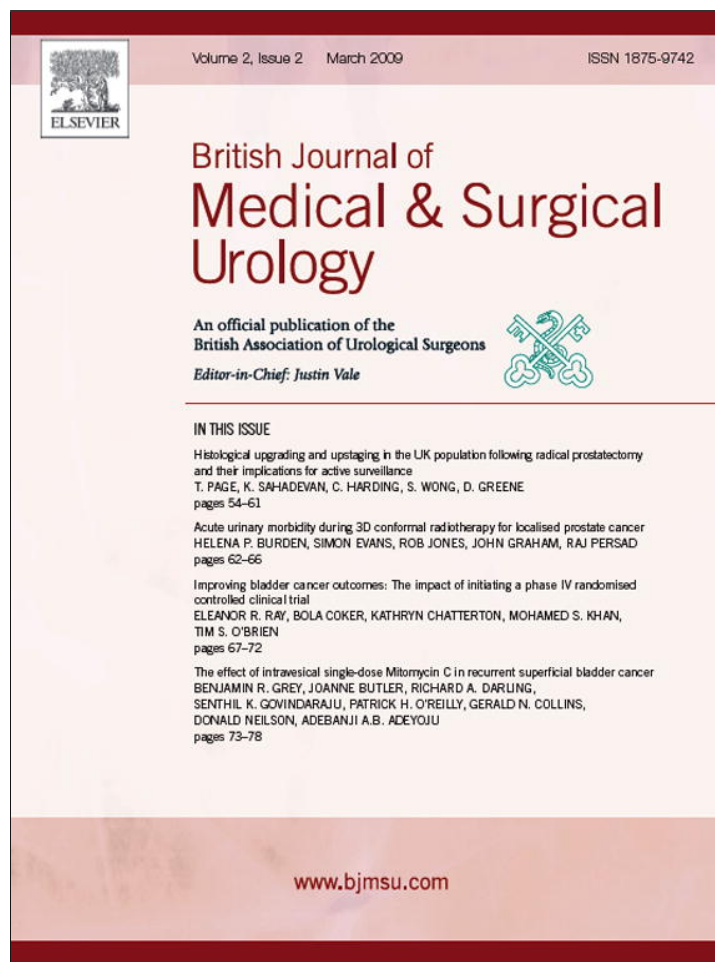


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The Comprehensive Clinical Research Network; implications for urological research in England

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Summary The UK Clinical Research Network (UKCRN) was established by the National Institute of Health Research to improve quality and delivery of clinical research in the UK. The Comprehensive Clinical Research Network (CCRN) is its newest element, made of Comprehensive Local Research Networks (CLRNs) covering the whole of England, and underpinning the infrastructure and delivery of NHS clinical research in a range of specialty groups. The Urogenital Specialty Group is responsible for advising the UKCRN on feasibility of potential studies, topic-specific training, overseeing the relevant parts of the UKCRN portfolio of research and brokering interactions with research funders or professional bodies developing clinical trials. The CLRNs will have a major impact on research activity of urologists; they can provide flexibility and sustainability funding, and support research infrastructure. However, the CLRNs are performance managed, such that delivery of projected recruitment to trials will be crucial. Furthermore, research activity not in the UKCRN portfolio will no longer be supported free of charge. Interactions with equivalent bodies in Wales, Scotland and Northern Ireland have not yet been formalised.
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Contents

Background	51
The CCRN	51
The UKCRN portfolio	51

Abbreviations: NIHR, National Institute of Health Research; UKCRN, UK Clinical Research Network; CCRN, Comprehensive Clinical Research Network; CLRN, Comprehensive Local Research Network; NCRN, National Cancer Research Network; TCRN, Topic-specific Clinical Research Network; PCRN, Primary Care Research Network; UGSG, Urogenital Specialty Group; FSF, Flexibility and sustainability funding; R&D, Research and Development; CSG, Clinical Studies Group; CSP, NIHR Co-ordinated System for gaining NHS Permission.

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Portfolio adoption process for studies not eligible for automatic inclusion	52
Clinical Studies Group for urogenital research.....	52
Implications for urogenital research and investigators.....	53
Conclusions	53
Conflict of interest statement.....	53

Background

The National Institute for Health Research (NIHR) was established by the Department of Health in answer to the government's Research and Development (R&D) strategy 'Best Research for Best Health'. A key element was the UK Clinical Research Network (UKCRN),^{1,2} run by a co-ordinating centre based in Leeds, and incorporating the primary care research network (PCRN) and several topic-specific Clinical Research Networks (TCRNs). The National Cancer Research Network (NCRN) is a TCRN comprising 33 regional networks in England, which provide dedicated research nurses, data managers, NHS service sessions and information systems. As a consequence of the improved support, and awareness of activity, recruitment to cancer trials has increased substantially. The NCRN also supports Clinical Studies Groups (CSGs), exemplified by those in bladder cancer and prostate cancer, which identify consensus opinion on areas of greatest priority.

