

David Campbell, MBBS,  
FACRRM, DRANZCOG,  
DCH, FRACGP<sup>1</sup>,  
Susan Williams,  
BSc (Hons), PhD<sup>2</sup>,  
Jill Konkin, BA (Hons),  
MCLSc, MD, CCFP,  
FCFP, FRRMS<sup>3</sup>,  
Isabella White, MBBS,  
FRACGP<sup>4</sup>,  
Ian Couper, BA, MBBCb,  
MFamMed, FCFP (SA)<sup>5</sup>,  
Ruth Stewart, MBBS,  
PhD, FACRRM,  
DRANZCOG (adv)<sup>6</sup>,  
Lucie Walters, MBBS,  
PhD, DCH, DRANZCOG,  
FRACGP, FACRRM<sup>7</sup>

<sup>1</sup>Australian College of  
Rural and Remote Medicine,  
Cunningham Arm Medical  
Centre, Lakes Entrance, Victoria,  
Australia, <sup>2</sup>Adelaide Rural  
Clinical School, The University  
of Adelaide, Nairne, Australia,  
<sup>3</sup>Department of Family Medicine,  
Edmonton Clinic Health  
Academy, University of Alberta,  
Edmonton, Alberta, Canada,  
<sup>4</sup>Adelaide Rural Clinical School,  
The University of Adelaide,  
Australia, <sup>5</sup>Ukwanda Centre  
for Rural Health, Stellenbosch  
University, Cape Town, South  
Africa, <sup>6</sup>College of Medicine  
and Dentistry, James Cook  
University, Thursday Island,  
Queensland, Australia, <sup>7</sup>Adelaide  
Rural Clinical School, Faculty  
of Health and Medical Sciences,  
University of Adelaide, Mount  
Gambier, Australia

Correspondence to:  
David Campbell,  
davidcam@bigpond.net.au

This article has been peer  
reviewed.

Access this article online

Quick Response Code:



Website:  
<https://journals.lww.com/cjrm>

DOI:  
10.4103/cjrm.cjrm\_67\_22

# New insights on rural doctors' clinical courage in the context of the unfolding COVID-19 pandemic

## Abstract

**Introduction:** Rural doctors typically work in low-resource settings and with limited professional support. They are sometimes pushed to the limits of their usual scope of practice to provide the medical care needed by their community. In a previous phenomenological study, we described the concept of clinical courage as underpinning rural doctors' work in this context. In this paper, we draw on rural doctors' experiences during the unfolding COVID pandemic to re-examine our understanding of the attributes of clinical courage.

**Methods:** Semi-structured interviews were conducted with rural doctors from 11 countries who had experience preparing for or managing patients with COVID-19. Interviews were transcribed verbatim and coded using NVivo. A deductive thematic analysis was undertaken to identify common ideas and responses related to the features of clinical courage.

**Results:** Thirteen interviews from rural doctors during the unfolding COVID-19 pandemic affirmed and enriched our understanding of the attributes of clinical courage, particularly the leadership role rural doctors can have within their communities.

**Conclusion:** This study extended our understanding that rural doctors' experience of clinical courage is consistent amongst participants in many parts of the world, including developing countries.

**Keywords:** Clinical courage, COVID-19 pandemic, rural physicians

## Résumé

**Introduction:** Les médecins ruraux travaillent généralement dans des environnements à faibles ressources et avec un soutien professionnel limité. Ils sont parfois poussés aux limites de leur champ d'action habituel pour fournir les soins médicaux dont leur communauté a besoin. Dans une étude phénoménologique précédente, et dans ce contexte, nous avons décrit le concept de courage clinique comme étant à la base du travail des médecins ruraux. Dans cet article, nous nous appuyons sur les expériences des médecins ruraux au cours de la pandémie de COVID pour réexaminer notre compréhension des attributs du courage clinique.

**Méthodes:** Des entretiens semi-structurés ont été menés avec des médecins ruraux de 11 pays ayant une expérience de la préparation ou de la prise en charge de

Received: 11-08-2022 Revised: 01-12-2022 Accepted: 05-12-2022 Published: 17-10-2023

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Campbell D, Williams S, Konkin J, White I, Couper I, Stewart R, *et al.* New insights on rural doctors' clinical courage in the context of the unfolding COVID-19 pandemic. Can J Rural Med 2023;28:163-9.

patients atteints de COVID-19. Les entretiens ont été transcrits mot à mot et codés à l'aide de NVivo. Une analyse thématique déductive a été entreprise pour identifier les idées et les réponses communes liées aux caractéristiques du courage clinique.

