

Pandemic research for older people: doing it better next time

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The COVID-19 pandemic has disproportionately affected older people, both in terms of hospitalizations and deaths, but also by the consequences of restrictions on social contact resulting in physical deconditioning and worsened mental health [1]. Yet the global research response to the COVID-19 pandemic has not been focused on the specific needs of older people; research has focussed on treatment more than prevention or rehabilitation, on hospital care rather than community care, on counting deaths rather than measuring function, and on younger people rather than older people [2,3]. Clinicians caring for older people find themselves making decisions by extrapolating evidence from younger populations or without evidence at all. Research was one of four pillars underpinning the UK COVID-19 response but has been largely lacking for older people. What has led us to this point and where do we go from here?

Previous pandemics found the healthcare research community unprepared. The research responses to the pandemic influenza outbreak in 2009 and the West African Ebola outbreak in 2014 were slow and fragmented, with studies failing to start early enough to complete recruitment in time to guide treatment. The infectious disease and respiratory research communities learned lessons from these experiences [4]. It is noteworthy that, in the current pandemic, studies that were able to start quickly and have delivered the most important results are either those that were predesigned and were dormant (for example the ISARIC-4c observational studies [5]), drew heavily on previous experience (e.g. the RECOVERY and SOLIDARITY trials) [6,7], or were repurposed from existing active studies (for example the REMAP-CAP critical care trial) [8]. Research using existing registries and benchmarking systems, for instance the ICNARC critical care system [9] have rapidly yielded important results from UK intensive care facilities.

The academic ageing research community has not been able to deliver research at sufficient speed and scale to meet the needs of older people, clinicians or healthcare providers. Whether it is inclusion of older people in vaccine or therapeutics trials [3], a resolution to the debate about frailty scoring in

prognostication [10], or an understanding of how to diagnose and manage care home outbreaks, the research response has fallen short of that delivered by other specialities and has not been commensurate with the clinical need. There are several reasons for this. Firstly, academic geriatric medicine is a small community, which lacks capacity to deliver research at scale. This is in part due to the small numbers of academics who specialise in clinical research for older people, but is also a result of the low numbers of non-academic clinicians who are active in research. Many clinicians caring for older people are, at best, ambivalent to research and lack skills or experience recruiting to studies. This group of clinicians bore a significant proportion of the workload in supporting COVID-19 wards and there was no opportunity to rapidly upskill. Secondly, academic geriatric medicine and allied academic professions lack the tradition or structures to support multicentre collaborative work at the scale seen in other specialties such as cardiology and respiratory medicine. Care homes and other sites outwith the hospital system have been neglected as research venues and are, for the most part, outside the existing research infrastructure, and so were unprepared for research despite bearing the brunt of deaths in the first wave of COVID-19 in many countries. The high number of small, descriptive, single-centre COVID-19 studies submitted to *Age and Ageing* over the last six months is testament to our failure as a research community to collaborate effectively and is a classic example of research waste [11]. The tens of thousands of patients receiving off-label treatments outside trials (such as convalescent plasma in the USA) represents a further wasted research opportunity. If all of these patients took part in clinical trials, we would have high-quality evidence of effectiveness or harm within weeks [12]. Thirdly, healthcare for older people often involves complex clinical interventions working over prolonged timeframes, not always amenable to study by simple trials, requiring research access to vulnerable populations and the navigation of complex governance procedures. Finally, the global academic geriatric medicine community has not experienced a global pandemic before. We have therefore not had the opportunity to benefit from the experience that some other research communities have had, although we have arguably also failed to learn lessons from colleagues in parts of the world affected by localised infection outbreaks such as SARS-CoV-1 [13].

Looking forwards there can be no excuse for failing to plan and prepare for future pandemics - or indeed other major challenges to the wellbeing of older people. Pandemics are likely to become more frequent given the increasing interconnectedness of the world and our closer proximity to wildlife due to human encroachment [14]. The first step is to identify the key issues for older people that require rapid answers in a pandemic. Disease prevention was at best partly successful and came at considerable collateral cost. From a disease perspective based on our experience with COVID-19, early priorities will include rapidly delineating the (often atypical and non-specific) presentation of illness in older people, prognostic factors, and accurate prediction of healthcare resource utilisation. In the intermediate to longer term, ascertainment of optimal rehabilitation strategies to minimise functional impairment and implementation of strategies to minimise the impact on delivery of usual healthcare will be paramount. In parallel, we will need to deliver rapid, high quality clinical trials of effective vaccines, therapeutics, prophylaxis and symptom relief strategies in early and late-phase illness, that enrol older people across community, care home and hospital settings. Multipurpose research platforms, whether for the trial of novel therapeutics (RECOVERY, PRINCIPLE), or new technologies (CONDOR) have shown great promise during the pandemic, and are the template for adaptive and responsive research models going forward. We need more of these to involve older people and to focus on clinical settings where older people are historically excluded from research, such as long-term care. This agenda is supported by a recent survey of international academic geriatric medicine experts [15] and could provide the beginnings of a blueprint for planning research for the next pandemic. To deliver this agenda, we need to redouble our efforts to build research capacity. We need clinicians willing and able to recruit to multicentre studies, and we need to build effective national and supranational networks that facilitate participation in multicentre studies. This is possible, as shown by the way that the GeMRC UK geriatric medicine trainees network rapidly designed and delivered the COVIDCollab study, collecting data on over 5000 patients from 55 centres [16]. Finally, we need to change our mindset. Every single centre study and every off-label therapeutic use in a pandemic is a

