



## National Registry of Rare Kidney Diseases (RaDaR) Protocol

### Purpose

The purpose of the National Registry of Rare Kidney Diseases (RaDaR; *rare disease registry*) is to facilitate translational and epidemiological research into rare kidney diseases by setting up and maintaining a comprehensive clinical database in partnership with Rare Disease Groups.

RaDaR facilitates the identification of well-characterized cohorts of patients who may be invited to participate in clinical trials, the development of biomarkers, phenotype-genotype correlations or outcome studies. This will inform the development of clinical guidelines for specific rare diseases and will audit treatment and outcome.

RaDaR has the capacity to feedback relevant information to registered patients, and in conjunction with Patient View, allows patients to provide information themselves including their own reported quality of life and outcome measures.

### Background

Rare diseases are arbitrarily defined as having an incidence such that they cannot be studied effectively on patient groups drawn from one or a few medical centres.

A high proportion of such disorders have a genetic background and often these diseases are first expressed in childhood. The success of chronic and end-stage renal failure programmes in childhood permit increased numbers of these patients to survive into adulthood. There are 13 centres for paediatric nephrology in the UK. For a rare disorder that a paediatric nephrologist might diagnosis only once a year, and assuming 100% survival to adulthood, a renal physician might be asked to take over such a case only once in seven or eight years of practice. Research is hampered by this dilution of clinical experience. Similarly in adult practice there are rare complications of diseases or their treatment so that a nephrologist might encounter such an event less often than once in every 5 years. National aggregation of clinical experience is essential to further study.

Research groups investigating a rare disease (Rare Disease Groups, RDGs) have difficulty accessing patients who are widely distributed. While rare disease groups are often successful in identifying novel genotypes in a few individuals, it is more difficult to define phenotype and undertake phenotype-genotype correlations. Moreover, the scarcity of patients makes it difficult to develop biomarkers or identify well-defined cohorts in which to test novel treatments. As a result, the progression and outcome for many rare diseases are unknown and treatment remains underdeveloped.

## **RaDaR**

RaDaR provides an infrastructure to capture both generic and disease-specific clinical information and to collate longitudinal information. Patients and clinicians can view information about the conditions covered by RaDaR on [Rarerrenal.org](http://Rarerrenal.org), which links closely with RaDaR.

RaDaR was set up following an initiative of the Medical Research Council (2008) to develop cohorts of well-categorized patients for translational research. RaDaR is a development of the Renal Association and is operated by the UK Renal Registry (UKRR). The governance structure is described below.

RaDaR is web-based and data is held on a secure server. Data entry is overseen by the clinician with responsibility for the patient - usually their nephrologist. Patients will be given a secure login and password and be able to view their own data on the Patient View (PV) website (where available), a well-established patient information system governed by the Renal Association.

Data from RaDaR will be made available to researchers investigating specific rare diseases in accordance with the operating policy enforced by the RaDaR Operational Management Board (OMB) (see below).

RaDaR is predominately aimed at UK patients; however international recruits who are consented in the UK by an NHS hospital are also eligible, subject to local approval.

## **Governance**

Governance will be undertaken under the authority of the Renal Association of Great Britain, the professional body for nephrologists in the UK, via its Rare Disease Committee (RDC) and Renal Information Governance Board (RIGB).

The business aspects and strategic direction of RaDaR are overseen by the OMB, comprising the Chair of the RDC together with the Director and General Manager of the UKRR and other relevant parties. The OMB meets face to face annually. Additional virtual meetings of the OMB are held as deemed necessary by the Chair throughout the year - face to face, by teleconference or email.

The RaDaR initiative follows from the Renal Association's 'Strategy for Patients with Rare Kidney Diseases' published in 2010. The RDC came into being in December 2010 on the appointment of its first chairman Dr C Mark Taylor. The rules of the Committee were approved by the Renal Association Executive in February 2011.

