Supplemental Table 1: Definitions of clinical outcomes

| Clinical Outcome | Definition | Source/Rationale |
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| Ventilator-associated pneumonia (VAP) | The primary outcome is adjudicated VAP. Clinically suspected VAP at participating sites is being centrally adjudicated independently and in duplicate by 2 physicians blinded to allocation and center, informed by the following standardized definition: receiving invasive mechanical ventilation for > 2 days, when there is a new, progressive or persistent radiographic infiltrate on chest radiograph plus any 2 of the following:<br>1) fever (temperature >38°C) or hypothermia (temperature <36°C);<br>2) relative leukopenia (<3.0 x 106/L) or leukocytosis (>10 x 106/L);<br>3) purulent sputum | The American College of Chest Physicians (ACCP) definition did not provide thresholds for leukopenia or leukocytosis. Therefore, the thresholds were obtained from Morrow et al [Morrow] as their VAP definition was also based on the ACCP definition [Grossman]. Any disagreement in adjudication will be resolved through discussion and consensus. Acknowledging that there is no universally accepted gold standard VAP definition [3] , and that in non-immunocompromised patients, routine invasive testing is not associated with improved outcomes [Canadian Critical Care Trials Group], we are also collecting data to allow VAP reporting according to several other definitions [46–49]. |
| Early VAP | Pneumonia arising on day 3, 4 or 5 after the initiation of mechanical ventilation. | We are classifying VAP by early VAP and late VAP, as the etiologic organisms may differ, the antimicrobials prescribed may differ, and the prognosis is often worse for late VAP [50,51]. We will also report a composite outcome of early VAP, late VAP, and post-extubation pneumonia, adjudicated independently and in duplicate by 2 physicians. For the timing of all pneumonia outcomes, we use days rather than hours to inform the classification. |
| Late VAP | Late VAP is defined as VAP arising on day 6 of mechanical ventilation or later, and including up to 2 days after | |

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| | discontinuation of mechanical ventilation (also relevant for patients with a tracheostomy) | |
| Post-extubation pneumonia | Pneumonia arising in the ICU following discontinuation of mechanical ventilation (3 or more days after discontinuation), labeled post-extubation pneumonia, to avoid suppressing potentially relevant lung infections that arise in ICU | |
| Diarrhea | Diarrhea in the ICU:<br>• World Health Organization definition (≥3 loose or watery bowel movements per day<br>• Bristol Stool classification for loose or watery stool (type 6 or 7) | We will record each bowel movement and define diarrhea incorporating 2 metrics [6,52] |
| Clostridioides difficile–associated diarrhea (CDAD) | Clostridioides difficile in the ICU and prior to discharge from hospital: diarrhea (as previously defined) and laboratory confirmation of C. difficile or colonoscopic or histopathologic findings demonstrating pseudomembranous colitis | Definition from Cohen et al. [53]. Will be adjudicated independently and in duplicate by 2 physicians |
| Antibiotic-associated diarrhea (AAD) | AAD: diarrhea (as above) defined as following the administration of antibiotics, any day antibiotics are administered or within 1 day after starting any antibiotic | Definition from Thibault et al. [54] |
| Other healthcare–associated infections | Any infection acquired during the ICU stay, including bloodstream infection, intravascular catheter-related bloodstream infection, intra-abdominal infection, C. difficile infection, urinary tract infection, skin and soft tissue infection, and others. | These individual infections are classified using definitions adapted from the International Sepsis Forum Consensus Conference on Definitions of Infection in the Intensive Care Unit [47], as adapted in prior studies [46]. We will also report a composite outcome of any infections (including pneumonia) acquired during the ICU stay. Secondary infectious outcomes (other than pneumonia and C. difficile) are being centrally adjudicated by 1 physician blinded to allocation and center, based on review of data collected at each participating site. |
| Serious adverse events (SAE) | Defined as isolation of Lactobacillus spp. in a culture from a sterile site or as the | The rationale for our approach to SAEs [Guidance |

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| | sole or predominant organism cultured from a non-sterile site and results in:<br>1) persistent or significant disability or incapacity;<br>2) that is life-threatening, or;<br>3) that results in death | Document for Industry] accords with our guidelines for academic drug trials in critical care [55]. Any culture obtained by the ICU team and processed by the clinical microbiology laboratory as positive for Lactobacillus spp. is recorded. Any such bacterial sample is sent to a McMaster University research laboratory for strain genotyping to evaluate consistency with the administered L. rhamnosus GG strain |