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# Hemodialysis management strategies for migrant patients with end-stage chronic renal disease

Raphaël Godefroy

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Faculté des sciences  
médicales et paramédicales

Aix-Marseille Université

**Stratégies de prise en charge en hémodialyse des patients migrants en  
insuffisance rénale chronique terminale.**

# **T H È S E**

**Présentée et publiquement soutenue devant**

**LA FACULTÉ DES SCIENCES MÉDICALES ET PARAMÉDICALES**

**DE MARSEILLE**

**Le 27 Octobre 2020**

**Par Monsieur Raphael GODEFROY**

**Né le 29 août 1991 à Croix (59)**

Pour obtenir le grade de Docteur en Médecine

D.E.S. de NÉPHROLOGIE

**Membres du Jury de la Thèse :**

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| <b>Madame le Professeur JOURDE-CHICHE Noémie</b> | <b>Assesseur</b> |
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| <b>Monsieur le Professeur AUQUIER Pascal</b>     | <b>Assesseur</b> |
| <b>Monsieur le Docteur ROBERT Thomas</b>         | <b>Directeur</b> |





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**Assesseur**

**Madame le Professeur JOURDE-CHICHE Noémie**

**Assesseur**

**Madame le Professeur MOAL Valérie**

**Assesseur**

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|    | COULANGE Christian     |    | MERCIER Claude            |
|    | DALMAS Henri           |    | METGE Paul                |
|    | DE MICO Philippe       |    | MICHOTEY Georges          |
|    | DESSEIN Alain          |    | MILLET Yves               |
|    | DELARQUE Alain         |    | MIRANDA François          |
|    | DEVIN Robert           |    | MONFORT Gérard            |
|    | DEVRED Philippe        |    | MONGES André              |
|    | DJIANE Pierre          |    | MONGIN Maurice            |
|    | DONNET Vincent         |    | MONTIES Jean-Raoul        |
|    | DUCASSOU Jacques       |    | NAZARIAN Serge            |
|    | DUFOUR Michel          |    | NICOLI René               |
|    | DUMON Henri            |    |                           |
|    | ENJALBERT Alain        |    |                           |

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POGGI Louis  
POITOUT Dominique  
PONCET Michel  
POUGET Jean  
PRIVAT Yvan  
QUILICHINI Francis  
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RIDINGS Bernard  
ROCHAT Hervé  
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ROUX Hubert  
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RUFO Marcel  
SAHEL José  
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SALDUCCI Jacques  
SAN MARCO Jean-Louis  
SANKALE Marc  
SARACCO Jacques  
SASTRE Bernard  
SCHIANO Alain  
SCOTTO Jean-Claude  
SEBAHOUN Gérard  
SERMENT Gérard  
SOULAYROL René  
STAHL André  
TAMALET Jacques  
TARANGER-CHARPIN Colette  
THOMASSIN Jean-Marc  
UNAL Daniel  
VAGUE Philippe  
VAGUE/JUHAN Irène  
VANUXEM Paul  
VERVLOET Daniel  
VIALETES Bernard  
WEILLER Pierre-Jean



**EMERITAT****2008**

|                   |                   |            |
|-------------------|-------------------|------------|
| M. le Professeur  | LEVY Samuel       | 31/08/2011 |
| Mme le Professeur | JUHAN-VAGUE Irène | 31/08/2011 |
| M. le Professeur  | PONCET Michel     | 31/08/2011 |
| M. le Professeur  | KASBARIAN Michel  | 31/08/2011 |
| M. le Professeur  | ROBERTOUX Pierre  | 31/08/2011 |

**2009**

|                  |                 |            |
|------------------|-----------------|------------|
| M. le Professeur | DJIANE Pierre   | 31/08/2011 |
| M. le Professeur | VERVLOET Daniel | 31/08/2012 |

**2010**

|                  |                |            |
|------------------|----------------|------------|
| M. le Professeur | MAGNAN Jacques | 31/12/2014 |
|------------------|----------------|------------|

**2011**

|                  |                   |            |
|------------------|-------------------|------------|
| M. le Professeur | DI MARINO Vincent | 31/08/2015 |
| M. le Professeur | MARTIN Pierre     | 31/08/2015 |
| M. le Professeur | METRAS Dominique  | 31/08/2015 |

**2012**

|                  |                      |            |
|------------------|----------------------|------------|
| M. le Professeur | AUBANIAC Jean-Manuel | 31/08/2015 |
| M. le Professeur | BOUVENOT Gilles      | 31/08/2015 |
| M. le Professeur | CAMBOULIVES Jean     | 31/08/2015 |
| M. le Professeur | FAVRE Roger          | 31/08/2015 |
| M. le Professeur | MATTEI Jean-François | 31/08/2015 |
| M. le Professeur | OLIVER Charles       | 31/08/2015 |
| M. le Professeur | VERVLOET Daniel      | 31/08/2015 |

**2013**

|                  |                            |            |
|------------------|----------------------------|------------|
| M. le Professeur | BRANCHEREAU Alain          | 31/08/2016 |
| M. le Professeur | CARAYON Pierre             | 31/08/2016 |
| M. le Professeur | COZZONE Patrick            | 31/08/2016 |
| M. le Professeur | DELMONT Jean               | 31/08/2016 |
| M. le Professeur | HENRY Jean-François        | 31/08/2016 |
| M. le Professeur | LE GUICHAOUA Marie-Roberte | 31/08/2016 |
| M. le Professeur | RUF0 Marcel                | 31/08/2016 |
| M. le Professeur | SEBAHOUN Gérard            | 31/08/2016 |

**2014**

|                  |                     |            |
|------------------|---------------------|------------|
| M. le Professeur | FUENTES Pierre      | 31/08/2017 |
| M. le Professeur | GAMERRE Marc        | 31/08/2017 |
| M. le Professeur | MAGALON Guy         | 31/08/2017 |
| M. le Professeur | PERAGUT Jean-Claude | 31/08/2017 |
| M. le Professeur | WEILLER Pierre-Jean | 31/08/2017 |

**2015**

|                  |                      |            |
|------------------|----------------------|------------|
| M. le Professeur | COULANGE Christian   | 31/08/2018 |
| M. le Professeur | COURAND François     | 31/08/2018 |
| M. le Professeur | FAVRE Roger          | 31/08/2016 |
| M. le Professeur | MATTEI Jean-François | 31/08/2016 |
| M. le Professeur | OLIVER Charles       | 31/08/2016 |
| M. le Professeur | VERVLOET Daniel      | 31/08/2016 |

**2016**

|                  |                   |            |
|------------------|-------------------|------------|
| M. le Professeur | BONGRAND Pierre   | 31/08/2019 |
| M. le Professeur | BOUVENOT Gilles   | 31/08/2017 |
| M. le Professeur | BRUNET Christian  | 31/08/2019 |
| M. le Professeur | CAU Pierre        | 31/08/2019 |
| M. le Professeur | COZZONE Patrick   | 31/08/2017 |
| M. le Professeur | FAVRE Roger       | 31/08/2017 |
| M. le Professeur | FONTES Michel     | 31/08/2019 |
| M. le Professeur | JAMMES Yves       | 31/08/2019 |
| M. le Professeur | NAZARIAN Serge    | 31/08/2019 |
| M. le Professeur | OLIVER Charles    | 31/08/2017 |
| M. le Professeur | POITOUT Dominique | 31/08/2019 |
| M. le Professeur | SEBAHOUN Gérard   | 31/08/2017 |
| M. le Professeur | VIALETTE Bernard  | 31/08/2019 |

**2017**

|                  |                     |            |
|------------------|---------------------|------------|
| M. le Professeur | ALESSANDRINI Pierre | 31/08/2020 |
| M. le Professeur | BOUVENOT Gilles     | 31/08/2018 |
| M. le Professeur | CHAUVEL Patrick     | 31/08/2020 |
| M. le Professeur | COZZONE Pierre      | 31/08/2018 |
| M. le Professeur | DELMONT Jean        | 31/08/2018 |
| M. le Professeur | FAVRE Roger         | 31/08/2018 |
| M. le Professeur | OLIVER Charles      | 31/08/2018 |
| M. le Professeur | SEBBAHOUN Gérard    | 31/08/2018 |

**2018**

|                  |                      |            |
|------------------|----------------------|------------|
| M. le Professeur | MARANINCHI Dominique | 31/08/2021 |
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| M. le Professeur | OLIVER Charles       | 31/08/2019 |