**Résultats:** Treize entretiens avec des médecins ruraux, durant la pandémie de COVID-19, ont confirmé et enrichi notre compréhension des attributs du courage clinique, en particulier le rôle de leadership que les médecins ruraux peuvent jouer au sein de leurs communautés.

**Conclusion:** Cette étude nous a permis de mieux comprendre que l'expérience des médecins ruraux en matière de courage clinique est la même pour tous les participants dans de nombreuses régions du monde, y compris dans les pays en développement.

**Mots-clés:** Courage clinique, médecins ruraux, pandémie de COVID-19

## INTRODUCTION

Clinical courage describes the lived experience of rural doctors who are pushed to the limits of their scope of practice to provide the medical care that is required by their community.<sup>1,2</sup> COVID-19 provided an internationally shared context where rural doctors suddenly found themselves responding to a rapidly evolving and challenging health crisis. The shared context enabled us to consider whether the previously identified attributes of clinical courage held true in this exceptional situation.

From our earlier phenomenological study, the six attributes of clinical courage rural doctors experience include:<sup>1,2</sup>

- A strong sense of belonging to and seeking to serve their community
- Accepting clinical uncertainty, persistently seeking to prepare for clinical challenges
- Working deliberately to understand and marshal resources
- Humbly seeking to know the limits of their own clinical practice
- Needing to clear a cognitive hurdle when deciding to act
- Gaining collegial support to continue their roles.

It has long been recognised that courage can be integral to clinical practice,<sup>3-6</sup> but, to our knowledge, our studies amongst rural doctors are unique in exploring the underlying attributes.<sup>1,2,7</sup> In late 2020, we interviewed rural doctors from 11 countries about their experiences during the emerging COVID-19 pandemic. Our analysis identified different coping strategies that were demonstrated by rural doctors across diverse

geographical locations.<sup>7</sup> In this study, we return to these interviews to ask: how do the attributes of clinical courage resonate with rural doctors in the face of the COVID-19 pandemic?

## METHODS

This qualitative study was undertaken from a constructivist epistemology which views reality as being actively created by social relationships and interactions. As researchers, we played a role in the co-construction of meanings from participants' interviews.

### Recruitment

The recruitment and data collection processes were described in our previous paper.<sup>7</sup> Emails distributed to the World Organisation of Family Doctors Working Party on Rural Practice and the Society of Rural Physicians of Canada email lists invited doctors currently working in rural areas to undertake an interview about their COVID-19 experiences and clinical courage. Inclusion criteria included: currently practising as a rural doctor, having experience preparing for or managing patients with COVID-19 and having proficiency in spoken English. Our aim was to understand the shared experiences of rural doctors across different demographic and geographical contexts, and participants were recruited to provide diversity across gender, career stage and geographical locations.<sup>1,2,7</sup>

### Ethics approval

Ethics approval was granted by the University of Adelaide Human Research Ethics Committee (Project H-2020-168).

## Interviews

Semi-structured interviews were undertaken in the last quarter of 2020 using Zoom video conferencing and were recorded with participants' consent. The interviewers were research team members who are experienced rural doctors. The questions explored the participants' stories of preparing for and managing COVID-19 in their community and interviews ranged between 25- and 77-min duration. For this paper, we analysed questions focussed on participant perceptions about drawing upon clinical courage<sup>1</sup> including how they responded to the aforementioned 6 attributes, their experiences with clinical courage during the COVID-19 pandemic and what lessons were learned from these experiences.

