.130	0.046	6.243	4.750	0.195
Time (β_1)	0.404	0.315	0.206	0.556	0.291	0.063
TimeSince (β_3)	-0.561	0.563	0.324	-1.219	0.521	0.024

(Unit: cases per 1,000 patient-months)
Abbreviations: SE (standard error).

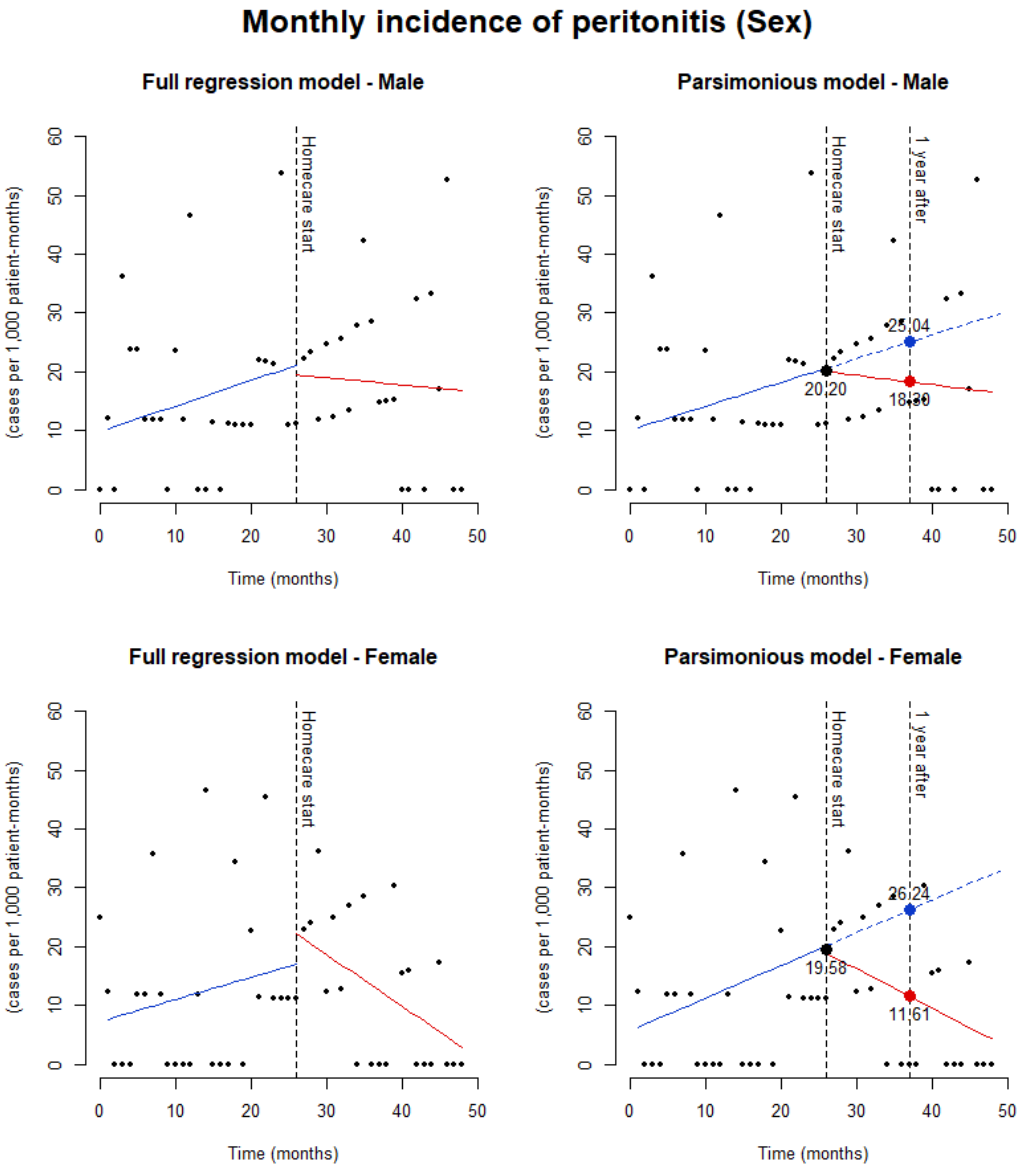

Figure 5. Impact of the home care program on peritonitis: ITS analyses (sex)

When analyzed by age subgroups, PD patients aged over 55 years showed significant improvement in the incidence of peritonitis (Table 22). The baseline trend was significantly increased by 0.850 cases per 1,000 patient-months (P-value for baseline trend = 0.027) and the trend declined by 1.439 cases per 1,000 patient-months after the intervention (P-value for trend change = 0.011). The parsimonious model without the Prepost(β_2) measure represented the results in those over 55-years of age (Figure 6). The incidence after 12 months (at Time = 36) in those <55 years became 11.02 cases per 1,000 patient-months (from a counterfactual value of 14.14) while for the ≥55 group it decreased to 18.52 cases per 1,000 patient-months (from a counterfactual value of 35.77). The one-year cumulative incidence of peritonitis was calculated, and we found that the <55 group decreased to 14.75% from 16.62% (P < .001), and the ≥55 group decreased to 26.37% from 36.72% (P < .001).

Table 22. Results of ITS analyses on the incidence of peritonitis (age)

	<55 years of age			**≥55 years of age**		
	Coefficient	SE	P-value	Coefficient	SE	P-value
Full regression model						
Constant (β_0)	13.485	4.730	0.007	4.865	5.201	0.355
Time (β_1)	-0.092	0.338	0.787	0.850	0.371	0.027
Prepost (β_2)	4.969	6.980	0.480	0.373	7.674	0.961
TimeSince (β_3)	-0.285	0.493	0.566	-1.439	0.542	0.011
Parsimonious model						
Constant (β_0)	12.414	4.460	0.008	4.785	4.877	0.332
Time (β_1)	0.048	0.274	0.862	0.861	0.299	0.006
TimeSince (β_3)	-0.260	0.489	0.597	-1.437	0.535	0.010

(Unit: cases per 1,000 patient-months)
Abbreviations: SE (standard error).

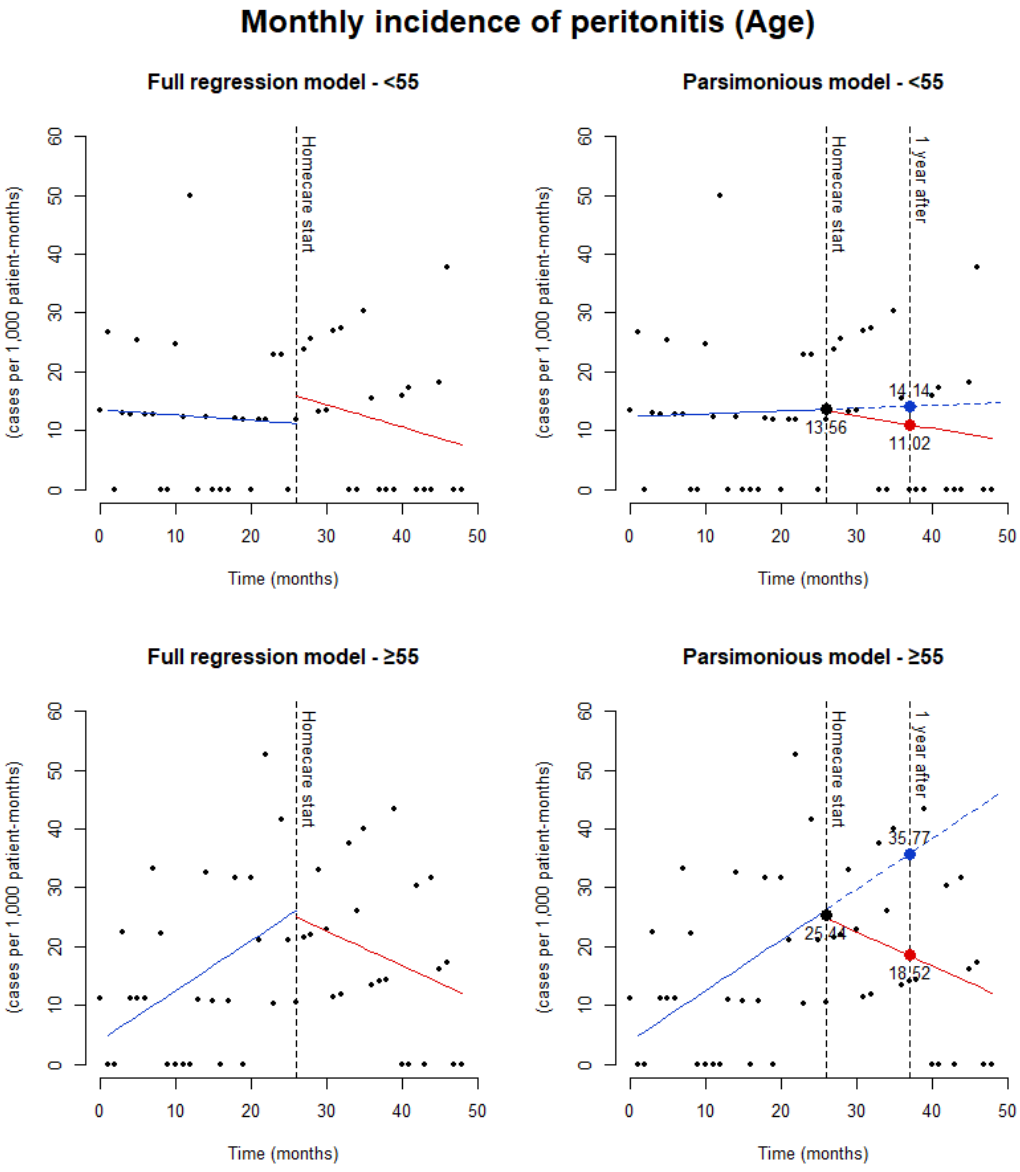

Figure 6. Impact of the home care program on peritonitis: ITS analyses (age)

The results of the subgroup (PD duration) analyses are presented in Table 23. PD patients above the six-year showed significant improvement in the incidence of peritonitis. The baseline trend was increasing to 0.819 cases per 1,000 patient-months (P-value for baseline trend = 0.027), but the trend decreased by 1.289 cases per 1,000 patient-months after the home care intervention (P-value for trend change = 0.017). The parsimonious model without the Prepost(β_2) variable clarified the impact of the home care program in the group whose PD was for more than six years. When this model is sustained for one-year, the incidence at Time = 36 (month) becomes 12.17 cases per 1,000 patient-months in the less than six-years group and 17.69 in the six or more years group (Figure 7). In cumulative value, the one-year incidence of peritonitis in the less than six-years group decreased to 16.84% from 20.11% (P < .001), while for the six or more years group it became 24.81% from 34.12% (P < .001).

Table 23. Results of ITS analyses on the incidence of peritonitis (PD duration)

	<6 years			**≥6 years**		
	Coefficient	SE	P-value	Coefficient	SE	P-value
Full regression model						
Constant (β_0)	13.792	4.674	0.005	4.401	5.004	0.384
Time (β_1)	-0.032	0.334	0.924	0.819	0.357	0.027
Prepost (β_2)	6.257	6.898	0.369	-0.868	7.384	0.907
TimeSince (β_3)	-0.486	0.487	0.324	-1.289	0.522	0.017
Parsimonious model						
Constant (β_0)	12.443	4.423	0.007	4.588	4.693	0.333
Time (β_1)	0.144	0.271	0.598	0.795	0.288	0.008
TimeSince (β_3)	-0.455	0.485	0.354	-1.293	0.515	0.016

(Unit: cases per 1,000 patient-months)
Abbreviations: SE (standard error).

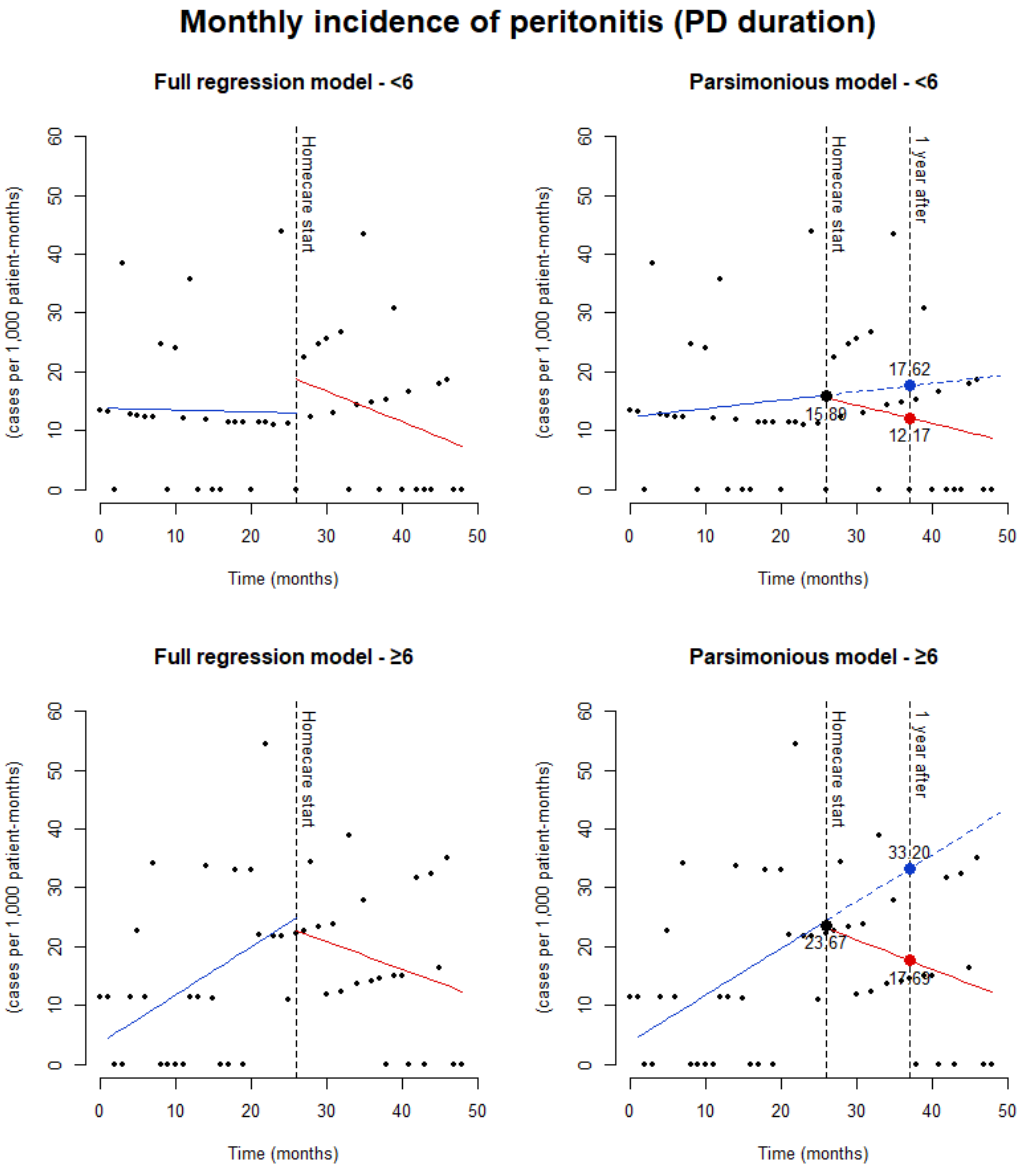

Figure 7. Impact of the home care program on peritonitis: ITS analyses (PD duration)

(2) Changes in clinical laboratory test results

A. Changes in the proportion achieving the target range over the two years

Table 24 and Figure 8 summarizes the hemoglobin outcome. The overall percentage of those achieving the target range significantly increased by 5.2%p (from 43.5% pre-homecare to 48.7% post-homecare, P = 0.002). In the subgroup analysis by sex, both males (5.2%p increase, P = 0.027) and females (4.8%p increase, P = 0.042) showed significant improvement. By age subgroups, those aged ≥55 years showed a statistically significant 6.2%p increase (P = 0.006). By PD durations, the <6 years group increased significantly by 6.9%p (P = 0.003).

