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# Somatic symptoms in patients with chronic kidney disease

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| **Submission date**<br>21/12/2021 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>18/02/2022 | **Overall study status**<br>Ongoing | |
| **Last Edited**<br>03/09/2025 | **Condition category**<br>Urological and Genital Diseases | |

## Plain English summary of protocol

Background and study aims
Patients with chronic kidney disease (CKD) report burdensome persistent somatic symptoms (PSS) in the early stages of renal dysfunction, long before requiring renal replacement therapy. Somatic symptom burden in CKD is an important predictor of health-related quality of life, disease progression, and also mortality. Their underlying aetiology in CKD remains unclear. The aim of this study is to improve the understanding on how PSS in CKD develop and maintain over time. It also aims to investigate biomedical, treatment-related and psychosocial predictors for the development of persistent somatic symptom burden in CKD.

The SOMA.CK study is part of the research unit RU5211 Persistent SOMAtic Symptoms ACROSS Diseases (SOMACROSS P3), funded by the German Research Foundation (DFG). SOMACROSS aims to identify generic and disease-specific risk factors and aetiological mechanisms of symptom persistence across a range of medical diseases, and thereby create a foundation for evidence-based interventions for PSS.

Who can participate?
Adults from the age of 18 years with a diagnosis of chronic kidney disease (CKD) stages 2-4.

What does the study involve?
The study investigates how somatic symptoms in CKD develop and evolve over time. We will investigate the role of biomedical and psychosocial factors in predicting CKD-specific symptom burden in n = 330 patients with CKD. To this end, an observational cohort study with assessments at baseline, 6 and 12 months will be conducted. An embedded experimental study as well as a qualitative study with newly diagnosed patients will further be conducted. The experimental study will compare individuals reporting high habitual symptoms with individuals reporting low symptom levels in order to test if symptom perception is influenced by general symptom burden, negative affectivity, emotion regulation deficits and disease severity. The qualitative study will explore individual mechanisms of symptom development and symptom perception after receiving a CKD diagnosis. A healthy control group will explore symptom perception between groups.

What are the possible benefits and risks of participating?
The study will investigate predictors of somatic symptom persistence in patients with chronic kidney disease, and will not influence patients' regular medical treatment. Patients will receive their medical care as usual and there are no disadvantages for participants compared to non-participants. Results will expand our knowledge of the underlying causes of CKD and increase our understanding of the predictive role of risk factors. The study results will be the basis for future treatment and intervention possibilities that aim to improve patients' quality of life.

Where is the study run from?
The study is being conducted by the III. Medicine Clinic and Policlinic and Clinic of Psychosomatic Medicine and Psychotherapy at the University Medical Centre Hamburg-Eppendorf, Germany and the Medical School Hamburg, Germany.

When is the study starting and how long is it expected to run for?
January 2021 to December 2025

Who is funding the study?
Deutsche Forschungsgemeinschaft, DFG (German Research Foundation, Germany)

Who is the main contact?
Prof. Dr. Meike Shedden Mora, meike.shedden-mora@medicalschool-hamburg.de
Prof. Dr. Tobias B. Huber, direktionsassistenz-3.med@uke.de

### Study website
https://www.uke.de/kliniken-institute/kliniken/psychosomatische-medizin-und-psychotherapie/forschung/studien/for-5211-somacross/index.html

## Contact information

### Type(s)
Scientific


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## Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
DFG SH 857/3-1 / HU 1016/13-1

