

The changing landscape of traumatic brain injury research

As this issue of *The Lancet Neurology* went to press, the traumatic brain injury (TBI) research community was eagerly anticipating an imminent call for proposals from the European Commission (EC). The new funding—expected to be included in the EC 7th Framework Programme (FP7) for cooperative health research—will be the first economic support from the EC for a unique research effort: the International Initiative for Traumatic Brain Injury Research (InTBIR). This initiative, which will also be supported by the Canadian Institutes of Health Research and the US National Institutes of Health, is an international multidisciplinary collaborative endeavour that aims to rapidly improve clinical practice in TBI.

A coordinated effort to boost TBI research by the major funding agencies of neurological research in North America and Europe was long overdue. TBI is an enormous public health problem, across all ages, and in all populations; even in North America and Europe, where TBI incidence is lower than in poorer regions, it has been estimated at 150 to 300 cases per 100 000 population per year. Over 200 per 100 000 individuals with TBI are admitted to European hospitals each year, with an average in-hospital case-fatality rate of 3%; in the USA, the average rate is 6.2%, and estimates indicate that 1–2% of the population live with disability caused by TBI. According to WHO, because incidence is increasing swiftly in low-income and middle-income countries (mostly owing to road traffic accidents), TBI is predicted to become the third leading cause of global mortality and disability by 2020. Furthermore, evidence suggests that TBI is a risk factor for dementia, substance abuse, and other psychiatric disorders. However, few improvements in clinical outcomes for patients with TBI have been achieved over the past two decades, and no effective therapy for TBI has been approved by any regulatory agency.

The InTBIR will gather the evidence that could lead to the improvement of patients' outcomes and decrease the global burden of TBI by 2020. These goals will be achieved by implementing a plan with three major components: the standardisation of data collection, the creation of an open-source registry to share the data, and the re-orientation of research questions by shifting towards a comparative effectiveness research (CER) approach. TBI is a heterogeneous and complex disorder; although

guidelines for the management of patients in different settings have been developed, many of these recommendations are not backed up by high-quality evidence. Clinical care and patients' outcomes vary greatly from centre to centre and in different countries. For instance, a recent study found large between-centre differences in clinical outcomes (about three times higher than expected by chance) even in the setting of large multicentre clinical trials. Hence, approaches to measure this variability in management and its effects on prognosis are urgently needed. Analyses of high-quality, large, observational data sets by use of CER statistical methods could provide specific answers on effective management more quickly—and more cheaply—than will traditional clinical trials. There is also an urgent need for comparative studies on the effects of access to acute and post-acute care, and it is unlikely that adequately powered clinical trials could be implemented soon to address these uncertainties across different settings. But by use of carefully designed collection methods, high-quality harmonised data, and prospective definition of any analyses plans, the InTBIR should enable researchers to learn more about the associations between management and clinical outcomes and improve prognostic models.

As the journal went to press, the participating funding agencies were preparing a document describing the specific goals and strategy of the InTBIR, its detailed governance, and the rules for participation; this document will be publicly available before the end of the year. Other funding agencies and philanthropists wishing to support the aforementioned goals of improved outcomes and decreased disease burden might be given the opportunity to contribute; the initiative should also attract the interest of the pharmaceutical industry, because the characterisation of patients with TBI will be key to development of effective therapies. A sizeable economic effort will indeed be required: the EC FP7 call for proposals is expected to offer only €30 million, a meagre sum that will fall short of that needed to implement the InTBIR across Europe. For the initiative to succeed, all interested stakeholders worldwide (TBI researchers, global health policy makers, funding agencies, and industry) have to support it and get involved—the possibility to tackle this crucial global health problem by 2020 should not be missed. ■ *The Lancet Neurology*

For more on **EC funding and InTBIR** see http://ec.europa.eu/research/health/medical-research/brain-research/international-initiative_en.html

For more on **TBI global burden** see *Neurological disorders: public health challenges*. Geneva: World Health Organization, 2006

For more on **data standardisation** see http://www.commondataelements.ninds.nih.gov/TB_Laspx#tab=Data_Standard

For more on the **open-source registry** see <http://fitbir.nih.gov/tbi-portal/>

For more on **comparative effectiveness research** see *J Neurotrauma* 2012; **29**: 32–46

For more on **differences in outcome** see *Neurosurgery* 2011; **68**: 601–7

For more on **prognosis after TBI** see *Review Lancet Neurol* 2010; **9**: 543–54