**2019**

|                  |                      |            |
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| M. le Professeur | BERLAND Yvon         | 31/08/2022 |
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| M. le Professeur | COZZONE Patrick      | 31/08/2020 |
| M. le Professeur | DELMONT Jean         | 31/08/2020 |
| M. le Professeur | FAVRE Roger          | 31/08/2020 |
| M. le Professeur | FONTES Michel        | 31/08/2020 |
| M. le Professeur | MAGALON Guy          | 31/08/2020 |
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PIRRO Nicolas

POINSO François

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RANQUE Stéphane

RAOULT Didier

REGIS Jean

REYNAUD/GAUBERT Martine

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SALAS Sébastien

*SAMBUC Roland Surnombre*

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SARLES/PHILIP Nicole

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SCAVARDA Didier

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SIELEZNEFF Igor

SIMON Nicolas

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TAIEB David

THIRION Xavier

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TREBUCHON-DA FONSECA Agnès

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VIENS Patrice

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| COZE Carole                                  | HRAIECH Sami                       | TOGA Isabelle                         |
| CUNY Thomas                                  | KASPI-PEZZOLI Elise                | TOMASINI Pascale                      |
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| DALES Jean-Philippe                          | LABIT-BOUVIER Corinne              | TROUSSE Delphine                      |
| DAUMAS Aurélie                               | LAFAGE/POCHITALOFF-HUVALE Marina   | TUCHTAN-TORRENTS Lucile               |
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ET DE LA REPRODUCTION ; GYNECOLOGIE MEDICALE 5405**

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MOUTARDIER Vincent (PU-PH)  
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BEGE Thierry (MCU-PH)  
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 FLECHER Xavier (PU PH)  
 PARRATTE Sébastien (PU-PH) *Disponibilité*  
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FOUILLOUX Virginie (MCU-PH)  
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 BOUFI Mourad (PU-PH)  
 MAGNAN Pierre-Edouard (PU-PH)  
 PIQUET Philippe (PU-PH)  
 SARLON-BARTOLI Gabrielle (PU PH)

LAGOUANELLE/SIMEONI Marie-Claude (MCU-PH)  
 RESSEGUIER Noémie (MCU-PH)

MINVIELLE/DEVICTOR Bénédicte (MCF)(06ème section)  
 TANTI-HARDOUIN Nicolas (PRAG)

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 PAULMYER/LACROIX Odile (MCU-PH)

**GASTROENTEROLOGIE ; HEPATOLOGIE ; ADDICTOLOGIE 5201**

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*BERNARD Jean-Paul (PU-PH) Retraite au 25/11/2019*  
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 DAHAN-ALCARAZ Laetitia (PU-PH)  
 GEROLAMI-SANTANDREA René (PU-PH)  
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 GRIMAUD Jean-Charles (PU-PH)  
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 DELAPORTE Emmanuel (PU-PH)  
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 MELLINAS Marie (MAST)  
 ROMAN Christophe (MAST)  
 TRINQUET Laure (MAST)

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GYNECOLOGIE MEDICALE 5404**

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 OLIVE Daniel (PU-PH)  
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FERON François (PR) (69ème section)

DEVILLIER Raynier (MCU PH)  
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 LAFAGE/POCHITALOFF-HUVALE Marina (MCU-PH)  
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BOUCRAUT Joseph (MCU-PH)  
 CHRETIEN Anne-Sophie (MCU PH)  
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 DESPLAT/JEGO Sophie (MCU-PH)  
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 DURAND Jean-Marc (PU-PH)  
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 HARLE Jean-Robert (PU-PH)  
 ROSSI Pascal (PU-PH)  
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ADNOT Sébastien (PR associé Méd. Gén. à mi-temps)  
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 NUSSELI Nicolas (MCF associé Méd. Gén. à mi-temps)  
 ROUSSEAU-DURAND Raphaëlle (MCF associé Méd. Gén. à mi-temps)  
 THERY Didier (MCF associé Méd. Gén. à mi-temps) (nomination au 01/10/2019)

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 VALERO René (PU-PH)

DUFOUR Henry (PU-PH)  
 FUENTES Stéphane (PU-PH)  
 REGIS Jean (PU-PH)  
 ROCHE Pierre-Hugues (PU-PH)  
 SCAVARDA Didier (PU-PH)

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CARRON Romain (MCU PH)  
 GRAILLON Thomas (MCU PH)

MARANINCHI Marie (MCF) (66ème section)

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 SOBOL Hagay (PR) (65ème section)

ATTARIAN Sharham (PU PH)  
 AUDOIN Bertrand (PU-PH)  
 AZULAY Jean-Philippe (PU-PH)  
 CECCALDI Mathieu (PU-PH)  
 EUSEBIO Alexandre (PU-PH)  
 FELICIAN Olivier (PU-PH)  
 PELLETIER Jean (PU-PH)

MAAROUF Adil (MCU-PH)



**OPHTALMOLOGIE 5502**

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 HOFFART Louis (PU-PH) *Disponibilité*  
 MATONTI Frédéric (PU-PH) *Disponibilité*

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 POINSO François (PU-PH)  
 GUIVARCH Jokthan (MCU-PH)

**OTO-RHINO-LARYNGOLOGIE 5501**

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 FAKHRY Nicolas (PU-PH)  
 GIOVANNI Antoine (PU-PH)  
 LAVIEILLE Jean-Pierre (PU-PH)  
 MICHEL Justin (PU-PH)  
 NICOLLAS Richard (PU-PH)  
 TRIGLIA Jean-Michel (PU-PH)

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PHARMACOLOGIE CLINIQUE; ADDICTOLOGIE 4803**

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 FAUGERE Gérard (PU-PH) *Surnombre*  
 MICALLEF/ROLL Joëlle (PU-PH)  
 SIMON Nicolas (PU-PH)

RADULESCO Thomas (MCU-PH)

BOULAMERY Audrey (MCU-PH)

REVIS Joana (MAST) (Orthophonie) (7ème Section)

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 CASSAGNE Carole (MCU-PH)  
 L'OLLIVIER Coralie (MCU-PH)  
 TOGA Isabelle (MCU-PH)

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 MATHIEU Marion (MAST)

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 MICHEL Gérard (PU-PH)  
 MILH Mathieu (PU-PH)  
 OVAERT Caroline (PU-PH)  
 REYNAUD Rachel (PU-PH)  
 SARLES Jacques (PU-PH)  
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## **AVANT-PROPOS**

L'insuffisance rénale chronique terminale (IRCT) est une pathologie fréquente dont la mortalité à l'échelle du globe dépasse maintenant les grandes maladies transmissibles comme le VIH, la tuberculose ou le paludisme. Le faible accès à au traitement de suppléance dans les pays les plus pauvres est responsable de 2 à 7 millions décès annuels. Le traitement de suppléance est réalisé soit par hémodialyse ou dialyse péritonéale, soit par la transplantation rénale qui représente le traitement de référence. Mais l'accès à ces traitements coûteux est inégalement réparti à la surface du globe et il n'est pas rare que des patients extra-européens atteints de maladie rénale chronique migrent en France et y soient pris en charge par notre système de santé.

L'accès aux soins des patients extra-européens est conditionné par l'obtention d'une assurance maladie. L'éligible à la Protection Maladie Universelle (PUMA) à leur arrivée sur le territoire est soumis à certains critères. L'Aide Médicale d'Etat (AME) n'est effective qu'après 3 mois et les demandes de soins urgents peuvent être longues à mettre en place en raison de difficultés linguistiques, financières, administratives ou du délai d'expiration d'un VISA touristique. Les patients migrants atteints d'IRCT sans couverture santé sont donc pris en charge selon des modalités différentes selon les centres d'hémodialyse, pouvant aller de trois dialyses hebdomadaires programmées jusqu'à la dialyse uniquement en cas d'urgence vitale, en attendant l'ouverture de droit à une assurance maladie.

Les modalités de dialyse dégradées ou uniquement en cas d'urgence font courir au patient le risque de complications pouvant aggraver son état de santé et impacter sa qualité de vie. Il nous semble également qu'elles mettent en tension le système de santé et augmentent le



recours aux services d'urgence, aux transports médicalisés parfois nocturnes, à l'utilisation de coûteuses filières de soins continus.

Deux études américaines portant sur une population de migrants sans assurance maladie montrent une augmentation de la mortalité à long terme, des hospitalisations et des coûts de prise en charge en cas de dialyse en urgence uniquement. Ces résultats sont en partie liés avec le système de santé américain qui ne prévoit pas d'accès à une assurance maladie universelle quelle que soit la durée de résidence sur le territoire. En France, cette période sans accès à une assurance maladie ne peut aller au-delà de 3 mois. Il n'y a pas d'étude publiée qui évalue la prise en charge des patients migrants en France avec une IRCT.

