improvement, readily equalled by patients not so mobilised in the weeks after hospital discharge.

Far less is known about these later effects of early mobilisation, whether provided by an additional physical therapist or by more effective coordination and communication of existing resources. Regrettably, the International Early SOMS-guided Mobilisation Research Initiative achieved only 42% (84 of 200 patients) follow-up at 3 months. Such low figures at follow-up are not uncommon in ICU RCTs, although not universal.6 A full endorsement of early mobilisation must wait for more data, even as many pragmatically attempt early mobilisation based on the hope that its effects on trajectory are durable. Large trials7 of mobilisation in other patient groups provide caution to making assumptions about its long-term benefit.

The future of early mobilisation research must move beyond the ICU and must include randomised tests of the hypothesis that early mobilisation provides enduring improvements for patients. Additionally, future research must go beyond the question of no mobilisation or some mobilisation. At some point—which will need more than 200 patients to be achieved—the different strategies for mobilisation need to be compared. These different strategies should include not only different specific regimes of active exercise, but also different approaches to integrate active exercise in the core interdisciplinary teamwork of the ICU. Use of these strategies will need use of all the tools of quality improvement, both RCTs and registries. Patients who are at particularly high risk for adverse outcomes of mobilisation need to be identified, cognizant of the non-significant difference in mortality seen in Schaller and colleagues8 and other RCTs. Furthermore, an understanding is needed of how early mobilisation can be integrated into coherent programmes of before ICU, in the ICU, and after ICU care to mitigate the post-intensive care syndrome, maximising recovery for all critically ill patients.

*Theodore J Iwashyna, Carol L Hodgson
Department of Internal Medicine, University of Michigan, Ann Arbor, MI 48109, USA (TJI); Center for Clinical Management Research, VA Ann Arbor Health System, Ann Arbor, MI, USA (TJI); Australian and New Zealand Intensive Care Research Centre, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC, Australia (TJI, CLH); and Department of Physiotherapy, Alfred Hospital, Melbourne, VIC, Australia (CLH)
iwashyn@umich.edu

The authors have proposed a large, international randomised clinical trial of early mobility to follow patients to well after hospital discharge. This proposal was submitted and under review before the invitation to write this Comment. This work does not necessarily represent the views of the US Government or the Department of Veterans Affairs.

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Clear-lens extraction as a treatment for primary angle closure

Glaucoma is a multifactorial spectrum of diseases in which progressive optic nerve damage leading to blindness occurs with raised intraocular pressure as the main risk factor. The outflow of fluids through the trabecular meshwork decreases when the iris moves forward and comes into contact with it. This condition is called “angle closure” and can lead to glaucoma damage if intraocular pressure remains sufficiently raised. When no other cause besides anatomical predisposition is present for the iridotrabecular contact, the condition is classified as primary angle closure, and if glaucomatous optic neuropathy is present it is classified as primary angle-closure glaucoma. The reported prevalence varies because of heterogeneity in definitions of primary angle-closure glaucoma and methods of angle assessment used in different surveys.1 Even more common than primary angle closure and primary angle-closure glaucoma is primary open-angle glaucoma. These three disorders have similarities, such as increasing prevalence after
Due to increased life expectancy and demographic expansion, the number of glaucoma cases worldwide is estimated to reach 76 million by 2020, of which 23 million will be primary angle-closure glaucoma. The established initial treatment for primary angle closure and primary angle-closure glaucoma is laser iridotomy with eye drops to reduce intraocular pressure. In the past decade, lens extraction (both clear or with cataract) with intraocular lens implantation has gained popularity due to good results in series of patients with various primary types of angle closure based on different definitions and anecdotal evidence.

Technological advances in surgical techniques have also improved the safety of phacoemulsification in patients with glaucoma. Lens extraction either clear or with cataract to treat primary angle closure, judged on an individual basis, has also been recommended by guidelines.

Augusto Azuara-Blanco and colleagues report in The Lancet the results of an international prospective randomised study comparing laser iridotomy with clear-lens extraction as the initial treatment of primary angle closure and primary angle-closure glaucoma. This is also the first prospective randomised therapeutic trial in ophthalmology in which one of the primary outcome measures is patient reported, through quality-of-life questionnaires. The co-primary endpoints were patient-reported health status, intraocular pressure, and incremental cost-effectiveness ratio per quality-adjusted life-year gained 36 months after treatment. 419 patients were randomised and followed up for 3 years, of whom 208 were assigned to clear-lens extraction and 211 to laser iridotomy. 351 (84%) had complete data on health status and 366 (87%) on intraocular pressure. The results show a small but unquestionable advantage of primary clear-lens extraction over laser iridotomy for all measured outcomes. The mean health status score (0.87 [SD 0.12]) on the European Quality of Life-5 Dimensions (EQ-5D) questionnaire, was 0.052 higher (95% CI 0.015 to 0.088, p=0.005) and mean intraocular pressure (16.6 [SD 3.5] mm Hg) 1.18 mm Hg lower (95% CI -1.99 to -0.38, p=0.004) after clear-lens extraction than after iridotomy. The incremental cost-effectiveness ratio was £14 284 for initial lens extraction versus standard care, although the costs were assessed only for the subset of patients treated in the UK and, therefore, are not conclusive for other settings.

