

THE ASSOCIATION OF INDIVIDUAL AND REGIONAL SOCIOECONOMIC STATUS ON INITIAL PERITONITIS AND OUTCOMES IN PERITONEAL DIALYSIS PATIENTS: A PROPENSITY SCORE-MATCHED COHORT STUDY

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◆ **Background:** Research indicates that the socioeconomic status (SES) of individuals and the area where they live are related to initial peritonitis and outcomes in peritoneal dialysis (PD). We conducted a retrospective, multi-center cohort study in China to examine these associations.

◆ **Methods:** Data on 2,171 PD patients were collected from 7 centers, including baseline demographic, socioeconomic, and laboratory data. We explored the potential risk factors for initial peritonitis and outcomes using univariate Cox regression and unadjusted binary logistic regression. Then, we used propensity score matching to balance statistically significant risk factors for initial peritonitis and outcomes, and Kaplan-Meier survival analysis to compare differences in peritonitis-free rates between different groups of participants after matching.

◆ **Results:** A total of 563 (25.9%) initial episodes of peritonitis occurred during the study period. The Kaplan-Meier peritonitis-free rate curve showed high-income patients had a significantly lower risk than low-income patients ($p = 0.007$) after matching for age, hemoglobin, albumin, and regional SES and PD center. The risk of treatment failure was significantly lower in the high-income than the low-income group after matching for the organism causing peritonitis and PD center: odds ratio (OR) = 0.27 (0.09 – 0.80, $p = 0.018$). Regional SES and education were not associated with initial peritonitis and outcomes.

◆ **Conclusions:** Our study demonstrates low individual income is a risk factor for the initial onset of peritonitis and treatment failure after initial peritonitis.

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Peritonitis continues to be the most frequent cause of peritoneal dialysis (PD) failure, having significant effects on patient morbidity and mortality (1). A clustered distribution of patients with a higher incidence of peritonitis has been consistently described. In addition, differences in the rate of peritonitis have been observed between medical centers and geographical regions (2). These observations suggest that patient characteristics, as well as factors related to therapy and the environment, may influence the risk of peritonitis.

Several demographic and physiological risk factors for peritonitis in PD patients have been described, including, black race (3,4), diabetes (3,4), advanced age (3), obesity (5), malnutrition (6), hypoalbuminemia (7), reduced residual renal function (8), and previous peritonitis (3). Moreover, the rate of peritonitis may be influenced by socioeconomic factors, such as income and education level (9–11), and geographic region (12,13). A previous study of ours found that patients with low individual income had a higher prevalence of peritonitis than other patients. Furthermore, patients with low individual income had significantly poorer nutrition status and biochemical factors, including hemoglobin and serum albumin, than other patients (14). Although multivariable Cox regression models have been used to adjust for potential confounding factors, bias may still be unavoidable. Previous studies of the association between socioeconomic status (SES) and risk of peritonitis have not used propensity score matching analysis to attenuate the effects of confounding variables and bias (9–13). Therefore, we aimed to investigate

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if individual and environmental characteristics and SES predict the first episode of peritonitis, using data from a large-scale multi-center retrospective cohort study and propensity score matching. This study's results should be helpful for implementing individualized treatment plans and training courses for patients with different SES backgrounds in order to decrease the rate of peritonitis and increase the survival rate of patients undergoing PD.

SUBJECTS AND METHODS

This study is affiliated with the Socioeconomic Status on the Outcome of Peritoneal Dialysis (SSOP) study, which is a retrospective multi-center cohort study. Seven centers located in 5 different provinces and 4 geographical regions of China were enrolled in this study. The center's enrollment criteria have been described in detail in our previous paper (14). Data from each center were collected within a strict quality-control framework and inspected and optimized to ensure the integrity and accuracy of the database. All study investigators and staff members completed a training program that taught them the study methods and procedures, and they received a manual that contained detailed instructions about data collection. The ethics committee of Peking University First Hospital, China, approved the study. Patients gave written consent for their information to be stored in the hospital database and used for research.

SUBJECT SELECTION

All patients receiving PD between the date the intact database was created and August 2011 were enrolled in this study. All study participants began the PD program within 1 month following catheter implantation and were given lactate-buffered glucose dialysate with a twin-bag connection system (Baxter Healthcare, Guangzhou, China). Patients who had been on PD for less than 3 months were excluded, as was the case in previous studies (15,16).

