

The KARMA-Dep-2 trial: Ketamine as a treatment for major depression

Researchers from the Department of Psychiatry at Trinity College Dublin are trialling a potential additional treatment for depression: the anaesthetic ketamine. Ketamine works differently from current antidepressants, although we are still finding out how. It may change dysfunctional brain cell pathways and connections (known as neuroplasticity). Previous studies showed it reduced depressive symptoms within one hour of single infusions, with peak effect at 24 hours.

The WHO says depression is now the leading cause of disability worldwide. For 60 years, standard pharmacological treatment has focused on monoamine neurotransmitters, such as selective serotonin re-uptake inhibitors (SSRIs). The large STAR*D study in the US found only 30% of patients achieved remission after first-line SSRI treatment and 50% after two trials. Fewer than 40% of patients had relief within 10-14 weeks.

More information is available at clinicaltrials.gov clinical trials identifier NCT04939649.

Professor Declan McLoughlin, Research Professor of Psychiatry at Trinity, and his team at St Patrick's Mental Health Services want to see if ketamine can help people who are hospitalised with severe depression. The randomised controlled trial, Ketamine as an Adjunctive Therapy for Major Depression (2) [KARMA-Dep-2], is a definitive pragmatic trial, involving over 100 patients in real-life clinical

“Depression is the most common reason in the EU for long-term sick leave and disability.”

Professor Declan McLoughlin
*Professor of Research Psychiatry
and Consultant in Old Age Psychiatry*

settings and building on an earlier pilot. Funded by the Health Research Board, it is the first-ever clinical trial sponsored by Trinity.

The main hypothesis in KARMA-Dep-2 is that repeated ketamine infusions (twice weekly, maximum of eight infusions) alongside routine care will improve the condition of patients hospitalised with severe depression. This has never been done in Ireland before on this scale. Working with Professor Ciaran O'Neill at Queen's University Belfast, we also predict that using ketamine will reduce healthcare costs and improve quality of life. Professor Ricardo Segurado, University College Dublin, provides statistical support.

