K-control

Interdialysis potassium level intensive monitoring

The Regional Health Service of Murcia (Servicio Murciano de Salud-SMS) provides healthcare to 1.47 million inhabitants (about 3.09% of the whole Spanish population). It integrates 11 hospitals, with 3,651 beds and more than 400 primary care centres. It is noteworthy that the Region of Murcia has been chosen by technological partners as a convenient living lab. Being a single-province region, political and administrative decision-making would be faster, which saves time, money and resources. The Region of Murcia owns the award of Reference site 2 stars in EIP AHA (European Innovation Partnership on Active & Healthy Ageing).

The Murcian Health Service has extensive experience in demand-driven co-creation, associated or not with innovative public procurement. Not in vain, SMS has obtained national and international awards such as the First International Prize in the category of “Outstanding Innovation Procurement in ICT” of the Procura+ 2021 awards for the 'InDemand' project or the Technology and Health Foundation Award for the *Best Technological Innovation in Health Driven by an Autonomous Community 2022* to the "InDemand" project.

Challenge description

Hyperkalaemia (HK) is an important cause of morbidity and mortality as it can generate life-threatening arrhythmias. The urgent approach to acute HP is an emergency frequently attended to in medical and nursing wards, and requires an extraordinary consumption of resources (pharmacological, care in emergency departments, hospital admissions and intensive care units, sessions of extra dialysis).

The HP rate worldwide is 2,8 cases per 100-person-year. In the general population, up to 3,2% of hospitalized patients may have potassium levels above normal. Its prevalence increases in patients with chronic kidney disease (CKD), in diabetics, cardiac patients, in the elderly and in patients taking drugs that prevent the renal elimination of potassium, such as blockers of the renin-angiotensin aldosterone axis, which are widely used. The population with advanced CKD and on dialysis is the one with the highest risk for HK. In haemodialysis (HD) up to 26.4% of patients have potassium levels above 5,1 mEq/L.

A low-potassium diet is a fundamental pillar in the treatment of chronic HK. Relying on potassium content tables of foods and recipe books, patients can prepare their daily menus in order to avoid an increase that could be life-threatening before the next dialysis.

However, this is a difficult effort to fulfil since:

- In Spain (and especially in Murcia), there is a deep root in the traditional Mediterranean diet rich in fruit and vegetables, and therefore rich in potassium.
- purification therapy in HD lasts around 4 hours and is performed intermittently every 2 or 3 days, so potassium accumulates between dialysis, especially when it comes to a long time.
- Demotivation of these patients is high as they are subjected to daily restrictions and live in ignorance of the effectiveness of their dietary actions.
- It involves confrontations with caregivers and health personnel in less compliant patients.
- It considerably worsens the patient's quality of life and limits social relationships by having to restrict eating.

- Potassium monitoring in the chronic HD population is carried out by pre-dialysis blood collection and in accordance with the Spanish Nephrology Society's recommendations at least once a month in stable chronic patients.

There is, therefore, an unmet need to monitor potassium levels more intensively in HD patients.

Challenge main objectives

- Optimize management of HK.
- Engage the patient in the low potassium diet and promote self-empowerment.
- Reduce the rate of complications due to HK.

Solution functional requirements

Compulsory functional requirements

- Reliable and non-invasive measurement of potassium in the patient's daily life.
- User's environment will be a dashboard for healthcare professionals and a mobile user-friendly app for patients.
- The solution will be hosted in the cloud and managed by the company with all the guarantees of privacy and security.
- It must be easy-to-use, through a gamified solution that manages information, recommendations and achievements.
- It must store patient data in order to show their progress.
- The solution will send automatically personalised recommendations to patients, according to guidelines.
- It will allow automating of responses to patients depending on the query.
- It will facilitate synchronous and asynchronous contact through chats and video conferencing.
- It will allow the administration of questionnaires and scales that the patient can complete autonomously and generate a tree of automatic recommendations.
- The healthcare team will manage the monitoring and be able to modify the rules and responses to the needs remotely.