DATA COLLECTION

Demographic and clinical data were collected at baseline, including age, gender, body mass index (BMI), primary renal disease, history of cardiovascular disease (CVD), and presence of diabetes mellitus (DM). Cardiovascular disease was recorded if one of the following conditions was present: angina, class III/IV congestive heart failure (New York Heart Association), transient ischemic attack, history of myocardial infarction or cerebrovascular accident, or peripheral arterial disease (17). Baseline biochemistry data, including hemoglobin and serum albumin, were calculated as the mean of measurements made during the first 3 months. Dialysis adequacy and residual renal function (RRF) were measured during the first 6 months. Dialysis adequacy was determined from total Kt/V and creatinine clearance. Center size was also recorded according to the number of enrolled patients from each center.

Socioeconomic status data were collected for each patient. Individual income level was defined as the yearly household income per person and was classified as low (<¥20,000, [<\$3,160]), median (¥20,000 – ¥40,000, [\$3,160 – \$6,320]), or high (>¥40,000, [>\$6,320]). Because most of the subjects were from urban areas, these groups were defined according to the average income for the urban population in 2011, obtained from the bureau of Statistics (www.bjststs.gov.cn/nj/main/2011-tjnj/index.htm). Education level was classified according to 4 categories based on the number of years of school completed: elementary school or less, middle school, high school, and more than high school. Other individual SES data included the proportion of individual income used for medical expenses (the percentage of yearly household income per person spent each year on self-paid medical expenses). Regional socioeconomic status was divided into undeveloped and developed regions, according to the median gross domestic product (GDP) per capita (¥95,000, [\$15,009]) of the regions.

DIAGNOSIS OF PERITONITIS

When patients experienced cloudy effluent or digestive tract symptoms of unknown origin, they were asked to make an emergency call to their respective dialysis centers as soon as possible. Then nurses and physicians in the PD unit assessed each patient. If peritonitis was suspected, a sample of PD effluent was sent for a cell count (WCC) (5 mL in an EDTA tube) and bacterial culture (10 mL in a blood culture bottle). The definition of peritonitis followed International Society for Peritoneal Dialysis (ISPD) guidelines (1).

TREATMENT AND FOLLOW-UP

The follow-up period for each patient was the interval from the first day of PD until 1 of the following events occurred: death; loss to follow-up; change of treatment modality; or until December 31st, 2012. The onset of initial peritonitis during follow-up was recorded and the time between starting PD and the initial episode of peritonitis was calculated.

Peritonitis episodes were treated using standard antibiotic protocol, as modified by ISPD guidelines (1,18). Treatment success was defined as the complete resolution of peritonitis (PD effluent WCC < 100/μL and clinical resolution) without the need for Tenckhoff catheter removal. Conversely, treatment failure was defined as death attributable to the peritonitis episode or transfer to hemodialysis (HD) during the course of peritonitis treatment.

STATISTICAL ANALYSIS

Continuous data are presented as means and standard deviations, except for RRF, the proportion of individual income used for medical expenses, and total Kt/V, which are presented as median and interquartile range because they are highly skewed. Categorical variables are presented as proportions. Expectation maximization algorithm was used

to account for missing covariate data imputation (typically < 5% per variable).

Patient data that were normally distributed continuous variables were compared using Student's *t*-test or ANOVA (F-test). Chi-square test was used for categorical variables, and Mann-Whitney U test was used for skewed continuous variables. Univariate Cox regression was used to determine predictors of peritonitis. The initial Cox models were constructed to explore potential individual risk factors for the first episode of peritonitis, including demographic and bioclinical data. In order to reduce confounding by variables and bias, we then used propensity score matching (1:2) to balance statistically significant risk factors between patients with and without an initial episode of peritonitis. Next, Kaplan-Meier analysis was used to compare the peritonitis-free rate between the different individual income groups and regional socioeconomic status groups. We calculated the univariate hazard ratios (HRs) with 95% confidence intervals (CIs). All probabilities were 2-tailed, and the level of significance was set at 0.05.