Nous avons donc réalisé une étude rétrospective médico-économique dans une population de patients hémodialysés migrant en France, dans le but d'analyser les coûts et les modalités de prise en charge dans les 3 mois suivant leur arrivée dans le centre.

## **ABSTRACT**

### **Introduction.**

In the setting of migration, extra-European patients with end-stage renal disease (ESRD) have a lower access to renal replacement therapy (RRT). Healthcare coverage access at arrival in France may influence hemodialysis strategy during the first 3 months. We aimed to study clinical healthcare costs and outcomes in this population in Marseille.

### **Methods.**

We conducted a retrospective cohort study of ESRD migrant patients admitted for hemodialysis in our center over a 4-years period. Patients were recently arrived in France and willing to stay regardless of their administrative status with a local follow-up of at least 3 months. The first group with access to Protection Universelle Maladie (PUMA) was compared to patients without access to PUMA. Patients with operational health coverage were scheduled in conventional dialysis and patients without health coverage had transient “emergency-only” dialysis before their rights were effective. We assessed the ESRD-related costs for the healthcare system and the medical outcomes during the 3-months period after arrival. Multivariate analysis was performed with partial least square regression.

### **Results.**

We included 25 patients aged in median 42.6 [31.7; 53.6] years old and 60% of them were males. Ten patients had access to PUMA on arrival and 15 patients did not. Baseline characteristics were similar between the two groups. Four patients (26%) in the No healthcare coverage group needed a switch from “emergency-only” to conventional strategy for medical reason. ESRD-related healthcare costs were also higher in the absence of medical coverage (20 813 [15 516; 28 609] vs 12 465 [11 957; 13 911],  $p < 0.001$ ). Patients in the No healthcare

coverage group spent more time in “emergency-only” dialysis (16.5 [6.5; 36.5] vs 0 [0; 7] days,  $p=0.002$ ) and had more ESRD-related complications (3 [1; 9] vs 1 [0; 1],  $p=0.02$ ) than patients with health coverage. Partial least square regression analysis show that the strongest independent predictor of healthcare costs was the number of ESRD-related complications ( $R^2_{Xy} = 0.96$ ).

### **Conclusion.**

This study is the first French cohort describing ESRD patients at their arrival in France with a medico-economic and outcome analysis. The absence of healthcare coverage and the subsequent “emergency-only” dialysis strategy are strongly associated with higher healthcare costs and more frequent ESRD-related complications in migrant patients with ESRD.

## ABBREVIATIONS

AME: *State Medical Aid*

ATIH: Agency for Data on Hospital Care

CKD: Chronic kidney disease

CSS: *Couverture Santé Solidaire*

DIM: Medical information department

DRG: diagnosis-related groups

ED: Emergency department

ESRD: End-stage renal disease

GHS: homogenous groups of stays

GHM: homogenous groups of patients

IOM: International Organization of Migration

ISN: International society of nephrology

OFII: French office for immigration and integration

PMSI: program for the medicalization of information systems

PUMA: *Protection Universelle Maladie*

SMUR: Mobile emergency and reanimation service

UNESCO: United Nations Educational, Scientific and Cultural Organization

## INTRODUCTION

Chronic kidney disease (CKD) affects 850 million people worldwide (11.2% of the world population), of which 5.3 to 10.5 million (0.1% of the world population) will progress to end-stage renal disease (ESRD) (1,2). The treatment is based on renal-replacement therapy by peritoneal dialysis, hemodialysis or ideally renal transplantation. Access to renal-replacement therapy suffers from important disparities between countries and may concern less than 10% of patients in low-income countries (2). Limited access to ESRD treatment is responsible for 2 to 7 million annual deaths worldwide (2–4).

Limited access to healthcare, particularly in the setting of ESRD diagnosis, lead people to immigrate in high-income country with broader availability of dialysis and improve healthcare quality for their kidney disease. Among the potentials factors influencing the decision to immigrate, 5 to 10% of migrants report healthcare access as the main reason to immigrate (5,6) but there is no specific study about kidney disease. Burden of migrants and refugees with ESRD in North America (7–10) and in Europe (11) is being increasingly studied and discussed by nephrologists. In Europe, a survey of the International Society of Nephrology (ISN) suggests that refugees represent about 1.5% of dialysis patients with a majority in the largest nephrology centers (12). The French Office for Immigration and Integration (OFII) estimates that migrant patients represent 1.6 to 3.2% of hemodialysis patients in France (unpublished data).

In France, migrants have poorer healthcare access, socioeconomic conditions, and housing access than the general population (5,13,14). Refugees, asylum-seekers and migrants working or being resident in France on a stable and regular basis have access to the Protection Universelle Maladie (PUMA) supplemented by the Couverture Santé Solidaire (CSS) which is a universal healthcare coverage and include maintenance dialysis (15–17). The State

Medical Aid (AME) is a healthcare coverage, including maintenance dialysis, for unemployed people or not being resident in France if they can prove its presence on French territory for at least 3 months (18). During these first 3 months, non-resident migrants may have access to the Emergency medical aid (AMU) which include maintenance dialysis. Complexity of procedures, availability of social workers, financial difficulties, and barrier language are likely to extend the period to obtain healthcare coverage by AMU and AME can lead to health aggravation of migrants with ESRD.

The “conventional” strategy of ESRD treatment includes three dialysis sessions per week, with clinical, biological and imaging surveillance, daily medication, treatments during the session, and reimbursement of transport to the dialysis center. Healthcare coverage limitation may constrain nephrologists to rely incomplete care, known as “degraded” strategies, the extreme being dialysis only in cases of vital emergency, known as the “emergency-only” strategy. Two comparative US studies have shown an association between “emergency-only” strategy with higher mortality, more frequent hospitalizations and higher healthcare costs than migrants which obtain healthcare coverage and being then treated by the “conventional” dialysis strategy (19,20).

In the French healthcare system, even if universal healthcare coverage, including maintenance dialysis, begins 3 months after a migrant’s arrival, we hypothesized that the waiting period to obtain universal healthcare coverage and the “emergency-only” strategy in migrants at their arrival in France could be more expensive for the French healthcare system and could generate additional ESRD-related complications than the “conventional” strategy. The aim of the present study was to compare the costs and the clinical outcomes in ESRD migrant patients with and without healthcare coverage during the next 3 months after their arrival in France.

## **METHODS**

### **Study design**

We conducted a retrospective cohort study of migrant patients with ESRD admitted for the first time for hemodialysis in our center over a 4-years period. The data used in this study was anonymized, approved and registered by the Health Data Portal of our institution under the reference PADS2-279. Reporting and redaction were made in accordance with the Strengthening the Reporting of Observational Studies (STROBE) guidelines.

### **Population**

We included all migrant patients aged 18 years or more with ESRD, treated by hemodialysis or with an indication for chronic dialysis on arrival in France, and who were received for the first time at the Center of Nephrology and Renal Transplantation in Marseille between May 1, 2014 and June 1, 2018. Migrants were defined as extra-European persons leaving their country of residence to live in France. We included refugees, defined as persons forced to leave their country in order to escape war, persecution or natural disaster, with asylum in France; asylum-seekers, defined as persons who are currently in demand to obtain asylum in France; and non-asylum-seeking migrants. Patients with acute kidney failure, treated with peritoneal dialysis and patients who had CKD without necessity for dialysis at their arrival in France were not included. Patients who left the center less than 3 months after the first dialysis were excluded from analysis.

### **Data collection**

Patients were screened from several sources: social service records from the social service of the Hospital de la Conception, notes taken during the daily medical staff and records from the Department of Medical Information (DIM). These sources were then cross-referenced, and inclusion criteria were checked for each patient to determine its eligibility. We collected

during the study period demographic data (age, sex, nationality, country of origin), administrative data (date of arrival in France, presence of family in national territory, mastery of French language, obtention of health coverage at arrival), and medical data (comorbidities, nephropathy, residual diuresis, type of vascular access, date of the first dialysis, date of the instauration of renal replacement therapy) from medical and social records. The occurrence of acute pulmonary edema, severe hyperkalemia, metabolic acidosis, severe hypertension, uremia-associated complication (for example pericarditis or encephalopathy) during the study period was considered as attributable to ESRD management strategy. Cardiovascular events and gastrointestinal hemorrhage occurring were also considered as related to the ESRD management strategy (**appendix 1**). Vascular access-related complications were also collected but not considered attributable to ESRD management strategy. We also collected long-term follow-up information, transfers in center with lighter modalities of hemodialysis, changes in the type of renal replacement therapy including transplantation, inscription in waiting list for transplantation and death.