Table 24. Proportion of patients who achieved the target hemoglobin (Hb) range

			Total	In range			Out of range		χ^2	p-value
				N	%	diff	N	%		
All		pre	2,423	1,054	43.5%	5.2%p	1,369	56.5%	9.44	0.002
		post	1,379	671	48.7%		708	51.3%		
Sex	Male	pre	1,173	535	45.6%	5.2%p	638	54.4%	4.86	0.027
		post	710	361	50.8%		349	49.2%		
	Female	pre	1,250	519	41.5%	4.8%p	731	58.5%	1.42	0.042
		post	669	310	46.3%		359	53.7%		
Age	<55 years	pre	1,137	509	44.8%	4.0%p	628	55.2%	2.52	0.113
		post	582	284	48.8%		298	51.2%		
	≥55 years	pre	1,286	545	42.4%	6.2%p	741	57.6%	7.60	0.006
		post	797	387	48.6%		410	51.4%		
Duration	<6 years	pre	1,463	646	44.2%	6.9%p	817	55.8%	8.66	0.003
		post	648	331	51.1%		317	48.9%		
	≥6 years	pre	960	408	42.5%	4.0%p	552	57.5%	2.71	0.100
		post	731	340	46.5%		391	53.5%		

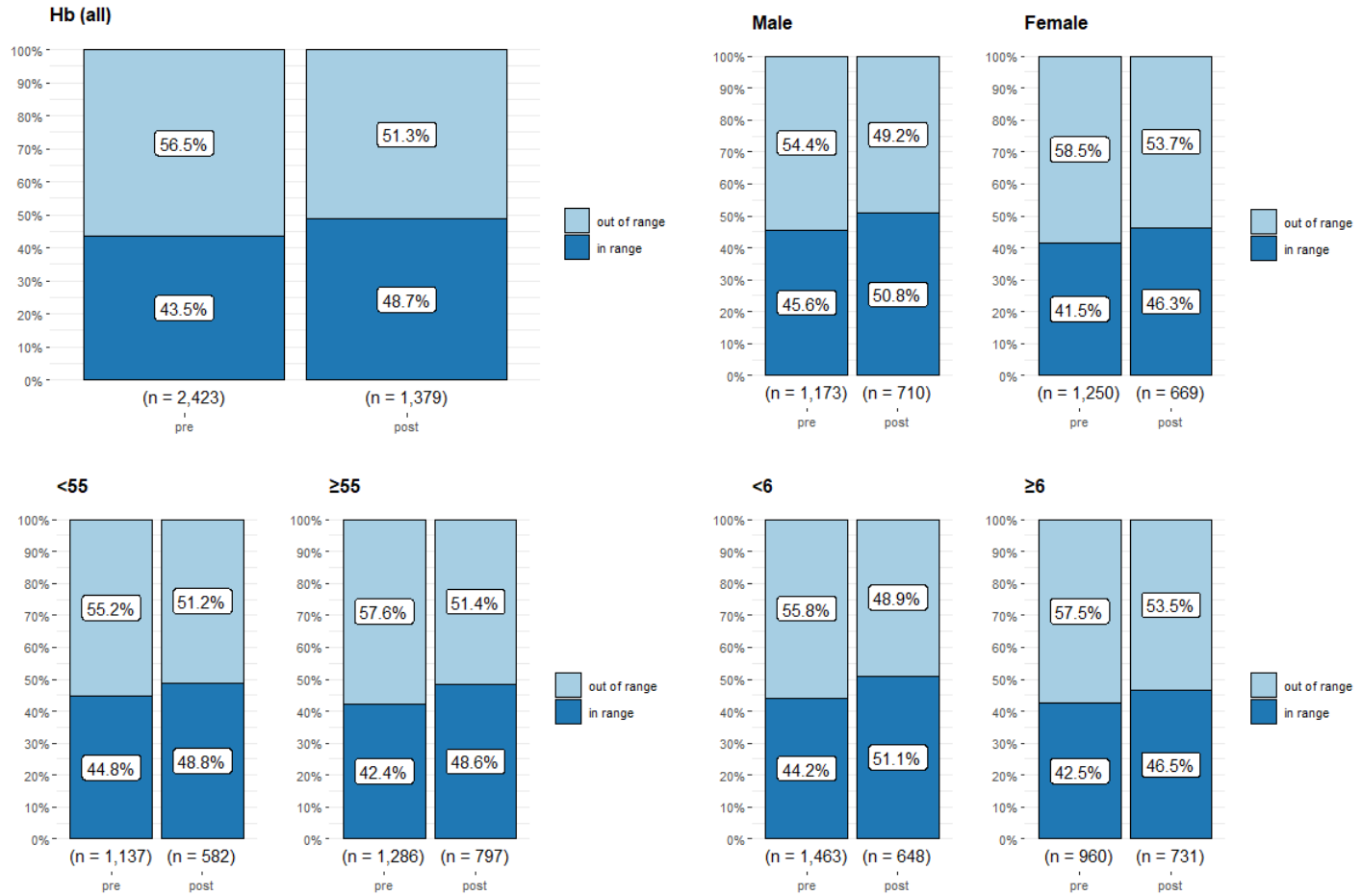

Figure 8. Proportion of the population in the target hemoglobin (Hb) range

The results of the calcium-phosphorus product are represented in Table 25 and Figure 9. The proportion of those achieving the target range after adopting the home care intervention was maintained as 79.6% from 78.5% in the pre-homecare group (P = 0.428). In the age subgroup analyses, those aged ≥55 years group significantly increased by 4.3%p, resulting in 85.5% of the cases achieving the target range.

Table 25. Proportion of patients who achieved the target calcium-phosphorus product (Ca x P) range

			Total	In range			Out of range		χ^2	p-value
				N	%	diff	N	%		
All		pre	2,175	1,707	78.5%	1.1%p	468	21.5%	0.63	0.428
		post	1,329	1,058	79.6%		271	20.4%		
Sex	Male	pre	1,038	800	77.1%	2.9%p	238	22.9%	2.07	0.150
		post	680	544	80.0%		136	20.0%		
	Female	pre	1,137	907	79.8%	-0.6%p	230	20.2%	0.08	0.773
		post	649	514	79.2%		135	20.8%		
Age	<55 years	pre	1,033	780	75.5%	-3.7%p	253	24.5%	2.64	0.105
		post	571	410	71.8%		161	28.2%		
	≥55 years	pre	1,142	927	81.2%	4.3%p	215	18.8%	5.98	0.014
		post	758	648	85.5%		110	14.5%		
Duration	<6 years	pre	1,292	1,002	77.6%	-0.1%p	290	22.4%	0.00	0.971
		post	635	492	77.5%		143	22.5%		
	≥6 years	pre	883	705	79.8%	1.7%p	178	20.2%	0.73	0.393
		post	694	566	81.6%		128	18.4%		

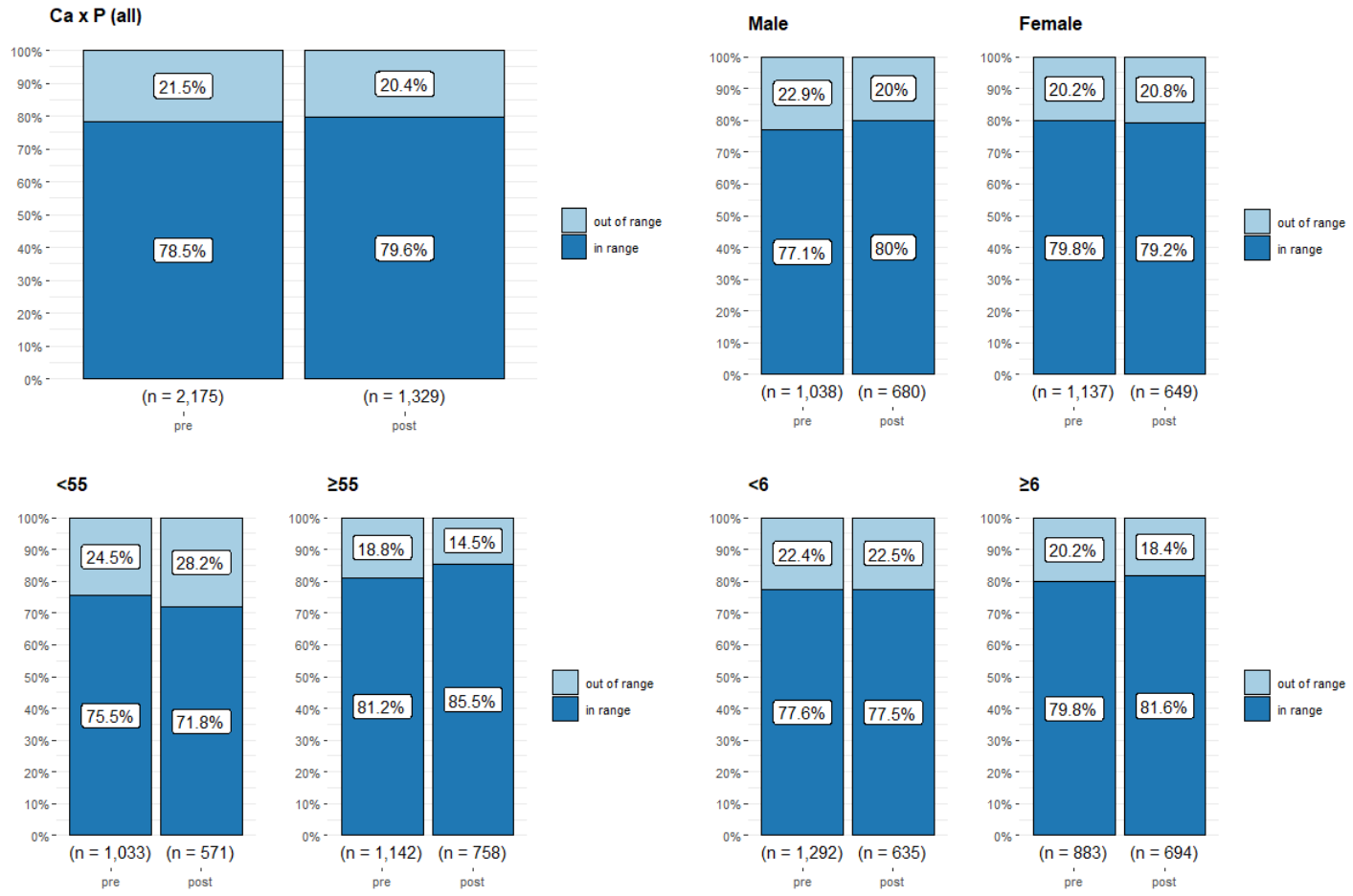

Figure 9. Proportion of the population in the target calcium-phosphorus product (Ca x P) range

The potassium measure outcomes are shown in Table 26 and Figure 10. The proportion of study subjects reaching the target range was maintained at 83.6% without statistically significant changes (P = 0.200). But there were some significant declines in the subgroup analyses, as the male subgroup decreased by 4.0%p (P = 0.027) and those undergoing PD for less than six years declined by 3.8%p (P = 0.020).

Table 26. Proportion of patients who achieved the target potassium (K) range

			Total	In range			Out of range		χ^2	p-value
				N	%	diff	N	%		
All		pre	2,372	2,020	85.2%	-1.6%p	352	14.8%	1.64	0.200
		post	1,321	1,104	83.6%		217	16.4%		
Sex	Male	pre	1,138	969	85.1%	-4.0%p	169	14.9%	4.92	0.027
		post	680	552	81.2%		128	18.8%		
	Female	pre	1,234	1,051	85.2%	0.9%p	183	14.8%	0.30	0.581
		post	641	552	86.1%		89	13.9%		
Age	<55 years	pre	1,131	969	85.7%	-1.2%p	162	14.3%	0.46	0.497
		post	572	483	84.4%		89	15.6%		
	≥55 years	pre	1,241	1,051	84.7%	-1.8%p	190	15.3%	1.10	0.294
		post	749	621	82.9%		128	17.1%		
Duration	<6 years	pre	1,472	1,281	87.0%	-3.8%p	191	13.0%	5.45	0.020
		post	642	534	83.2%		108	16.8%		
	≥6 years	pre	900	739	82.1%	1.8%p	161	17.9%	0.92	0.337
		post	679	570	83.9%		109	16.1%		

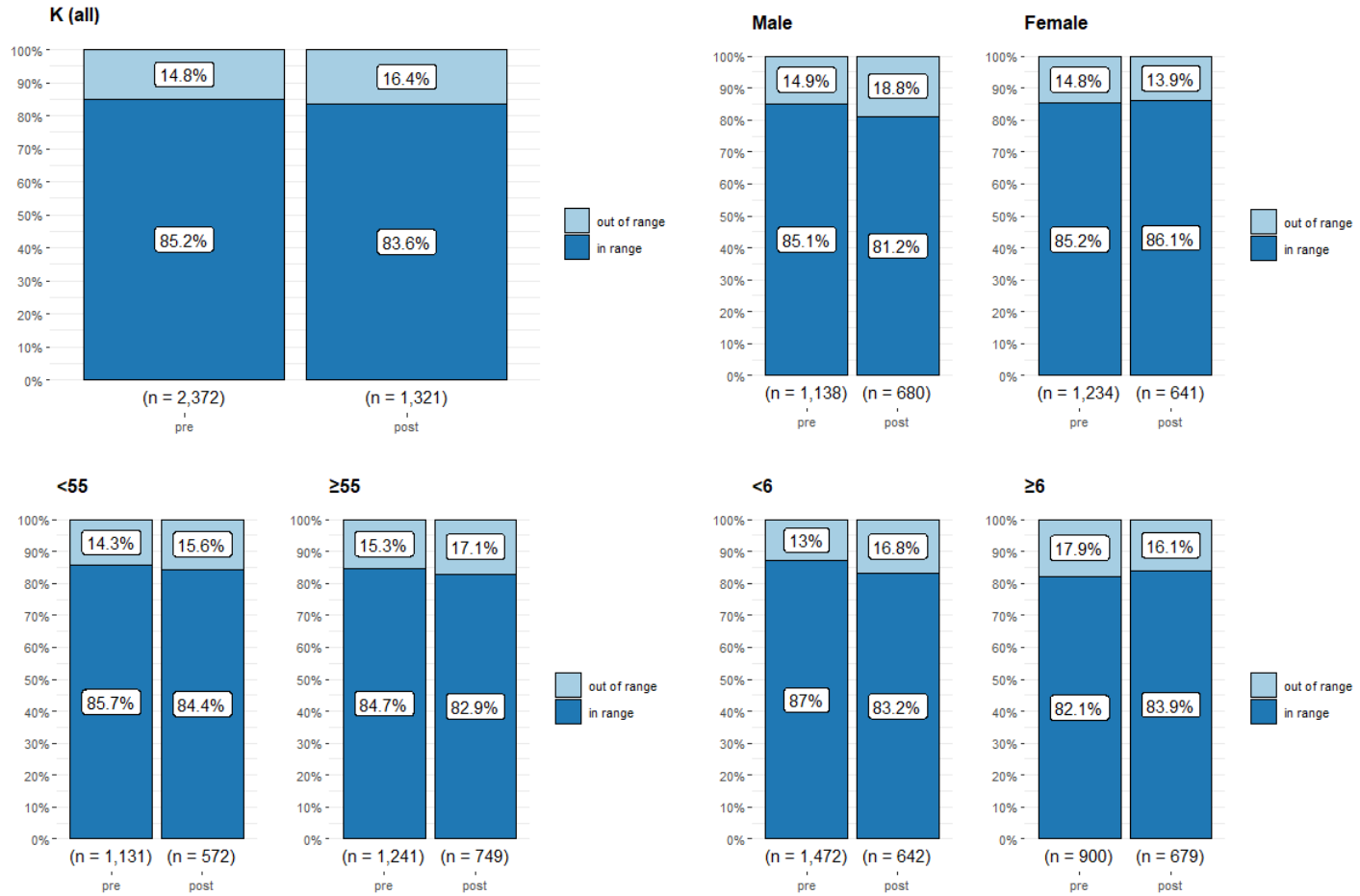

Figure 10. Proportion of the population in the target potassium (K) range

Lastly, the results of the parathyroid hormone outcome measure are summarized in Table 27 and Figure 11. Unlike other measures analyzed above, the proportion of the populations achieving the target range has significantly decreased by 11.0%p (from 69.5% to 58.5% in the overall population, $P < 0.001$). Although the iPTH outcomes got worse, the average values for both the pre-homecare (242.0 pg/mL) and post-homecare (287.0 pg/mL) groups were in the target range (Appendix Table 4 and Appendix Figure 1).

Table 27. Proportion of patients who achieved the target parathyroid hormone (iPTH) range

			Total	In range			Out of range		χ^2	p-value
				N	%	diff	N	%		
All		pre	924	642	69.5%	-11.0%p	282	30.5%	22.33	0.000
		post	783	458	58.5%		325	41.5%		
Sex	Male	pre	456	302	66.2%	-10.3%p	154	33.8%	9.26	0.002
		post	379	212	55.9%		167	44.1%		
	Female	pre	468	340	72.6%	-11.8%p	128	27.4%	13.60	0.000
		post	404	246	60.9%		158	39.1%		
Age	<55 years	pre	464	300	64.7%	-10.1%p	164	35.3%	9.03	0.003
		post	394	215	54.6%		179	45.4%		
	≥55 years	pre	460	342	74.3%	-11.9%p	118	25.7%	13.88	0.000
		post	389	243	62.5%		146	37.5%		
Duration	<6 years	pre	417	297	71.2%	-15.8%p	120	28.8%	21.93	0.000
		post	397	220	55.4%		177	44.6%		
	≥6 years	pre	507	345	68.0%	-6.4%p	162	32.0%	3.95	0.047
		post	386	238	61.7%		148	38.3%		

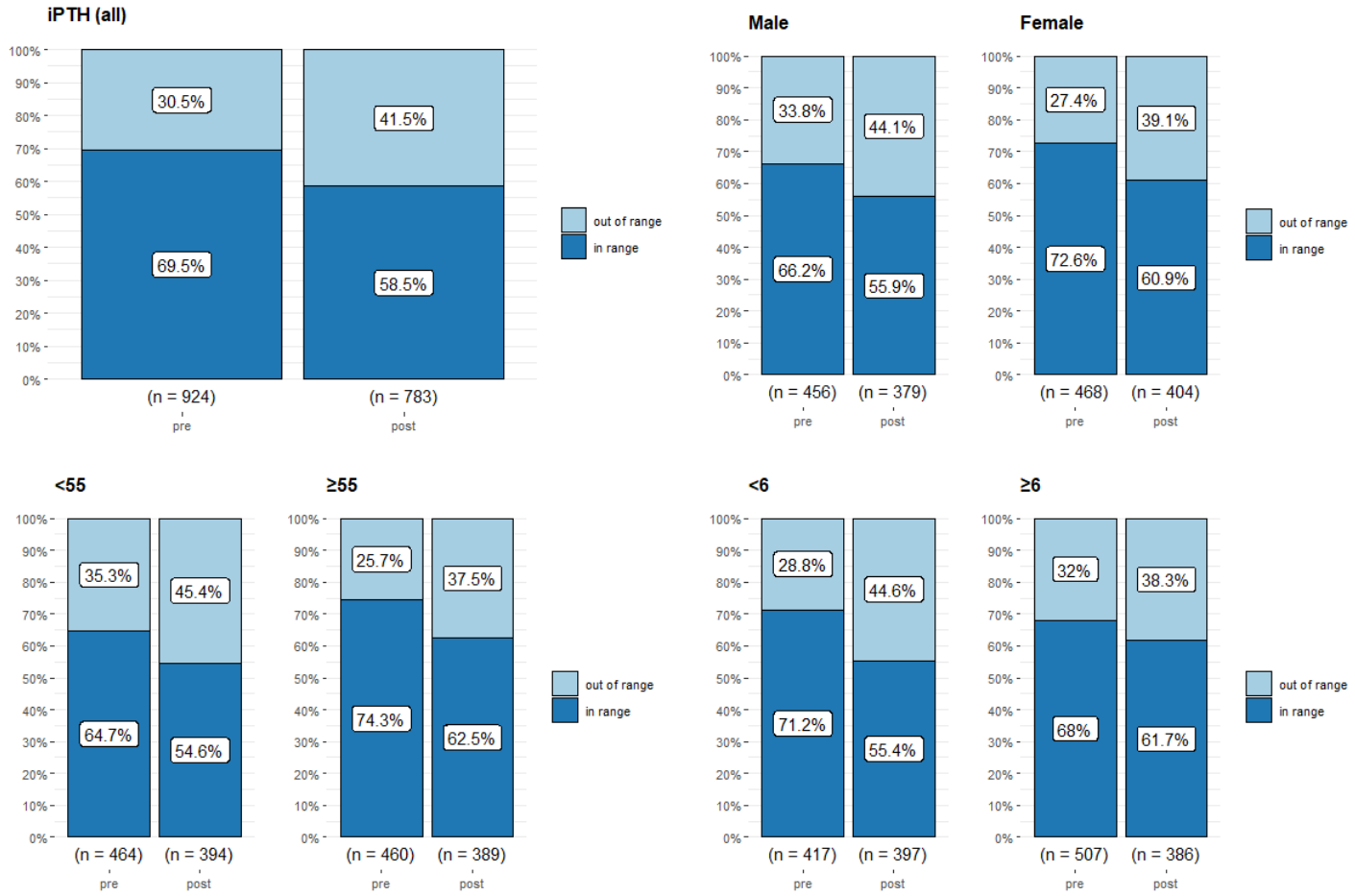

Figure 11. Proportion of the population in the target parathyroid hormone (iPTH) range

B. Changes in the trend of clinical laboratory test results over the four years

We performed ITS analyses to identify the changes in clinical laboratory test results over time. With the time interval of one-month, we observed the clinical outcomes reported in the pre-homecare (two years) and post-homecare (two years) periods. Table 28 and Figure 12 summarizes the overall outcomes. The level of hemoglobin in the pre-homecare period significantly decreased by 0.023 g/dL per month (P-value for baseline trend = 0.007). After adopting the home care program, the value immediately increased by 0.490 g/dL (P-value for level change = 0.006) and its month-to-month value increased by 0.016 g/dL (P-value for trend change = 0.196). The calcium-phosphorus product showed no significant changes overall but maintained its stable value. For potassium, the monthly trend in the pre-homecare period significantly declined by 0.008 mEq/L per month (P-value for baseline trend = 0.018), but the level and its slope slightly increased with no significance. Parathyroid hormone levels significantly increased monthly by 2.829 pg/mL per month (P-value for trend change = 0.015) after the home care intervention.

