Title: Safeguarding the future of Urological research and delivery of clinical excellence: harnessing the power of youth to spearhead Urological research

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Research has a key role in driving the specialty forward and improving the care of our patients. However, conducting large multi-centre studies can be extremely challenging. As an individual surgeon, it is difficult to gather the appropriate methodological, administrative and financial support to run them or have the time to do so. Driven by novel forms of electronic communication, one solution to this problem are resident-led research collaboratives, typified by that of the British Urology Researchers in Surgical Training (BURST), Australian Young Urology Researchers Organisation (YURO), Young Academic Urologist section of the European Association of Urology (EAU) and Young Urologic Oncologists (YUO) section of the Society of Urological Oncology. Whilst resident-led collaboratives have achieved success in other surgical specialities, they have only been gathering attention within Urology in recent years (Table 1).

Resident-led research collaboratives provide a central network of expertise in methodology, mentoring and knowledge of research processes. The committee of such organisations are typically comprised of residents or junior Urologists with close support from senior academic Urologists and clinical trials groups. Clinicians with ideas for research projects can present ideas to the collaborative who provide a detailed peer review, modify the protocol to make the design more robust, before assessing feasibility to roll out the study amongst their vast network of interested collaborators. The collaborative can carry out time-consuming approvals required to run the study, creates databases for data entry and provides the administrative resource to coordinate and run the study across many different centres.

A fundamental principle is that residents take the lead in coordinating the study and collecting data at individual sites under the supervision of a local consultant. Contributors are recognised with PubMed-indexed collaborative authorship. Each resident is only required to obtain data for a small number of patients, which gives them a very achievable goal but between many residents this scales up exponentially to make a well-powered study that recruits quickly. An excellent example of this would be the Multi-centre cohort study assessing the role of Inflammatory Markers in spontaneous stone passage In ureteric Colic (MIMIC), which had 220 collaborators across 71 sites collecting data for 4181 patients in 7 countries over a 4-month period, concluding that white cell count did not influence the likelihood of spontaneous stone passage in patients with acute renal colic [1].

One interesting aspect about this approach is that residents often have fewer conflicts of interest than their seniors and can be more flexible in their views meaning they tend to have reasonable equipoise when considering study designs or recruiting patients to a study (Table 2). This may allow the conduct of studies in areas of Urology that it might otherwise be difficult. The geographical flexibility provided by residents who are spread over regions allows access to a wide range of different practices which can increase the generalisability of the results and provide large samples sizes that are powered to investigate associations and disease areas that may otherwise be difficult to. Types of research projects that work well within resident-led collaboratives are observational cohort studies [1, 2], case-control studies [3], systematic reviews [4-6], meta-analysis [7], and randomised controlled trials [8-10].

Challenges of this approach include the lack of dedicated managerial infrastructure to coordinate large numbers of clinicians across different geographical areas. Open-source software such as Slack, social media platforms such as Twitter and meeting forums provided by organisations such as the European Association of Urology and British Association of Urological Surgeons help to mitigate this issue. Set up of clinical trials-compliant databases for data collection can be done with software such as Redcap which gives clinicians anywhere at any time access to a robust electronic data entry system. Systematic reviews can be aided by Cochrane endorsed-software such as Covidence which has enabled reviewers in different time zones to collaborate together easily.

Engagement with residents and consultants may be variable at first until they are convinced that the concept works. As a result, lower-risk projects such as cohort studies in areas of a common pathology with short-term outcomes that can be easily run in most centres and study designs such as systematic review are often used to consolidate the network in the early stages of a collaborative. Typical areas of investigation here include stone disease, treatment of lower urinary tract symptoms, bladder and prostate cancer management.

Support from established senior surgeons who are recognised in their units, region or country is essential for this model to have success. Obtaining funding can be challenging but one of the advantages of the collaborative approach is that within the network there are usually technology-savvy residents who are able to contribute project infrastructure, specialist IT and database skills that would otherwise be expensive to fund. Funders are now beginning to recognise the potential that these networks have in successfully delivering clinical studies and large grants have been awarded to resident-led collaboratives for the delivery of randomised studies of surgical interventions with longer-term follow up [8-10].

One of the key reasons for success of this model is the motivation of residents to be part of something that is not only successful and high profile but enhances their portfolio at a point in their careers where esteem is important. Residents gain transferrable team-working skills and specific research methodology skills. They learn how to critically appraise the literature, to write a protocol, to gain governance approvals for projects, to recruit patients to studies, to analyse data, to write scientific papers and to present the findings. Thus, this provides the consultant workforce of tomorrow with the skills required to deliver practice-changing clinical studies in Urology. There is the potential that these collaboratives could drive the "everyone as a researcher" mentality in which there is the possibility that every surgical patient could be offered a trial or the opportunity be involved in a clinical study that can improve patient care. In summary, resident-led collaboratives offer exciting new perspectives and approaches to Urological research and time will tell whether they have the potential to deliver on their early promise.