### **Healthcare coverage status**

Patients were categorized in 2 groups according to their healthcare coverage status at their arrival in France. Patients with the PUMA coverage were assigned to the Health coverage group (16,17). Patients without PUMA coverage or with a touristic VISA were assigned to the No health coverage group (18). In the absence of VISA, patients in the No health coverage group may have benefit Emergency medical aid (AMU) triggered by social workers before obtention of AME to begin conventional dialysis (21).

### **ESRD Management**

Two strategies could be performed in the center depending on health coverage rights.



In the “emergency-only” strategy, patients had clinical and biological evaluation at an emergency department (ED) before being eventually admitted in the nephrology department to receive hemodialysis session in intensive care or chronic dialysis unit. To receive emergency-only hemodialysis, the patient must present ESRD-related complications described in **appendix 1** including acute pulmonary edema, hyperkalemia, symptomatic hypertension, metabolic acidosis, uremia-related symptoms. Transport could include medical monitoring if needed. Acute medical conditions not related to ESRD were managed at the ED. Depending on the hour, the patient could have a social workers assistance to request healthcare coverage. When the health coverage is operational, patients are switched to “conventional” strategy. In case of any medical condition with necessity of regular hemodialysis, the medical team could trigger conventional strategy even in the absence of health coverage.

The “conventional” strategy consisted in three regular dialysis sessions per week with transportation to the center. In case of acute ESRD-related complication, the patient could directly contact nephrology intensive care or chronic dialysis unit (depending on the hour and degree of emergency) to be admitted without mandatory passage to ED. This strategy implied also daily medication for ESRD including hypertension, CKD-Mineral and Bone Disorder, adjunctive dialysis treatments like iron therapy or erythropoiesis-stimulating agents and additional screening tests when needed, for example to evaluate arteriovenous fistula or cardiac function.

### **Economic analysis**

We performed a cost analysis based on the Society’s perspective. Total costs were calculated and compared between the two groups, corresponding to the difference in mean costs (expressed in Euros). Patients still alive were censored at the date of the end of the follow-up period, precisely 3 months after enrolment in the study. The economic analysis considered all

direct healthcare costs in relation with haemodialysis, transport and management care. All input data were collected individually and retrospectively for each patient enrolled into the study. This included costs relating to 1) administration of haemodialysis, which include haemodialysis sessions, transports performed by the Mobile Emergency Medical Services (SMUR) and ambulance transports, and 2) inpatient care for managing adverse events, ESRD-related complications and surveillance. For example, the total cost of each inpatient stay included the cost of the diagnosis-related groups (DRGs), with costs calculated according to the National Reference Costs (ENC), as well as any additional costs due to any short passages in ED, ongoing observation, amount of expensive molecules, or any transports except transfers between institutions already included in the National Reference Costs (ENC) estimates. As the follow-up time horizon was short, discounting was not applied. Unit costs were obtained from the French national health coverage system and inpatient costs derived for valuation of DRGs, according to CIM-10 coding, and based on 2017 hospital activity and associated expenditures, based on the ENC. The French public Agency for Data on Hospital Care (ATIH) database was used (22). In the study population, the CIM-10 codes 28, 11 and 10 were mainly observed. The ESRD healthcare cost was defined as the sum of hospital and transportation costs related to complications attributable to the management strategy of ESRD as detailed in **appendix 2**. The transport costs were based on national health coverage reimbursement rates for in-agglomeration transportation of 5 kilometers (23). Transport from out-hospital to our department were estimated to 68.75€ for an ambulance transportation and 23.62€ for a car/cab transportation. Transportation costs with personal or public means were considered as negligible. The cost transport between the ED and our department was included in the ENC estimates.

## **Statistical analysis**

Clinical characteristics upon enrolment were compared at inclusion in the study using either Student's t or Mann-Whitney (for quantitative variables), chi-squared or Fisher's exact tests (for qualitative variables), as appropriate. Descriptive statistics were performed on costs and secondary outcomes, in order to identify those characteristics that may influence cost outcomes and ESRD-related complications. The primary endpoint, quantitative data, was analysed using Mann-Whitney U test in accordance with the variable distribution. For the secondary endpoints, also quantitative data, similar descriptive analyses were conducted. Statistical significance was defined as  $p=0.05$  in two-sided tests. These analyses were performed using Microsoft Excel 365 ProPlus, PASW Statistics version 18.0.0 and JMP Statistics 14.2.0.

Due to a relative small sample size ( $N=25$ ), and in the context of multicollinearity of predictors, unstable inferences using standard linear regression models may occurred. Therefore, Partial Least Squares (PLS) regression was performed. PLS regression extracts a set of orthogonal factors called latent variables which are used to capture most of the information in the explanatory variables useful for predicting the dependent variable (24). First, pair-wise correlation matrix of the study variables was provided. Second, PLS regression models were developed and proportion of variance explained ( $R^2_{Xy}$ ) were taken as a measure of the models Goodness of Fit. The final model was optimized with a  $R^2_{Xy}$  value of 0.73 at three latent factors. Finally, PLS standardized regression coefficients were provided. For this analysis, we used the R packages "pls" and "plsdepot".

## RESULTS

### Population

We identified 33 patients eligible during the study period. Five patients (15.1%) did not meet the inclusion criteria: 3 of them were resident in France for several years before initiation of dialysis, one had CKD without need of dialysis at arrival and one died during dialysis in intensive care unit before contact with the nephrology team. Three patients (9.1%) did not complete the follow-up of three months and were excluded from analysis. Twenty-five patients were included (**figure 1**). The median age was 42.6 [31.7; 53.6] and most patients (60%) were male. 9 patients (36%) had undetermined nephropathy and half (52%) had significant residual diuresis (more than 500ml). **Table 1** describes baseline characteristics of the cohort and **table S1** summarizes parameters at admission.

### Healthcare coverage and dialysis strategy

Ten patients were categorized in the group with healthcare coverage because of rapid access to PUMA after their arrival: 2 patients with political refugee status and 3 with asylum request which benefits from PUMA respectively at the 1st, 7th and 13th day of their arrival; 2 patients were Franco-Algerian bi-national living in Algeria who returned in France respectively 2 and 42 months after hemodialysis initiation in Algeria ; 2 patients benefited from rights in other EU countries and one patient had already health coverage rights from a former stay in France. All those patients received the “conventional” strategy.

Fifteen patients were categorized in the group without healthcare coverage. All those patients were programmed to receive the “emergency-only” strategy. However, four of them (26.6%) needed a switch to the “conventional” strategy for medical reasons: one patient had superior vena cava syndrome and needed hospitalization for vascular procedure and anticoagulation, another patient was anuric (bilateral nephrectomy history) and 2 patients had severe ESRD-

related complications (uremic encephalopathy and hypertension with microangiopathy), respectively at day 1st, 4th, 12th and 23th from the first dialysis session in the center.

There were no significant differences between the two groups in terms of age, BMI, dialysis vintage, vascular access, region of origin, time since arrival, French language or presence of family in France.

### **Healthcare costs**

The use of health care resources in each group during the period study was compared in **Table 2**. Duration of “emergency-only” period was shorter in the group with health coverage at arrival compared to the group without health coverage (0 [0; 7.5] and 16 [6.5; 36.5] days,  $p = 0.002$ ). The median global healthcare cost was higher in the No health coverage group compared to the Health coverage group (€22 090 [16 141; 29 176] vs 12 930 [12 224; 15197],  $p < 0.001$ ). In the whole cohort, ESRD-related costs represented 90.1% of global healthcare costs. The median ESRD-related cost was higher in the group without health coverage group compared to the health coverage group (€20 813 [15 516; 28 609] vs 12 465 [11 957, 13 911],  $p < 0.001$ ). The No health coverage group spent more time at hospital compared to the health coverage group especially in intensive care (2 [0; 9.5] vs 0.5 [0; 2] days,  $p = 0.002$ ), where emergency dialysis were performed. ED visits and SMUR transportation were also more frequent (4 [2; 7.5] vs 1 [1; 2] and 2 [1; 6] vs 0.5 [0; 1] respectively;  $p = 0.002$  and  $p = 0.011$ ). The total number of hemodialysis sessions (emergency-only and conventional) over the study period was not significantly different between the two groups (38.5 [33; 39] vs 36 [27.5; 37.5],  $p = 0.14$ ) (**Table 2**).