Table 28. Results of ITS analyses on clinical laboratory tests (all)

	Coefficient	SE	P-value
Hb			
Constant (β_0)	10.040	0.115	0.000
Time (β_1)	-0.023	0.008	0.007
Prepost (β_2)	0.490	0.170	0.006
TimeSince (β_3)	0.016	0.012	0.196
Ca x P			
Constant (β_0)	45.099	0.593	0.000
Time (β_1)	0.027	0.042	0.522
Prepost (β_2)	-1.003	0.873	0.257
TimeSince (β_3)	0.020	0.062	0.751
K			
Constant (β_0)	4.427	0.048	0.000
Time (β_1)	-0.008	0.003	0.018
Prepost (β_2)	0.108	0.070	0.132
TimeSince (β_3)	0.003	0.005	0.501
iPTH			
Constant (β_0)	228.128	10.656	0.000
Time (β_1)	0.997	0.761	0.198
Prepost (β_2)	17.570	15.686	0.269
TimeSince (β_3)	2.829	1.111	0.015

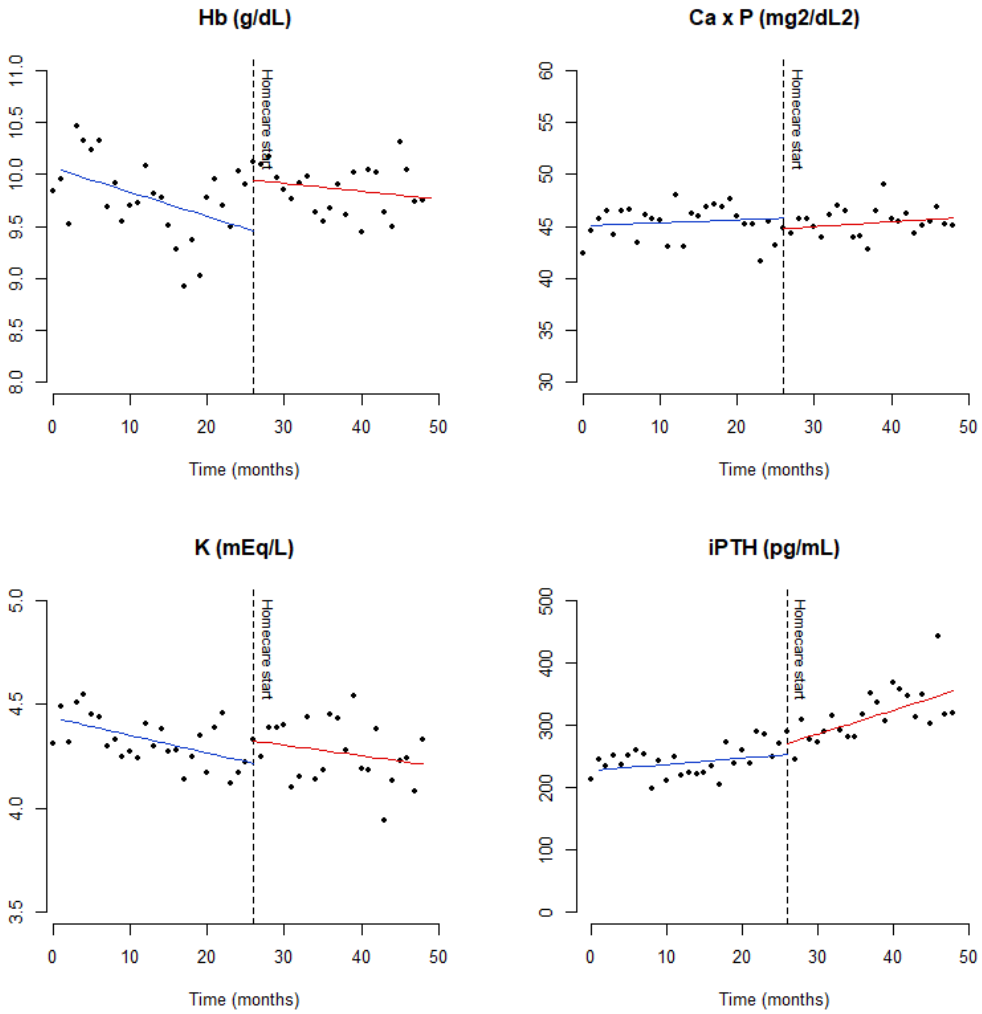

Figure 12. Impact on lab test results: ITS analyses (all)

Table 29 and Figure 13 shows the results of subgroup (sex) analyses. For hemoglobin, the decreasing baseline trend for both males (0.025 g/dL per month, P = 0.049) and females (0.027 g/dL per month, P = 0.024) increased by 0.324 g/dL (P-value for level change = 0.202) and 0.540 g/dL (P-value for level change = 0.028), respectively.

Table 29. Results of ITS analyses on clinical laboratory tests (sex)

	Male			Female		
	Coefficient	SE	P-value	Coefficient	SE	P-value
Hb						
Constant (β_0)	10.260	0.169	0.000	9.931	0.160	0.000
Time (β_1)	-0.025	0.012	0.049	-0.027	0.011	0.024
Prepost (β_2)	0.324	0.250	0.202	0.540	0.236	0.028
TimeSince (β_3)	0.025	0.018	0.157	0.023	0.017	0.184
Ca x P						
Constant (β_0)	48.154	0.810	0.000	42.277	0.948	0.000
Time (β_1)	-0.076	0.058	0.196	0.124	0.068	0.074
Prepost (β_2)	-2.346	1.195	0.056	0.327	1.400	0.817
TimeSince (β_3)	0.180	0.084	0.039	-0.129	0.099	0.200
K						
Constant (β_0)	4.578	0.078	0.000	4.316	0.051	0.000
Time (β_1)	-0.014	0.006	0.021	-0.005	0.004	0.186
Prepost (β_2)	0.040	0.116	0.732	0.151	0.076	0.053
TimeSince (β_3)	0.015	0.008	0.078	-0.002	0.005	0.732
iPTH						
Constant (β_0)	259.291	15.892	0.000	197.568	15.270	0.000
Time (β_1)	0.019	1.135	0.987	1.910	1.091	0.087
Prepost (β_2)	20.680	23.452	0.383	10.350	22.533	0.649
TimeSince (β_3)	2.476	1.657	0.143	3.263	1.592	0.047

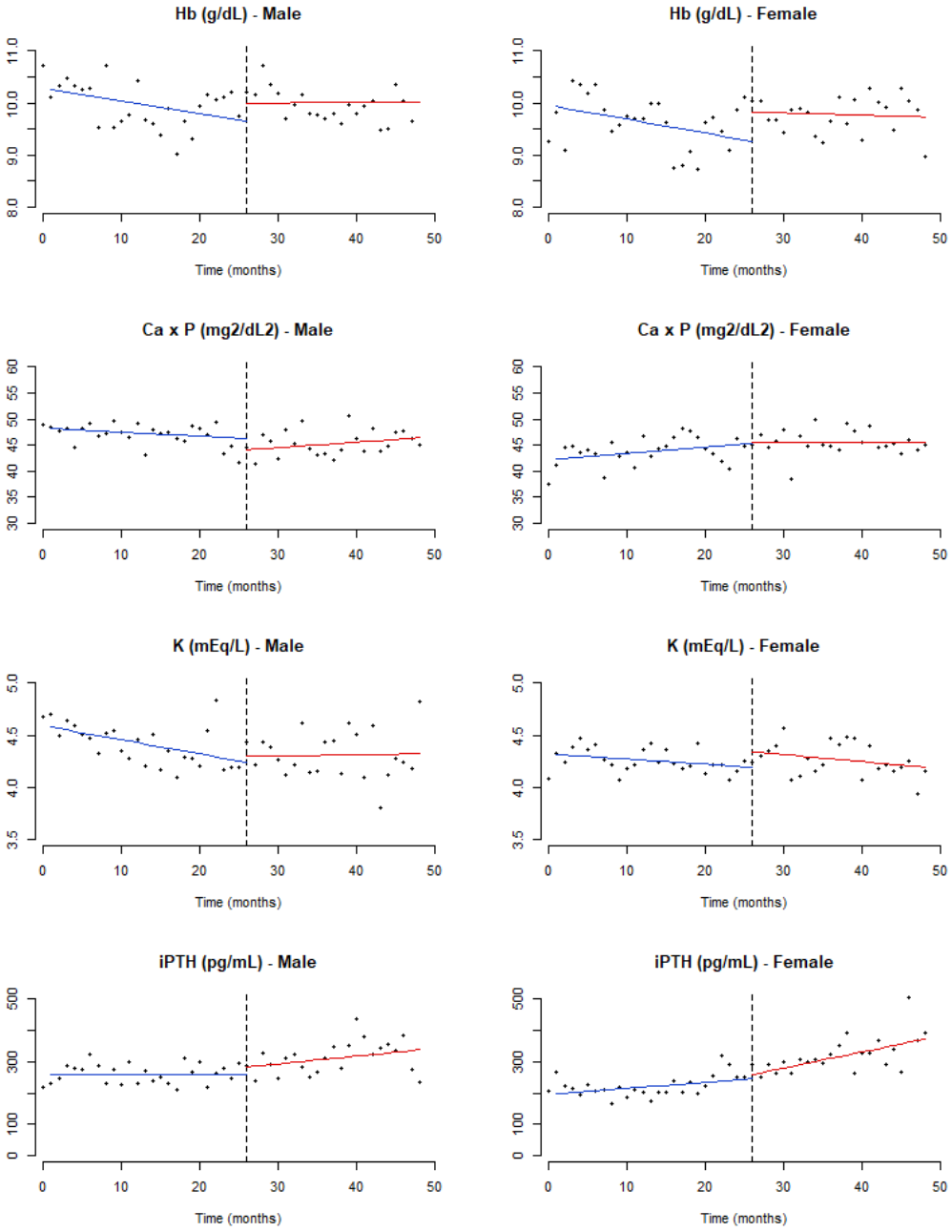

Figure 13. Impact on lab test results: ITS analyses (sex)

We then performed a subgroup (age) analysis (Table 30 and Figure 14). There were no major differences between the <55 and ≥55 years of age groups in general. But the intact parathyroid hormone levels in the ≥55 group showed significant increases (4.115 pg/mL per month, P-value for trend change = 0.007) after the implementation of the home care program.

Table 30. Results of ITS analyses on clinical laboratory tests (age)

	<55 years of age			**≥55 years of age**		
	Coefficient	SE	P-value	Coefficient	SE	P-value
Hb						
Constant (β_0)	10.009	0.136	0.000	10.132	0.154	0.000
Time (β_1)	-0.022	0.010	0.032	-0.027	0.011	0.017
Prepost (β_2)	0.463	0.201	0.026	0.491	0.227	0.037
TimeSince (β_3)	0.004	0.014	0.785	0.027	0.016	0.095
Ca x P						
Constant (β_0)	47.986	1.081	0.000	42.572	0.900	0.000
Time (β_1)	-0.021	0.077	0.792	0.075	0.064	0.249
Prepost (β_2)	0.677	1.596	0.674	-2.601	1.327	0.057
TimeSince (β_3)	0.110	0.113	0.334	0.006	0.094	0.946
K						
Constant (β_0)	4.479	0.067	0.000	4.383	0.059	0.000
Time (β_1)	-0.007	0.005	0.127	-0.008	0.004	0.061
Prepost (β_2)	-0.005	0.099	0.961	0.163	0.088	0.070
TimeSince (β_3)	0.013	0.007	0.077	-0.003	0.006	0.671
iPTH						
Constant (β_0)	245.721	14.138	0.000	209.327	13.874	0.000
Time (β_1)	0.921	1.010	0.367	1.054	0.991	0.294
Prepost (β_2)	28.488	20.863	0.179	-1.444	20.473	0.945
TimeSince (β_3)	1.913	1.474	0.201	4.115	1.446	0.007

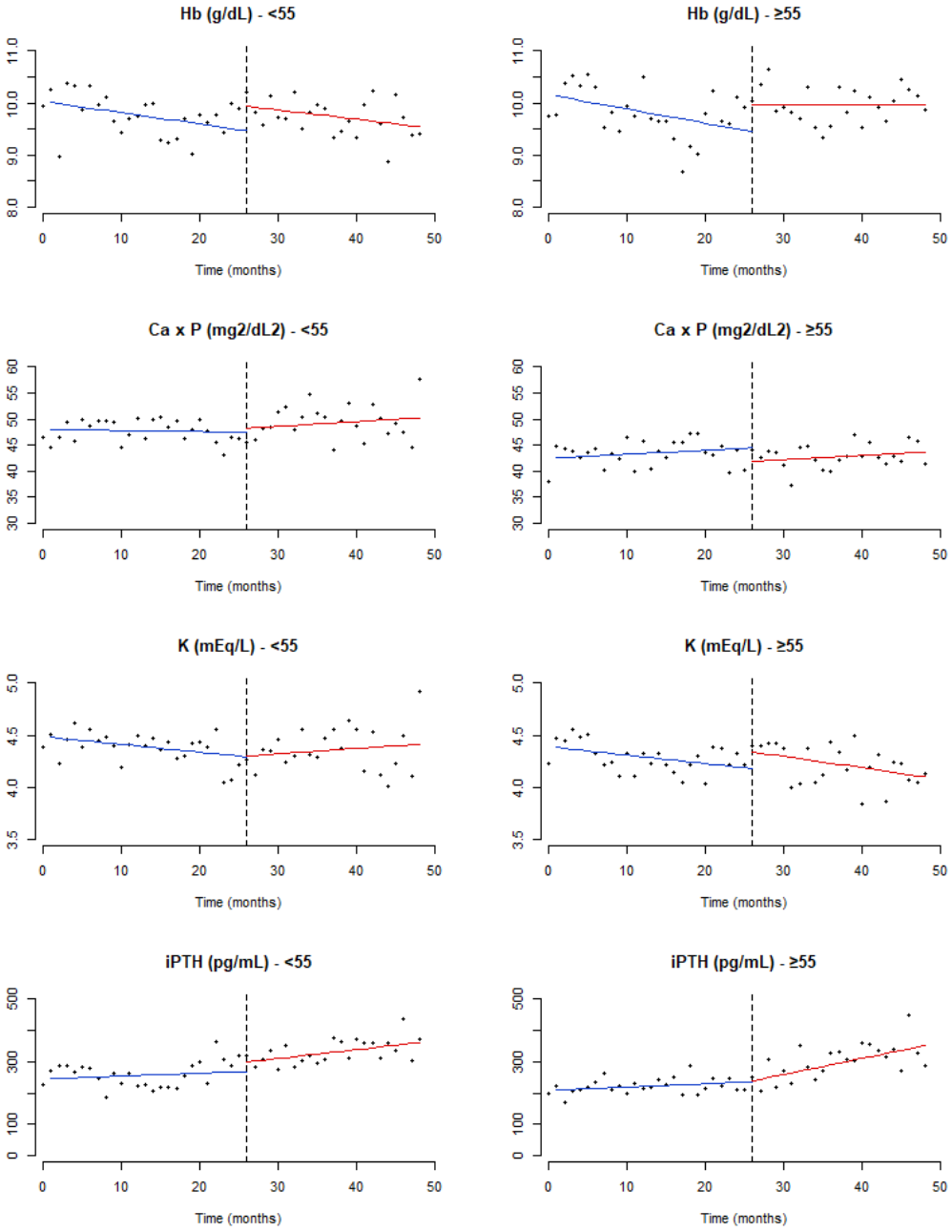

Figure 14. Impact on lab test results: ITS analyses (age)

The results of a subgroup analysis concerning PD duration are shown in Table 31 and Figure 15. In general, the subgroup that underwent PD for less than six years showed significant improvement, especially for the hemoglobin value, which decreased by 0.042 mg/dL monthly (P-value for baseline trend = 0.001) and enhanced by 0.699 mg/dL after the home care intervention.