The Rare Disease Committee meets at least twice yearly, a minimum of one meeting being a face-to-face meeting. In addition, committee business is maintained using e-mail and telephone conferences between meetings. The Chair will prepare written reports of the business of the Committee for UKRR and the Research Committee of the Renal Association, or delegate this task to a secretary chosen from among the Committee membership. The Chair is responsible for keeping the membership of the Renal Association informed of the registry's activity and keeping the committee's website area up to date with information about the current committee membership, minutes of committee meetings, research activity, patient recruitment opportunities and other relevant information. Members of the Committee will usually serve for no more than one term of three years. Members of the Committee are expected to attend at least one Committee meeting annually and will contribute actively to the work of the Committee as required by the Chair.

## **Research access**

Researchers wishing to use RaDaR to investigate a specific rare disease are required to form a Rare Disease Group (RDG). The Rare Disease Committee (RDC) of the Renal Association will adjudicate applications. To be successful, a RDG will need to demonstrate compliance with the Good Practice guidelines of the Renal Association Strategy for Rare Kidney Disease (2010) and sign a Standard Operating Procedure with the OMB. The RDG will specify their required disease-specific data fields. Generic data fields are the responsibility of the Rare Disease Committee and will be designed and modified where necessary. The RDG will require separate research ethical committee approval to involve patients in any further research studies.

## **Ethics**

The patient, or in the case of a minor their parents/guardians, is informed about RaDaR by their nephrologist or a member of their clinical team. Information will be offered in the patient's first language using translation services provided locally within the NHS. Age appropriate information will be provided for children and adolescents. Written consent is obtained by the patient's nephrologist or a member of their research team. Consent can be obtained in person or via post providing that the patient has suitable opportunity to discuss any concerns they may have with a member of the research team. Copies of the consent documents are stored in the patient's hospital record. Confirmation that consent has been obtained forms part of the data entry process.

For paediatric patients the period of consent will be capped at 18 years. Upon transition to adult care, paediatric renal units should ask the receiving adult unit to re-consent the patient as an adult. If a research subject reaches 18 years of age and has neither consented for themselves nor withdrawn, their RaDaR record will be frozen and they will no longer be contacted by the RDG or the central RaDaR team.

Patients may withdraw from RaDaR at any time by notifying the RaDaR team in writing or by contacting their doctor. If they do so their data will cease to be updated, and any contact with the RDG prevented. They will be notified in writing that this has been done according to their instruction.

RaDaR has received ethical approval from the South West – Central Bristol Research Ethics Committee, reference number 14/SW/1088.

## **Patient information**

RaDaR will capture both generic and disease specific information. The former will include patient identifiers. This is justified by the intention of RaDaR which is to contact patients about relevant research opportunities as they arise. Patient information will only be released to a RDG under the terms of the agreement between the OMB and a RDG, and with appropriate ethical agreement in place concerning the specific proposal that a RDG will make towards the patient.

The data fields that are specific for a given disease will be specified by the RDG. RaDaR will be capable of handling data generated after contact between the patient and the RDG. For example, if a RDG proposed expert pathological review of renal biopsies or genetic analyses that are central to the development of a cohort, and have obtained separate consent to obtain the same, the results of this would be added to patient data held in RaDaR.

## **Funding**

The set-up costs and the first 3 years of operation were funded by grants from the MRC, KRUK and BKPA. The MRC grant funded pediatric cohort development of two diseases - nephrotic syndrome with focal segmental glomerulosclerosis (SRNS) and mesangiocapillary glomerulonephritis (MPGN). This permitted the setting up not only of the generic registry but also the first two RDGs. These two examples were used to develop and test the system that has now been rolled out to additional rare kidney diseases. The long-term aim is to maintain funding so that data acquisition can continue during periods when projects become inactive and project funding lapses. This has been achieved from 2016 with an increase in capitation fee to cover both RaDaR and RareRrenal.org. We expect this model of a rare disease registry to be an exemplar for the understanding of all rare diseases within the NHS. We propose that the structure will become integrated with the Map of Medicine and Connecting for Health and will be supported by the National Clinical Audit Advisory Group and the National Institute of Health Research.

The annual budget will meet the cost of staff required to support and maintain RaDaR as well as other maintenance, infrastructure, implementation and development costs. Staff employed for RaDaR will mostly work in the UKRR offices in Bristol, under the same HR arrangements as UKRR staff. If RaDaR employs UKRR staff on a part-time or freelance basis, appropriate arrangements for cross cover and necessary training will be agreed between the OMB Chair and the management team of the UKRR.