### **ESRD-related complications**

The median number of ESRD-related complications was higher in the group without health coverage compared to the health coverage group (3 [1; 9] vs 1 [0; 1],  $p = 0.023$ ) (**Table 2**). In

the whole cohort, 105 ESRD-related complications occurred during 2250 days of follow-up but most of them (n=96, 91.4%) occurred during “emergency-only” period and only 9 occurred during conventional dialysis (**Figure 2**). The most frequent complications were severe hyperkalemia (n=46, 43.8%), acute pulmonary edema (n=32, 30.5%) and severe hypertension (n=20, 19.0%). Other complications included uremic encephalopathy (n=1), uremia-associated incoercible vomiting (n=1), severe metabolic acidosis (n=1) and acute coronary syndrome (n=4) in hypertensive context. One patient needed percutaneous coronarography and was treated with transluminal angioplasty of a coronary lesion. 75 of these complications (71.4%) required SMUR transportation for emergency dialysis session. During the study period, we also observed 5 vascular access complications: one superior vena cava syndrome, two catheter-related bacteremia, one AVF drainage vein thrombosis and one digital ischemia from AVF steal syndrome. Other medical conditions unrelated to ESRD during the follow-up were septic knee arthritis, community-acquired pneumonia, uncontrolled diabetes mellitus and cardiac defibrillator placement for a preexisting cardiopathy.

### **Predictors of ESRD healthcare costs**

**Table 3** depicts the correlation between predictors and the response variable estimated. The absence of health coverage ( $r=0.72$ ,  $p<0.001$ ), the number of ESRD-related complications ( $r=0.55$ ,  $p=0.004$ ), ED visits ( $r=0.50$ ,  $p=0.010$ ) and SMUR transportation ( $r=0.48$ ,  $p=0.014$ ) were significantly correlated ( $p<0.05$ ) with ESRD-related healthcare cost variable. Time spent on conventional hemodialysis was negatively correlated with ESRD-related healthcare cost variable ( $r= -0.53$ ,  $p=0.006$ ). Some predictors were also correlated with each other; for example the number of ESRD-related complications were positively correlated with the ESRD-related healthcare cost ( $r= 0.56$ ,  $p=0.004$ ) and negatively correlated with the number of hemodialysis sessions ( $r= -0.50$ ,  $p=0.043$ ) and the time spent in conventional hemodialysis ( $r= -0.83$ ,  $p=0.006$ ).

**Table 4a** and **4b** present the results of PLS regression. The models' components were chosen by maximizing the variance in the dependent variable (ESRD-related healthcare costs): three components were fitted on the PLS model, explaining 73.0% of the variance in ESRD healthcare costs (Table 4a). **Table 4b** provides the value of the correlation between each component and each predictive variable, in specifying the direction of the relation (columns X-loadings).

A range of predictive variables had strong associations with total healthcare cost ( $R^2_{Xy} > 0.80$ ). ESRD-related complications and time in "Conventional" strategy were the most relevant predictor variables, followed by the number of SMUR transportations and ED visits; ESRD-related complications, SMUR transportations and ED visits were positively associated with total healthcare cost (standardized  $\beta = 0.888, 0.019$  and  $0.040$ ;  $R^2 = 0.960, 0.932$  and  $0.884$ , respectively); the association was inverse for time in "Conventional" strategy (standardized  $\beta = -0.014$ ;  $R^2 = 0.921$ ).

### **Long-term follow-up**

After a median follow-up time of 2.6 [2.1 ; 3.8] years, 11 patients (44%) were still under renal-replacement therapy in our center, 13 patients (52%) were transferred in others hemodialysis center and one patient (4%) was lost. None had been transferred to peritoneal dialysis. Two patients underwent kidney transplantation, one in our center and another after transfer in another transplantation center and six patients were on transplantation waiting list. Three patients died: two patients 77 and 58 years, both with advanced cardiopathy and another 35 years old, from an infectious complication in the first year after transplantation.

## DISCUSSION

This is the first French cohort describing ESRD patients at their arrival in France with a medico-economic and outcome analysis. We found that absence of health coverage in the first 3 months increased global healthcare cost and ESRD-related complications with subsequent acute care utilization. These results favor our initial hypothesis that medical care with universal health coverage for migrants arriving in France is the best strategy from both medical and economic point of view.

The medico-economic analysis tried to fit as much as possible to the reality of public healthcare depenses in a societal perspective. In our study, healthcare costs unrelated to ESRD represented less than 10%. ESRD-related healthcare costs are strongly and independently associated to ESRD-related complications and to ED visits, SMUR transports and in-hospital stays as observed in the first component of the PLS regression. The former variables, which represent the acute care management, are intimately connected and the PLS regression categorizes them as the same latent variable. Another strong determinant is the time spent in “emergency-only” dialysis, which basically works by waiting for complications and therefore triggers avoidable healthcare depenses. Noteworthy, Migrant patient with cardiopathy history has a full-fledged impact in the healthcare cost in relation with greater dialytic needs as show in component 2 of the PLS regression. In our cohort, migrant have median dialysis vintage around 3 years before their arrival in France. Similarly to the literature data, we observed in component three of the PLS regression that irregular dialysis in long-term dialysis patients increased the ESRD cost probably due to the accumulated morbidity related to the dialysis condition.

Our analysis shows that patients without health coverage at their arrival in France undergo more acute pulmonary edema, hyperkalemia and hypertension episodes than patient with



effective coverage. Nearly all of the complications occurred during the “emergency-only” dialysis period, which is longer in patients without healthcare coverage at arrival. Four patients even needed transfer from “emergency-only” to conventional strategy, suggesting that this degraded strategy is not sufficient to manage severe medical condition or increases the gravity of complications related to ESRD. These considerations strongly suggest that early use of conventional thrice-a-week dialysis strategy is likely to provide protection against ESRD-related complications. Interestingly, during the first three months, the number of hemodialysis sessions was not significantly different between groups. This highlights that regular frequency in dialysis session is the key parameter to reduce the incidence of ESRD-related complications.

Two comparative US studies shows that emergency-only strategy was associated with higher mortality, more hospitalizations and higher healthcare cost than conventional dialysis over longer study periods (19,20). However, US healthcare system does not provide universal healthcare coverage to non-resident migrant and “emergency-only” dialysis could last for years. In France, the 2nd Pasqua law of August 24, 1993, relating to the control of immigration and the conditions of entry, reception and residence of foreigners, makes the affiliation to the health coverage subject to the regularity of the residency. Finally, according to the finance law of December 30, 2003, a condition of stability of a 3-month residency in France is opposed to any foreigner in order to claim health coverage regardless of the legality of the residency. The waiting situation of migrant patients after their arrival to obtain healthcare coverage is the result of these different legislations, which intended to reduce public expenses but are harmful for patients. Facilitating the health coverage in migrant population will probably result in health system and societal benefits.

Our work has significant limitations. The little sample size, the possible center effect and selection bias are inherent to its retrospective and monocentric study. We did not include patients who only had transient dialysis and left the center before obtaining health coverage. Moreover, our study only highlights correlation and not causality between the absence of health coverage and a lower efficiency of our healthcare system.

In the current state of the French legislation, ESRD migrant patients at their arrival in France without health coverage have not access to thrice-a-week dialysis. In reaction, nephrologists are forced to use degraded strategy like “emergency-only” dialysis. Our data suggests that “emergency-only” dialysis leads to ESRD-related complications and is not cost-effective. If degraded strategy has to be implemented, a regular frequency in dialysis session is surely more efficient than emergency-only dialysis on clinical outcome and healthcare cost. However, the proven standard-of-care in hemodialysis patients remains three weekly dialysis sessions. Our legislation has to evolve in order to allow nephrologists to provide the optimal care for all patients with ESRD.

## **CONCLUSION**

Our study provides evidence that immediate health coverage access to ESRD migrant at their arrival in France is associated with less ESRD-related complications and few related healthcare costs. The associated morbidity and lack of economic benefit of the “emergency-only” strategy in migrant patients with ESRD should prompt nephrologists to avoid this strategy and implement the “conventional” strategy regardless of the health coverage status.