This pragmatic trial is clinically relevant because it addresses a topic with widespread practical implications. Patients undergoing clear-lens extraction became emmetropic (final refraction 0.08 [SD 0.95]), whereas those assigned to laser iridotomy remained hyperopic (0.92 [2.8]). Uncorrected visual acuity, therefore, improved greatly for distance and near vision in the clear-lens extraction group only, which was associated with improvements in patient-reported outcome questionnaires. How this purely refractive result affected the observed improvement in the clear-lens extraction group compared with the laser iridotomy group (a change in absolute terms of almost 6% for the EQ-5D, 7% for the Glaucoma Utility Index, and 2.58% for the National Eye Institute Visual Function Questionnaire-25) remains to be determined.

The clinical relevance of the small difference between groups in intraocular pressure (1.18 mm Hg) is unclear since patients with advanced glaucoma damage were excluded from the study. The use of eye drops to lower intraocular pressure, however, was less in the clear-lens extraction group than in the laser iridotomy group (mean 0.4 [SD 0.8] vs 1.3 [1.0]). This finding partly explains the small difference recorded for intraocular pressure. There was also a difference between groups...
in the need for further surgery to control intraocular pressure (one patient in the clear-lens extraction group vs 24 patients in the laser iridotomy group); of the 24 patients in the laser iridotomy group who had further surgery, 16 (67%) underwent cataract surgery. However, the need for some cataract operations within 3 years is not surprising and this finding should not to be interpreted as an increased occurrence of an unfavourable outcome in the laser iridotomy group.

Cataract extraction by phacoemulsification causes continued progressive endothelial cell loss,6,7 and increasing age is associated with decreasing endothelial cell counts. The mean corneal endothelial cell loss after phacoemulsification in patients whose eyes have shallow anterior chambers and short axial lengths—both features of primary angle closure—is around 19%.8 Azuara-Blanco and colleagues9 did not address corneal endothelial cell loss, possibly because such an assessment is not always part of the routine preoperative preparation for phacoemulsification in most centres.

Primary angle closure and primary angle-closure glaucoma are very different disorders, especially according to the definitions used by Azuara-Blanco and colleagues. They noted that their results are applicable only to patients with primary angle closure and intraocular pressure greater than 30 mm Hg—who represent a minority of patients with this disorder—or to those with primary angle-closure glaucoma without advanced damage, implying that these two groups would be expected to respond to treatment in a similar way. However, how generalisable the study’s findings are to other patients remains elusive.

Phacoemulsification to treat primary angle closure can be technically challenging. The surgeons involved in Azuara-Blanco and colleagues’ study were highly experienced. Training for routine cataract surgery might not provide the skills needed to reach consistently good results for phacoemulsification clear-lens extraction in primary angle closure cases that would achieve the safety margin and avoid the few but potentially severe intraoperative complications reported in this study, and less experienced surgeons might incur more difficulties and complications. Nevertheless, the study highlights the great advances made in phacoemulsification techniques.

While not yet sufficient to justify using clear-lens extraction to treat all patients with primary angle closure with or without glaucoma, the findings of this trial could have positive implications for areas where angle closure is most prevalent, particularly east Asia, or where health-care resources are scarce and patients might not have easy access to medications and monitoring. A not yet proven potential additional benefit with clear-lens extraction is that early intervention might prevent blindness due to primary angle-closure glaucoma. The findings of Azuara-Blanco and colleagues underline the need for further efforts to improve phenotyping of angle closure and for more randomised prospective therapeutic trials that include other subtypes of primary angle closure and assess the effects of laser iridotomy in eyes with narrow but not yet closed angles.

Carlo E Traverso
Clinica Oculistica, DINOGMI, Università di Genova, Genoa, Italy; and IRCCS Azienda Ospedaliera, Universitaria San Martino IST, 16132 Genoa, Italy
mc8620@mclink.it

I am co-investigator with Augusto Azuara-Blanco, an author of the Article, in a HORIZON 2020 project (H2020 FTIPILOT-2015-3) on the effects of a novel laser trabeculoplasty method to lower intraocular pressure in patients with primary open-angle glaucoma. I am a member, with Augusto Azuara-Blanco, of the Executive Committee of the European Glaucoma Society.

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