## Analysis

Analysis was undertaken concurrently with data collection. A deductive thematic analysis was used to identify common ideas and narratives across the interviews,<sup>8</sup> using the original 6 attributes of clinical courage as an initial coding framework in NVivo 12 (QSR International Pty Ltd., Doncaster, Australia). Four transcribed interviews were read aloud in research group meetings and meanings were discussed, and additional codes and themes were developed and refined through these discussions. The NVivo coding framework was then used by SW and LW to code the remaining interviews. New findings about each attribute

were presented back to the research team with a discussion about how they added to the group's original understanding. After completing 13 interviews, we had identified cumulative evidence to support each of our themes. We were aware that the pandemic was evolving quickly, and doctors' experiences and responses would be changing over time. For these reasons, we decided to cease data collection at that point.

## RESULTS

The sample included 13 rural doctors from 11 countries [Table 1], with 6 participants from low-resource countries. This allowed us to consider a broad range of experiences from the international community of rural doctors.<sup>1</sup>

Participants were asked to reflect on their experiences of drawing on clinical courage in the context of COVID-19 and specifically asked to reflect on the 6 features of clinical courage. Participants identified with the attributes and drew on examples from their own experiences to affirm them. Their narratives described common feelings of fear and anxiety but a strong commitment to their clinical responsibilities, to providing local leadership and even a need to show bravery.

When I'd leave the house, I had to leave all my fears behind and, like, just show them (staff) that we can manage this. I mean just show them that we can all do this, it's like I had to keep up a front of being brave, even though I feel deep inside I'm not really brave enough. –09Philippines

**Table 1: Participant's characteristics and geographical contexts**

Career stage	World Bank income level of country <sup>a</sup>	Country	Gender	Participant reference number
Early and mid-career rural doctor	High income	Australia	Male	4
		Wales	Female	10
	Middle income	South Africa	Female	1
		Democratic Republic of Congo	Male	3
		Philippines	Female	9
		Zimbabwe	Female	1
Experienced rural doctor	High income	Australia	Male	7
		New Zealand	Female	13
	Middle income	Bosnia and Herzegovina	Male	2
		South Africa	Male	5
		Thailand	Male	6
		Nigeria	Male	8
	Lower income	Pakistan	Male	12

<sup>a</sup>World Bank. World Bank Country and Lending Groups. <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups>

## Standing up to serve anybody and everybody in the community

Consistent with findings from our original study,<sup>1</sup> these rural doctors described feelings of commitment to their communities, with their motivation to serve being grounded in relationships with the community.

If I think back to that day when we got the first COVID-19 diagnosis, we went to the patient's home to go and see their family and check that they were okay, and test those that need to be tested. Because we wanted to make sure that the community was going to be okay. –11South Africa

In the context of COVID-19, there was a heightened significance in standing up to serve the community because of the risks to the doctors and their families' personal safety. Serving the community often involved providing local pandemic leadership, founded on the doctors' broad understanding of, relationships with, and sense of belonging to their community. The descriptions of working together with their communities highlighted that belonging to a community required understanding and valuing diverse community worldviews.

One was just a community experience, that one of the roles of rural doctors is to use your intellect for good, I suppose, and to – with the connections that you have and the understanding you have of the health system to try and help the community come to terms with what you do, and we did a few things. One of them was I, at fairly short notice, just got all the community leaders together and said, 'Let's have a meeting' and I just fielded questions about COVID and how we might need to respond and how we could respond, and – but it was a very collaborative meeting with the community about what do we do if we all have to go into lockdown? –07Australia

## Accepting uncertainty and persistently seeking to prepare

This feature resonated very strongly in the context of COVID-19 due to the overwhelming sense of uncertainty throughout the early stages of the pandemic. These doctors sought to understand the threat within their local context and to plan what resources would be needed.

Well, after the [initial] peak, which was end of June, beginning of July, because all the time we were told to expect these huge numbers. And all the time, we kind of plan based on these numbers. And

we don't know if they're right, and we don't know if they're not right. And we're looking at what the numbers say, what are our actual figures say? And what's our oxygen usage like? What's the patient number doubling time? –11South Africa

New approaches to manage COVID-19 patients were rapidly adopted. The importance of teams was a common thread and there were genuine examples of clinical teamwork which supported rapid system change and the capacity to provide care to COVID-19 patients.