Table 31. Results of ITS analyses on clinical laboratory tests (PD duration)

	<6 years			**≥6 years**		
	Coefficient	SE	P-value	Coefficient	SE	P-value
Hb						
Constant (β_0)	10.321	0.159	0.000	9.741	0.146	0.000
Time (β_1)	-0.042	0.011	0.001	-0.001	0.010	0.919
Prepost (β_2)	0.699	0.234	0.005	0.196	0.216	0.370
TimeSince (β_3)	0.024	0.017	0.150	0.003	0.015	0.842
Ca x P						
Constant (β_0)	43.583	0.810	0.000	47.110	0.920	0.000
Time (β_1)	0.119	0.058	0.046	-0.099	0.066	0.140
Prepost (β_2)	0.223	1.195	0.854	-1.434	1.357	0.297
TimeSince (β_3)	-0.036	0.084	0.676	0.117	0.096	0.229
K						
Constant (β_0)	4.484	0.052	0.000	4.366	0.062	0.000
Time (β_1)	-0.009	0.004	0.019	-0.007	0.004	0.114
Prepost (β_2)	0.083	0.077	0.287	0.129	0.092	0.165
TimeSince (β_3)	0.012	0.005	0.034	-0.004	0.006	0.534
iPTH						
Constant (β_0)	215.900	14.631	0.000	242.782	15.002	0.000
Time (β_1)	1.470	1.045	0.167	0.004	1.072	0.997
Prepost (β_2)	48.835	21.591	0.029	-10.551	22.137	0.636
TimeSince (β_3)	-0.462	1.525	0.764	6.599	1.564	0.000

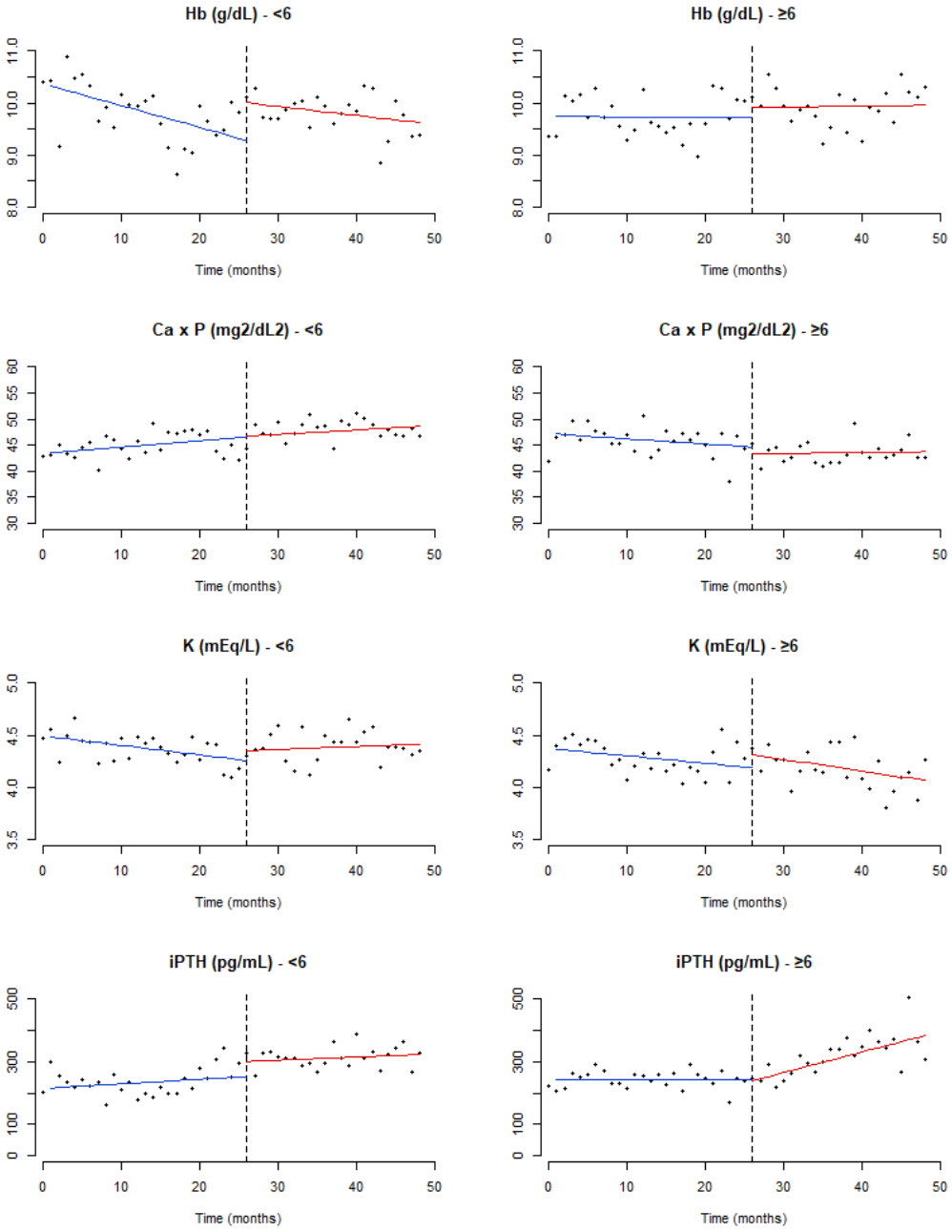

Figure 15. Impact on lab test results: ITS analyses (PD duration)

3. Cost-utility analysis

(1) Base-case analysis

Table 32 summarizes the results of a cost-effectiveness analysis for the PD home care program. In the base-case analysis (Scenario 1) with the annual discount rate of 4.5% for both cost and effectiveness, the QALYs for the usual care and home care groups were 7.015 and 7.535, respectively, while the total costs were KRW 247,773,231 and KRW 250,151,127, respectively. With the WTP threshold of KRW 40,043,036 in this study, the ICER was calculated as KRW 4,571,500 per QALY (USD 3,874 when converted using the 2020 exchange rate of KRW 1,180.01 per one USD) which is in the range of the WTP threshold. INMBs were represented to be KRW 18,450,757 (USD 15,636). In Scenario 2 (changes in probabilities from PD to peritonitis), the ICER and INMB were calculated as KRW 4,009,978 and KRW 15,864,731 with the changes in both cost and QALY, respectively. When cost differed in Scenario 3, the ICER slightly increased to KRW 5,601,567. In Scenario 4, when the utility values differed, the ICER was KRW 4,834,818. The results of the base case analyses were in the range of the WTP threshold (KRW 40,043,036) which means that the home care intervention group is a relatively more cost-effective strategy than the usual care group.

Table 32. Base case analysis

(Units: KRW, QALY)	Cost	ΔCost	Effectiveness	ΔEffectiveness	ICER	NMB	INMB
Scenario 1							
Usual care	247,773,231	2,377,896	7.015	0.520	4,571,500	33,112,070	18,450,757
Home care	250,151,127		7.535			51,562,827	
Scenario 2							
Usual care	248,158,633	1,765,524	7.065	0.440	4,009,978	34,743,913	15,864,731
Home care	249,924,157		7.505			50,608,644	
Scenario 3							
Usual care	256,145,692	2,913,693	7.015	0.520	5,601,567	24,739,609	17,914,960
Home care	259,059,385		7.535			42,654,569	
Scenario 4							
Usual care	247,773,231	2,377,896	7.089	0.492	4,834,818	36,075,930	17,316,369
Home care	250,151,127		7.580			53,392,299	

Descriptions: Scenario 1 (Base case), Scenario 2 (probability changes), Scenario 3 (cost changes), Scenario 4 (utility changes).
Abbreviations: QALY (quality-adjusted life years); ICER (incremental cost-effectiveness ratio); NMB (net monetary benefit); INMB (incremental net monetary benefit).

(2) Sensitivity analysis

A. Deterministic sensitivity analysis (DSA)

(A) One-way sensitivity analysis

To examine the uncertainty and identify which parameter impacted the results the most, a one-way sensitivity analysis was performed in two ways. For the ICER outcome measure, the most sensitive parameter was the cost of PD home care and PD usual care in every scenario (Figure 16 and Figure 17), but this was considered to be less impactful since the ranges are under our WTP threshold (KRW 40,043,046). In Scenario 3, however, the results show that the ICER would exceed the WTP threshold when the cost of PD (home care) is higher than KRW 32,289,300 or that of PD (usual care) is below KRW 24,801,014.

For the INMB measure, the costs of PD (home care) and PD (usual care) were also sensitive, and the utility of PD (home care) and PD (usual care) were critical (Figure 18 and Figure 19). Except for Scenario 3 (costs of PD (home care) and PD (usual care)), all parameters were in the range of INMB > 0 criteria.