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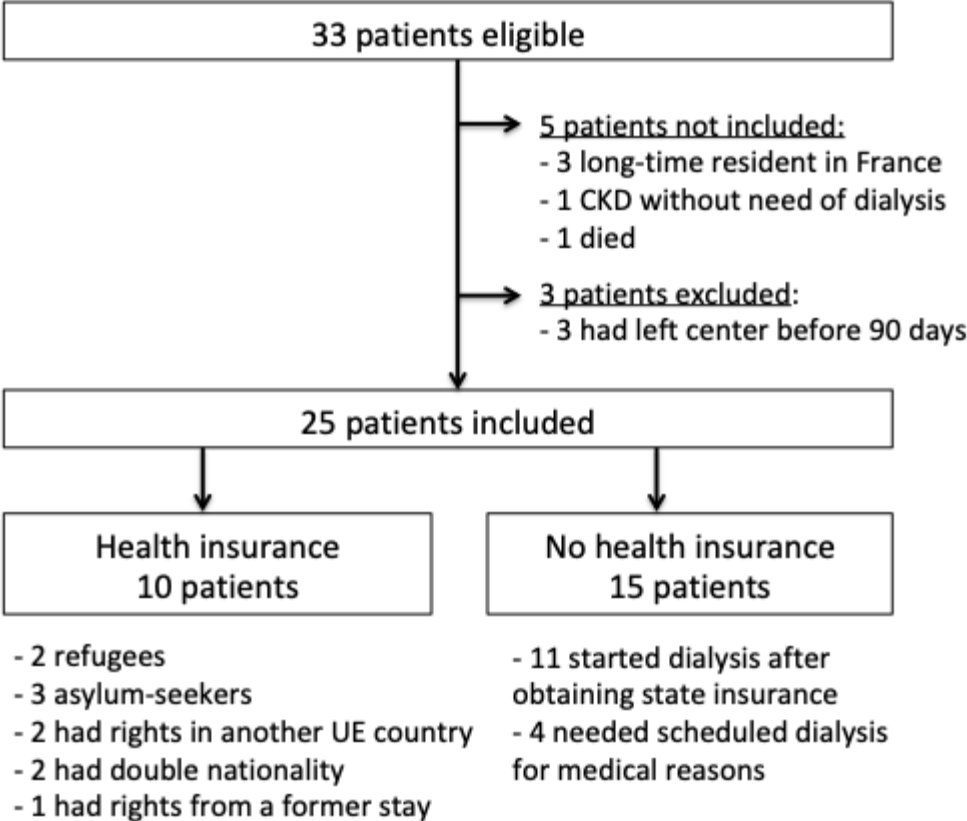
The authors thank Alexandra Elbakyan for help in the literature review.

## **Conflict of interest**

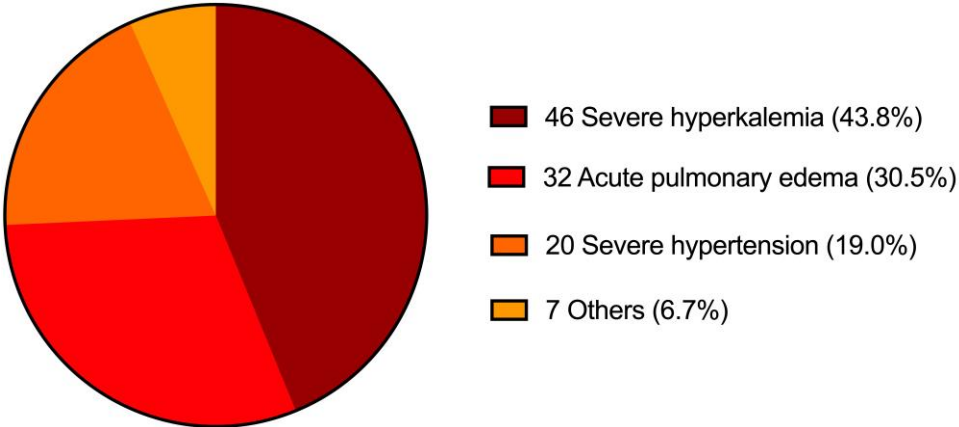
The authors have no conflict of interest to declare.

**FIGURES**

**Figure 1. Flow chart of the study**



**Figure 2. ESRD-related complications in the whole cohort during the study period**



**Table 1. Baseline characteristics of the patients.**

|   | <b>Population<br/>N = 25</b> |
|---|------------------------------|
| <b>Age</b>                                | 42.6 [31.7 ; 53.6]           |
| <b>Women</b>                              | 10 (40%)                     |
| <b>BMI</b>                                | 22 [19 ; 25.8]               |
| <b>Comorbidities</b>                      |                              |
| - Hypertension                            | 21 (84%)                     |
| - Diabetes mellitus                       | 5 (20%)                      |
| - Renal transplantation                   | 1 (4%)                       |
| - Cardiopathy                             | 6 (24%)                      |
| <b>Nephropathy</b>                        |                              |
| - Undetermined                            | 9 (36%)                      |
| - Interstitial                            | 6 (24%)                      |
| - Diabetic                                | 5 (20%)                      |
| - Glomerular                              | 2 (8%)                       |
| - Vascular                                | 2 (8%)                       |
| - Hereditary                              | 1 (4%)                       |
| <b>Residual diuresis</b>                  | 13 (52%)                     |
| <b>Time on dialysis, months</b>           | 36 [10 ; 54]                 |
| <b>Vascular access at admission</b>       |                              |
| AVF                                       | 16 (64%)                     |
| Catheter                                  | 4 (16%)                      |
| None                                      | 5 (20%)                      |
| <b>Region of origin</b>                   |                              |
| North Africa                              | 11 (44%)                     |
| Balkans / Caucasus                        | 7 (28%)                      |
| Sub-Saharan Africa                        | 4 (12%)                      |
| Middle East                               | 2 (8%)                       |
| Asia                                      | 1 (4%)                       |
| <b>Time since arrival in France, days</b> | 2.5 [0.5 ; 8]                |
| <b>Health coverage at arrival</b>         | 10 (40%)                     |
| <b>Family in France</b>                   | 11 (44%)                     |
| <b>French-speaking</b>                    | 9 (36%)                      |
| <b>Tourist VISA</b>                       | 6 (24%)                      |

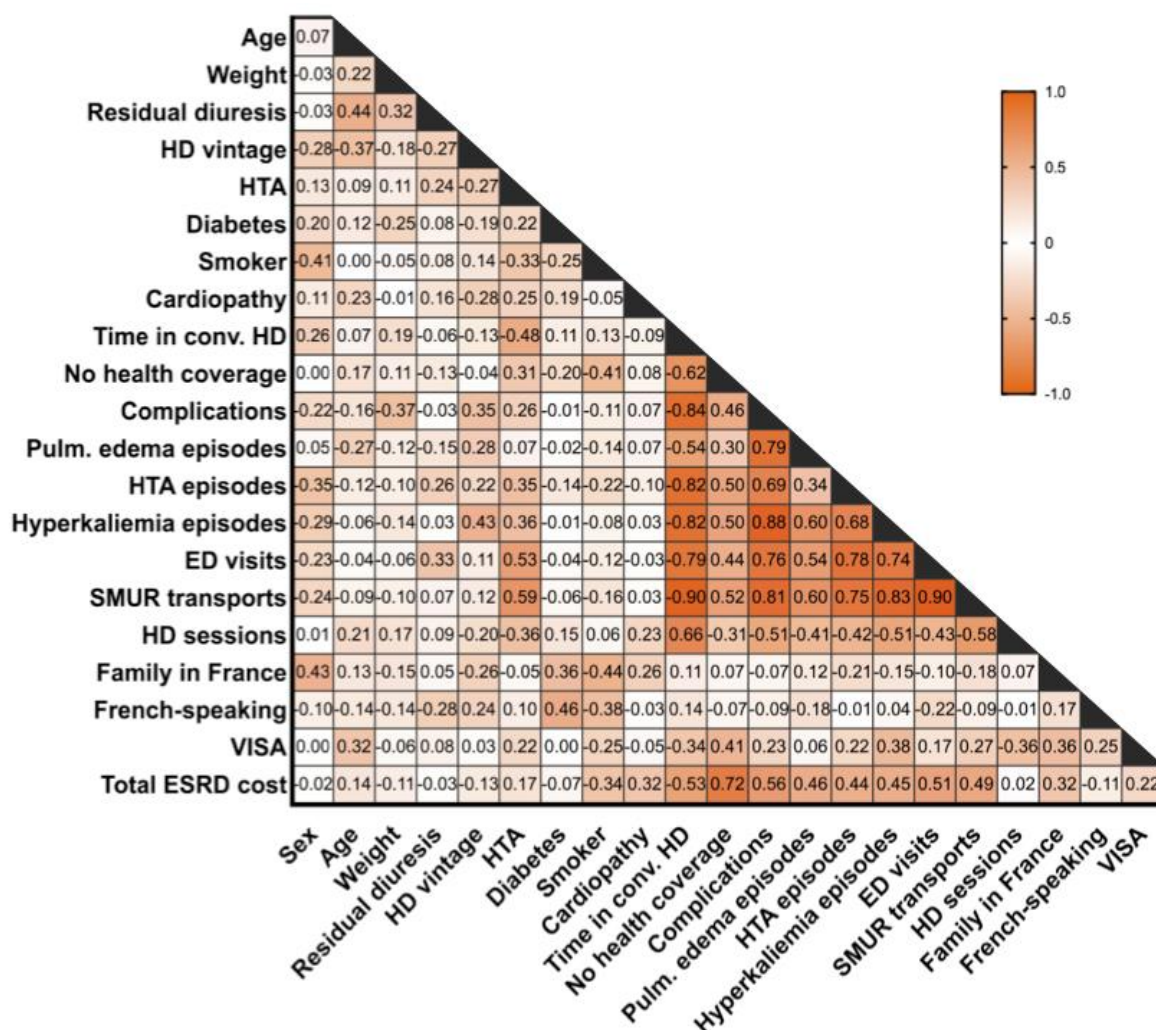
*AVF, arteriovenous fistula ; IQR, interquartile range ; NS, non-significant.* Qualitative variables are described with number and percentage. Quantitative variables are described by median and interquartile range (IQR).