# Study information

### Scientific Title
Predictors of somatic symptom persistence in patients with chronic kidney disease

### Acronym
SOMA.CK

### Study objectives
Hypothesis 1: Somatic symptom burden at 12 months in CKD can be predicted as a function of biomedical factors, treatment-related factors, psychosocial factors and their interplay.
Hypothesis 1 is broken down into three testable partial hypotheses and an exploratory research question:
Hypothesis 1a: Biomedical factors, namely renal function, comorbidity, altered DNA methylation in an epigenome-wide association study, and elevated suPAR levels, predict somatic symptom burden at 12 months.
Hypothesis 1b: Treatment-related factors, namely concurrent treatments and side-effects, predict somatic symptom burden at 12 months.
Hypothesis 1c: Psychosocial factors, specifically cognitive-perceptual variables in terms of somatosensory amplification, illness perceptions, symptom and treatment expectations, affective factors in terms of depression, (health) anxiety, and behavioural factors in terms of physical inactivity, predict somatic symptom burden at 12 months.
Hypothesis 1d: exploratory: Biopsychosocial risk factors interact in the development and maintenance of PSS in CKD.
Hypothesis 2a: Distinct symptom trajectories over a 12-months course can be predicted by biopsychosocial variables.
Hypothesis 2b: Changes in symptoms over time are predicted by biopsychosocial variables.
Hypothesis 3a: Inducing negative affect increases symptom perception in patients with CKD, particularly in patients with high baseline symptom burden, high trait negative affectivity, and deficits in emotion regulation.
Hypothesis 3b: The effect is moderated by disease severity, i.e., less pronounced symptom reporting after negative affect induction is expected in patients with high disease severity.
Hypothesis 3c: Higher symptom reporting after negative affect induction predicts greater symptom burden at 12 months.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 25/01/2021, Ethics Committee of the Hamburg Medical Association (Ethik-Kommission der Ärztekammer Hamburg, Weidestraße 122b, 22083 Hamburg, Germany; +49 (0) 40 202299-240; ethik@aekhh.de), ref. 2020-10195-BO-ff

## Study design
Observational prospective cohort study mixed-methods design

## Primary study design
Observational

## Secondary study design
Cohort study

## Study setting(s)
Hospital

## Study type(s)
Diagnostic

## Participant information sheet
See additional files

## Health condition(s) or problem(s) studied
Chronic kidney disease (CKD) stages 2-4

## Interventions
Previous interventions as of 25/09/2023:
An observational mixed methods cohort study will be conducted in order to develop a multivariate prognostic prediction model for CKD-specific symptom burden. Using a mixed-methods approach, mechanisms of symptom perception and development of CKD in a subgroup with newly diagnosed patients will be examined.

Prospective cohort study:
A mixed methods cohort study with assessments at baseline, 6, and 12 months will explore multivariate predictors of PSS in 330 patients with CKD stages 2-4. The primary outcome will be CKD-specific somatic symptom burden. Secondary outcomes include CKD-specific quality of life, general somatic symptom burden, and functioning. Predictors based on the adapted biopsychosocial working model of RU SOMACROSS include relevant biomedical (including epigenetic mechanisms and the biomarker suPAR), treatment-related (e.g., side effects), and psychosocial variables (e.g., expectations). Patient data will be collected through self-report questionnaires, semi-structured interviews, as well as blood, stool and urine samples. Longitudinal structural equation models, latent class growth and cross-lagged panel analyses will be used.

Experimental study:
In an experimental study in a subgroup of patients newly diagnosed with CKD, the influence of inducing negative affect on symptom perception will be examined using an affective picture paradigm. Also, it will be tested if symptom perception is moderated by baseline symptom burden, negative affectivity, emotion regulation and disease severity.

Qualitative study:
Qualitative interviews will be conducted in a subsample of patients newly diagnosed with CKD stages 2-4 in order to complement the quantitative data. Patients will undergo semi-structured interviews at baseline, 6 and 12 months. Interview questions will assess patients' symptom development, expectations of symptoms and treatment, as well as their own coping abilities.

In addition to the patient group, a healthy control group started recruiting for the experimental study in May 2023. The target number for this group will also be 100 participants. This is done to compare symptom perception after negative affect induction in healthy and physically ill individuals. Before taking part in the experiment and watching the three picture series of the IAPS, the controls are asked to fill in the following questionnaires: PHQ-15, PANAS trait, ERQ, SSAS, CSQ-CAT, and TAS-20.

Previous interventions:
An observational mixed methods cohort study will be conducted in order to develop a multivariate prognostic prediction model for CKD-specific symptom burden. Using a mixed-methods approach, mechanisms of symptom perception and development of CKD in a subgroup with newly diagnosed patients will be examined.

Prospective cohort study:
A mixed methods cohort study with assessments at baseline, 6, and 12 months will explore multivariate predictors of PSS in 330 patients with CKD stages 2-4. The primary outcome will be CKD-specific somatic symptom burden. Secondary outcomes include CKD-specific quality of life, general somatic symptom burden, and functioning. Predictors based on the adapted biopsychosocial working model of RU SOMACROSS include relevant biomedical (including epigenetic mechanisms and the biomarker suPAR), treatment-related (e.g., side effects), and psychosocial variables (e.g., expectations). Patient data will be collected through self-report questionnaires, semi-structured interviews, as well as blood, stool and urine samples. Longitudinal structural equation models, latent class growth and cross-lagged panel analyses will be used.