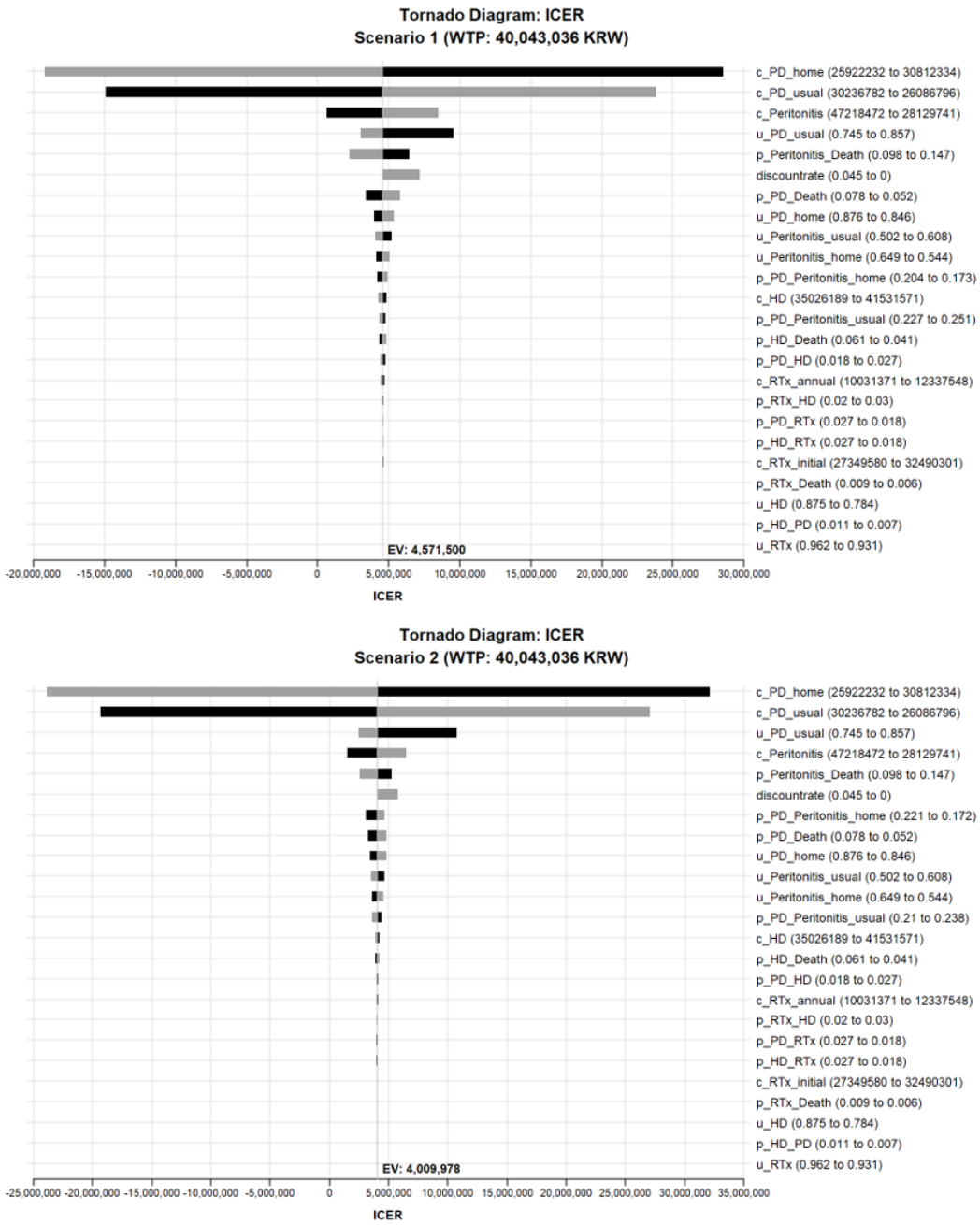

Figure 16. One-way sensitivity analysis (ICER) – Scenarios 1 &2

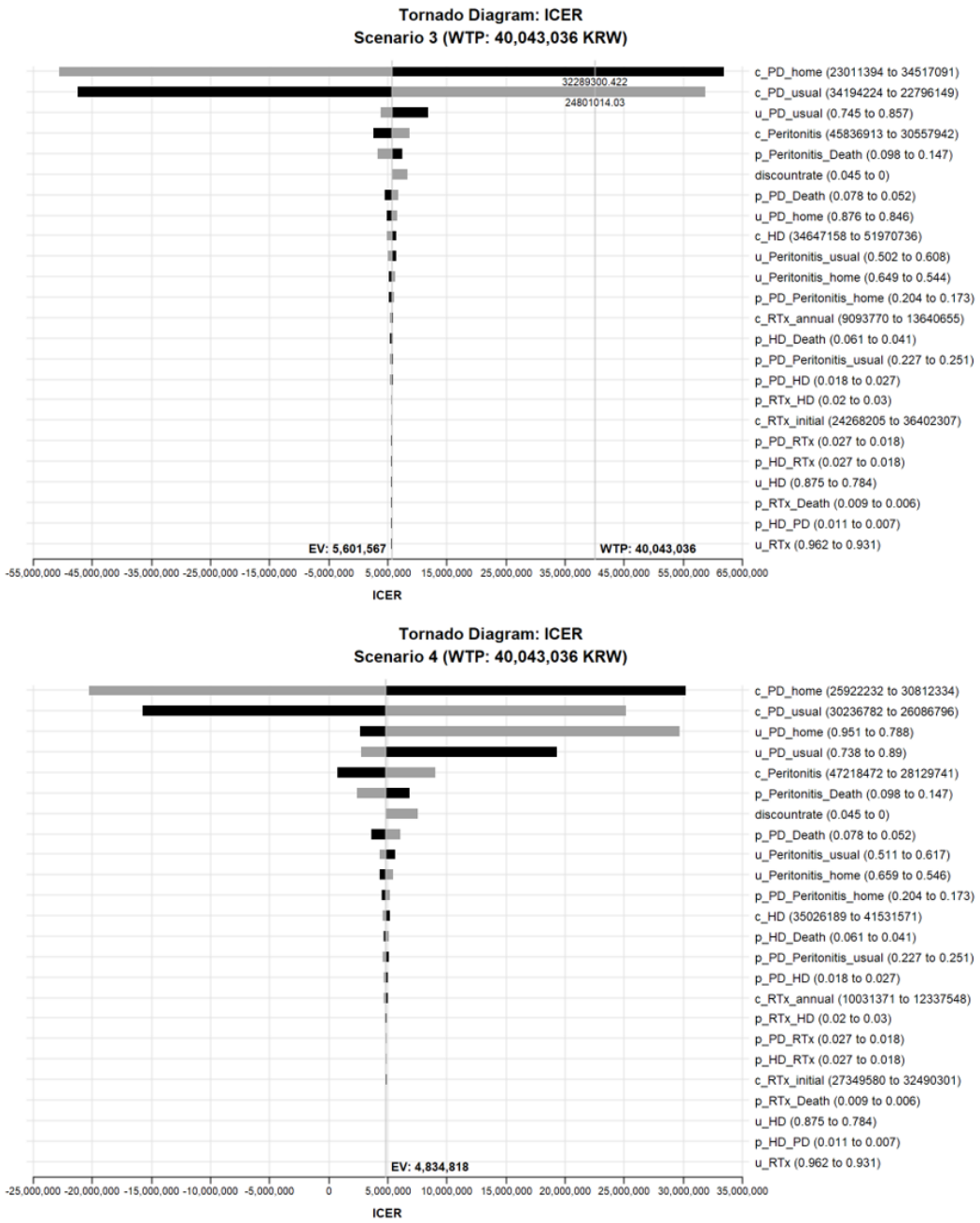

Figure 17. One-way sensitivity analysis (ICER) – Scenarios 3 & 4

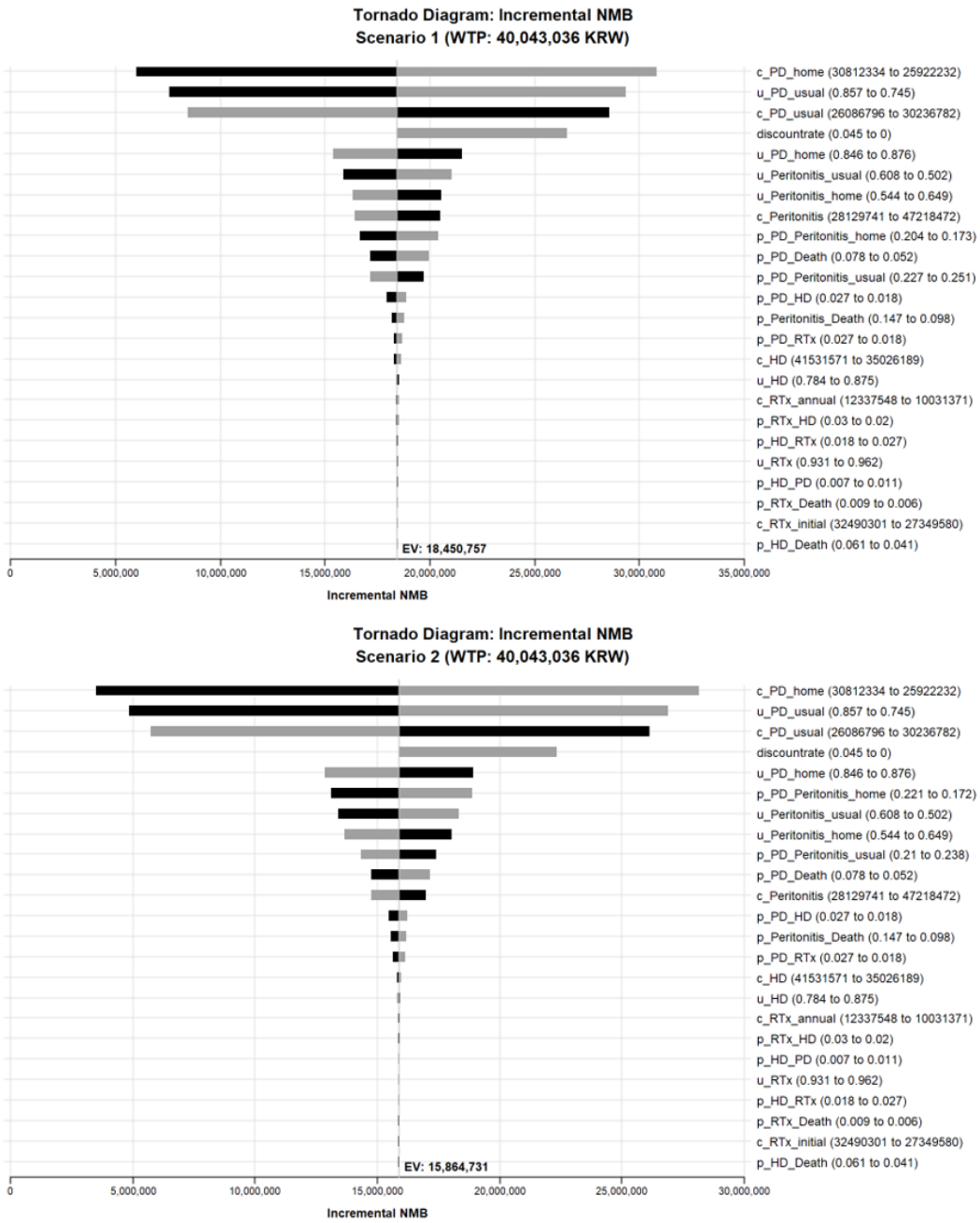

Figure 18. One-way sensitivity analysis (INMB) – Scenarios 1 &2

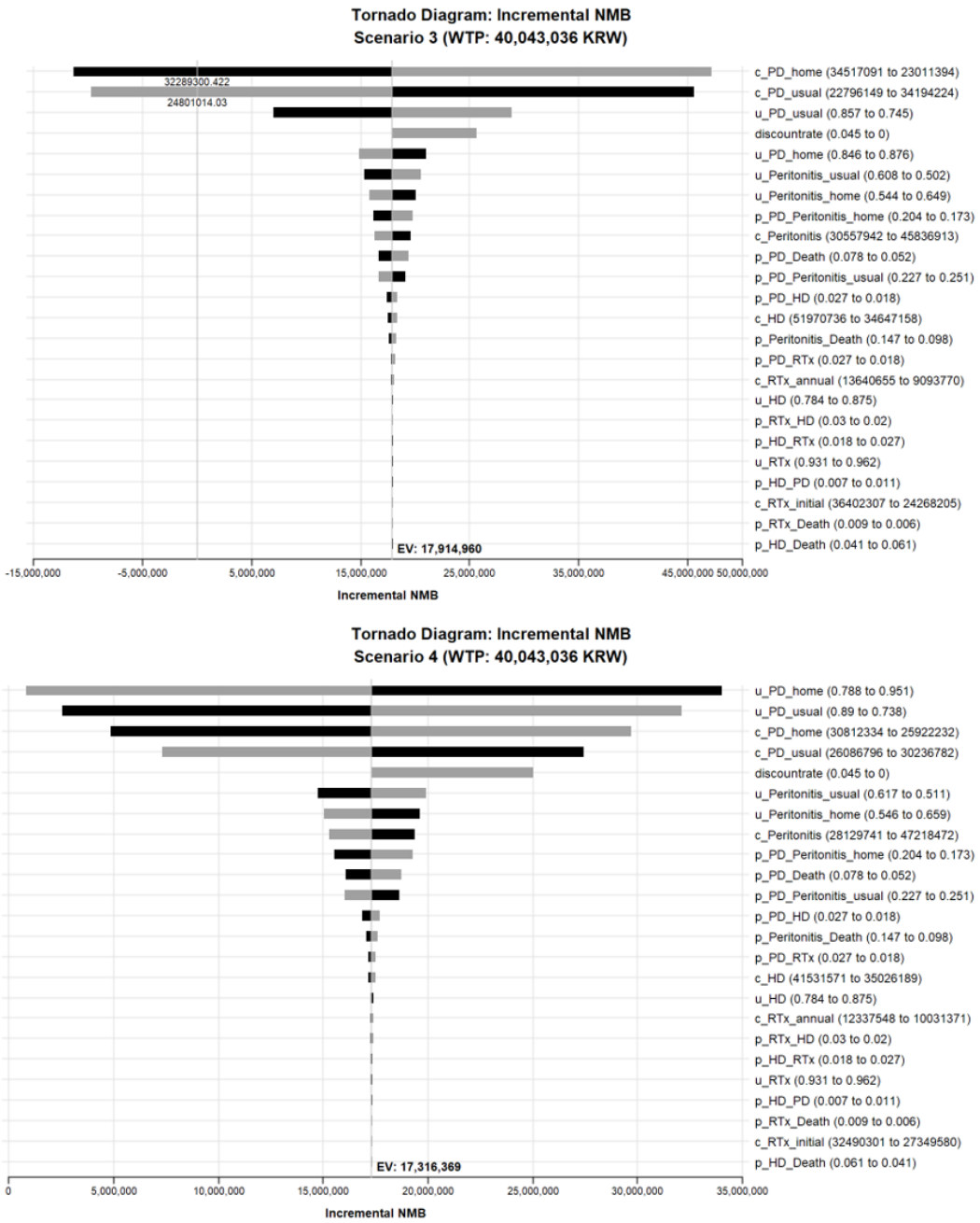

Figure 19. One-way sensitivity analysis (INMB) – Scenarios 3 & 4

(A) Two-way sensitivity analysis

We identified that the two most impactful parameters on the ICER results are the costs of PD (home care) and costs of PD (usual care) from the one-way sensitivity analysis. To demonstrate how the cost-effectiveness outcomes depend on the two parameters, we conducted a two-way sensitivity analysis by changing the range of both variables at the same time (Figure 20 and Figure 21).

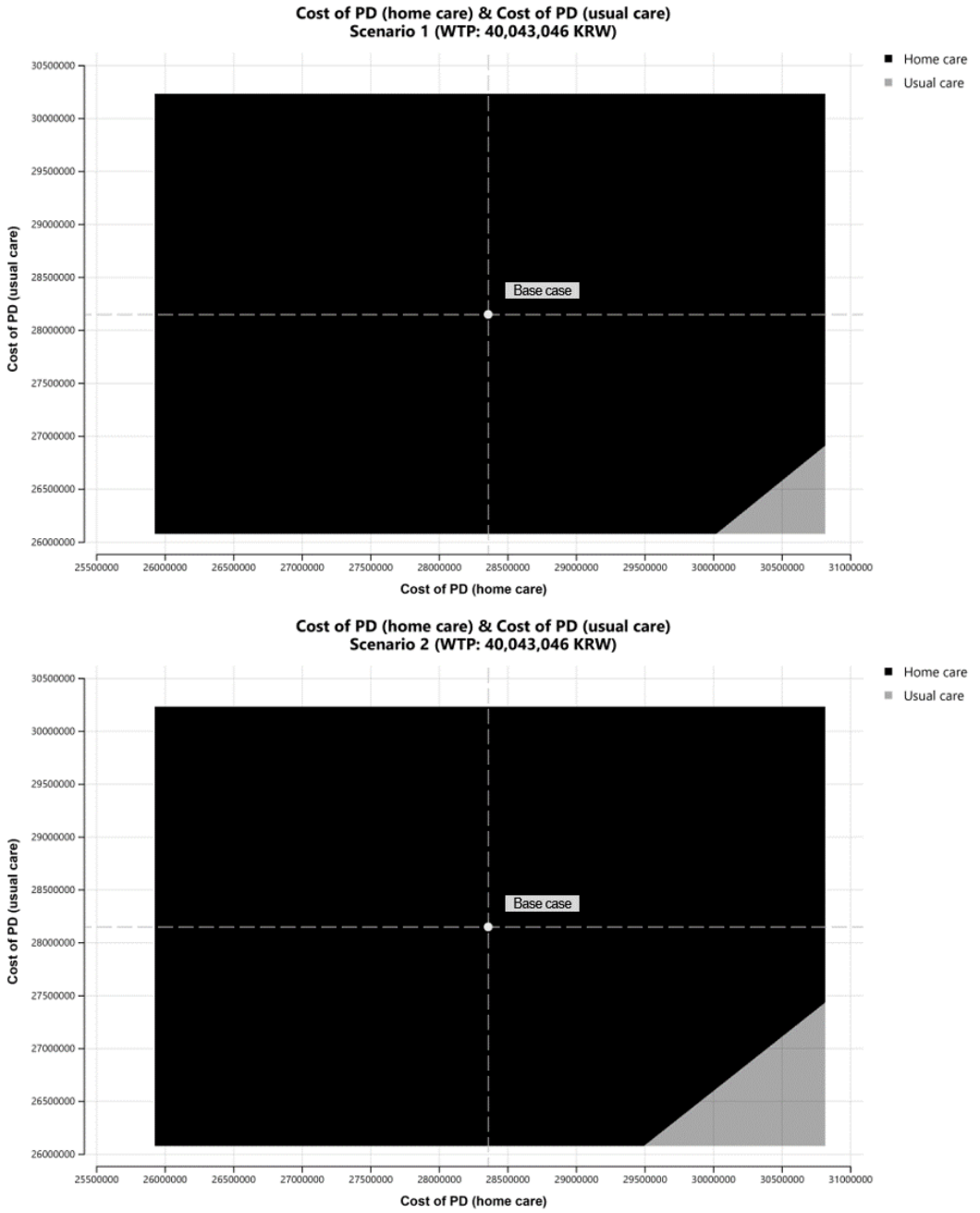

Figure 20. Two-way sensitivity analysis – Scenarios 1 & 2

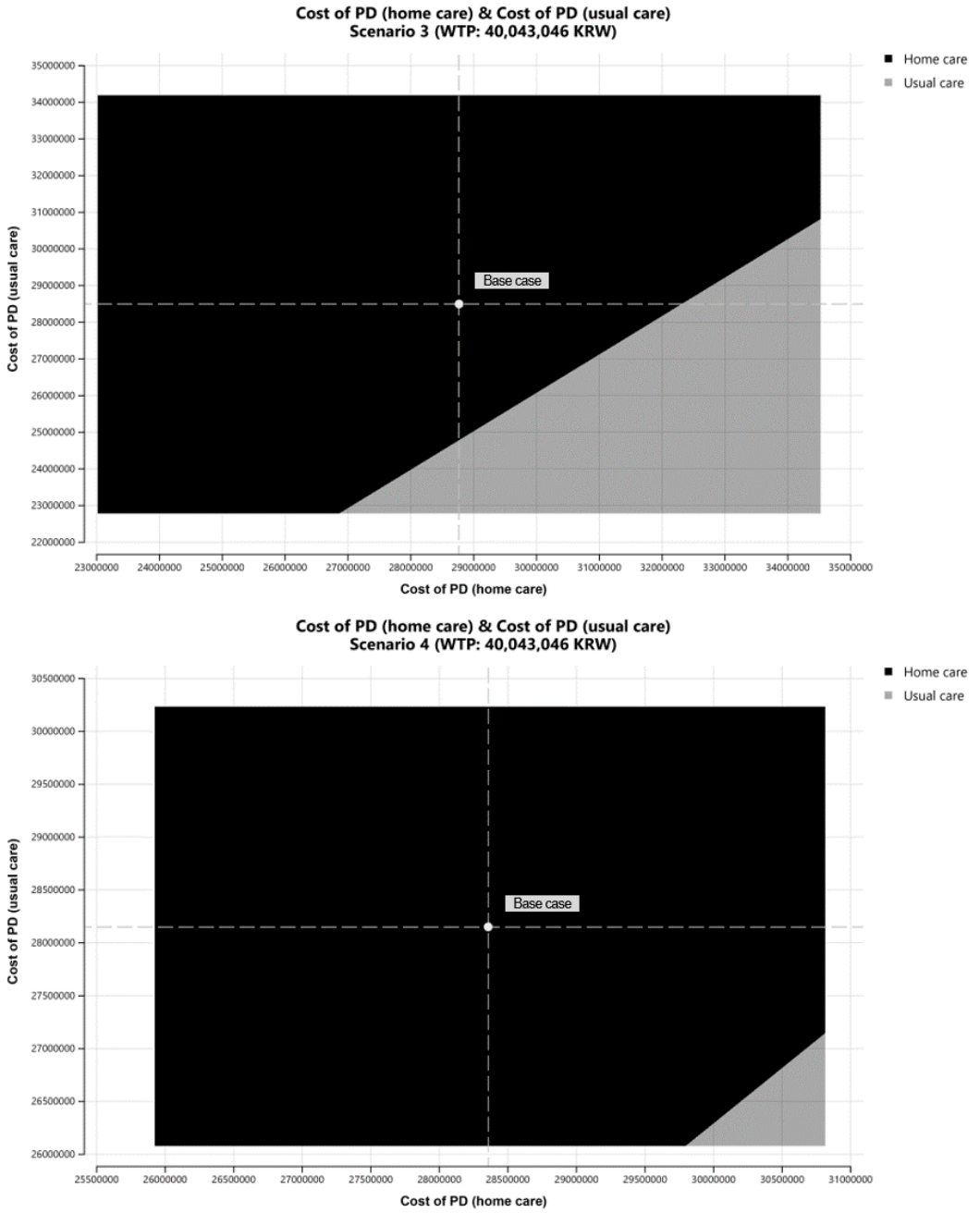

Figure 21. Two-way sensitivity analysis – Scenarios 3 & 4

B. Probabilistic sensitivity analysis (PSA)

For the Monte Carlo simulation (10,000 iterations), we presented the results of PSA as incremental cost-effectiveness (ICE) scatterplots and a cost-effectiveness acceptability curve (CEAC). Figure 22 and Figure 23 shows the ICE scatterplot when the WTP threshold was KRW 40,043,036 per QALY. The home care group was the overall optimal strategy, with the probabilities of 62.05% in Scenario 1, 59.95% in Scenario 2, 61.70% in Scenario 3, and 89.41% in Scenario 4.

The CEAC graphs in Figure 24 and Figure 25 describes the probabilities of certain strategies being optimal when WTP changes. With the WTP threshold of KRW 40,043,036 per QALY in our study, we already identified the probabilities of the home care group being optimal in the ICE scatter plot results. Rather, we evaluated the WTP threshold where the probabilities of the home care group were optimal to be above 50%: KRW 7,380,000 in Scenario 1, KRW 4,725,000 in Scenario 2, KRW 6,760,000 in Scenario 3, and KRW 6,020,000 in Scenario 4.