We had a guy who arrived, he was extremely short of breath and obviously needed oxygen. We didn't have a high-flow machine at that point and we didn't have easy access to referral at all, and we'd been discussing in the morning meeting the things that we can do to mitigate it, including prone positioning and nursing. ...our community service doctor was actually in the ward at the time, allocated there, and he went back from that meeting and he was, like, 'This patient needs proning and let's do it'. He literally heard about it half an hour before, the nurses knew nothing about it and it was like, 'Let's work out how we can do this'. I mean, we've seen the pictures, we've discussed how to do it, but nobody at all had any experience of it, but clearly this patient needed it and that kind of ability to go and take what you've just learnt, quite literally, and work together with your nursing colleagues and put it into practice, I was so chuffed. –05South Africa

The COVID-19 pandemic also highlighted the importance of persistence in situations where current practices and systems are not ideal, particularly in low-resource rural settings.

I couldn't just then sit back, even though the resources were not enough. Yeah, I think that was the main reason why, in the end, I got up and said, 'We can just work with what we have and see what we can do'.... And so it's drawing from the things that we've already been practising and applying them to a new situation. –01Zimbabwe

## Deliberately understanding and marshalling resources

Preparing for COVID-19 involved establishing new infection control procedures, new systems to screen and consult patients, ways of working in teams and improvising existing facilities. When facing the likely influx of patients and potential collapse of health services, these rural doctors were innovative in how they reached out to people to marshal available resources.



I really had to just reach out to people I know who are also starting their responses during that time, like, the other municipal health officers in the area.... I even said to my staff that I personally do not know how to do this, but if we work together, I think we can manage to get through this pandemic and everyone would just share resources,..... We were able to innovate, we were able to do the improvised handwashing facilities that we could use, like, using a drum as a storage of water for handwashing facilities in different areas that we can use. –09Philippines

Being innovative, pragmatic and proactive enabled them to access local facilities and resources, to get up-to-date information and to mobilise clinical team members. These rural doctors understood the local context and reported being better placed than external administrators in recognising and marshalling resources for their medical services.

When the pandemic began, a lot of administrations were worried about getting ventilators and all these things, when the basic infrastructure that people had could have been more useful, like oxygen concentrators, particularly here.... And we were worried about getting ventilators, but we didn't have people trained to use those. And we didn't have enough things to intubate,... so I think, if we are stepping into an unknown situation, I think I learned that we should primarily focus on what we have and see how we can improve what we have, the little that we have, to help us fight an unknown situation. –01Zimbabwe

### **Humbly seeking to know one's own limits**

In the context of the emerging pandemic, 'knowing one's limits' was interpreted in relation to coming to terms with one's own limitations and lack of knowledge about COVID-19.

This experience, more or less, it really humbled me a lot because as a doctor I thought I could manage anything, I mean if you have a disease you need to manage or treat, you'd know what to do because you are the doctor, but with COVID everything is just so uncertain. And you know that it's something that you cannot really rely on the skills you developed during medical school. So, it really humbled me a lot. That I know I do not know everything and that I need other people to work with. 09Philippines

Participants also spoke about the limits to their own personal resources in the context of unrelenting stress and workload, and of recognising the limits of their colleagues:

... I know that everyone has his or her own limits, so we have to know or we have to understand, highly understand about that – about that limit

and don't push them go forward, but you have to support them and stay along with them until they know their own limit, and also support them every moment in that situation. –06Thailand

Another aspect of knowing one's limits was weighing the risks they would take on for themselves and their families. Although none of our participants made the decision to distance themselves from COVID-19 patients, they described how some colleagues had chosen to do so, and how they assessed their own personal risks:

In our department we had the father of some young children who just did not want to have anything to do with it because he was worried that he was going to infect his children, he just couldn't tolerate that. 04Australia

Every risk I take, I think about the repercussion to my family for their health, their wellbeing. Every risk I take, I think what will happen to them if something goes wrong. That is my somehow moral and cautious parameter. 02Bosnia Herzegovina

In many cases, these doctors described pushing beyond their limits of feeling personally safe:

I was really uncomfortable doing all that work. I had to push myself each time.... But the whole time, I was worried that the PPE that I had was inadequate, and I was exposing myself each time. At some point I had to test about 40 members of staff who had been involved in the care of two patients who turned out to be COVID-positive and with severe symptoms. So testing all those 40 people was quite a challenge. 01Zimbabwe

