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Author's reply

Ioan Milosevic and colleagues pointed out that the outcomes presented in our Article[1] were different from those in the ISRCTN registry (number ISRCTN37118456). They stated that one pre-specified primary outcome ("hospital costs") was not reported, and a new co-primary outcome ("physician diagnosed post-stroke pneumonia") added. We have clarified in the Methods section that physician diagnosed pneumonia was not a primary outcome but was presented as an alternative to algorithm-based diagnosis to harmonise with diagnostic criteria used in previous studies.[2] Our innovative approach to post-stroke pneumonia (PSP) diagnosis helped to minimise detection bias in physician diagnosis arising from overdependence on fever and stroke severity as principal determinants.[3] With regards to cost outcomes, both the primary and four of the eight so-called missing secondary outcomes (therapy costs, quality of life, institutionalisation, and cost-effectiveness ratios) will be presented in a later publication as stated in the headline paper, because cost-effectiveness in the absence of clinical effectiveness has little value. The five so-called new endpoints include four of eight "unreported" pre-specified endpoints (National Institutes of Health Stroke Scale [NIHSS] score, change in NIHSS score at 14 days, mortality at 14 days, and modified Rankin Scale 0–2 at 90 days). Length of stay in survivors and days to death (the fifth so-called new endpoint) are components of length of hospital stay, but they were presented separately to prevent bias from higher mortality in either group that resulted in a difference in length of stay between groups. We commend the vigilance shown by Milosevic and colleagues, but also believe that diligence needs to be exercised in analysing published data for the COMPare project to be credible.

In Hermann Neugebauer and colleagues' letter, the PSP incidence rates quoted are for all stroke patients and include non-dysphagic patients, in whom the risk of PSP is 2%—compared with 16% in dysphagic patients,[4] the patient population for the STROKE-INF study. Routine use of fibre-endoscopic evaluation of swallowing is not recommended by UK guidelines, and PSP incidence in dysphagic patients is likely to be determined by dysphagia management rather than the method used for screening. For clarification, dysphagia screening and management were initiated at admission for all patients; 48 h was the maximum interval between stroke to randomisation and trial intervention. Finally, any bias caused by screening methods or management of dysphagia between the control and intervention groups would have been controlled for by randomisation in this study.

I declare no competing interests.

Lalit Kalra
lalit.kalra@kcl.ac.uk

Department of Basic and Clinical Neuroscience, IoPPN, King's College London, London SE5 8AF, UK

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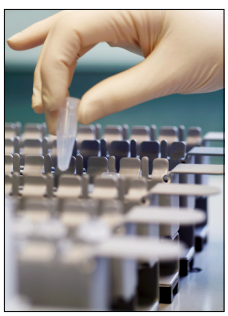
The promise of personalised medicine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Genomics are anticipated to have an important role in promoting population health by being used to target at-risk individuals. In 2015, Victor Dzau and colleagues[1] proposed that identification of genomic variants in major complex diseases would lead to modulation of health-related behaviours, with a 10–50% reduction in disease incidence. Most studies in a Cochrane review,[2] however, showed no evidence of incremental behavioural changes by patients after provision of genetic risk information alongside lifestyle interventions. Given that genomics can currently explain only a small fraction of inherited complex disease risks, such testing is also unlikely to lead to behavioural changes.

A broad, genomic, health-risk factor modification approach to major complex diseases has not yet proven to be effective. An alternative strategy is needed to deliver on the promise of personalised medicine.

Genomic medicine achieved its initial success with its application to serious diseases caused by highly penetrant alleles. Large health benefits have already been shown from the provision of genomic information to individuals at high risk of imminent, serious, preventable, and penetrant disorders, even when the behavioural modification need is arduous.