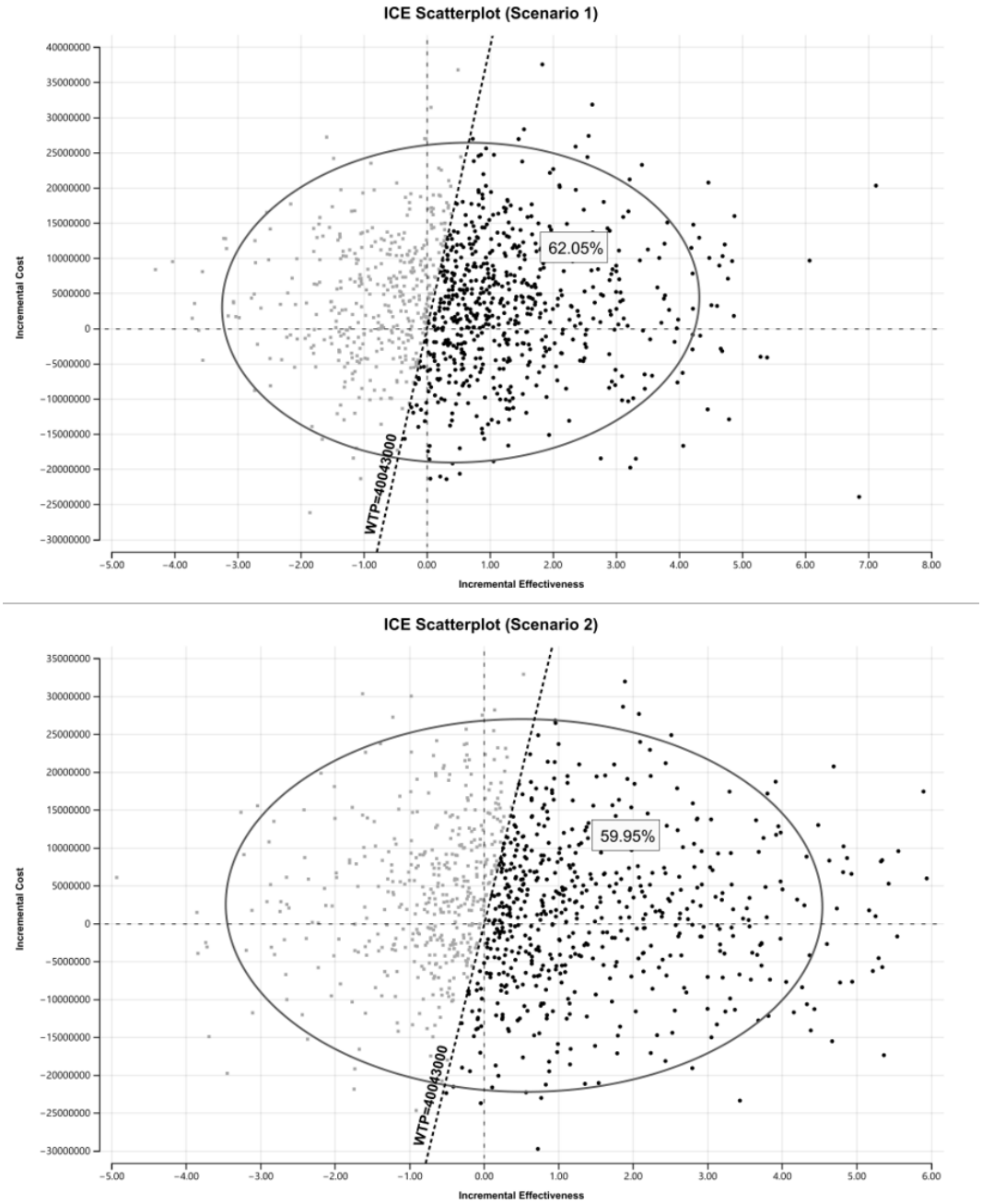

Figure 22. ICE scatterplot – Scenarios 1 & 2

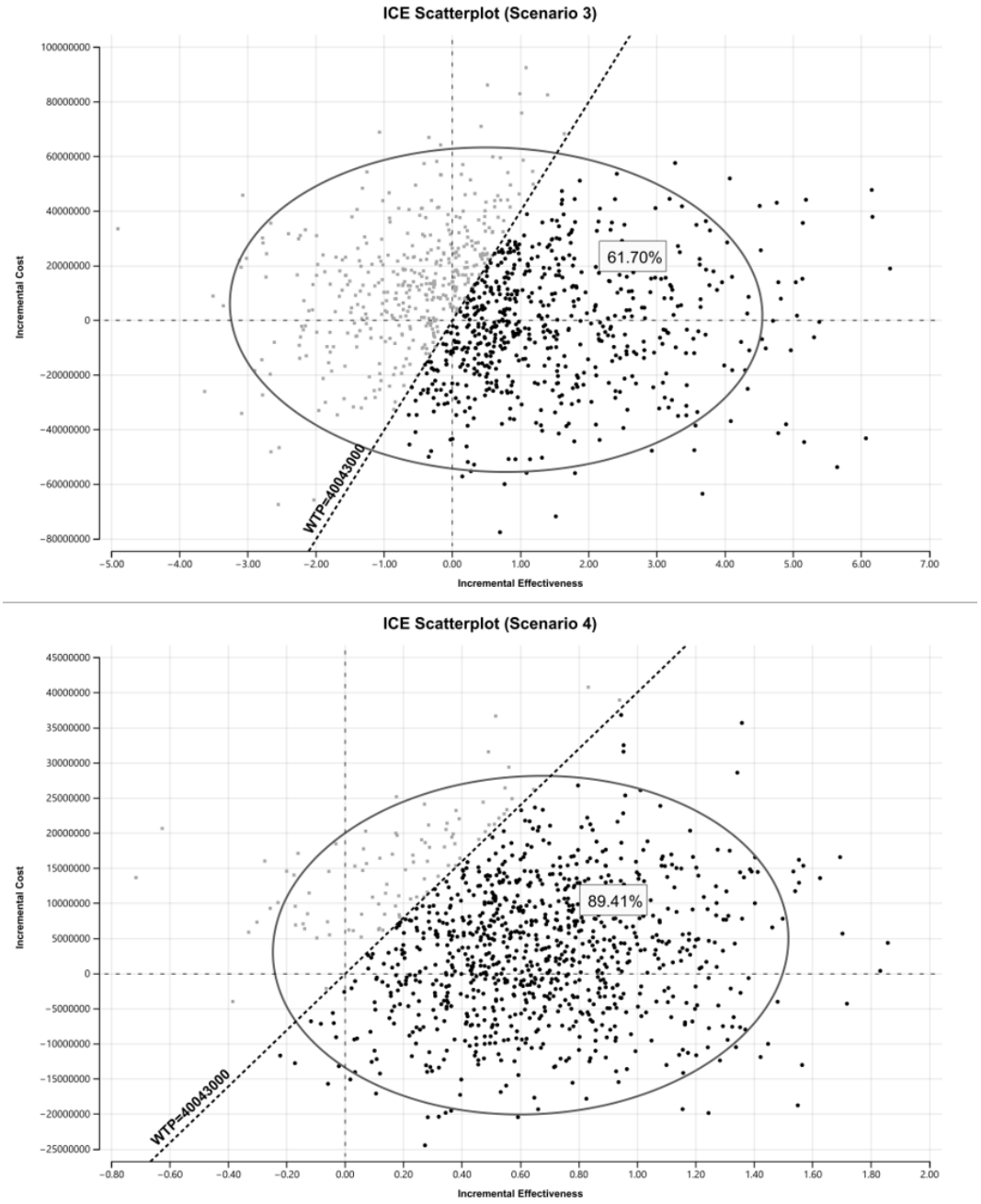

Figure 23. ICE scatterplot – Scenarios 3 & 4

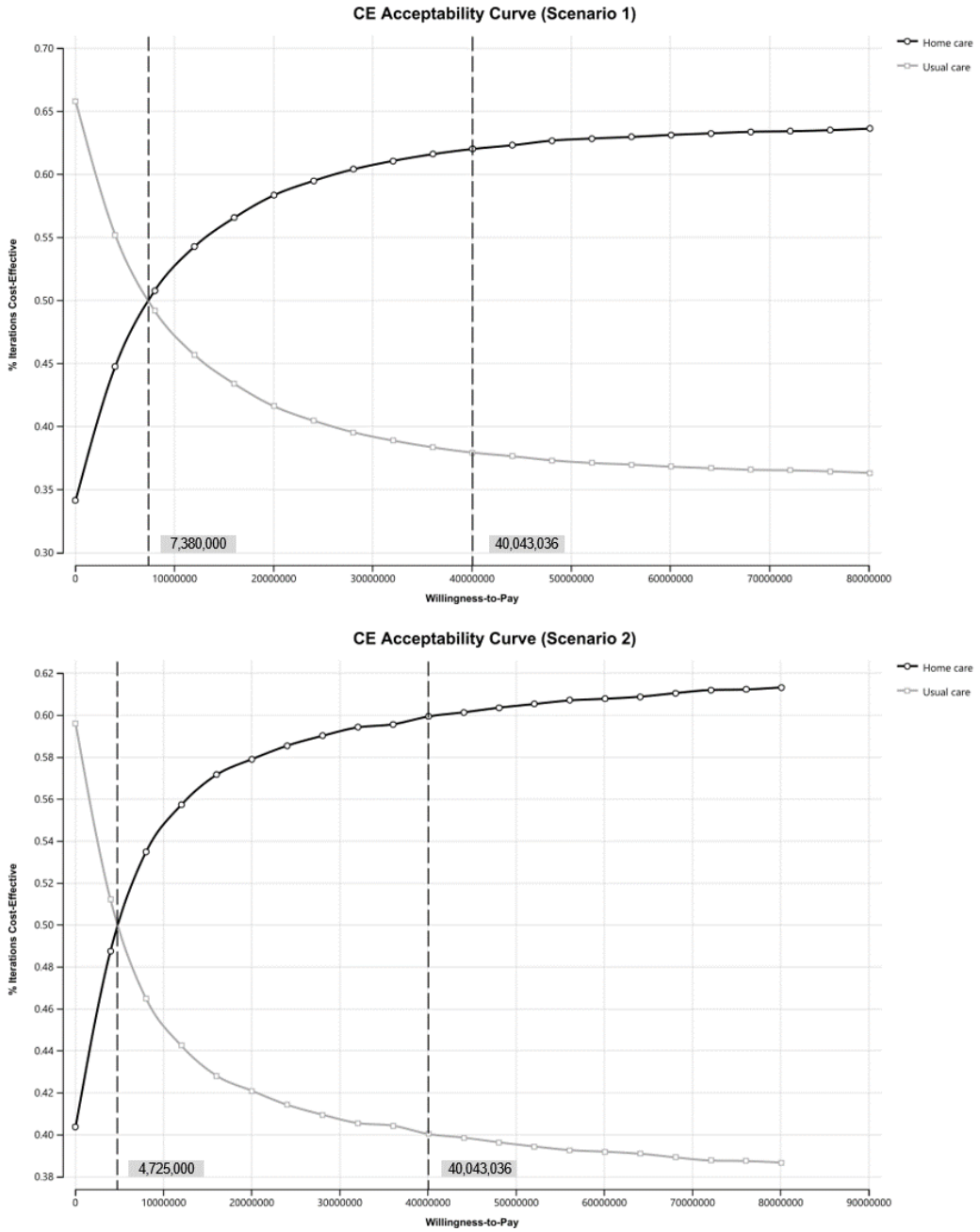

Figure 24. Cost-effectiveness acceptability curve – Scenarios 1 & 2

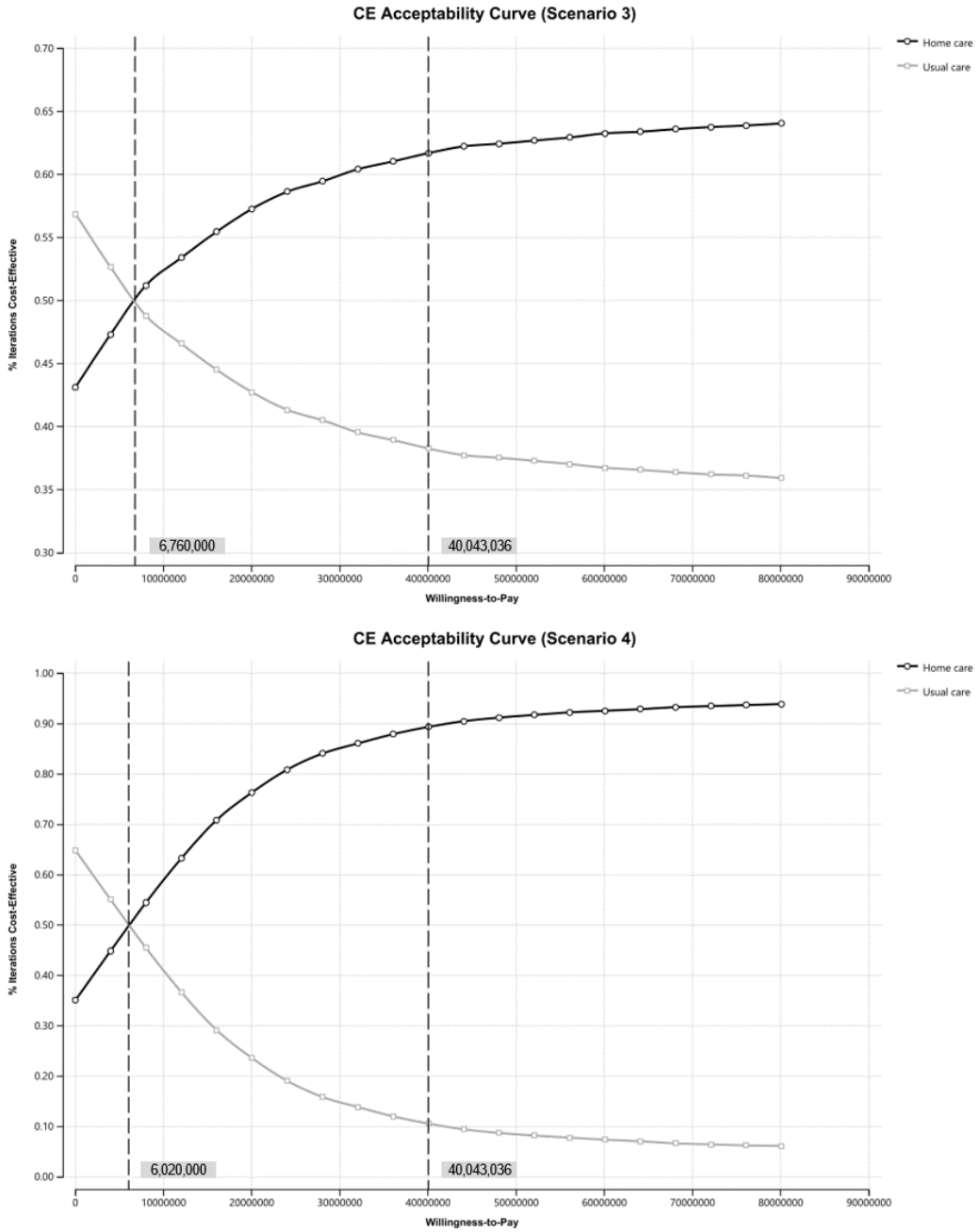

Figure 25. Cost-effectiveness acceptability curve – Scenarios 3 & 4

C. Value of information analysis – The expected value of perfect information (EVPI)

Finally, EVPI was measured to identify the net benefit when perfect information was given without any uncertainty. We chose net monetary benefit to present the results rather than net health benefit to clarify the monetary impacts of the home care program. For Scenarios 1, 2, and 3, an additional KRW 14,818,960, KRW 15,218,841, and KRW 16,229,695 per patient can be gained, respectively, when the information is perfect and the parameters have no uncertainty. In Figure 26, we demonstrated the probabilities of the home care group being cost-effective, and Scenario 4 showed the highest probability (89.41%), which also expressed that we already got nearly perfect information for decision-making in Scenario 4. With a high rate of certainty, the EVPI in Scenario 4 was the lowest among the four scenarios; that is, an additional KRW 891,048 per patient can be gained once perfect information is provided (Figure 26).

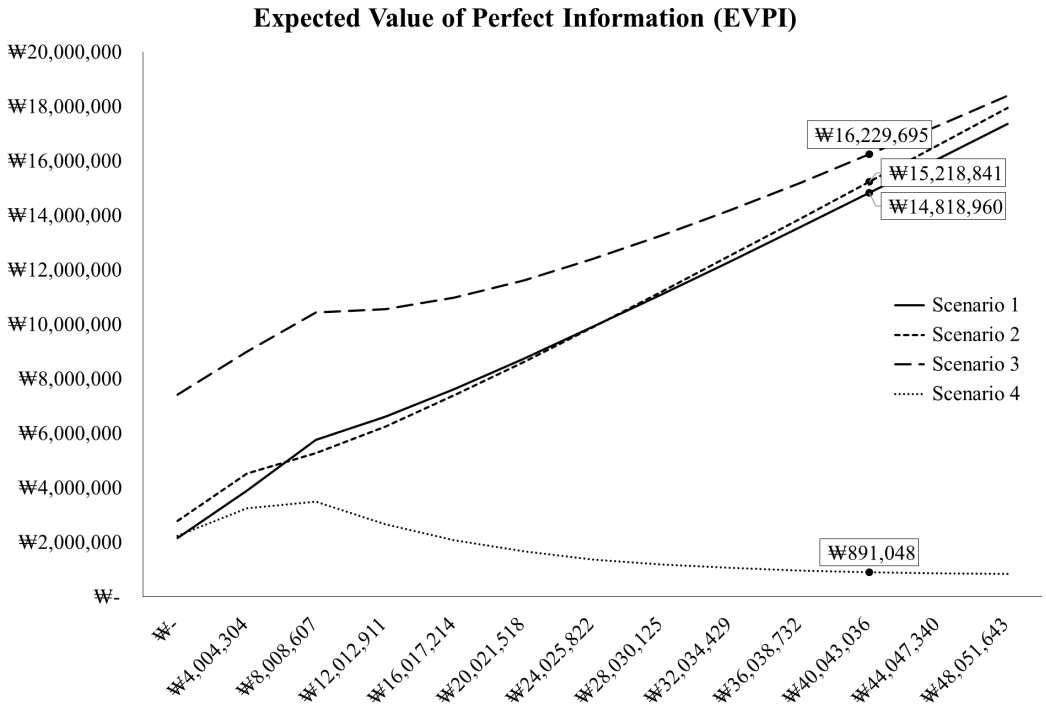

Figure 26. The expected value of perfect information

V. Discussion

1. Study Methods

With the increasing interests of implementing digital health (1, 65, 66), our study offers the evidence justifying the clinical effectiveness of adopting digital health services in an analysis of a PD home care program. To follow up on potential complications in PD patients, we used long-term (five-year) hospital data to examine the clinical effectiveness of the home care program. Since one of the major concerns of PD patients when choosing PD modality was the complications (25), we analyzed any changes in the incidence of peritonitis after adopting home care program using long-term data. Also, we evaluated the clinical laboratory test results which are accumulated when patients visit hospital every 2-month, because the changes in some value can be interpreted as the effectiveness of improved self-care. This enabled us to demonstrate the trend of clinical outcome changes in PD patients using ITS analyses and the proportion of patients achieving the clinical target range. In here, the results of ITS analyses should be cautiously interpreted. We used the hospital data in an aggregate-level to observe the overall changes in incidence of peritonitis over 4-year, not an individual patient level. Also, the number of populations in each (monthly) time point varies; keep decrease over time (Appendix Table 3). When calculated the 1-year cumulative incidence to compare pre-homecare and post-homecare, we measured the area under parsimonious regression model.

Markov models are widely used in nephrology studies (20-22, 39, 40), but they are not often combined with digital health. We constructed a Markov model to investigate the lifetime cost-effectiveness of the home care program for the first time in Korea. Although our study is a Markov model-based economic evaluation, we used clinical outcomes derived from long-term hospital data to blend the advantage of model-based and trial-based economic evaluation. In this study, we tried to utilize accurate clinical and costs data. The utility of the PD (home care) health state was measured and calculated from an EQ-5D survey of 402 Korean PD patients participating in the home care program. It was the first time the utility of the home care program (including face-to-face educational consultation and remote monitoring such as text messaging or phone calls) was measured and it is expected to be widely used in further cost-effectiveness studies. Also, when collecting healthcare utilization data (e.g., the number of outpatient visits, hospitalizations, etc.), we referred to the national level HIRA data (25) collected based on reimbursed medical services in Korea.

With the uncertain nature of economic evaluation, we tried to evaluate the outcomes besides the base case analysis. First, we made four scenarios by changing the main parameters in transition probabilities, utilities, and costs. Using four scenarios, we could identify the changes in results when certain parameters were altered. Also, we performed sensitivity analysis via DSA and PSA. This enabled us to interpret which parameter was the most sensitive and how the outcomes differ when the distributed variables are randomly chosen. Finally, to identify the net benefit when perfect

information is provided, we performed a value of information analysis via EVPI. For the cost-utility analysis in this study, we referred to the recently updated Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 checklist in planning and conducting the economic evaluation.

2. Study Results

(1) Clinical effectiveness analyses

The Health Insurance Review & Assessment Service (HIRA) in Korea conducted a study (25) to identify the short-term effectiveness of the home care program. Our study continued this research to determine its long-term effectiveness and found that the home care program helped maintain or improve both the incidence of peritonitis and the percentage of those reaching the target range of clinical laboratory test results. Especially, in a subgroup of females, aged populations, and those with longer PD vintages showed significant improvement after a home care program. ESRD patients have 2.6 to 3.2 times higher risk of cognitive impairment than non-ESRD populations (67). That is, those who are aged and have longer PD vintages need education regarding dialysis and nutrition and exercise guidelines. The remote home care program became a great advisor for PD patients not to forget the crucial steps when conducting dialysis and fulfilled the medical gaps between regular hospital visits.

The percentage subjects reaching the iPTH target range was the only clinical laboratory result that decreased after home care program implementation. This may be because iPTH keeps rising due to secondary hyperparathyroidism in ESRD patients when PD vintages get longer (68, 69). Previous studies indicate that 47% of PD patients had abnormal iPTH levels (514.9 pg/mL on average), a high prevalence of hyperparathyroidism, and increasing iPTH during follow-up (70). Also, even with

increasing iPTH, the changes in our data (a 15.7% increase from 242.0 to 287.0 pg/mL) are considerable compared with a previous study (71) that followed the iPTH trends over two years (a 64.4% increase from 94.3 to 264.0 pg/ml). Finally, there were huge individual variations in iPTH (pg/mL) levels. There was a mean (SD) of 242.0 (191.0) in the pre-homecare group and 287.0 (220.0) in the post-homecare group (Appendix Table 4). The aggregated data should be considered individually. If iPTH increases, other clinical parameters should worsen as well, but our data showed these values were maintained (Ca x P and K) or even improved (Hb) from the initial value. Despite the nature of iPTH described above, other parameters are manageable with the home care program by educating and reminding PD patients about the dialysis and guidelines for nutrition and exercises. It is recommended to execute further studies comparing the home care and usual care group, so able to demonstrate the impact on the outcomes of iPTH.