Desirable functional requirements

- It would show patients information about the potassium content of foods.
- It would be able to record the food eaten by the patient and count its potassium content.
- To be interactive through an assistant who would reinforce the patient and reward their progress.
- Possibility of translation to avoid language barriers.
- The solution would apply Artificial Intelligence embedded in the workflow manager to alert of possible problems at the 'process' level not perceived by the actors or nodes.
- We want technology to help in the adherence and sharing with third parties of good practices in potassium monitoring management, as well as community resources in a sustainable and cost-efficient way for SMS.
- If blood glucose and TCO2 could be determined at the same time, intensive potassium monitoring could help characterize the behaviour of this cation, its circadian cycle, as well as its exact relationship with the patient's daily diet.

Pilot scope

The pilot will be developed in a total period of 12 months, including design, validation, testing and measuring of the impact of the co-created solution.

It will include at least 30 patients, who will test the solution for 6 months.

The healthcare professionals' team will be composed by different profiles and specialities. The main professional actors in the pilot will be nurses and nephrologists from a dialysis unit.

Type and number of targeted end-users:

End-user type	Role	Number
Patients	With different skills and condition's level	At least 30
Nurses	Closer patient´s follow up and main interlocutor with patients.	5
Nephrologists	Leading the design and compliance of the plan	At least 2

Table 1. Target users

Language

- The solution must be in Spanish. Other languages would be desirable (English, French, German, Arabian).

Other aspects

- Synchronous and asynchronous contact through chats and video conferencing.
- Possibility of synchronization with other devices such as a smart watch for reducing the digital gap, with autonomy >5 days, allowing personalized alerts and recommendations to be displayed to patients.

Pilot set-up conditions

The pilot set-up conditions are based on three pillars: a data processing contract, the use of standards as HL7 or FHIR, and an agile and short integration with the corporative system during the pilot, focused on validating a Minimum Viable Product (MVP).

Ethical, legal or regulatory

The Entity undertakes to process the personal data to which it has access as a result of the execution of the contract, observing the principles required by the legislation on data protection, in particular those relating to data quality, data security and duty of secrecy, as well as in accordance with the specific instructions received from the data controller, not using the data for any purpose other than the provision of services described in the object of the contract. Likewise, it undertakes to observe professional secrecy, maintaining absolute confidentiality and confidentiality on any data it may come to know on the occasion of compliance with the contract, in accordance with the level of protection established in the European data protection Regulation (EU 2016/679)of the European Parliament and of the Council, of 27 April 2016, relating to the protection of individuals with regard to the processing of personal data and Organic Law 3/2018 of 5 December, on the Protection of Personal Data and guarantee of digital rights, not communicating to any third party the data provided by the data controller. The data controller will determine whether, at the end of the services provided by the data processor, the personal data should be destroyed, returned to the data controller or handed over, where appropriate, to a new data processor. The destruction of the data shall not proceed when there is a legal provision obliging their conservation, in which case they shall be returned to the data controller, who shall guarantee their conservation for as long as such obligation persists. This obligation will continue even after the end of their relationship with the person in charge. The Entity will ensure and be responsible for its employees and / or collaborators receive the data only to the extent that it is necessary to their knowledge for the

provision of the object of the contract. In the event that the Entity uses the data for purposes other than those stipulated, communicates them or uses them in breach of the instructions set out in this contract, it shall be liable for the infringements set out in Articles 70 et seq. of Organic Law 3/2018, of 5 December, on the Protection of Personal Data and the guarantee of digital rights, in which it has incurred.

Technological

The user identification will be then provided through the OAuth standard. The solution may notify SMS systems about certain events and situations. Ideally via ´HL7´ messaging, but web services could also be an option. This information may include registration status, activity, progress and periodic (summarized) clinical information. The IT systems needed for running the solution will be hosted by the solver. If the complexity of the connections is too high or the personal data could be at risk, these systems could be hosted in local servers of the SMS. This will be established in a technical session at the beginning of the project. Anyway, the solver will provide mechanisms to guarantee that the Servicio Murciano de Salud can exploit the data. Data No prior Challenger data is expected to be available, meaning all users will start as new users in the system. The repository of documents and resources to be shared with the end users will be supplied and / or validated by the SMS.

Data access

No initial data will be provided for pre-load. All participants will have to register for free and fill their own data.