Binary logistic univariate regression was used to determine the risk factors for the outcomes of the first episode of peritonitis. The initial regression models were constructed to explore the relationships among the bioclinical data, SES, and the outcomes of the first episode of peritonitis. Then we used propensity score matching (1:7) to balance statistically significant risk factors between patients with and without treatment failure. The causative agents (i.e., organisms) of the first episode of peritonitis were divided into 2 groups (Group 1: culture-negative infections and non-*Staphylococcus aureus* gram-positive infections; Group 2: *Staphylococcus*, gram-negative, and polymicrobial infections) (19). The contribution of individual income level, education level, and regional SES were analyzed as categorical variables. We report the odds ratios (ORs) and 95% CIs. All probabilities were 2-tailed, and the level of significance was set at 0.05. Statistical analyses were performed using SPSS for Windows software version 13.0 (SPSS Inc., Chicago, IL, USA)

RESULTS

BASELINE CHARACTERISTICS

The 2,171 patients included in the study had a mean age of 57.97 ± 15.45 years and BMI 22.92 ± 3.60 kg/m²; 38.1% were diabetic, and CVD was present in 40.9% of the patients at baseline. Chronic glomerulonephritis (CGN) was the most common cause of end-stage renal disease (ESRD) (34.8%), followed by diabetic nephropathy and hypertensive nephropathy. The detailed data were presented in our previous paper (14).

SOCIOECONOMIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH AND WITHOUT INITIAL PERITONITIS

The median time from start of PD to the first episode of peritonitis was 18.13 (7.2 – 34.5) months. A total of 563 (25.9%) initial episodes of peritonitis occurred until December 31st,

2012; 203 episodes (36.1%) were due to gram-positive organisms, 130 (23.1%) to gram-negative organisms, and 11 (2.0%) to fungi. Twelve (2.1%) were polymicrobial, 147 (26.1%) were culture-negative, and 60 (10.7%) had no culture result.

Patients with an initial peritonitis episode tended to be older and have lower levels of serum albumin than patients without a peritonitis episode. The rate of peritonitis was lower among patients who lived in undeveloped regions (see Table 1).

ASSOCIATION BETWEEN SES AND INITIAL PERITONITIS

The univariate Cox regression analysis showed that initial peritonitis was significantly associated with age, hemoglobin, albumin, individual income, and regional SES (see Table 2). Patients with high individual income had a significantly lower risk of initial peritonitis than those with low individual income (log rank: 7.21, $p = 0.007$), after propensity score matching for age, hemoglobin, albumin, regional SES, and PD center (1 to 2 match). The peritonitis-free rate in the median-income group was not significantly different from that in the low-income group (log rank: 2.11, $p = 0.146$) or the high-income group (log rank: 2.22, $p = 0.136$) (see Figure 1). Moreover, there was no difference in peritonitis-free rate between patients living in developed regions and those living in undeveloped regions (log rank: 1.37, $p = 0.241$), after propensity score matching for age, hemoglobin, albumin, individual income, and PD center (1 to 2 match).

ASSOCIATION BETWEEN SES AND OUTCOMES OF INITIAL PERITONITIS

Of the 563 episodes of initial peritonitis, 482 (85.6%) continued on PD, and 81 (14.4%) were reported as treatment failure. Among these 81 patients, 51 transferred to HD, 28 died due to peritonitis, and the outcomes of the other 2 patients were unknown.

Individual income and the organism causing the peritonitis (2 categories) were significant risk factors for treatment failure of the initial peritonitis in the unadjusted binary logistic regression (see Table 3). The risk of treatment failure was significantly lower in the high-income group than the low-income group—OR = 0.27 (0.09 – 0.80, $p = 0.018$)—after propensity score matching (1 to 7 match, $n = 488$) for the organism causing peritonitis and PD center. However, no significant difference in treatment failure risk was observed between the low- and median-income groups (see Figure 2).

DISCUSSION

The key finding of this large, multi-center, retrospective cohort study is that low individual income is a significant risk factor for initial peritonitis and treatment failure. And living in developed regions is a significant risk factor for initial peritonitis. To our knowledge, this is the first study to evaluate the roles of SES variables on initial peritonitis and its outcomes in PD patients, using propensity score matching analysis.