wasted opportunity and a step further away from providing best evidence-based care for older patients. COVID-19 has taught us lessons in all areas of our lives; it is our duty as an academic community to learn these lessons and do better in our research response anticipating and responding to the next pandemic.

Acknowledgements:

MDW acknowledges support from the NIHR Newcastle Biomedical Research Centre

Funding:

No external funding supported the writing of this editorial

Conflicts of interest:

MDW is deputy editor of *Age and Ageing*, and is National Speciality Lead for the NIHR Ageing Clinical Research Network

RHH is editor in chief of *Age and Ageing*

ALG is President-elect of the British Geriatrics Society and outgoing chair of the BGS Research and Academic Committee

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References

- [1] Briguglio M, Giorgino R, Dell’Osso B et al. Consequences for the Elderly After COVID-19 Isolation: FEaR (Frail Elderly amid Restrictions). *Front Psychol* 2020. <https://doi.org/10.3389/fpsyg.2020.565052> [online ahead of print]
- [2] Fraser S, Lagacé M, Bongué B et al. Ageism and COVID-19: what does our society's response say about us? *Age Ageing* 2020;49:692-5.
- [3] Lithander FE, Neumann S, Tenison E et al. COVID-19 in older people: a rapid clinical review. *Age Ageing* 2020; 49, 501–15.
- [4] Dunning J, Merson L, Rohde GGU et al. Open source clinical science for emerging infections. *Lancet Infect Dis* 2014; 14: 8-9.
- [5] Docherty AB, Harrison EM, Green CA et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ*. 2020;369:m1985.
- [6] Horby P, Mafham M, Linsell L et al. Effect of hydroxychloroquine in hospitalised patients with COVID-19. *N Engl J Med* 2020. doi: 10.1056/NEJMoa2022926. Online ahead of print.
- [7] Pan H, Peto R, Karim QA et al. Repurposed antiviral drugs for COVID-19 –interim WHO SOLIDARITY trial results [Preprint] *MedRxiv* <https://doi.org/10.1101/2020.10.15.20209817>
- [8] Angus DC, Berry S, Lewis RJ et al. The REMAP-CAP (Randomized Embedded Multifactorial Adaptive Platform for Community-acquired Pneumonia) Study. Rationale and Design. *Ann Am Thorac Soc* 2020;17:879-91.
- [9] Richards-Belle A, Orzechowska I, Gould DW, Thomas K, Doidge JC, Mouncey PR et al. COVID-19 in critical care: epidemiology of the first epidemic wave across England, Wales and Northern Ireland. *Intensive Care Med* 2020;46:2035-47.
- [10] Lewis EG, Breckons M, Lee RP, Dotchin C, Walker R. Rationing care by frailty during the COVID-19 pandemic. *Age and Ageing* 2020. <https://doi.org/10.1093/ageing/afaa171> [online ahead of print]

[11] Chalmers I, Glasziou P. Avoidable waste in the production and reporting of research evidence. Lancet 2009;374:86-9.

[12] Convalescent plasma treatment for covid-19 has been oversold by the US. New Scientist. 25th August 2020. Downloaded from: <https://www.newscientist.com/article/2252737-convalescent-plasma-treatment-for-covid-19-has-been-oversold-by-the-us> [Accessed 10th November 2020]

[13] Chow L. Care homes and COVID-19 in Hong Kong: how the lessons from SARS were used to good effect. Age Ageing 2020. <https://doi.org/10.1093/ageing/afaa234> [online ahead of print]

[14] United Nations Environment Programme and International Livestock Research Institute (2020). Preventing the Next Pandemic: Zoonotic diseases and how to break the chain of transmission. Nairobi, Kenya. Available from: <https://www.unenvironment.org/resources/report/preventing-future-zoonotic-disease-outbreaks-protecting-environment-animals-and> [Accessed 16th November 2020]

[15] Richardson SJ, Carroll CB, Close J et al. Research with older people in a world with COVID-19: identification of current and future priorities, challenges and opportunities. Age Ageing 2020;49:901-6.

[16] Geriatric Medicine Research Collaborative, Covid Collaborative. Age and Frailty Are Independently Associated with Increased Mortality in COVID-19: Results of an International Multi-Centre Study. Available at SSRN: <https://ssrn.com/abstract=3709847> or <http://dx.doi.org/10.2139/ssrn.3709847> [Accessed 17th November 2020]