Expected impact and KPIs

To define the expected impact, a control group could be compared with an intervention group in which potassium was intensively monitored.

We will quantify in each group:

- Episodes of HK above 5.5 meq/L (reference value above normal in our laboratory).
- Episodes of moderate-severe HK defined by potassium above 6 meq/L.
- Number and type of complications associated with HK: emergency care, hospital admissions, ICU admissions, sudden deaths from unknown causes in a long period of dialysis.
- Number and type of intervention performed in relation to HK: dietary adjustment, dialysis adjustment, blood glucose correction, correction of acidosis, increase in potassium binders, urgent dialysis, and admission to ICU.
- Decrease in the use of potassium binders.

Finally, a quality-of-life questionnaire will be carried out before and after the intervention.

In 2022, 129 admissions with HK and 35 urgent assistances for severe HK were registered at the Reina Sofía Hospital.

Expected impact in one year:

- Reduction of more than 10% in HK episodes.
- Reduction of at least 20% in episodes of severe HK and/or the need for urgent dialysis.
- Any improvement in the reduction of long-term mortality from unrelated causes in HD patients.
- Quality of life of patients and their relatives before / after, valued through the SF12 short questionnaire. Goal: 20% improvement.
- Decreased need for potassium binders.

- Improved efficiency by reducing the healthcare resources used and lowering morbidity and mortality measured by the significant decrease of:
  - days of hospitalization, stays in the emergency room.
  - the number of dialysis performed by HK in chronic patients.
  - pharmaceutical prescriptions of potassium binders.

Business opportunity

Market size

The need of a more intensive and non-invasive way to monitor interdialysis potassium level is a universal pending task and its trend is growing year by year. The HK rate worldwide is 2,8 cases per 100-person-year. In the general population, up to 3,2% of hospitalized patients may have potassium levels above normal. Its prevalence increases in patients with CKD, diabetics, cardiac patients, in the elderly and in patients taking drugs that prevent the renal elimination of potassium, such as blockers of the renin-angiotensin aldosterone axis, which are widely used. The population with advanced CKD and on dialysis is the one with the highest risk for HK. In HD, up to 26.4% of patients have potassium levels above 5,1 mEq/L.

This new solution could be easily expanded to other healthcare systems after a hypothetical success in this pilot, which would be based on less complications and optimization of costs.

The challenger group offers their cooperation in the following:

- Advice on business model.
- In case of success of the pilot experience, the SMS undertakes to manage the possible resulting solutions in the volume to be determined, through the appropriate legal means, in particular as provided by the contractual regulations.
- Dissemination of results with the support of clinicians and patient associations, in order to make patient organizations aware of the solution at national and international level.
- Collaboration with a study of cost saving based on the published evidence, as well as with its publication and dissemination.
- Identification and contact with other potential customers.
- Advice on collaboration with the pharmaceutical industry by shortening treatment evaluation times in collaborative clinical trials.

Adoption plans

If the pilot is successful, SMS intends to adopt the solution, by a shared ownership of the solution co-created and procure its maintenance.

Intellectual Property Rights

This section sets the rules for the evaluation, ownership, and exploitation of Intellectual and Industrial Property Rights.

Evaluation and Documentation: Each party shall evaluate and document in the Pilot Action Plan their respective contributions to the new solution. This assessment will consider each party's background knowledge, resources, and tasks undertaken in the co-creation pilot project, determining the ownership and rights of the resulting shared IP&IPR.

Intellectual Property (IP) Rights: The intellectual property rights developed or contributed by SMS are inalienable, reflecting the knowledge and resources provided by SMS, including work time, patient access, and real-world validation. Usage of such intellectual property by other parties shall require a formal licensing agreement with mutually agreed terms.

Industrial Property Rights (IPR): SMS may opt-out of the commercial exploitation of the solution due to its lack of capacity in this area. In such a case, the exploitation rights will defer to the two companies, subject to compensations to SMS. These compensations will be based on the IP generated during the K-control project, where SMS will have an active role in the validation of the technology, and they are defined as the following future benefits: Reduced overall cost in licensing and maintenance of the solution.

- Allocated hours for corrective and evolutionary maintenance.
- Priority status for SMS in incident handling.
- Priority status for new developments related with the software developed by the follower SME.
- Collaboration by SMS in promoting the solution, including identifying customer networks and assisting in presentations.