**Table 2. Healthcare use and costs in patients with and without health coverage costs in the next 3 months after arrival in France**

|  | <b>Health coverage<br/>N = 10</b> | <b>No health coverage<br/>N = 15</b> | <b>P</b> |
|--|-----------------------------------|--------------------------------------|----------|
| Global healthcare cost                   | 12 930 [12 224; 15 197]           | 22 090 [16 141; 29 176]              | < 0.001  |
| ESRD-related healthcare cost:            | 12 465 [11 957; 13 911]           | 20 813 [15 516; 28 609]              | < 0.001  |
| “Emergency-only” strategy duration, days | 0 [0; 7]                          | 16 [6.5; 36.5]                       | 0.002    |
| “Emergency-only” period                  |                                   |                                      |          |
| - Dialysis sessions                      | 0.5 [0; 2]                        | 4 [1.5; 8]                           | 0.003    |
| - SMUR transports                        | 0 [0; 1]                          | 2 [1; 5]                             | 0.01     |
| “Conventional” period                    |                                   |                                      |          |
| - Dialysis session                       | 38.5 [33; 39]                     | 32 [22; 35.5]                        | 0.01     |
| Days at hospital                         |                                   |                                      |          |
| - In intensive care                      | 0.5 [0; 1]                        | 2 [0; 9.5]                           | 0.002    |
| - In conventional unit                   | 0 [0; 0]                          | 4 [2; 7.5]                           | 0.06     |
| ED visits                                | 1 [1; 2]                          | 4 [2.5; 8]                           | 0.002    |
| SMUR transports                          | 0.5 [0; 1]                        | 2 [1; 6]                             | 0.011    |
| Dialysis sessions                        | 38.5 [33; 39]                     | 36 [27.5; 37.5]                      | 0.14     |
| ESRD-related complications               | 1 [0; 1]                          | 3 [1; 9]                             | 0.023    |

*ED: Emergency department; ESRD: End-stage renal disease; SMUR: Mobile emergency and reanimation service.* The costs are expressed in euros (€) over three months after first dialysis. Quantitative variables are described by median and interquartile range (IQR). Comparisons are performed with the U Mann-Whitney test for independent samples.

**Table 3: Pair-wise correlation matrix of study variables**



Qualitative variables are tested with U-Mann Whitney rank sum test; quantitative variables are tested with spearman correlation test = rho.

*Sex: female sex; HD vintage: Hemodialysis vintage; HTA: history of hypertension; Time in conv. HD: Time spent in conventional dialysis strategy; Complications: number of complications overall the study period; ED: Emergency department; SMUR: Mobile emergency and reanimation service; HD session: number of HD sessions overall the study period*



**Table 4a. Summary of the PLS model results.**

| Model | Component | R <sup>2</sup> X (%) | Cumulative R <sup>2</sup> X (%) | R <sup>2</sup> Y (%) | Cumulative R <sup>2</sup> Y (%) |
|-------|-----------|----------------------|---------------------------------|----------------------|---------------------------------|
| PLS   | First     | 26.0                 | 26.0                            | 38.3                 | 38.3                            |
|       | Second    | 16.9                 | 42.9                            | 25.5                 | 63.8                            |
|       | Third     | 10.0                 | 52.9                            | 9.2                  | 73.0                            |

The models' components were chosen by maximizing the variance in Y (dependent variable).

Three components were fitted on the PLS model, explaining 73.0% of the variance in Y. The

first 3 components explained 52.9% of the variation in predictive variables

*R<sup>2</sup>X; R-square scores for the independent variables; R<sup>2</sup>Y: R-square scores for the dependent variable (ESRD-related healthcare cost)*

**Table 4b. Standardized PLS regression coefficients using 3 components and cumulative R-squared in predicting ESRD-related costs.**

|                               | ESRD-related costs |                 |                  |                 | Cumulative R-squared ( $R^2_{XY}$ )*** |
|-------------------------------|--------------------|-----------------|------------------|-----------------|--|
|                               | Standardized Beta* | X-Loadings**    |                  |                 |  |
|                               |                    | First Component | Second Component | Third Component |  |
| Sex (female)                  | 0.040              | 0.024           | 0.246            | <b>-0.353</b>   | 0.410                                  |
| Age                           | 0.087              | 0.021           | 0.243            | -0.268          | 0.307                                  |
| Weight                        | -0.052             | -0.077          | 0.055            | -0.088          | 0.044                                  |
| Residual diuresis             | -0.237             | -0.032          | -0.251           | -0.319          | 0.198                                  |
| Hemodialysis vintage          | -0.017             | 0.025           | -0.278           | <b>0.368</b>    | 0.480                                  |
| Hypertension                  | -0.027             | 0.218           | -0.021           | -0.308          | 0.350                                  |
| Diabetes                      | -0.037             | 0.103           | 0.286            | -0.330          | 0.254                                  |
| Smoker                        | -0.079             | -0.292          | -0.155           | 0.292           | 0.534                                  |
| Cardiopathy                   | 0.351              | 0.111           | <b>0.368</b>     | 0.024           | 0.432                                  |
| Time spent in conventional HD | -0.014             | <b>-0.419</b>   | 0.319            | -0.045          | <b>0.921</b>                           |
| No health coverage            | 0.402              | <b>0.372</b>    | 0.105            | 0.108           | 0.547                                  |
| Complications                 | 0.089              | <b>0.420</b>    | -0.310           | 0.172           | <b>0.960</b>                           |

|                          |        |              |              |        |              |
|--------------------------|--------|--------------|--------------|--------|--------------|
| Pulmonary edema episodes | 0.253  | 0.318        | -0.120       | 0.336  | 0.617        |
| HTA episodes             | 0.119  | 0.338        | -0.278       | 0.228  | 0.726        |
| Hyperkalemia episodes    | -0.008 | <b>0.353</b> | -0.351       | -0.053 | <b>0.801</b> |
| ED visits                | 0.040  | <b>0.401</b> | -0.328       | 0.047  | <b>0.884</b> |
| SMUR transports          | 0.019  | <b>0.409</b> | -0.342       | 0.036  | <b>0.932</b> |
| HD sessions              | 0.301  | -0.306       | <b>0.363</b> | 0.095  | 0.730        |
| Family in France         | 0.225  | 0.199        | 0.299        | -0.256 | 0.522        |
| French-speaking          | -0.073 | 0.112        | -0.076       | -0.142 | 0.099        |
| VISA                     | 0.042  | 0.253        | -0.012       | -0.249 | 0.345        |

\* Standardized coefficients allow for interpretation in terms of standard deviations; for example, an increase by 1 standard deviation in the number of Complications increases by 0.089 standard deviation ESRD-related costs.