TABLE 1
Baseline Characteristics According to Prevalence of Initial Peritonitis

Variables	Peritonitis (-) (n = 1,608)	Peritonitis (+) (n = 563)	p
Age (years)	57.44±15.75	59.39±14.49	0.010
Male (%)	49.3%	50.3%	0.695
DM (%)	38.0%	38.3%	0.878
Primary disease			0.420
CGN (%)	35.1%	34.1%	
DN (%)	29.9%	28.4%	
HTN (%)	15.7%	14.9%	
Others or undefined	19.3%	22.6%	
BMI (kg/m ²)	22.87±3.61	23.04±3.58	0.352
Hb (g/L)	104.31±19.30	102.95±18.47	0.148
ALB (g/L)	35.86±5.34	34.58±4.97	<0.001
Total Kt/V	1.94 (1.63~2.36)	1.97 (1.67~2.40)	0.323
RRF (mL/min)	3.29 (1.60~5.32)	3.15 (1.68~5.67)	0.484
Center size (>300)	64.2%	65.4%	0.645
Individual income level			0.409
Low (<¥20,000, i.e., <\$3,160) (%)	41.4%	45.6%	
Median (¥20,000–¥40,000, i.e., \$3,160–\$6,320) (%)	39.7%	37.7%	
High (>¥40,000, i.e., >\$6,320) (%)	17.8%	16.7%	
Education level			0.756
Elementary or less (%)	26.3%	25.7%	
Middle school (%)	29.4%	30.3%	
High school (%)	22.6%	24.1%	
More than high school (%)	21.8%	20.0%	
Regional socioeconomic status			<0.001
Undeveloped region (GDP per capita <¥95,000, i.e., <\$15,009)	63.1%	53.5%	
Developed region (GDP per capita >¥95,000, i.e., >\$15,009)	36.9%	46.5%	

DM = diabetes mellitus; CGN = chronic glomerulonephritis; DN = diabetic nephropathy; HTN = hypertensive nephropathy; BMI = body mass index; Hb = hemoglobin; ALB = albumin; RRF = residual renal function; GDP = gross domestic product.

Consistent with Rubin's research (9), low income was a significant risk indicator of the onset of initial peritonitis and treatment failure in PD patients. There are a number of potential explanations for this finding based on our data. First, patients with low individual income were prone to be hypoalbuminemic and malnourished (14), both of which have been reported to be significant risk factors for peritonitis in PD patients (6,7). However, after propensity score matching for statistically significant biochemical factors, the net effect of individual income on initial peritonitis still remained statistically significant. There may have been other confounders of peritonitis risk that we did not take into account in our study. Second, as shown in our previous paper, the proportion of individual income used for medical expenses in the low-income group was significantly higher than the proportion in the median- and high-income groups (14). According to data from the World Health Organization (WHO) website (20), the average total expenditure on health as a percentage of gross domestic product (GDP) in China from 2009 to 2011 was 5.1%, which was the lowest percentage among China, the United States (17.7%), Brazil (8.9%), and Portugal (10.6%). However, the average out-of-pocket expenditures as a percentage of private expenditures on health in China, the United States, and

Brazil were 78.3%, 22.13%, and 57.6%, respectively. Therefore, individual income plays a particularly important role in medical expenditures in China. This may be a potential explanation for the difference in our findings compared with research findings in the United States, Brazil, and Portugal (15,21–23), which have reported no relationship between income and initial peritonitis. We also found low individual income to be a risk factor for the treatment failure of PD after the initial incidence of peritonitis, compared with the high-income group. This result could probably be ascribed to the delay in referrals to nephrologists when symptoms of peritonitis developed in low-income patients. Poorer patients often chose to take oral antibiotics, rather than see a nephrologist, to try to control the infection without extra expenditures, which may have led to severe infections. This leads us to suggest that several strategies should be applied to improve the treatment of peritonitis for poorer patients in order to maintain their utilization of PD.

However, no impact of regional GDP per capita on initial peritonitis and outcomes was observed, which is consistent with previous findings (24,25). One possible reason for our finding is that, in our study, the patients in the developed regions were older, there were more cases of diabetes, and baseline serum albumin levels were lower than in the undeveloped regions.