(2) Cost-utility analysis

There are many economic evaluation studies regarding RRT (20-22, 39, 40) or digital health solutions (72), but the study for PD patients in home care program as a digital health is quite meaningful. When performing economic evaluation to identify the relatively cost-effective alternative, it is optimal when the cost takes less than the alternatives with higher effectiveness. But in general cases, both effectiveness and costs are increased in the intervention group; so, we should identify whether the incremental cost is allowable compared to the incremental effectiveness. With a WTP threshold of KRW 40,036,043, the ICER results of a cost-utility analysis were less than the WTP threshold, which means that the home care program was more effective than anticipated. Also, the results from sensitivity analysis in four scenarios indicate that the home care program has a high probability of being an optimal strategy among several alternatives. The costs for PD (home care) and PD (usual care) were sensitive which may change the results of cost-effectiveness. But considering that we've used the cost data in a tertiary care hospital, the costs for PD patients may not be higher than our cases; when compared with the average Korean PD patients data (25), our cost data was 30.4% higher. This is the reason why we expect the results of cost-effectiveness may not change even with the changes in cost data. Prior to conduct the home care program, the expected medical costs must be identified and the uncertainty of information should be unveiled for additional net benefits on EVPI.

(3) Implications

Clinical Implications

After the COVID-19 pandemic, New York City health officials started telehealth visits for home dialysis patients using Zoom for Healthcare or FaceTime. Especially for PD patients, they used a remote patient management platform and home dialysis nurses visited patients' homes if needed (such as for requiring blood samples) (7). Unlike these non-billable medical services, Korea's home care program can be reimbursed. Based on 2020 satisfaction surveys (N = 398) on our home care program (25), 97.6% of APD[6] and 100% of CAPD patients were satisfied with the medical staff's early detection of concerning symptoms, and the majority wished to continue the home care program (93.7%).

Our study indicates the clinical effectiveness of this home care program, but it is unclear how best to reinforce its service contents and system. To improve patient self-care behavior, an integrated and patient-centered monitoring app containing bidirectional messengers and data management functions can motivate PD patients (73) to manage their diseases by themselves and enhance medical staff productivity at the same time. CAPD requires a high level of self-management, while APD automatically transfers medical data from the patient's home to staffs. Educational content must be updated

6 APD (automated peritoneal dialysis)

regularly and used to remind PD patients about lifestyle guidelines.

Many digital health solutions are preparing for the post-pandemic world (74), and remote monitoring care from medical staffs is necessary for PD patients who require integrated self-care management for entire lifetime. The key question for adopting the RPM technologies for PD patients was whether it can help reduce the rates of technique failure, which mainly occurs due to peritonitis (24). Since we found out that the home care program helped reduce the incidence of peritonitis, the home care program is meaningful for ESRD patients. The informed decision making is also feasible when choosing their RRT types.

Further attention is needed when applying digital health solutions in an aged population, as they may struggle with digital technologies, including a lack of confidence/experiences in e-health, struggles using a small screen and text, and troubleshooting issues (75). But when digital health resources are limited, it is recommended to focus on females, older individuals, and those with a longer PD vintages group, as these individuals demonstrate compliance and improvement after the home care program in our study. Older individuals are often motivated to learn and confident when they receive dedicated support (75).

Managerial Implications

The frequency of healthcare utilization changed after the home care program, including an increased number of outpatient visits and decreased hospitalizations and the

length of stay (25). The number of outpatient visits has increased, even during the COVID-19 pandemic, which is anticipated due to the early detection of any symptoms during the home care program. This may potentially lead to a decrease in the total healthcare expenditures and may allow medical staff to focus more on other medical services.

In the value of information analysis, we found improved net benefits by resolving uncertainty, when additional evidence is given. Especially, the transition probabilities from PD to peritonitis states in Scenario 2 and costs in Scenario 3 were the two most impactful parameters in the ICE scatter plot results. It means that the cost-effectiveness of the home care program can be increased by managing the incidence of peritonitis and its costs. Since we can establish patient management plans based on the ultimate value of each parameter derived from this study, hospitals can use this to decide whether to start a home care program and which patients to target first when resources are limited.

Considering that the results of the cost-utility analysis were the ICER of KRW 4,571,500 per 1 QALY which is just about 11.4% of the WTP threshold of KRW 40,036,043 (equals to 1 GDP), the home care program requires a small budget to bring about positive outcomes. In the hospital, we can utilize our limited human resources more effectively by remotely managing PD patients and potentially reducing their healthcare utilization by preventing predictable events. In the communities, the responsibilities of the home care program should be expanded, as it is potentially cost-effective when used with advanced digital health technologies.

3. Limitations

This study has several limitations, so it should be cautiously interpreted. First, the clinical effectiveness analyses in this study used data from a single tertiary care hospital. Our data includes only 186 individual PD patients which may not reflect the demographics of PD patients in Korea. Also, we need to consider the nature of a tertiary care hospital and interpret cautiously; the characteristics of PD patients are more severe than others, leading to higher healthcare expenditures and worse clinical outcomes. Also, the hospitals may have sufficient medical staff and high-quality infrastructures, enabling us to provide a home care program without supplementing any additional resources.

Second, we could not set the control group not involved in the home care program since every PD patient in our center was enrolled in the program. Thus, we could not compare the differences between the two groups, but rather we compared the pre-homecare and post-homecare groups in a single-arm pre-post study design. As we mentioned in the discussion for study results, the outcomes for iPTH couldn't be compared with non-homecare group but just interpreted its anticipated meanings from previous studies. Further studies are needed to prove the real effectiveness of home care program in the results of iPTH. This may also include several limitations, such as unnoticeable interruptions like the COVID-19 pandemic, that may affect the results.

Third, there are many assumptions and uncertainties associated with collecting parameters to conduct a cost-utility analysis. In the *overall analysis*, when we mixed our

clinical data and data from several other studies, each parameter had a different study population, which may not reflect the real world. In the *transition probability* parameters, we used our hospital data to collect probabilities from the PD to peritonitis states. Although we analyzed the one-year cumulative incidence of peritonitis from ITS analyses, these were estimated values. As our clinical analysis is a pre-post study design, the home care group and usual care group in the cost-utility analysis corresponded to the post-homecare and pre-homecare groups, respectively, in the clinical effectiveness analyses. In the *utilities* measure, we calculated EQ-5D from a survey conducted on PD patients who participated in the home care program. Since this outcome excludes the PD patients who are in the usual care group, we could not compare the difference of utilities between the home care and usual care groups, but had to refer to the utility value of PD (usual care) from a previous study. For the *costs* data, we extracted PD medical costs from our hospital data, which may be considered high, so it may not reflect the average value in Korea. But considering that the home care program is performed in tertiary care and general hospitals, the medical costs may not differ all that much. There may be some uncertainties when executing with the *limited societal perspective*. We only included patients' time costs to measure productivity loss, but further studies are needed to calculate the productivity loss using Work Productivity and Activity Impairment (WPAI) index or Health and Labour Questionnaire (HLQ) (47, 76).

Lastly, we used a Markov chain model when conducting the cost-utility analysis based on the memoryless property of Markov model. A model can be built that can

remember the previous health state (where this patient came from). This kind of Markov process model would need additional clinical data, such as the peritonitis mortality rate depending on the number of people who were developing infections.

Despite of the mentioned limitations, this study is meaningful as we demonstrated the clinical and cost-effectiveness of the PD home care program in Korea for the first time. Considering that we examined using the tertiary care hospital data which led to the high medical costs and low incidence of peritonitis, the cost-effectiveness of the PD home care program may be increased in the real-world circumstances. Other than a few assumptions and data collected from published studies, the majority of parameters used in this study were derived from accurate national-level data or individual hospital data. Several sensitivity analyses were also conducted to track any possibilities of different outcomes, but identified to be obvious that the home care program for PD patients is expected to be cost-effective in any scenarios.

VI. Conclusions

This study evaluated the clinical and cost-effectiveness of a home care program for PD patients in Korea for the first time. We demonstrated the clinical effectiveness using long-term clinical data and discovered that the program reduced the incidence of peritonitis and improved/maintained laboratory test results. Then we established the lifetime Markov model and identified the cost-effectiveness with the results of ICER which was under the WTP threshold.

Therefore, with the social needs of remote medical services after COVID-19 pandemic, our study has proved that conducting a home care program for PD patients is clinically effective and has the potential to be cost-effective. With meaningful clinical and social implications, there is no doubt in implementing the home care program but decide how to effectively operate and expand the program. Further study is needed to develop the ultimate system and methods to run a home care program more effectively using advanced digital technologies.

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Appendix

Appendix Table 1. Background mortality

Age	Cycle	Mortality	Age	Cycle	Mortality
50	0	0.0020	76	26	0.0233
51	1	0.0022	77	27	0.0243
52	2	0.0024	78	28	0.0323
53	3	0.0025	79	29	0.0303
54	4	0.0027	80	30	0.0356
55	5	0.0032	81	31	0.0453
56	6	0.0033	82	32	0.0474
57	7	0.0033	83	33	0.0544
58	8	0.0042	84	34	0.0633
59	9	0.0039	85	35	0.0717
60	10	0.0046	86	36	0.0787
61	11	0.0046	87	37	0.0878
62	12	0.0050	88	38	0.1041
63	13	0.0056	89	39	0.1111
64	14	0.0058	90	40	0.1268
65	15	0.0067	91	41	0.1454
66	16	0.0071	92	42	0.1566
67	17	0.0075	93	43	0.1702
68	18	0.0092	94	44	0.1803
69	19	0.0088	95	45	0.2200
70	20	0.0109	96	46	0.2264
71	21	0.0124	97	47	0.2576
72	22	0.0130	98	48	0.2620
73	23	0.0149	99	49	0.2682
74	24	0.0153	100+	50+	0.2772
75	25	0.0164			

Appendix Table 2. Consumer price index

Year	Overall	Healthcare	Transportation
2000	63.15	71.00	70.87
2001	65.72	79.08	73.67
2002	67.53	78.64	74.40
2003	69.91	80.40	77.40
2004	72.42	81.56	80.11
2005	74.41	83.36	84.13
2006	76.08	85.00	88.02
2007	78.01	86.48	91.15
2008	81.66	88.15	99.17
2009	83.91	90.06	95.66
2010	86.37	91.64	100.35
2011	89.85	93.25	107.37
2012	91.82	94.11	110.85
2013	93.01	94.44	110.27
2014	94.20	95.11	108.50
2015	94.86	96.30	99.99
2016	95.78	97.25	97.78
2017	97.65	98.11	101.28
2018	99.09	98.06	103.73
2019	99.47	98.52	101.87
2020	100.00	100.00	100.00

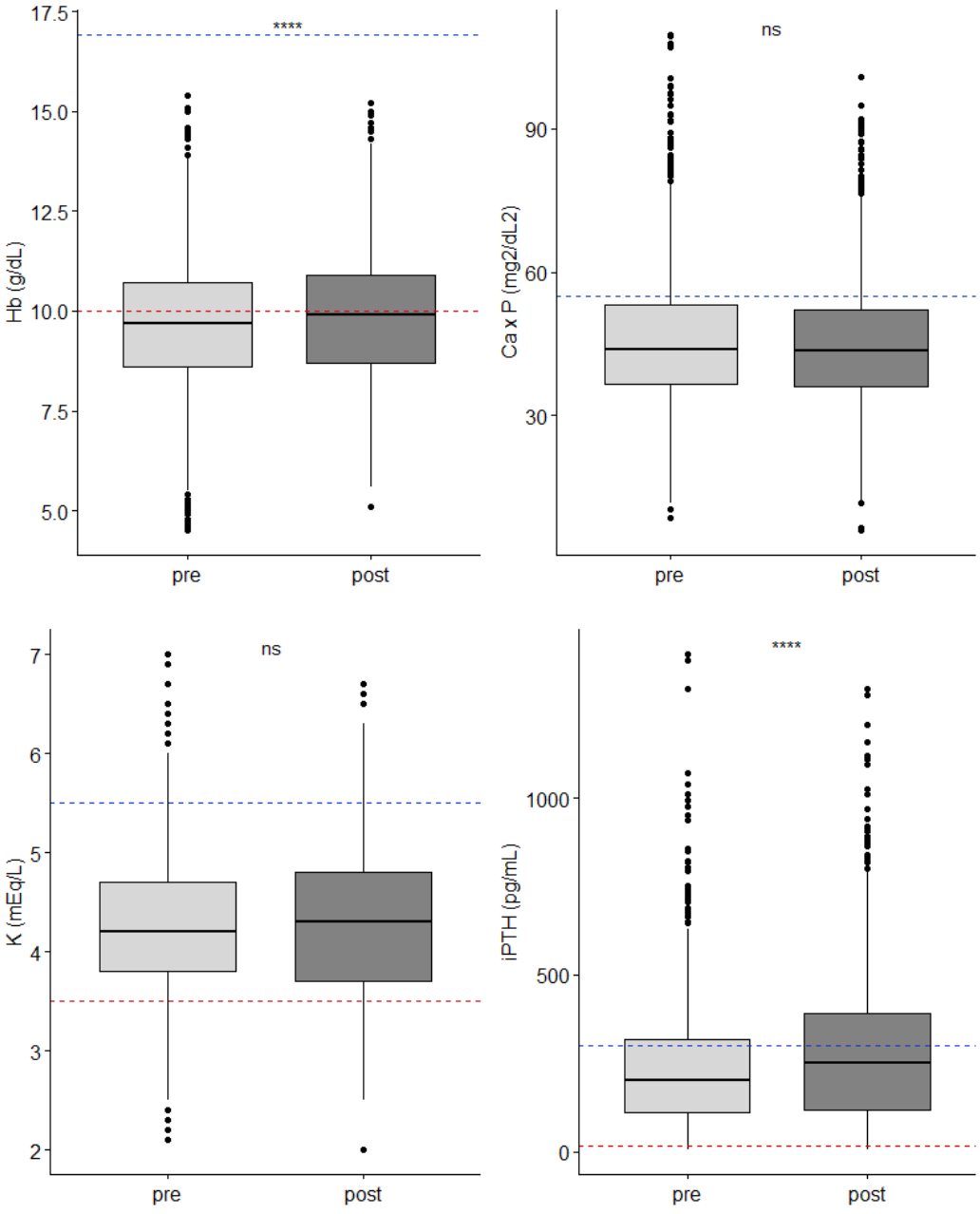
Reference: Korean Statistical Information Service (77)

Appendix Table 3. Dataset for ITS analyses

Time (month)	N	Peritonitis	Time (month)	N	Peritonitis
0	163	2	25	180	2
1	164	2	26	179	2
2	165	0	27	177	4
3	166	3	28	169	4
4	167	2	29	167	4
5	168	3	30	162	3
6	169	2	31	161	3
7	169	4	32	157	3
8	169	2	33	149	3
9	170	0	34	143	2
10	171	2	35	141	5
11	171	1	36	139	2
12	171	4	37	136	1
13	171	1	38	134	1
14	173	4	39	132	3
15	174	1	40	131	1
16	175	0	41	126	1
17	177	1	42	123	2
18	178	4	43	121	0
19	179	1	44	118	2
20	179	3	45	117	2
21	179	3	46	111	3
22	180	6	47	97	0
23	184	3	48	74	0
24	183	6			

Appendix Table 4. Changes in the laboratory test results (all)

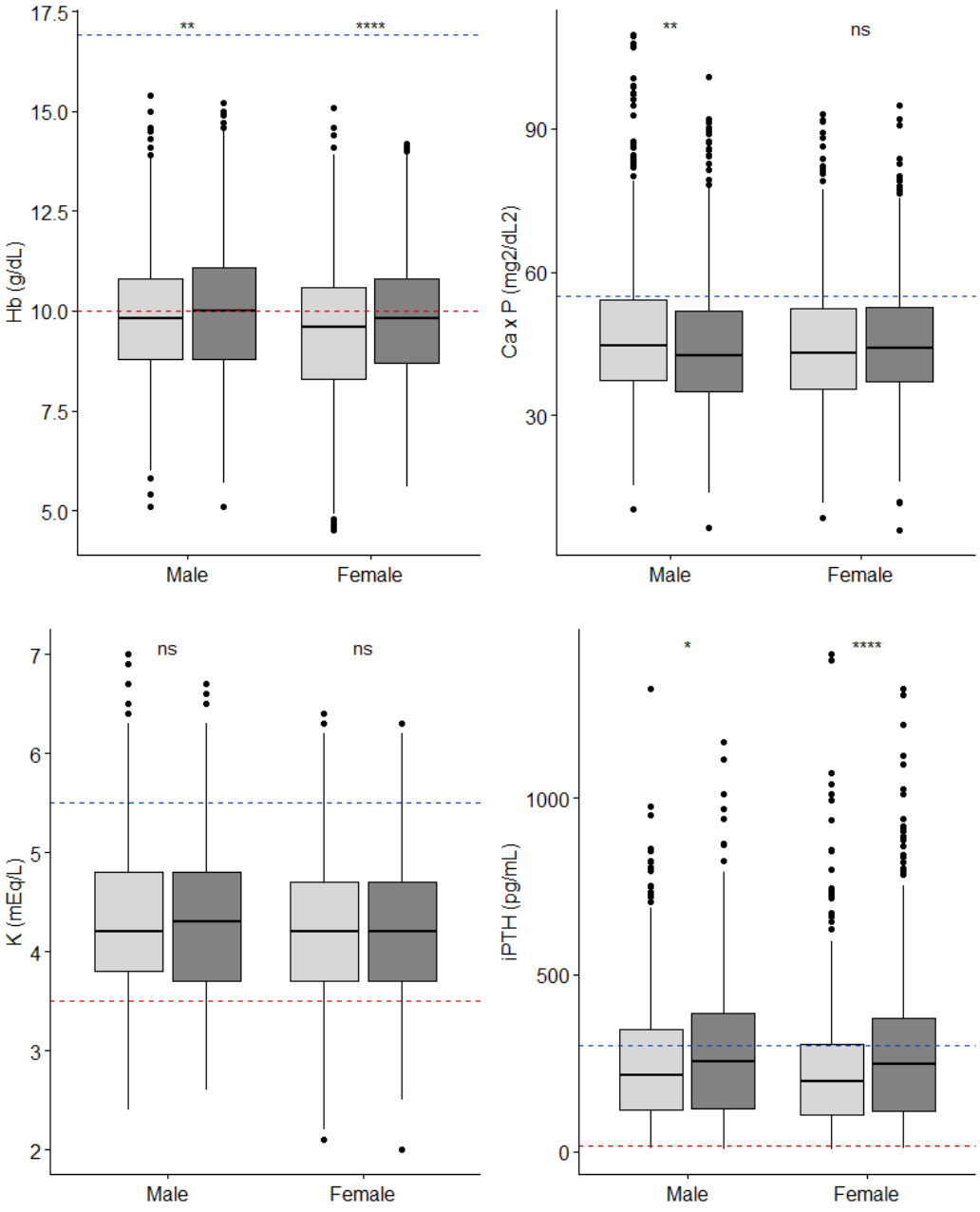
	Pre			Post			p-value
	N	Mean	SD	N	Mean	SD	
Hb	2,423	9.59	1.66	1,379	9.89	1.60	0.000
Ca x P	2,175	45.6	13.6	1,329	44.9	13.7	0.160
K	2,372	4.26	0.70	1,321	4.28	0.72	0.230
iPTH	924	242.0	191.0	783	287.0	220.0	0.000