Leading SME

GENERAL INFORMATION	
NAME OF THE SME	**CREATSENS HEALTH S.L.**
DESCRIPTION OF THE SME	renalyse Renalyse (CreatSens Health S.L.) is a biotech company that focuses its activity on the development of medical platforms and devices to improve the quality of life of patients by monitoring different relevant biochemical parameters. The company was established in September 2017, being a spin-off of the Universitat Rovira i Virgili (URV) in Tarragona. During these years, through many scientific publications, awards, and media appearances, Renalyse has demonstrated a great capacity to solve a market need. The company aims to provide unique screen-printed-based electrochemical sensor solutions that help patients and healthcare professionals to better manage the information generated in primary care centers, doctor's offices, or at the patient's home. For that, Renalyse centers its activity on developing novel healthcare platforms that aim to improve people's well-being by enabling decentralized analysis of relevant biochemical parameters in the blood to enable prediction, early detection, and prevention of serious diseases at home. There is a high level of experience among Renalyse team members in the field of business management, research and development, electronics, and implementation of quality system and regulatory. The activities in the Healthchain project are suitable for Renalyse, especially for the challenge K-control, as the aim is to increase the capacity of healthcare organization through the introduction of a new POC device and deliver solutions for doctors for a better management of their patients.
WEBSITE URL	http://www.renalyse.com

Table 2. Leading SME general information

Solution proposed:

Kontrol-IT: Pilot test for the Uncertainty Reduction Tool in ambulatory monitoring of interdialysis potassium

Kontrol-IT will be a point-of-care tool that allows rapid and affordable monitoring of Chronic Kidney Disease (CKD) via measuring the potassium ion from the patient's home or while in the dialysis machine. The core patented technology consists of a **chemical sensor integrated into a single system**, combining blood sampling, sensor calibration and sample measurement. Data will then be sent to a database through wireless technology to an application. The application will include content on dietary recommendations for CKD patients with special attention in potassium content from the diet. The information will help patients to know exactly the potassium they will ingest and ideally contain resources to reduce potassium content in foods. Based on the potassium intake data that the patient fills in into the app and the comparison with the potassium values determined by the device, the app should reinforce the patient's achievements in a gamification environment, In the event that potassium approaches the limits, the app will be able to provide reminders regarding the limitations in the intake of those foods with a higher potassium content. In any case, the application will only be able to estimate the potassium content according to food and portion ingested as a guideline and according to general recommendations.

Kontrol-IT is a disruptive solution, significantly size-reduced, with high accuracy, affordable, that will compete with current alternatives.

The solution includes a **self-calibration system** which simplifies the interaction device-user as patients will only need to introduce their blood to the system. Our capsules have a microfluidic system that can move the fluids inside to auto-calibrate the sensor. **For the first time, an appropriate self-management CKD diagnostic tool will be available in the day-to-day life of the patient to guide the choice of their daily menu in order to mitigate uncertainty.**

In a CKD situation, patients must follow strict indications regarding their diet and medication. By measuring the parameter several times per week, doctors will know exactly their patients' habits and its relationship with the diet, to try to establish dietary modifications, needs in potassium binders or changes in dialysis schedule in each case.

Kontrol-IT allows greater knowledge between diet and potassium levels to improve outpatient care, patient quality of life, reduction of hyperkalaemia episodes, and enables significant savings in the healthcare system as well as decreasing hospital congestion. The solution will create a patient-physician channel in which patients are more attended and monitored from their homes/residencies.

Current stage of development

CreatSens Health S.L is preparing for the final product fabrication, and it is especially focused on the industrial scalability of the microfluidic piece with the calibrators. The electronic part, including the pump for the microfluidics, is being tested and it is expected to study the viability for a scalable fabrication. The chemical sensor for potassium detection has already been validated with real blood samples (N=700) from dialysis patients and CreatSens will have an alpha app version ready to start the project in September 2024. It is expected to have a full functional KIT (sensoring + electronics + alpha app), ready for its optimization during the KONTROL-IT development.