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TABLE 2
Univariate Cox Regression for Predictors of Initial Peritonitis

Variables	HR	95% CI	p
Age	1.01	1.00–1.01	0.001
Female gender	0.86	0.73–1.02	0.088
DM	1.07	0.90–1.28	0.395
BMI	1.01	0.98–1.03	0.512
Hb	0.99	0.99–0.99	0.008
ALB	0.94	0.93–0.96	<0.001
Total Kt/V	0.93	0.80–1.08	0.358
RRF	1.01	0.98–1.03	0.620
History of CVD	1.15	0.97–1.36	0.112
Center size	1.00	0.84–1.19	0.990
Education level			
Elementary or less	Ref		
Middle school	0.93	0.74–1.16	0.551
High school	1.04	0.82–1.32	0.697
More than high school	0.90	0.70–1.16	0.439
Regional socioeconomic status			
Undeveloped region (GDP per capita <¥95,000, i.e., < \$15,009)	Ref		
Developed region (GDP per capita >¥95,000, i.e., > \$15,009)	1.39	1.18–1.64	<0.001
Individual income level			
Low (< ¥20,000, i.e., < \$3,160)	Ref		
Median (¥20,000–¥40,000, i.e., \$3,160–\$6,320)	0.85	0.71–1.03	0.100
High (>¥40,000, i.e., > \$6,320)	0.78	0.62–0.99	0.049

HR = hazard ratio; CI = confidence interval; DM = diabetes mellitus; BMI = body mass index; Hb = hemoglobin; ALB = albumin; RRF = residual renal function; CVD = cardiovascular disease; GDP = gross domestic product.

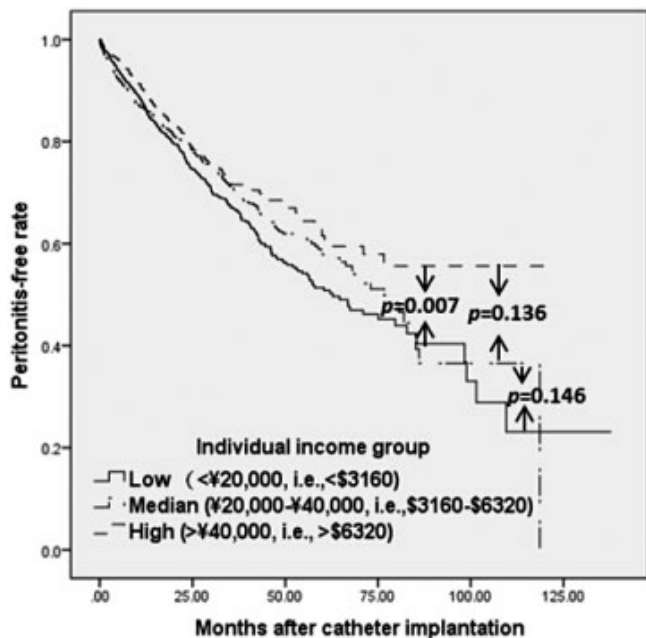


Figure 1 — Kaplan-Meier peritonitis-free rate curve for patients with low (< ¥20,000, i.e., < \$3,160), median (¥20,000–¥40,000, i.e., \$3,160–\$6,320), and high (> ¥40,000, i.e., > \$6,320) individual income, after propensity score matching for age, duration, hemoglobin, albumin, regional socioeconomic status and PD center (1 to 2 match). PD = peritoneal dialysis.

Given that age, diabetes and serum albumin have been recognized as significant predictors by previous studies (3,4,8), these favorable individual factors in our study possibly offset the disadvantages of regional SES. Moreover, as shown in our previous paper (14), no association between regional SES and initial peritonitis had been observed, even after adjustment for age, proportion of patients with diabetes, serum albumin, and so on. We hypothesize that unknown confounding factors related to regional SES are also associated with PD outcome.

Our analysis did not find any correlation between education level and the onset of initial peritonitis or its outcome. This result is consistent with an analysis of a regional ESRD registry in the United States, in which 1,595 new PD patients were observed over 2 years (26), but is contrary to recently published data from Brazil and Canada (15,27). One possible explanation is that our selected centers had highly professional PD doctors and nurses and well-established training programs. Patients and their homecare helpers often were trained simultaneously, which probably led to stronger family support (28). Whether better compliance among Asian individuals (29,30) plays a role in this phenomenon is unclear.