The Comprehensive Clinical Research Network (CCRN)³ is the latest UKCRN network, covering clinical areas not supported by the TCRNs. The implications are considerable and represent a substantial opportunity, given that support for high-quality research will be improved and streamlined. However, the urological profession has yet to take full advantage of the opportunities and knowledge of the CCRN is patchy. This review article describes the structures which are being established and briefly reviews some of the opportunities and threats.

The CCRN

The CCRN is an umbrella organisation devolved into 25 Comprehensive Local Research Networks (CLRNs)⁴ covering England. The CLRNs provide

the NHS infrastructure for non-oncology clinical research, under a clinical director and dedicated manager. Support teams cover critical areas including information technology and industry liaison, and there is provision for clinical research support staff, sessional support for investigators and funding of other NHS support costs, such as clinical services (e.g. Pharmacy) and diagnostic tests (e.g. Radiology and Pathology).

The CCRN covers a substantial proportion of medicine and surgery, which therefore has to be broken down into manageable chunks known as Specialty Groups. Non-oncological urology falls into the Urogenital Specialty Group (UGSG). Regional specialty group leads have been appointed by some of the CLRNs, who are expected to encourage clinical research in their CLRN, and are members of the UGSG; membership of the UGSG will soon include multi-disciplinary input with patient and public involvement, and future members will be sought by invitation and advertisement. UGSG activity is summarised in Table 1. A crucial aspect is to ascertain whether a clinical trial can actually be delivered in the NHS context, i.e. feasibility assessment. The overall responsibility for the activity and performance of the UGSG rests with the Chairman and members of the group, which is accountable to the UKCRN Co-ordinating Centre.

The UKCRN portfolio⁵

The UKCRN is developing a database of clinical research studies active in the UK, including separate portfolios for England and the devolved nations. The requirement for automatic inclusion is funding awarded by open competition, high quality peer review, clear value to the NHS, and priority strategic direction; studies funded by the NIHR, other areas of government and NIHR non-commercial partners (e.g. the MRC) will be eligible automatically. Other studies can be adopted into the portfolio after formal review by the UGSG. Importantly, studies funded by overseas governments and agencies such as the EU Framework

¹ UKCRN website; www.ukcrn.org.uk.

² UKCRN Industry team; <http://www.ukcrn.org.uk/index/industry/contacts.html>.

³ CCRN; www.ukcrn.org.uk/index/networks/comprehensive.html.

⁴ CLRNs; <http://www.ukcrn.org.uk/index/networks/comprehensive/clrns.html>.

⁵ Portfolio; http://www.ukcrn.org.uk/index/clinical/portfolio_new.html.

Table 1 Activities of the UGSG funded by the CCRN.

1. Advice^a on feasibility of potential studies.
2. Advice to the UKCRN Co-ordinating Centre on aspects of the research portfolio covered by the UGSG.
3. Input to topic-specific training.
4. Overseeing of the relevant parts of the CCRN portfolio of research.
5. Provision of contacts for research funders or professional bodies developing clinical trials.

^a Regulatory and governance issues; www.ukcrc-rgadvice.org.

Program and the U.S. National Institute of Health will be considered of only medium priority.

The portfolio determines resource allocation for support of recruitment and follow-up of patients in clinical trials. Crucially, it is only the portfolio studies that will receive infrastructure support from the CCRN (delivered through the CLRNs). This will include NHS service support costs—studies outside the portfolio will have to pay a fee in order to receive R&D support in the NHS. Those areas which are most successful in attracting the resources will be able to build up skills and expertise in the research workforce for future research activity.

Portfolio adoption process for studies not eligible for automatic inclusion

A formal process assesses whether studies meet the criteria required, which runs in parallel with the Co-ordinated System for gaining NHS Permissions (CSP)⁶ and is run by the UGSG. The first part (level 1 feasibility) is a broad statement as to whether such a study could be done in the NHS. Level 1 includes a preliminary review on the potential clinical benefit, compatibility with UK practice, protocol issues, whether investigators are likely to be interested and an estimate of prevalence of the condition. Level 2 is an in-depth feasibility assessment, with a more detailed assessment of the costed final draft study protocol, information from potential network sites to identify named investigators, potential patient availability, suitability of facilities and other resources. This culminates in an adoption panel review, which would allow entry to the portfolio. The Level 2 feasibility is ideally performed with the IRAS application so that the study can be flagged as potentially adoptable in the CSP. The above measures are not yet fully active

and each application currently therefore has to go through interim measures.

Expert review for final adoption evaluates the following criteria:

1. Is there a genuinely testable hypothesis or research question with future benefit for patients as its objective?
2. Is there a statistically valid trial design reasonable for the main objective?
3. Has the trial and its design been subjected to adequate protocol review?
4. Does network infrastructure have current capacity to deliver the trial data reliably and on time?