Work to be done by the leading SME

The project will be divided into four phases that contribute to the clinical validation of the KONTROL-IT platform as described below:

WP 1	**Design of the study (M1-M4)**
Activities	1.1 Design of the Clinical study: establish with the medical team which information will be collected from the patients, number of patients, repetitions, and periodicity. 1.2 Clinical Committee protocol: Servicio Murciano de Salud (SMS). 1.3 Patients' recruitment: information for the patients following all the clinical and ethical guidelines. 1.4 Patients' education on the platform: trainings on how to use the device and the platform and support with educational contents. 1.5 Usability study & KPI: consensus of indicators for measuring the impact of the solution.
Milestones	*M3: Protocol for the clinical trial signed.*

WP 2	Software (M1-M12)
Activities	3.1 Software adaptation to the study: together with the medical team and the patients the software will be adapted to collect all the information needed for the study in a simple and visual way. 3.2 Iterations of software, data and visualization: several iterations of the software and in situ study of the trial will be done to assess the adoption of the end user and the usefulness to the specialist. 3.3 Medical recommendations based on the study: the final outputs of the study will be incorporated as medical recommendations in the RENALYSE software upon medical validation of the results.
Milestones	*M4: Software ready for this specific study (M4).* *M5: Improved software with feedback from the study (M12).*

WP 3	Clinical Trial (M5-M10)
Activities	4.1 Potassium measurement: measurement of the potassium levels in blood from all the participants according to the procedure established during the design of the study. 4.2 User experience: all the other information introduced by the patient to the software (diet, other medical parameters e.g. sugar, blood pressure, etc.) will be constantly evaluated to perform recommendations and iterate the software according to the results.
Milestones	*There are no milestones in this phase.*

WP 4	Validation of the solution (M5-M12)
Activities	5.1. Data collection: results will be collected during all the clinical trial to iterate the software and incorporate immediate feedback to adapt it to the needs of the patients and the medical team. 5.2 Data analysis: the final results will be analysed statistically and also from a medical perspective to further improve the software interface, the user experience and the medical management.
Milestones	*M6: Report of the study with the chemical results, the user experience and the medical recommendations (M12).*

	WORKING PACKAGES	PRE-PROJECT			PROJECT START											
		-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12
1	**Design of the study**															
1.1	Design of the Clinical study															
1.2	Clinical Committee protocol					M3										
1.3	Patients' recruitment															
1.4	Patients' education on the platform															
1.5	Usability study & KPI															
2	**Software**															
2.1	Software adaptation to the study							M4								
2.2	Iterations of software, data and visualization															
2.3	Medical recomendations based on the study															M5
3	**Clinical trial**															
3.1	Potassium measurement															
3.2	User experience															
4	**Validation of the solution**															
4.1	Data recopilation															
4.2	Data analysis															M6

Figure 1. Kontrol-IT Gantt Chart

Follower SME

Scope of work performed by the follower SME

The consortium detected a specific profile that will perfectly fit with the development of the K-control Challenge:

Medical software provider: That Follower SME profile must have previous experience in the development of medical software based on IEC 62304:2006 or knowledge in the compliance and/or implementation of the ISO 13485 applied to software and app development. It is also highly valuated to have previous knowledge in the development of diet recommendations for Chronic Kidney patients. It is expected to be part of the development of the app and diet protocols for the K-control Challenge with the final goal of enhancing/ complementing KONTROL-IT's tool, to improve patient education on healthy diet awareness and adding new information between potassium levels and patient diet for the clinician.

Main tasks for the Follower SME to address the K-control Challenge are:

- Improve Renalyse's app to integrate potassium values with symptomatology, diet, weight and lifestyle information though a machine learning algorithm.
- Co-create with Renalyse (Leading SME) and SMS (Healthcare organisation), for the development of a device that provides cutting-edge information on potassium for both the patient and the doctor. For the patient, the device can be an educational tool to help guide daily dietary choices. For the physician, intensive inter-dialysis potassium monitoring will increase knowledge about inter-dialysis potassium variations and their relationship to the patient's diet.
- Design an alarm protocol system for several CKD patient's profile.
- Create an easy-to-use interface for elderly people that will be validated during the clinical trial through a usability study.
- Develop a security protocol for patient's clinical data transferring and storaging.