### **Clearing the cognitive hurdle when something needs to be done for your patient**

This feature resonated with participants who faced new clinical challenges with COVID-19 patients. In one case, this involved shifting from life preservation to a palliative care focus for patients with poor prognosis:

I feel like I know that feeling. When you first get the situation and you think, no, I can't, I can't do this, there isn't a way that it can be done. And to come back and look at it again and say, 'Okay, can I make a mind shift'? Can I say, 'All right, maybe there's a way that we can do this. Maybe even the mind shift to the palliative care comes under that? ...But sometimes the obstacle is in your own mind. 11South Africa

### **Collegial support to stand up again**

Collegial support was a strong theme in the

context of COVID-19. It was described in terms of sharing the load and supporting each other in the local context.

I think trying to also get a couple of people around me who were like-minded in their understanding of what was going on within the hospital, obviously, was helpful as well. Getting people to help with some of the day-to-day stuff, like data management and stuff which was obviously important, but was taking a lot of time. –05South Africa

Sharing experiences more broadly with national and international colleagues was an important source of support and reassurance for these doctors. It provided opportunities for problem-solving and gaining access to new information and normalising experiences through shared conversations.

So we built a Zoom meeting to talk about the situation, the COVID situation and how to deal with the COVID in COVID era, something like that; that's the theme of the meeting. So every week, we have the guest or the speaker from every, every province in Thailand that shows how family physician can deal with the COVID situation. So that's helped a lot. That's helped our practice, that's helped our spirit, that we have another family physician that fights COVID along with us, that's helped a lot. 06Thailand

## DISCUSSION

The emergence of COVID-19 and its impact on rural doctors presented a rare but timely opportunity to explore the relevance of the attributes of clinical courage as described in our previous phenomenological study. In the current study, we found evidence that affirms and extends our understanding of these attributes, as well as highlighting the role of rural doctors as community leaders during this crisis.

In relation to 'standing up to serve the community' we broadened our understanding to include the drive to respectfully bring community members along in managing the new threat of COVID-19. More than in our previous work,<sup>1</sup> an important community leadership role for doctors was articulated, and this highlighted the intersectionality of rural doctors who belong to the rural community and to the medical profession. Some doctors were driven to push beyond the limits of personal safety to provide care, an expression of clinical courage drawn out by exceptional circumstances.

In our original phenomenological work, we described 'accepting clinical uncertainty' in relation to rural doctors undertaking unfamiliar procedures, and using their adaptive expertise to apply familiar skills to new clinical circumstances.<sup>1</sup> In the context of COVID-19, these doctors used their adaptive expertise to transfer basic clinical knowledge to manage a complex new disease, and to adopt different treatment strategies, such as proning or palliative care for COVID-19 patients with poor prognosis. Adaptive expertise was also used more broadly to develop and implement disaster preparation strategies within their communities. These examples concur with other accounts of rural doctors' adaptive responses in relation to COVID-19<sup>9,10</sup> or in relation to healthcare barriers.<sup>11</sup>

To prepare for COVID-19 in their communities, these rural doctors marshalled available resources by reaching into and beyond their local communities. They described sharing information with other communities, 'the more local the better'. Information from international sources was accessed via webinars and professional networks. Where our previous research had uncovered the challenges in marshalling resources for locums who do not know the local context,<sup>1</sup> this study demonstrated how external systems can fail to provide appropriate resources for rural medical facilities, which are often lacking basic infrastructure.

In the early stages of the pandemic, the participants described being humbled by their own uncertainty and powerlessness to manage COVID-19. This resonated with the attribute of 'Knowing one's limits' which was previously understood in relation to recognising the limits to the scope of practice.<sup>1</sup> These doctors also felt pushed to the limits of their own personal reserves, and mindful of their colleagues due to the unrelenting stress and workload. Where our previous work had hinted at the personal risks of burnout when communities had unrealistic trust in or expectations of their rural doctors, this study highlighted the challenges faced by some doctors in coming to terms with their own uncertainties and limitations, especially in low-resource settings.