Item 4 will look at patient numbers and whether there are conflicting studies in the current portfolio competing for the same patient group. The entire process is undertaken confidentially with all participants signatory to confidential disclosure agreements.

Industry-sponsored studies are eligible for inclusion where they have been assessed by the UGSG and meet specific criteria; where this is achieved, the study will be rated as high priority for delivery. Where the industry provides funding but not sponsorship, the research is referred to as investigator-initiated, and attracts a lower priority rating, so may not attain successful completion if there are higher priority studies in similar clinical areas. This is important to urologists, as a substantial part of urological research is investigator-initiated, so will be at a disadvantage. The same adoption panels as used in industry studies will evaluate whether non-commercial studies are of value to the NHS. If not adopted, such "own account" research will not be supported by R&D departments in hospitals. Individual investigators would therefore need to identify additional funds to support NHS infrastructure costs.

Clinical Studies Group for urogenital research

NCRN Clinical Studies Groups (CSGs) drive the development of future research by identifying priorities. The CCRN does not specifically fund CSGs, but the UGSG will be looking to identify such priority research issues and to establish funding from sources outside the NIHR to setup an autonomous urogenital CSG. This will link the process of clinical research delivery (the CLRNs) with clinical need and funding bodies; collaboration between specialty areas will also be easier. For example, a metabolic stone disease programme could be

⁶ CSP; <http://www.ukcrn.org.uk/index/clinical/csp.html>.

setup within the UGSG CSG, interacting with the Metabolic and Endocrine Specialty Group and with the Renal Specialty Group; cross-specialty research can thereby arise through a well-organised and systematic approach.

Implications for urogenital research and investigators

Despite a perception that the UK is active in the arena of Urological Research only a small proportion of CLRNs have expressed expertise in the urogenital arena—in fact the UGSG is the smallest specialty group, lagging behind equivalent specialties, such as Gynaecology (Reproductive Health and Childbirth SG). A priority for the UGSG is to increase investigator participation.

Recruitment performances are a major indicator for pharmaceutical companies when deciding where to place planned research. The UK is falling behind other countries; the establishment of the CCRN aims to address this. Implicit within this is the expectation that CLRNs will be performance-managed with accrual data being crucial. The tendency of investigators to overestimate the number of patients and speed of recruitment is counter-productive and networks will therefore evaluate estimated times and patient numbers. The implications for urologists undertaking research are that the network may provide partial infrastructure support, but that failure to deliver will make it harder for the investigator to gain support for future research projects.

Flexibility and sustainability funding (FSF) is a financial resource that networks have been allocated to set up infrastructure needs. In the initial stages, 'priming FSF' can be used to help investigators to establish support needed for research activity. This will soon shift towards an FSF stream used to maintain infrastructure, based on the CLRN's performance in recruiting patients and meeting targets. FSF will be distributed to the most active investigators, effectively providing a reward for successful trial delivery. FSF can also be used to maintain infrastructure which might otherwise be lost through lack of funding during quiet periods between research projects (for example research nurse expertise).

Experienced investigators applying for European Union or U.S. National Institute of Health fund-

ing need to be aware that obtaining funding from these bodies will not automatically mean CCRN support. If the CCRN adoption panel perceives that the study is unfeasible, then the project would not be adopted into the portfolio. It would then not have NHS R&D support, which will make it very difficult to deliver the study. This embarrassing possibility means investigators planning major applications would be prudent to discuss them with the UGSG.

Across the United Kingdom, the processes differ for the four nations. The CCRN is an English body interacting with the equivalent bodies for Wales, Scotland, and Northern Ireland. However, the processes are different for the respective organisations and the UKCRN has yet to communicate how cross-border activity will be achieved in practice.

The CCRN is a research body, contrasting somewhat with the NCRN, which additionally supports clinical management. There are no plans for additional clinical support provision through the CCRN.

Conclusions

The CCRN comprises numerous CLRNs, active in specific clinical areas defined by "Specialty Groups". The networks provide infrastructure support for NHS clinical research, with funding based on successful delivery of clinical trial activity. Such funding will be available only to projects in the NIHR portfolio. At this stage, the urology profession is only marginally aware of the developments. Anyone considering undertaking research needs to be informed about the considerable changes. It is urgent that investigators approach their CLRN to express an interest in setting up a regional urogenital specialty group. Regional leads will then join the national committee of the UGSG so as to maximise urogenital research in England. There is substantial benefit available for researchers in the form of greater opportunity for collaboration, knowledge of research activity in the UK, input to the CSG for identifying research priority, and access to support through FSF. For those not participating within the network, research may become even more difficult.

Conflict of interest statement

None.

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