Phenylketonuria is such a disease that genomic medicine can help. For every 4 weeks that dietary treatment is delayed after birth there is an associated decrease of 7–10 intelligence quotient (IQ) points.[3] Yet, despite the burden to maintain a phenylalanine-restricted diet being more onerous than the uptake of healthy lifestyle behaviours, the prevalence of the disabling effects of phenylketonuria has been reduced by 92% with introduction of newborn screening and dietary advice.[4] Reductions in the prevalence of conditions with high health-care costs, such as fragile

X syndrome (reduced by 47%) and β-thalassaemia (90%),[5,6] have been reported as a result of informed family planning after genetic testing, with the added benefit of restored reproductive confidence. Similarly, identification of patients with homozygous familial hypercholesterolaemia via genetic testing and prophylactic therapy (predominantly statins), resulted in reductions of 66% of patient deaths and 51% of major adverse cardiovascular events.[7] Genomic testing also has the potential to reduce the large economic burden associated with adverse drug reactions through personalised drug prescriptions.

The priority for genomic testing should be to identify individuals at high risk of imminent, serious, preventable, penetrant disorders that have large health-care costs. These patients and their families will be uniquely placed to gain immediate benefits from personalised genomic medicine.

We declare no competing interests.

*Brett Doble, Deborah J Schofield, Tony Roscioli, *John S Mattick*
j.mattick@garvan.org.au

Garvan Institute of Medical Research, Darlinghurst, NSW 2010, Australia (BD, DJS, TR, JSM); Centre for Health Economics, Monash Business School, Monash University, Melbourne, VIC, Australia (BD); Faculty of Pharmacy, University of Sydney, NSW, Australia (DJS); Murdoch Childrens Research Institute, Royal Children's Hospital, Parkville, VIC, Australia (DJS); Department of Medical Genetics, Sydney Children's Hospital, Sydney, NSW, Australia (TR); and St Vincent's Clinical School, University of New South Wales, Sydney, NSW, Australia (TR, JSM)

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Frailty in emergency departments

Population ageing is placing a heavy demand on health-care systems worldwide. This pressure is being particularly felt by hospital emergency departments, which are facing an unprecedented influx of older patients (65 years and older).[1] Of concern, more than half of these older patients are likely to be frail.[2] Frailty signifies an increased vulnerability to external stressors and has been purported to be the largest global problem associated with an ageing population.[3]

Is admission to an emergency department for a frail older adult, particularly one with an advanced care directive in place, really appropriate care? Appropriate care is hallmarked by the fundamental concept of patient welfare.[4] At present, emergency departments are not specifically equipped to deal with the extra service and care requirements a frail patient needs.[5]

If progress is to be made to manage the rapidly increasing influx of frail older patients to emergency departments, then rapid recognition and response systems are imperative for frailty. Such a system should not only incorporate a frail patient's right to prompt medical treatment but should also protect these patients from harm, including the avoidance of any unnecessary tests and treatments. At present, several major barriers prevent frailty from being rapidly recognised and treated in the emergency department. First, methods to identify frailty are too complicated for use in emergency departments and are usually completed after a decision about a patient's care has been made. Second, no standard measurement for frailty exists and frailty classifications can differ vastly depending on which frailty measurement is used. Third, frailty is often erroneously judged to be part of the normal ageing process, and in turn, older patients might be treated based on their medical disorders, rather than their physiological vulnerability to external stressors.[3] Finally, clinical guidelines for frailty are sparse and those that do exist, do not encompass frailty management in emergency departments.

Research and investment in technologies, such as health informatics and electronics (inertial sensors), might prove invaluable for a rapid recognition-response system for frailty in emergency departments. In the meantime, there is no question that a patient-focused system for rapid recognition and response for frailty has the potential to become a promoter of improvement in the management of frail, older patients admitted to emergency departments.

We declare no competing interests.

**Elsa Dent, Emiel O Hoogendijk, Magnolia Cardona-Morrell, Kenneth Hillman*
elsa.dent@adelaide.edu.au

School of Public Health, University of Adelaide, 5000 Adelaide, Australia (ED); Gérontopôle, Department of Internal Medicine and Geriatrics, Toulouse University Hospital, Toulouse, France and Department of General Practice and Elderly Care Medicine and Department of Epidemiology and Biostatistics, Institute for Health and Care Research, VU University Medical Center, Amsterdam, Netherlands (EOH); Simpson Centre for Health Services Research, University of New South Wales, Sydney, NSW, Australia, (MC-M, KH); and Liverpool Hospital, South Western Sydney Clinical School, Sydney, NSW, Australia (KH)

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