\*\* X-loadings; the loadings captured the proportion of explained variance by each predictive variable, in specifying the direction of the relation (i.e., capture correlation between components and predictive variables); in black: |X-loadings| >0.35 for significant relation

\*\* Cumulative R-squared gives the cumulative proportion of variance explained for each variable

|                                 | <b>Population<br/>N = 25</b> |
|---------------------------------|------------------------------|
| Time since last dialysis (days) | 4 [3 ; 7]                    |
| Acute indication                |                              |
| - No complication               | 5 (20%)                      |
| - Hyperkalemia                  | 7 (28%)                      |
| - Pulmonary edema               | 4 (16%)                      |
| - Severe hypertension           | 4 (16%)                      |
| - Other / unknown               | 5 (20%)                      |
| Arterial blood pressure (mmHg)  |                              |
| - Systolic                      | 153 [139 ; 162]              |
| - Diastolic                     | 84 [73 ; 97]                 |
| Sodium (mmol/l)                 | 138 [135.5 ; 141]            |
| Potassium (mmol/l)              | 5.8 [5.4 ; 6.45]             |
| Bicarbonate (mmol/l)            | 18 [16 ; 20]                 |
| Azotemia (mmol/l)               | 27.5 [22 ; 36]               |
| Serum Creatinine ( $\mu$ mol/l) | 1185 [875 ; 1420]            |
| Hemoglobin (g/dl)               | 11.2 [8.5 ; 12.3]            |
| Ultrafiltration rate (ml/kg/h)  | 8.6 [2.7 ; 11.6]             |
| Duration (minutes)              | 240 [240 ; 240]              |

**Table S1. Baseline characteristics at initiation of dialysis**

Qualitative variables are described with number and percentage. Quantitative variables are described by median and interquartile range (IQR).

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## **APPENDIX 1. ESRD-related complications**

- Acute pulmonary edema: presence of signs of respiratory distress with necessity of oxygen, due to a state of pulmonary overload that improves with ultrafiltration.
- Hyperkalemia: defined by association of blood potassium greater than 6.5mM and electrocardiographic disorders related to hyperkalemia.
- Metabolic acidosis: defined as the association of a blood pH below 7.38 and a level of blood bicarbonate below 22mM.
- Severe arterial hypertension: combination of hypertension above 180/110 mmHg and symptoms attributable to hypertension regressing with the decrease of the blood pressure.
- Uremia-associated complications: pericarditis, encephalopathy or any complication associated to ESRD with need of hospital admission
- Acute coronary syndrome: defined by the association of acute chest discomfort and compatible electrocardiographic modifications (ST-segment elevation or depression, T-wave inversion, flat T-wave).
- Stroke: focal neurological deficit of abrupt onset with a brain imaging compatible with transient arterial ischemic attack (TIA), constituted cerebral infarction, or cerebral hemorrhage.
- Acute limb ischemia: association of a sharp pain in a limb with clinical signs of interrupted arterial blood flow in distal arteries.
- Digestive hemorrhage: occurrence of bleeding whose origin is between the mouth and the anal canal.

## APPENDIX 2. Hospital stays and management strategy of ESRD

| Hospital stays (GHM) related to the management of ESRD |   | Cost (€) |
|--|---|----------|
| 01M122   | Other nervous system disorders, level 2                                 | 3702     |
| 04M111   | Respiratory signs and symptoms, level 1                                 | 969      |
| 04M131   | Pulmonary edema and respiratory distress, level 1                       | 1745     |
| 04M132   | Pulmonary edema and respiratory distress, level 2                       | 4847     |
| 04M13T   | Pulmonary edema and respiratory distress, very short duration           | 1258     |
| 05K051   | Vascular stents with myocardial infarction, level 1                     | 4975     |
| 05M09T   | Heart failure and circulatory shock, very short duration                | 1033     |
| 05M13T   | Chest pain, very short duration   | 821      |
| 05M17T   | Other conditions of the circulatory system, very short                  | 813      |
| 10C081   | Other interventions for endocrine and metabolic disorders, level 1      | 2997     |
| 10M162   | Metabolic disorders, age over 17 years, level 2                         | 2708     |
| 10M163   | Metabolic disorders, age over 17 years, level 3                         | 4644     |
| 10M16T   | Metabolic disorders, age over 17 years, very short duration             | 728      |
| 11K021   | Renal failure, with dialysis, level 1                                   | 2233     |
| 11K022   | Renal failure, with dialysis, level 2                                   | 6872     |
| 11K023   | Renal failure, with dialysis, level 3                                   | 12855    |
| 11K024   | Renal failure, with dialysis, level 4                                   | 23476    |
| 11K02J   | Renal failure, with dialysis, outpatient                                | 2217     |
| 11M06T   | Renal failure, without dialysis, very short term                        | 916      |
| 16M11T   | Other disorders of the erythrocyte lineage, very short duration         | 958      |
| 21M161   | Other iatrogenic complications not elsewhere classified, level 1        | 1749     |
| 23M20T   | Other symptoms and reasons for seeking care for CMD 23, very short term | 762      |
| 28Z04Z   | Hemodialysis, in sessions   | 319      |

*CMD: Major diagnostic categories ; ESRD: End-stage renal disease ; GHM, homogenous groups of patients.*



| <b>Hospital stays (GHM) unrelated to the management of ESRD</b> |  | <b>Cost (€)</b> |
|---|--|-----------------|
| 01M221  | Migraines and headaches, level 1   | 1021            |
| 05C191  | Cardiac defibrillator placement, level 1   | 15646           |
| 05C211  | Creation and repair of arteriovenous fistulas for CMD 05, level 1                            | 2614            |
| 05C21J  | Creation and repair of arteriovenous fistulas for CMD 05, ambulatory                         | 1782            |
| 05K101  | Vascular Diagnostic Procedures, Level 1  | 1881            |
| 05K261  | Therapeutic acts on vascular accesses or veins by vascular route, age over 17 years, level 1 | 2259            |
| 06M18T  | Symptoms and other health care utilization of CMD 06, very short term                        | 685             |
| 08C611  | Major Interventions for Osteoarticular Infections, Level 1                                   | 5332            |
| 10M022  | Diabetes, age over 35 years, level 2   | 2670            |
| 11C091  | Creation and repair of arteriovenous fistulas for CMD 11, level 1                            | 2093            |
| 11C09J  | Creation and repair of arteriovenous fistulas for CMD 11, ambulatory                         | 1610            |
| 23M101  | Surgical follow-up care, level 1   | 1414            |

*CMD: Major diagnostic categories ; ESRD: End-stage renal disease ; GHM, homogenous groups of patients*

## SERMENT D'HIPPOCRATE

Au moment d'être admis(e) à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences.

Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admis(e) dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçu(e) à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonoré(e) et méprisé(e) si j'y manque.



## **ABSTRACT**

### **Introduction.**

In the setting of migration, extra-European patients with end-stage renal disease (ESRD) have a lower access to renal replacement therapy (RRT). Healthcare coverage access at arrival in France may influence hemodialysis strategy during the first 3 months. We aimed to study clinical healthcare costs and outcomes in this population in Marseille.

### **Methods.**

We conducted a retrospective cohort study of ESRD migrant patients admitted for hemodialysis in our center over a 4-years period. Patients were recently arrived in France and willing to stay regardless of their administrative status with a local follow-up of at least 3 months. The first group with access to Protection Universelle Maladie (PUMA) was compared to patients without access to PUMA. Patients with operational health coverage were scheduled in conventional dialysis and patients without health coverage had transient “emergency-only” dialysis before their rights were effective. We assessed the ESRD-related costs for the healthcare system and the medical outcomes during the 3-months period after arrival. Multivariate analysis was performed with partial least square regression.

### **Results.**

We included 25 patients aged in median 42.6 [31.7; 53.6] years old and 60% of them were males. Ten patients had access to PUMA on arrival and 15 patients did not. Baseline characteristics were similar between the two groups. Four patients (26%) in the No healthcare coverage group needed a switch from “emergency-only” to conventional strategy for medical reason. ESRD-related healthcare costs were also higher in the absence of medical coverage (20 813 [15 516; 28 609] vs 12 465 [11 957; 13 911],  $p < 0.001$ ). Patients in the No healthcare coverage group spent more time in “emergency-only” dialysis (16.5 [6.5; 36.5] vs 0 [0; 7] days,  $p=0.002$ ) and had more ESRD-related complications (3 [1; 9] vs 1 [0; 1],  $p=0.02$ ) than patients with health coverage. Partial least square regression analysis show that the strongest independent predictor of healthcare costs was the number of ESRD-related complications ( $R^2_{Xy} = 0.96$ ).

### **Conclusion.**

This study is the first French cohort describing ESRD patients at their arrival in France with a medico-economic and outcome analysis. The absence of healthcare coverage and the subsequent “emergency-only” dialysis strategy are strongly associated with higher healthcare costs and more frequent ESRD-related complications in migrant patients with ESRD.

### **Keywords :**

End-stage renal disease (ESRD), chronic kidney disease, hemodialysis, migrant patient.