References

- [1] Shah T, O'Keefe A, Gao C, Manning T, Peacocke A, Cashman S, et al. A multi-centre cohort study evaluating the role of inflammatory markers in patient's presenting with acute ureteric colic (MIMIC). European Urology Supplements. 2017;16:e723-e4.
- [2] Silay MS, Spinoit AF, Undre S, Fiala V, Tandogdu Z, Garmanova T, et al. Global minimally invasive pyeloplasty study in children: Results from the Pediatric Urology Expert Group of the European Association of Urology Young Academic Urologists working party. J Pediatr Urol. 2016;12:229 e1-7.
- [3] Sanguedolce F, Montanari E, Alvarez-Maestro M, Macchione N, Hruby S, Papatsoris A, et al. Use of XenX, the latest ureteric occlusion device with guide wire utility: results from a prospective multicentric comparative study. World J Urol. 2016;34:1583-9.
- [4] Manning TG, Perera M, Christidis D, Kinnear N, McGrath S, O'Beirne R, et al. Visual Occlusion During Minimally Invasive Surgery: A Contemporary Review of Methods to Reduce Laparoscopic and Robotic Lens Fogging and Other Sources of Optical Loss. J Endourol. 2017;31:327-33.
- [5] Eggener SE, Badani K, Barocas DA, Barrisford GW, Cheng JS, Chin AI, et al. Gleason 6 Prostate Cancer: Translating Biology into Population Health. J Urol. 2015;194:626-34.
- [6] O'Brien JS, Perera M, Manning T, Bozin M, Cabarkapa S, Chen E, et al. Penile Cancer: Contemporary Lymph Node Management. The Journal of Urology. 2017;197:1387-95.
- [7] Perera M, Papa N, Christidis D, Wetherell D, Hofman MS, Murphy DG, et al. Sensitivity, Specificity, and Predictors of Positive 68Ga-Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol. 2016;70:926-37.
- [8] Pinkney TD, Calvert M, Bartlett DC, Gheorghe A, Redman V, Dowswell G, et al. Impact of wound edge protection devices on surgical site infection after laparotomy: multicentre randomised controlled trial (ROSSINI Trial). BMJ. 2013;347.
- [9] the Reinforcement of Closure of Stoma Site C, the West Midlands Research C. Feasibility study from a randomized controlled trial of standard closure of a stoma site vs biological mesh reinforcement. Colorectal Disease. 2016;18:889-96.
- [10] Cornish J, Harries RL, Bosanquet D, Rees B, Ansell J, Frewer N, et al. Hughes Abdominal Repair Trial (HART) Abdominal wall closure techniques to reduce the incidence of incisional hernias: study protocol for a randomised controlled trial. Trials. 2016;17:454.

Table 1: Examples of Resident-led research projects in Urology and allied surgical specialities with contact details of collaboratives