Experimental study:
In an experimental study in a subgroup of patients newly diagnosed with CKD, the influence of inducing negative affect on symptom perception will be examined using an affective picture paradigm. Also, it will be tested if symptom perception is moderated by baseline symptom burden, negative affectivity, emotion regulation and disease severity.

Qualitative study:
Qualitative interviews will be conducted in a subsample of patients newly diagnosed with CKD stages 2-4 in order to complement the quantitative data. Patients will undergo semi-structured interviews at baseline, 6 and 12 months. Interview questions will assess patients' symptom development, expectations of symptoms and treatment, as well as their own coping abilities.

## Intervention Type
Mixed

## Primary outcome measure
CKD-specific somatic symptom burden will be assessed with the CKD Symptom Burden Index (CKD-SBI) at baseline, after 6 and after 12 months.

## Secondary outcome measures
1. CKD-related quality of life will be measured using the Kidney Disease Quality of Life 36-Item Short-Form Survey (KDQOL-36) which includes the general health-related quality of life scale SF-12 at baseline, 6 months, and 12 months.
2. General somatic symptom burden in CKD will be measured using the Patient Health Questionnaire-15 (PHQ-15) at baseline, 6 months, and 12 months.
3. Symptom intensity and interference measured using a Numeric Rating Scale (NRS) at baseline,

6 months, and 12 months.
4. Symptom-related disability measured using the Pain Disability Index (PDI) at baseline, 6 months, and 12 months.
5. General quality of life measured using the above-mentioned SF-12 at baseline, 6 months, and 12 months.
6. Disease-related variables, i.e. CKD cause, duration and severity as well as current and prior renal and comorbid illnesses measured using the Cumulative Illness Rating Scale (CIRS), core serum and urine laboratory parameters (glomerular filtration rate), venous, blood gas analysis, blood cell count, serum albumin, and cystatin c. Medication, allergies, pulse, blood pressure, respiratory rate, saturation, abdominal circumference, genetic predisposition, first diagnosis of CKD and first symptoms are measured asking the patients directly or taking missing information out of the patients' physician's letter.
7. Epigenetic variables, namely DNA methylation and histone modification.
8. Urokinase-type plasminogen activator receptor (suPAR) levels in the plasma measured with the suPARnostic ELISA kit (IBL international).
9. Concurrent treatments, assessed from the patients' physicians.
10. Subjective side effects measured using a Numeric Rating Scale (NRS) at baseline, 6 months, and 12 months.
11. Adherence of treatment measured using the Medication Adherence Rating Scale (MARS-D) at baseline, 6 months, and 12 months.
12. Somatosensory amplification measured using the Somatosensory Amplification Scale (SSAS) at baseline, 6 months, and 12 months.
13. Illness perceptions measured using the Brief Illness Perception Questionnaire (B-IPAQ) at baseline, 6 months, and 12 months.
14. Catastrophizing measured using the Coping Strategies Questionnaire – Catastrophizing Subscale (CSQ-CAT) at baseline, 6 months, and 12 months.
15. Expectations of symptom severity, symptom coping treatment measured using a Numeric Rating Scale (NRS) and the Treatment Expectation Questionnaire (TEX-Q) at baseline, 6 months, and 12 months.
16. Perceived stress measured using the Perceived Stress Scale (PSS-10) at baseline, 6 months, and 12 months.
17. Depression measured using the Patient Health Questionnaire-9 (PHQ-9) at baseline, 6 months, and 12 months.
18. Anxiety measured using the Generalized Anxiety Disorder-7 (GAD-7) at baseline, 6 months, and 12 months.
19. Health anxiety and illness behaviour measured using the Somatic Symptom Disorder – B Criteria Scale (SSD-12) at baseline, 6 months, and 12 months.
20. Physical inactivity measured using the International Physical Activity Questionnaire (IPAQ-SF) at baseline, 6 months, and 12 months.

