Statement on waiver of Informed Consent

The FENICE Executive committee consider that IRB's / Ethics Committees in most Countries should grant a waiver of informed consent for the FENICE Study.

We suggest this based on the following grounds:

(1) ***Observational Study**:* This study is entirely observational with no risk to participants since no additional tests or examinations will be performed. The data collected is data generated as part of routine clinical care and are usually already recorded for clinical purposes.

(2) ***Data is De-Identified**:* The data is de-identified and cannot be traced back to the individual patients once the database is closed [1].

(3) ***Scientific Value**:* To generate truly generalizable scientific insights in a study such as this, a large (several thousand patients) and globally geographically dispersed patient population is required. The first FENICE study [2] study enrolled 2,213 patients, but the importance of the results suggests aiming at enrolling more than 10,000 patients in the FENICE II, as in other settings for similar studies about mechanical ventilation [3, 4], for obtaining an authoritative and widely generalizable study. A requirement for informed consent may impact on participation and, consequently, prejudice the scientific value and the generatability of the results of the study by creating biases in the study population, as previously demonstrated for similar studies [5].

(4) ***Risk of Population Bias**:* There is clear risk of bias where informed consent is required for these types of studies, in that certain populations may be over or under-selected. This results in a study population that does not represent the typical patient, potentially introducing a bias due to consent requirements, as highlighted in previous studies [5, 6].

(5) ***Difficulties in Informed Consent in Population****:* Requiring informed consent in a study of this size in this specific patient population is often impractical. Patients admitted to ICU for shock may be unable to consent due to their illness. Requiring consent from next-of-kin or another third party and/or deferred consent are possibilities, but will serve to reduce participation, further exacerbating bias in the study sample.

(6) ***Cost and Workload****:* Requiring informed consent greatly increases workload in observational studies, due to the study requirement for large patient populations, and this greatly increases the associated cost, as clearly demonstrated in the study by Tu et al. [5] This would greatly reduce the feasibility of the study.

(7) ***Risk of Geographic Bias****:* The greatly increased workload from requiring informed consent may mean that certain study sites, or even whole countries, may choose not to participate in this study, limiting generalisability of the results and constituting a significant disadvantage to future critically ill patients from these countries.

(8) ***Public Interest****:* There is significant public interest in the findings of a large study such as FENICE II study. Medical advances generated by this study will benefit all people receiving fluid in intensive care. This should also be weighed against any arguments for informed consent.

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