Study	Collaborative	Study design	Status	Findings
Multi-centre cohort study	British Association of Urological	Retrospective	Complete	White cell count was not
assessing the role of	Surgeon's in Surgical Training (BURST)	cohort study		associated with likelihood of
Inflammatory Markers in	3, 3, 3, 3, 3, 3, 3, 3, 3, 3, 3, 3, 3, 3			spontaneous stone passage.
spontaneous stone passage In	www.bursturology.com	n = 4181		Key predictors were stone
ureteric Colic (MIMIC) [1]	Twitter: @BURSTUrology			size and stone position.
	Email: <u>bursturology@gmail.com</u>			
The Investigation and DEtection	British Association of Urological	Prospective	Pilot study in	Multi-centre prospective
of urological Neoplasia in	Surgeon's in Surgical Training (BURST)	cohort study	800 patients	study feasible.
paTlents reFerred with suspected			complete.	
urinary tract cancer: A	www.bursturology.com	n = 5000	Main study	Progress to main study phase.
multicentre analysis (IDENTIFY)	Twitter: @BURSTUrology		open to	
,	Email: <u>bursturology@gmail.com</u>		registration.	
International Post-operative	Australian Young Urology Researchers	Prospective	In set up	In set up
Intravesical Chemotherapy study	Organisation (YURO)	cohort study		
(IPIC)	http://ausyuro.wixsite.com/yuro			
()	Twitter: @AusYURO	n =		
	Email: ausyuro@gmail.com			
Global minimally invasive	Young Academic Urology (YAU)	Restrospective	Complete	Shorter hospitalization time
pyeloplasty study in children:	Section of the European Association of	Cohort study		and lower postoperative
Results from the Pediatric	Urology			complication rates with
Urology Expert Group of the	<u> </u>	n = 575		robotic pyeloplasty compared
European Association of Urology	http://uroweb.org/education/young-			to laparoscopic approach in
Young Academic Urologists	urologists-office-yuo/yau/			treating ureteropelvic
working party [2]	Twitter: @EAUYAUrology			junction obstruction in
				children.
Use of XenX, the latest ureteric	Young Academic Urology (YAU)	Prospective case	Complete	XenX was a safe and effective
occlusion device with guide wire	Section of the European Association of	control study	- Cop.c.c	device for the treatment of
utility: results from a prospective	Urology	Control study		upper ureteric tract stones; It
multicentric comparative study	or or or or or	n = 82		may reduce the risk for the
[3]	http://uroweb.org/education/young-	02		need of auxiliary procedures
	urologists-office-yuo/yau/			and for the insertion of a JJ
	Twitter: @EAUYAUrology			stent.
Gleason 6 Prostate Cancer:	Young Urologic Oncologists (YUO)	Systematic	Complete	The metastatic potential of
Translating Biology into	Section of the Society of Urological	review	·	contemporary Gleason 6
Population Health [5]	Oncology			disease is negligible but not
, , , , , , , , , , , , , , , , , , , ,	, , , , , , , , , , , , , , , , , , ,			zero.
	http://suonet.org/y-u-o.aspx			
	Twitter: @SUO_YUO			
	Email: info@suonet.org			
Sensitivity, Specificity, and	Australian Young Urology Researchers	Systematic	Complete	For biochemically recurrent
Predictors of Positive 68Ga-	Organisation (YURO)	review and		prostate cancer, there is a
Prostate-specific Membrane	http://ausyuro.wixsite.com/yuro	meta-analysis		favourable sensitivity and
Antigen Positron Emission	Twitter: @AusYURO			specificity profiles compared
Tomography in Advanced	Email: ausyuro@gmail.com			to choline-based PET imaging
Prostate Cancer: A Systematic				techniques
Review and Meta-analysis [7]				
Randomized controlled trial:	West Midlands Research Collaborative	Randomised	Complete	Wound edge protection
Reduction of Surgical Site	(WMRC)	controlled trial		devices did not reduce
Infection using a Novel	http://wmresearch.org.uk			surgical site infection rate
Intervention (ROSSINI) [8]	Twitter: @WMRC_UK	n = 760		when used during laparotomy
	enquiries@wmresearch.org.uk			
A randomized controlled twist of	Wort Midlands Passaveh Callaharetter	Dandomics d	Intornal	Multicontro randoreitatia a da
A randomized controlled trial of reinforcement of closure of	West Midlands Research Collaborative (WMRC)	Randomised	Internal	Multicentre randomization to
		controlled trial	feasibility	this trial of biological mesh
stoma site using a biological	http://wmresearch.org.uk Twitter: @WMRC UK	n = 560	complete.	was feasible, with no early
mesh (ROCSS) [9]	enquiries@wmresearch.org.uk	n = 560	Main study	safety concern. Progress to main study phase
	enquires@winresedich.org.uk	1	recruiting	main study phase

Table 2: Advantages and limitations of resident-led collaborative research

Advantages	Limitations		
Methodologically robust studies due to	Engagement of residents can be variable		
peer-review process	until the concept has been shown to work		
Large sample sizes achievable by	Engagement of established Urologists can		
distributing over collaborative network	be challenging as they may be unfamiliar		
	with the concept		
Studies can recruit and complete quickly	Central coordination is required and takes		
	time to set up in the absence of a dedicated		
	managerial infrastructure		
Studies can be more generalizable as	Challenging to design explanatory trials		
patients are from a wide range of centres	when such a large number of sites are		
	involved		
Can investigate rare diseases	Easier to successfully deliver studies in		
	areas with of a common pathology		
Efficient and cheap as the collaborative	Complex interventional studies are		
utilises expertise within existing network	challenging to deliver and big funding is still		
	required for success of the study		
Residents have fewer fixed views and fewer	Individual units may have biases which limit		
conflicts of interest, thus priority is on	involvement in a collaborative study		
studies that may improve patient care			
Residents gain transferrable team-working	Transferrable skills gained are dependent		
skills important for career	on how well the team functions		
Residents gain specific research skills	Research skills gained are dependent on		
equipping them to run clinical trials as	the expertise level within the collaborative		
consultants	network		
Residents and consultants are recognised	Not all national training bodies will		
for their contribution with authorship on	recognise collaborative authorship		
PubMed indexed peer-reviewed papers			