### Overall study start date
25/01/2021

### Completion date
31/12/2025

## Eligibility

### Key inclusion criteria
Current participant inclusion criteria as of 27/09/2023:
Inclusion criteria for the patient group:

1. Clinical diagnosis of CKD stages 2-4
2. Newly diagnosed with CKD
3. Age ≥18 years
4. Sufficient oral and written German language proficiency
5. Provision of written consent

Inclusion criteria for the healthy control group:
1. To be at least 18 years old (equivalent to the patient group)
2. Sufficient knowledge of the German language

1. Clinical diagnosis of CKD stages 2-4
2. Newly diagnosed with CKD
3. Age ≥18 years
4. Sufficient oral and written German language proficiency
5. Provision of written consent

## Participant type(s)
Healthy volunteer, Patient

## Age group
Adult

## Lower age limit
18 Years

## Sex
Both

## Target number of participants
330

## Total final enrolment
222

## Key exclusion criteria
Current participant exclusion criteria as of 27/09/2023:
Exclusion criteria for the patient group:
1. Acute severe somatic or psychiatric disease
2. Florid psychosis
3. Substance abuse disorder
4. Acute suicidality
5. Cognitive impairment
6. Planned dialysis within the next 6 months
7. Current dialysis
8. Dialysis in history longer than 3 months
9. Kidney transplantation
10. Life expectancy shorter than 6 months

Exclusion criteria for the healthy control group:
1. Existence of a chronic kidney disease
2. Cognitive impairment (equivalent to the patient group)

3. Diagnosis of psychosis, schizophrenia etc. (equivalent to the patient group)
4. Drug addiction (also equivalent to the patient group)
5. Acute suicidality

Previous participant exclusion criteria:
1. Acute severe somatic or psychiatric disease
2. Florid psychosis
3. Substance abuse disorder
4. Acute suicidality
5. Cognitive impairment
6. Planned dialysis within the next 6 months
7. Current dialysis
8. Dialysis in history longer than 3 months
9. Kidney transplantation
10. Life expectancy shorter than 6 months

### Date of first enrolment
12/05/2022

### Date of final enrolment
28/02/2024

## Locations

### Countries of recruitment
Germany

### Study participating centre
**University Medical Centre Hamburg-Eppendorf**
Department of Psychosomatic Medicine and Psychotherapy
Martinistraße 52
Hamburg
Germany
20246

### Study participating centre
**Medical School Hamburg**
Department of Psychology
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### Study participating centre

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**Study participating centre**
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**Study participating centre**
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**Study participating centre**
**Nephrocare Hamburg-Altona GmbH**
Mörkenstraße 47
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**Study participating centre**
**Nephrocare Hamburg-Barmbek GmbH**
Hebebrandstraße 6
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**Study participating centre**
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# Sponsor information

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University Medical Center Hamburg-Eppendorf

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### Sponsor type
Hospital/treatment centre

### Website
http://www.uke.de/

### ROR
https://ror.org/01zgy1s35

### Organisation
Medical School Hamburg

### Sponsor details
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### Sponsor type
University/education

### Website
https://www.medicalschool-hamburg.de/

### ROR
https://ror.org/006thab72

# Funder(s)

### Funder type
Research organisation

### Funder Name
Deutsche Forschungsgemeinschaft

### Alternative Name(s)
German Research Association, German Research Foundation, DFG

### Funding Body Type
Government organisation

### Funding Body Subtype
National government

### Location
Germany

## Results and Publications

### Publication and dissemination plan
The study protocol will be submitted for publication. According to the WHO Statement on Public Disclosure of Clinical Trials (https://www.who.int/ictrp/results/reporting/en/), the main findings will be submitted for publication in a high-impact peer-reviewed journal within 12 months of study completion.

### Intention to publish date
01/03/2026

### Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be stored in a publicly available repository (e.g., DRYAD Digital Repository; https://datadryad.org/stash). The study protocol and statistical analysis plan will be available at the ISRCTN registry. Individual participant data that underlie the reported results in a published article will be shared after de-identification beginning 3 months and ending 5 years following article publication. Data can be shared with researchers who provide a methodologically sound proposal to achieve the aims in the approved proposal. Proposals should be directed to Prof. Dr. Meike Shedden Mora (meike.shedden-mora@medicalschool-hamburg.de). To gain access, data requestors will need to sign a data access agreement. Informed consent from participants was obtained.

### IPD sharing plan summary
Stored in publicly available repository

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | | 22/12/2021 | 22/12/2021 | No | Yes |
| Protocol article | | 17/11/2022 | 18/11/2022 | Yes | No |