To the best of our knowledge, our study, which examined a large cohort of adult PD patients in China, is the first study to analyze the relationship between SES and initial peritonitis using propensity score matching analysis. There were 563 outcome events, accounting for 25.9% of the total episodes, which

TABLE 3
Unadjusted Binary Logistic Regression for Predictors of Treatment Failure of Initial Peritonitis

	OR	95% CI	<i>p</i>
Age	1.01	0.99–1.03	0.240
Female gender	0.94	0.55–1.60	0.823
Duration	1.00	0.99–1.01	0.556
History of CVD	1.56	0.89–2.75	0.120
DM	1.22	0.70–2.13	0.466
Hb	0.98	0.97–1.00	0.094
ALB	0.97	0.92–1.03	0.396
Organism of peritonitis			
Non- <i>Staphylococcus aureus</i> gram-positive cocci and culture negative	Ref		
<i>Staphylococcus aureus</i> , gram-negative and polymicrobial	1.78	1.04–3.07	0.036
RRF	0.93	0.84–1.03	0.179
BMI	1.02	0.94–1.10	0.577
Education level			
Elementary or less	Ref		
Middle school	1.32	0.63–2.78	0.459
High school	1.39	0.64–3.01	0.396
More than high school	1.09	0.46–2.55	0.839
Regional socioeconomic status			
Undeveloped region (GDP per capita <¥95,000, i.e., < \$15,009)	Ref		
Developed region (GDP per capita >¥95,000, i.e., > \$15,009)	1.30	0.76–2.23	0.332
Individual income level			
Low (<¥20,000, i.e., <\$3,160)	Ref		
Median (¥20,000–¥40,000, i.e., \$3,160–\$6,320)	0.77	0.43–1.36	0.371
High (>¥40,000, i.e., >\$6,320)	0.27	0.09–0.79	0.017

OR = odds ratio; CI = confidence interval; CVD = cardiovascular disease; DM = diabetes mellitus; Hb = hemoglobin; ALB = albumin; RRF = residual renal function; BMI = body mass index; GDP = gross domestic product.

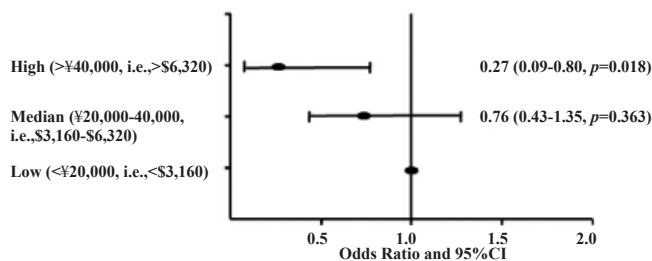


Figure 2 — Odds ratio of individual income for risk of treatment failure after initial peritonitis, after propensity score matching for the organism causing peritonitis and PD enter (1 to 7 match). CI = confidence interval; PD = peritoneal dialysis.

allowed us to build a regression model containing SES and a few recognized confounders to explore the predictive ability of SES. The demographic characteristics and the distribution of causative organisms are typical of those previously reported, supporting the generalizability of our findings to other PD cohorts elsewhere.

This study has several limitations. First, there may be other confounders of peritonitis risk that we did not take into account in our study, such as personal and environmental hygiene, psychological factors, and center-related factors, e.g., climate or medical conditions. Second, we have no detailed data on

dialysate cell count, treatment protocols, or treatment duration, which might be associated with outcomes of peritonitis. However, peritonitis episodes were treated using the standard antibiotic protocol in each center, as modified by the ISPD guidelines. This should have reduced any selection bias on clinical outcomes due to different antibiotic therapies. Third, similar to other studies (15,31), there was a high proportion of culture-negative episodes (25.6%), which makes a precise analysis of peritonitis risks by different etiologies difficult.

CONCLUSION

Our study demonstrates that low level of individual income is a risk factor for the initial onset of peritonitis and for treatment failure in Chinese PD patients, whereas regional SES and education were not associated with the initial onset of peritonitis. As our study found a significantly higher risk of treatment failure in low-income patients than high-income patients, the reinforcement of healthy policies in this population may be beneficial, especially for low-income patients. National expenditure on health and medical insurance should be improved, especially for patients with low individual incomes. Moreover, given the critical role of infections related to PD in patient survival, regional economic status should not be considered as a limitation for PD in low-income areas, in particular when

offered by dedicated healthcare professionals who use international clinical practice guidelines. Lastly, medical insurance for low-income patients should be improved.

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DISCLOSURES

The authors have no financial conflicts of interest to declare.

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