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Protein quantification platforms for use in critical care precision medicine trials: a scoping review

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Introduction: Critical care syndromes demonstrate significant underlying biological heterogeneity. To address this issue, researchers are increasingly using enrichment methods to identify putative treatment-responsive subphenotypes. A parsimonious model for the allocation of acute respiratory distress syndrome (ARDS) subphenotypes has been developed that utilises the plasma cytokines interleukin-6 (IL-6) and soluble tumour necrosis factor receptor 1 (sTNFR1) along with bicarbonate from an arterial blood gas. In order to use models like this to guide treatment decisions, automated platforms that can quantify these plasma cytokines rapidly are needed. This scoping review aims to identify and collate data on such platforms as an aid to critical care researchers who are planning trials that stratify patients based on plasma biomarkers.

Methods: A protocol for this scoping review was previously published online (https://doi.org/10.17605/OSF.IO/FU546). Searches of MEDLINE, Embase, OpenGrey, and the Espacenet patent database were conducted. References relating to automated devices that could be used to quantitatively measure human proteins in the blood, plasma, or serum were included. “Proof of concept” studies, animal studies, and semi-quantitative assays were excluded. Screening was completed by two independent reviewers and disagreements were resolved with a third reviewer.

Results: 489 records met the inclusion criteria (Figure 1). 151 protein measurement devices across 59 manufacturers and several indications were identified. The most cited devices were the Cobas® series (Roche, Basel, Switzerland), the ADVIA Centaur® series (Siemens, Munich, Germany), the ARCHITECT™ series (Abbott Laboratories, Abbott Park, Illinois), the AU5800 (Beckmann-Coulter Inc, Pasadena, California), and the LUMIPULSE® G1200 (Fujirebio, Tokyo, Japan). Together these comprise most high-throughput hospital laboratory immunoassay devices. All support

IL-6 measurement following the COVID-19 pandemic. Multiplex devices supporting simultaneous cytokine measurements were also identified from 7 manufacturers: Ella™ (BioTechne, Minneapolis, Minnesota), Evidence series (Randox Laboratories, Crumlin, Northern Ireland), IMMULITE® 2000 XPi (Siemens, Munich, Germany), AFIAS (BodiTech Med Inc, Chuncheon, South Korea), sqidlite® (SQI Diagnostics, Toronto, Canada), READ (EnLiSense, Allen, Texas), and BV® (MeMed, Tirat Carmel Park, Israel). All multiplex devices except the MeMed BV® can quantify IL-6. The Randox multiSTAT (part of the Evidence series), the BioTechne Ella™ and the sqidlite® can quantify both IL-6 and sTNFR1.

Conclusions: Multiple automated protein quantification devices are available. Researchers will be able to leverage existing multiplex devices for precision medicine trials in critical care.

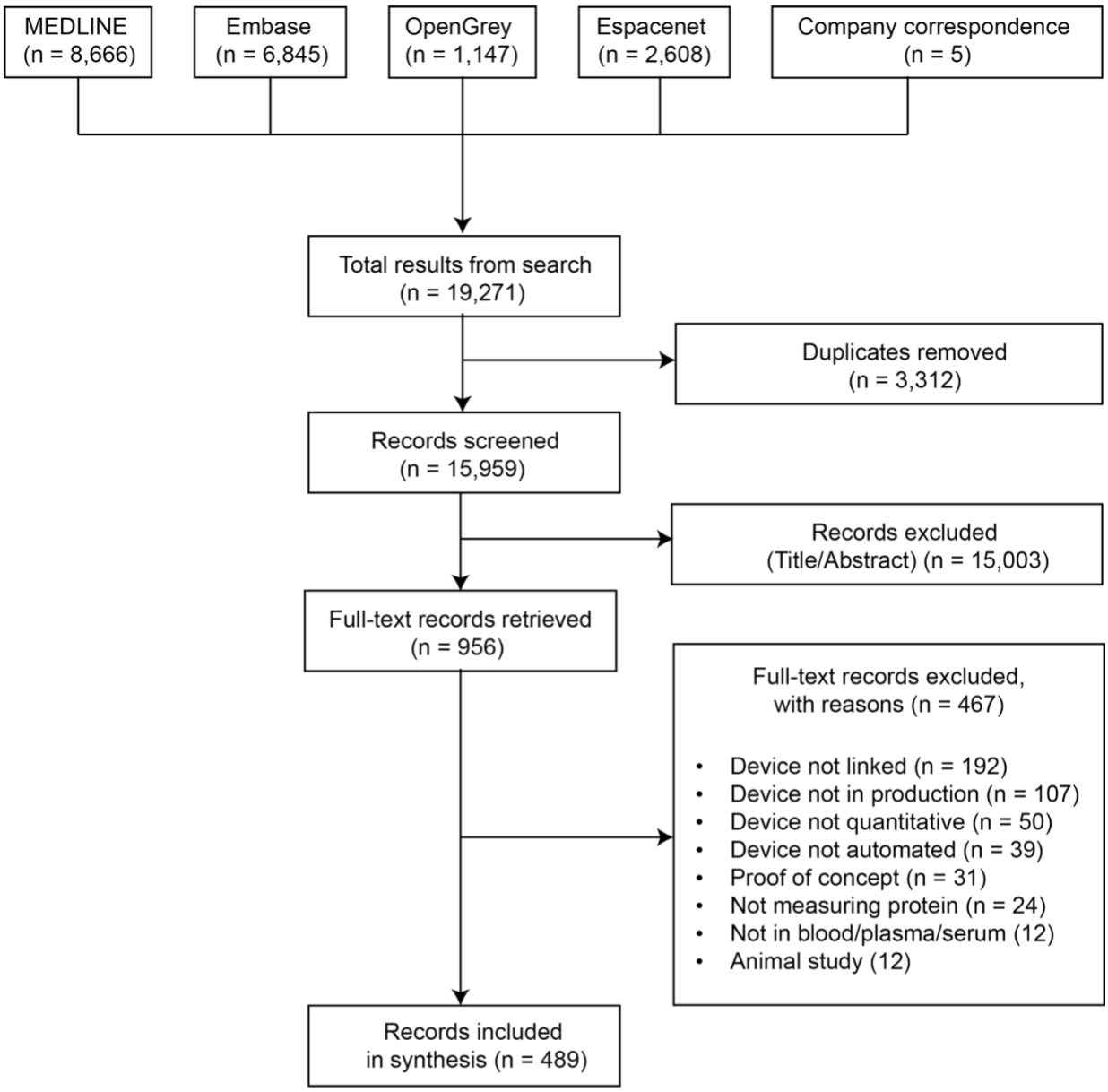

Figure 1: PRISMA Extension for Scoping Reviews (PRISMA-ScR) flow diagram. For those records that were removed on full text screening, reasons were recorded in keeping with inclusion and exclusion criteria published in the prospective protocol (https://doi.org/10.17605/OSF.IO/FU546).