Appendix Figure 1. Changes in the laboratory test results (all)

Appendix Table 5. Changes in the laboratory test results (sex)

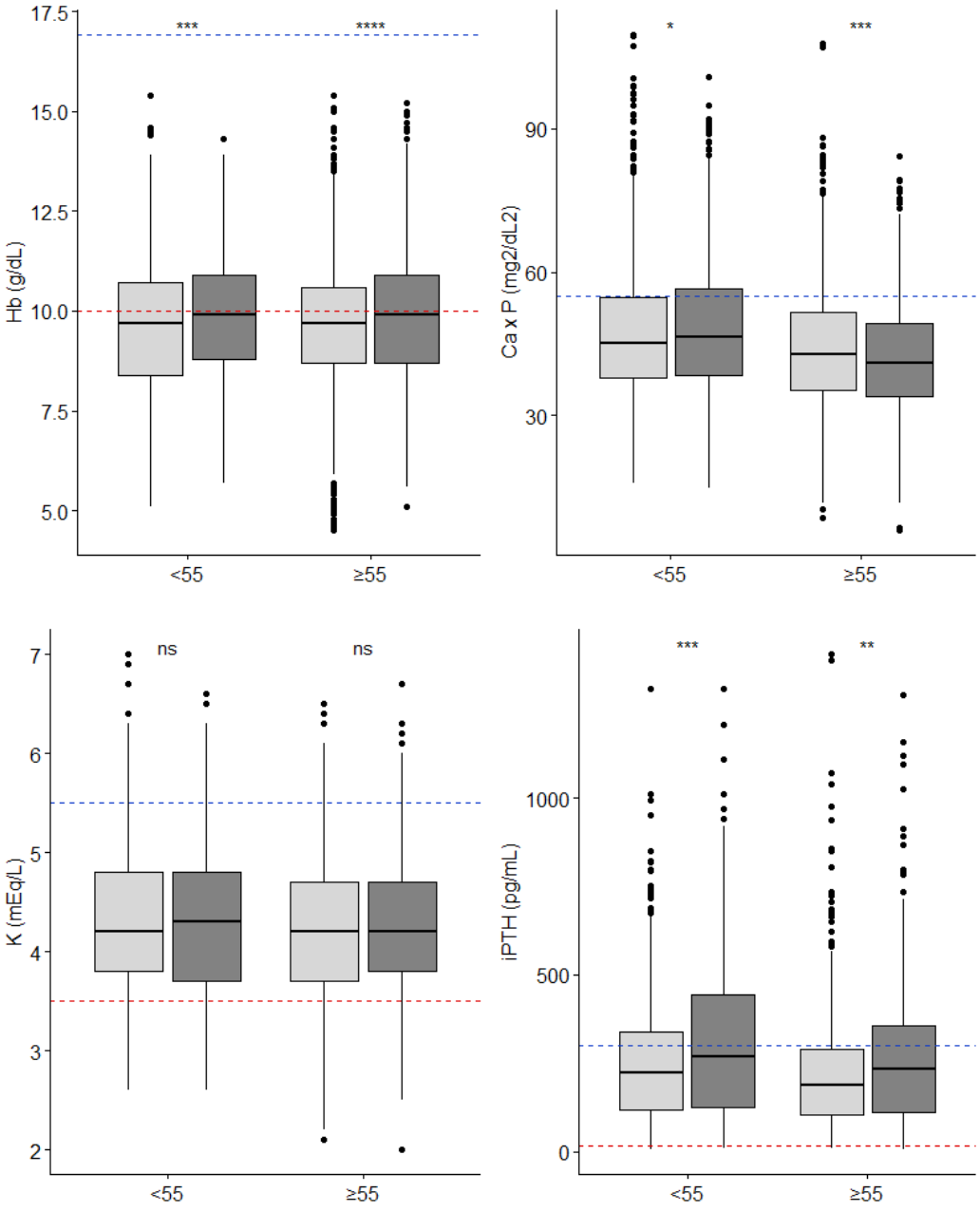
	Pre			Post			p-value
	N	Mean	SD	N	Mean	SD	
Hb							
Male	1,173	9.80	1.52	710	10.00	1.68	0.003
Female	1,250	9.39	1.76	669	9.75	1.51	0.000
Ca x P							
Male	1,038	46.5	14.1	680	44.4	14.4	0.003
Female	1,137	44.7	13.0	649	45.4	13.0	0.299
K							
Male	1,138	4.30	0.71	680	4.29	0.74	0.814
Female	1,234	4.22	0.69	641	4.28	0.70	0.058
iPTH							
Male	456	254.0	189.0	379	284.0	202.0	0.028
Female	468	231.0	192.0	404	289.0	236.0	0.000



Appendix Figure 2. Changes in the laboratory test results (sex)

Appendix Table 6. Changes in the laboratory test results (age)

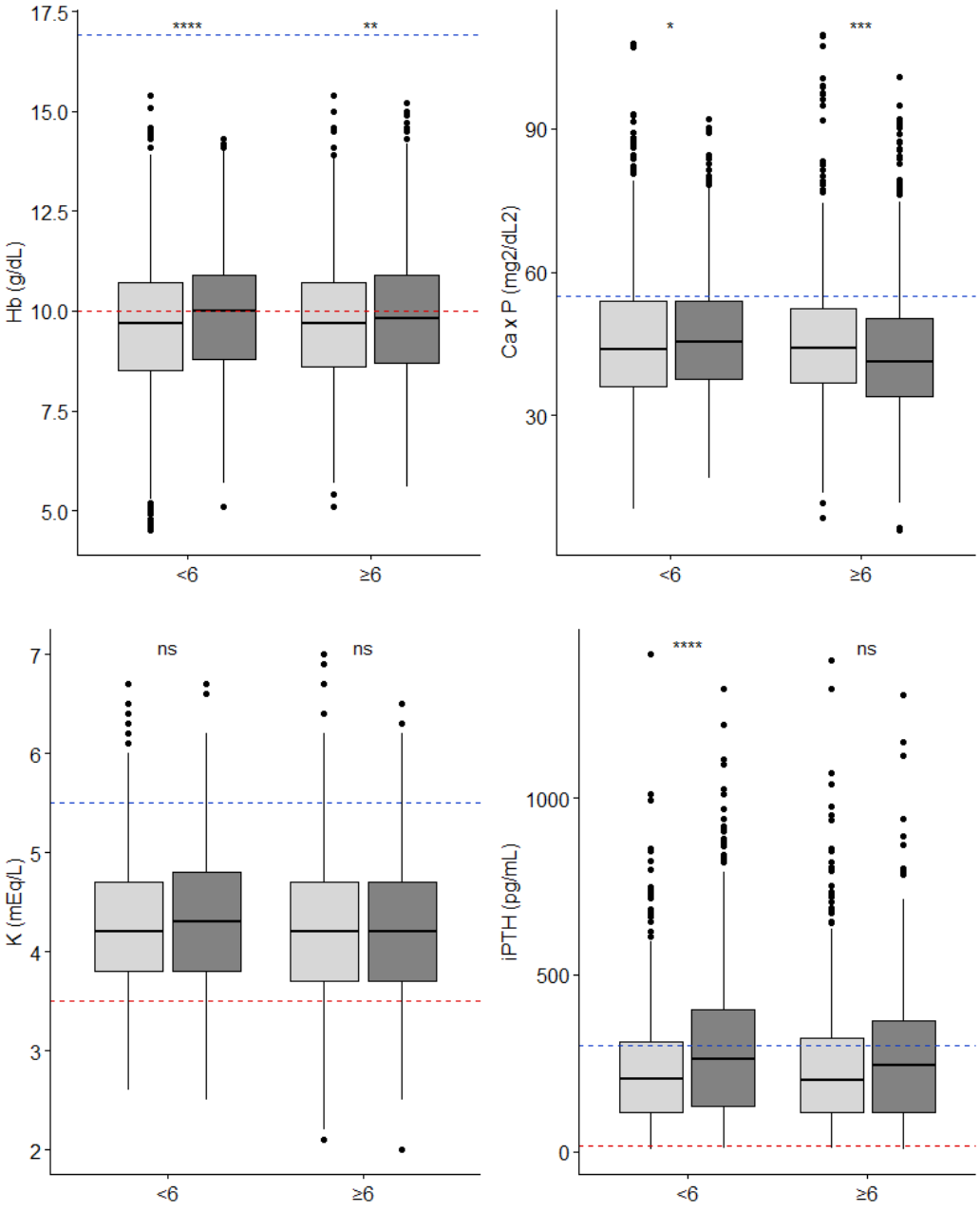
	Pre			Post			p-value
	N	Mean	SD	N	Mean	SD	
Hb							
< 55	1,137	9.61	1.63	582	9.89	1.61	0.001
≥ 55	1,286	9.57	1.69	797	9.90	1.60	0.000
Ca x P							
< 55	1,033	47.2	14.0	571	48.8	14.7	0.032
≥ 55	1,142	44.1	13.0	758	41.9	12.2	0.000
K							
< 55	1,131	4.29	0.70	572	4.31	0.72	0.560
≥ 55	1,241	4.23	0.70	749	4.27	0.72	0.220
iPTH							
< 55	464	256.0	188.0	394	308.0	233.0	0.000
≥ 55	460	229.0	192.0	389	265.0	203.0	0.008



Appendix Figure 3. Changes in the laboratory test results (age)

Appendix Table 7. Changes in the laboratory test results (PD duration)

	Pre			Post			p-value
	N	Mean	SD	N	Mean	SD	
Hb							
< 6	1,463	9.54	1.74	648	9.90	1.58	0.000
≥ 6	960	9.66	1.53	731	9.88	1.62	0.004
Ca							
< 6	1,292	45.6	13.3	635	46.8	12.7	0.046
≥ 6	883	45.5	13.9	694	43.1	14.4	0.001
K							
< 6	1,472	4.28	0.67	642	4.33	0.74	0.110
≥ 6	900	4.22	0.74	679	4.24	0.70	0.580
iPTH							
< 6	417	239.0	181.0	397	302.0	235.0	0.000
≥ 6	507	245.0	198.0	386	270.0	202.0	0.062



Appendix Figure 4. Changes in the laboratory test results (PD duration)

Appendix Table 8. CHEERS 2022 Checklist

Section	No	Guidance for reporting
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.
Introduction		
Background and Objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.
Methods		
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).
Setting and location	6	Provide relevant contextual information that may influence findings.
Comparators	7	Describe the interventions or strategies being compared and why chosen.
Perspective	8	State the perspective(s) adopted by the study and why chosen.
Time horizon	9	State the time horizon for the study and why appropriate.
Discount rate	10	Report the discount rate(s) and reason chosen.
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.
Measurement and valuation of resources and costs	14	Describe how costs were valued.
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.
Rationale and description of model	16	If modeling is used, describe in detail and why used. Report if the model is publicly available and where it can be assessed.
Analytics and assumptions	17	Describe any methods for analyzing or statistically transforming data, any extrapolation methods, and approaches for validating and model used.
Characterizing heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.
Characterizing distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.

Characterizing uncertainty	20	Describe methods to characterize any sources of uncertainty in the analysis.
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (eg, clinicians or payers) in the design of the study.
Results		
Study parameters	22	Report all analytic inputs (eg, values, ranges, references) including uncertainty or distributional assumptions.
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure.
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affects findings. Report the effect of choice of discount rate and time horizon, if applicable.
Effect of engagement with patients and others affected by the study	25	Report any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study.
Discussion		
Study findings, limitations, generalizability, and current knowledge	26	Report key findings, limitations, ethical, or equity considerations not captured and how these could impact patients, policy, or practice.
Other relevant information		
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis.
Conflicts of interest	28	Report authors' conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.

Korean Abstract

상급종합병원 복막투석 환자 재택의료 프로그램의 비용-효용분석

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김경이

서론: 코로나바이러스 감염증(COVID-19) 대유행 이후 다양한 디지털 헬스 기술이 빠르게 도입되었다. 여러 종류의 솔루션 중 한국의 보건복지부는 환자들의 의료접근성을 높여 궁극적으로는 삶의 질을 향상시키기 위하여 재택의료 사업을 시작했다. 이 사업은 대면 교육상담과 전화 또는 양방향 메신저를 활용한 비대면 환자 모니터링을 포함하고 있다. 본 연구에서는 복막투석을 시행하고 있는 말기신부전 환자를 대상으로 재택의료 사업을 평가한다. 복막투석 환자는 국내 말기신부전 환자의 3.9%에 불과하지만, 재택에서 투석을 하는 것에 대한 임상적 이점을 다룬 연구가 많다. 또한 의료비 부담이 증가함에 따라 복막투석은 다른 신대체요법에 비해 비용-효과적인 대안으로 간주된다. 복막투석에 대한 관심이 높아지면서, 새롭게 시작한 재택의료 사업의 장기적인 임상적, 경제적 효과를 검증하기 위한 연구가 필요하다.

연구방법: *(임상효과분석)* 복막투석 재택의료 사업의 사전-사후 임상적 효과를 평가하기 위하여 단일 상급종합병원에서 후향적 코호트 연구를 설계하였다.

2017년 6월부터 2022년 5월까지 총 186명의 복막투석 환자가 연구대상으로 선정되었다. 5년 간의 데이터는 재택의료 사업 시행 후 복막염 발생과 임상검사결과 (Hb, Ca x P, K, iPTH) 변화와 같은 임상적 변화 분석에 사용되었다. 분석방법으로는 카이제곱검정, 독립표본 t-검정, 시계열분석(ITS)을 사용하였다. *(비용-효용분석)* 재택의료 사업의 평생(lifetime) 비용-효과성을 평가하기 위해 마콥모형을 설계하고, 재택관리군과 기존 였다. 50세 복막투석 환자 1,000명을 포함한 가상의 코호트를 구축하고 모두 복막투석 단계에서 시작하여 매 1년 주기마다 상태(state) 전이를 확인하였다. 효과 변수는 질보정수명(QALY)으로 설정하고 제한적 사회적 관점으로 비용-효용분석을 수행했다. 1 QALY 당 지불의사(WTP) 임계치로는 1 GDP에 해당하는 40,043,036원으로 설정하였고, 비용과 효과(QALY) 데이터에 모두 4.5%의 할인율을 반영하였다. 반주기보정 후 주요 결과인 ICER와 INMB를 산출하였다. 불확실성이 큰 경제성평가의 제한점을 보완하기 위해 시나리오분석, 민감도분석 및 완벽한 정보의 기대값(EVPI)을 활용하여 결과의 변화를 확인하였다.

결과: *(임상효과분석)* 재택의료 사업 이후 복막염 발생이 감소했다. 1,000명의 환자-월 당 8.345건 발생(SE = 3.181, P = 0.012)하던 기준값은 매월 0.480건씩 증가하던 추세였다 (P = 0.018). 재택의료 사업 도입 후 복막염 발생 추이는 매월 0.886건 감소하는 추세로 변하였다 (P = 0.015). 1년 간 누적 발생으로 산출하면, 이는 27.31%의 발생이 20.93%로 감소한 것과 같다. 임상검사결과 분석 역시 개선되었다. 목표 수치에 도달한 비율이 Hb은 5.2%p 증가 (P = 0.002), Ca x P (1.1%p, P = 0.428) 및 K (-1.6%p, P = 0.200)는 유지된 반면, iPTH는 감소하였다 (-11.0%p, P = 0.000).

(비용-효용분석) 기본분석에서 ICER는 1 QALY 당 4,571,500원으로 본 연구에서 설정한 WTP 임계치 이내에 속했으며, 시나리오에 관계없이 모든 기본분석 결과는 WTP 임계치를 벗어나지 않았다. 일원민감도분석을 시행하였고, 모든 시나리오에서 가장 민감한 변수는 복막투석비용 (재택사업)과 복막투석비용 (기존)으로 확인하였다. 10,000회의 몬테카를로 시뮬레이션 분석 결과, 재택의료 사업이 최적의 대안일 확률은 시나리오 1에서 62.05%, 시나리오 2에서 59.95%, 시나리오 3에서 61.70%, 시나리오 4에서 89.41%인 것으로 나타났고, 재택의료 사업이 최적의 대안일 확률이 50%를 넘는 WTP 임계치는 7,380,000원이었다. 마지막으로 EVPI를 측정하였고, 불확실성 없이 모든 변수에 대한 완벽한 정보를 가지고 있는 상황이라면 환자당 14,818,960원을 추가로 얻을 수 있다.

결론: 본 연구는 국내 최초로 복막투석 환자를 위한 재택의료 사업의 임상적 효과와 비용-효과를 평가하였다. 연구에서 복막염 발생 감소와 임상검사결과 개선의 임상적 효과성을 확인하였고, ICER가 WTP 임계치 미만이라는 점에서 비용-효과성을 확인하였다. 따라서 연구진은 복막투석 재택의료 사업이 임상적으로 효과적이며, 비용-효과적일 가능성이 높음을 시사하는 바이다.

핵심어: 디지털 헬스, 재택의료, 복막투석, 말기신부전, 시계열분석, 마콥모형, 비용-효용분석, 코로나바이러스 감염증