Dear Colleagues,

We are pleased to invite your center to participate in a national multicenter study entitled **"Anticholinergic Drug Burden and Delirium Occurrence in Critically Ill Patients: A Prospective Multicenter Cohort Study (ADEL-ICU)."**

Delirium is a common and serious complication in critically ill patients, associated with prolonged mechanical ventilation, increased intensive care unit (ICU) stay, and higher mortality. Identifying potentially modifiable risk factors for delirium is essential for improving patient outcomes. Anticholinergic medications are frequently administered in ICUs; however, their contribution to delirium remains unclear. Previous studies have reported inconsistent findings, and evidence regarding the longitudinal relationship between anticholinergic drug burden and delirium is limited.

This prospective, multicenter longitudinal cohort study aims to investigate whether anticholinergic drug burden may represent a potentially modifiable risk factor for delirium in critically ill adult patients. Anticholinergic burden will be assessed daily using the Anticholinergic Drug Scale (ADS) and the Anticholinergic Cognitive Burden (ACB) Scale.

The primary objective is to evaluate the association between daily anticholinergic drug burden and daily delirium status. Secondary objectives include:

- To evaluate the association between pre-ICU anticholinergic drug burden and delirium occurrence during ICU stay.
- To identify the most frequently used medications with anticholinergic properties in the ICU, their frequency of use, and their contributions to the overall anticholinergic burden.
- To investigate the association between anticholinergic drug burden and time to first delirium occurrence following ICU admission.
- To assess the association between anticholinergic drug burden and delirium burden, including the number of days with delirium and the proportion of ICU days with delirium.
- To evaluate the association between cumulative anticholinergic drug burden during ICU stay and clinical outcomes.

The ADEL-ICU Study aims to provide valuable multicenter evidence regarding the longitudinal relationship between anticholinergic drug burden and delirium. The findings may help clarify whether anticholinergic drug burden represents a potentially modifiable risk factor for delirium and inform medication optimization and delirium prevention strategies in critically ill patients.

Authorship will be assigned in accordance with the International Committee of Medical Journal Editors (ICMJE) criteria. Each participating center may nominate one intensivist and

one clinical pharmacist as co-authors, provided that both meet the ICMJE authorship criteria. The order of authorship will be primarily determined by the number of eligible patients enrolled by each center, with priority given to centers contributing the highest number of patients. In addition, principal investigator of the study will be the first author and national coordinator will be the last author.

Once the participating centers have been finalized, the study protocol will be submitted to the Hacettepe University Health Sciences Research Ethics Committee for ethical approval. Patient enrollment will commence only after all required ethical and institutional approvals have been obtained. Participating centers will be provided with the study protocol and necessary documents to facilitate institutional approval.

We sincerely invite your center to join the **ADEL-ICU Study** and contribute to this national collaborative research initiative.

Contact Persons

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