Participants' narratives strongly emphasised the value and importance of clinical teams and support workers and articulated the terrible sadness and responsibility of having to care

for workmates who became COVID-19 cases. Distress, separation from the support of family, and self-care were prominent in the interviews. While this was unsurprising considering the context and the nature of our questions, these issues may have broader relevance in the praxis of rural medicine. Previous studies have described the importance of self-care to prevent burnout,<sup>12</sup> and the importance of personal and professional relationships for developing and sustaining rural doctors' context-specific clinical courage.<sup>2</sup>

Participants displayed a range of coping strategies in response to COVID-19, and we have explored these in a separate paper.<sup>7</sup> Consistent with the Lazarus and Folkman stress and coping model,<sup>13</sup> we identified problem-focussed, emotion-focussed, and meaning-based coping strategies. These parallel some attributes of clinical courage; preparing for uncertainty and working to marshal resources are consistent with problem-focussed coping strategies; while collegial support to continue through adversity represents emotion-focussed coping.

Although there may be further features of clinical courage, this study has affirmed the existing attributes in the context of the COVID-19 crisis and added richness to our overall understanding of this phenomenon. The strengths of the study include interviewing doctors from very low-resource settings; the rich detail provided by all participants; and finally, the rapport between the participants and experienced interviewers who have worked as rural doctors. We do not seek to generalise from this diverse sample of rural doctors, rather, we sought to understand whether the attributes of clinical courage were transferable to this group and in this context. Although the group was small, the sample specificity and high quality of the interview dialogue strengthened the information power and validity of the study.<sup>14</sup>

## CONCLUSION

This international study affirms the attributes of

clinical courage amongst a group of rural doctors during the emerging COVID-19 pandemic. It also highlights the important role of rural doctors as community leaders during crises.

**Financial support and sponsorship:** LW, IC, RS, DC, IW and JK have all worked as rural doctors. LW, IC, RS, DC, and JK have leadership roles in rural medical undergraduate or vocational training. This research was supported through funding from the Australian Government Rural Health Multidisciplinary Training grant scheme to the Adelaide Rural Clinical School.

**Conflicts of interest:** There are no conflicts of interest.

## REFERENCES

1. Konkin J, Grave L, Cockburn E, Couper I, Stewart RA, Campbell D, *et al.* Exploration of rural physicians' lived experience of practising outside their usual scope of practice to provide access to essential medical care (clinical courage): An international phenomenological study. *BMJ Open* 2020;10:e037705.
2. Walters L, Couper I, Stewart RA, Campbell DG, Konkin J. The impact of interpersonal relationships on rural doctors' clinical courage. *Rural Remote Health* 2021;21:6668.
3. Shelp EE. Courage and tragedy in clinical medicine. *J Med Philos* 1983;8:417-29.
4. Shelp EE. Courage: A neglected virtue in the patient-physician relationship. *Soc Sci Med* 1984;18:351-60.
5. Hawkins SF, Morse J. The praxis of courage as a foundation for care. *J Nurs Scholarsh* 2014;46:263-70.
6. Spence D, Smythe L. Courage as integral to advancing nursing practice. *Nurs Pract N Z* 2007;23:43-55.
7. Couper I, Walters L, Williams S, Campbell D, White I, Stewart R, *et al.* Exploring rural doctors' early experiences of coping with the emerging COVID-19 pandemic. *J Rural Health* 2022;38:923-31.
8. Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3:77-101.
9. Yan W. Rural health care for coronavirus requires collaboration, creativity. *IEEE Pulse* 2020;11:17-20.
10. Kedar E, Scott R, Soule DM, Lovelett C, Tower K, Broughal K, *et al.* COVID-19 in a rural health system in New York – Case series and an approach to management. *Rural Remote Health* 2021;21:6464.
11. Chipp CL, Johnson ME, Brems C, Warner TD, Roberts LW. Adaptations to health care barriers as reported by rural and urban providers. *J Health Care Poor Underserved* 2008;19:532-49.
12. Chipp C, Dewane S, Brems C, Johnson ME, Warner TD, Roberts LW. "If only someone had told me...": Lessons from rural providers. *J Rural Health* 2011;27:122-30.
13. Lazarus RS, Folkman S. *Stress, Appraisal, and Coping*. New York: Springer Publishing Company; 1984.
14. Malterud K, Siersma VD, Guassora AD. Sample size in qualitative interview studies: Guided by information power. *Qual Health Res* 2016;26:1753-60.