Supplementary Material S1. PICO chart of the study objectives

Primary objective 1.

P: All cases with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, severe also non-severe CDID, and concordant also non-concordant treatment
I: Concordant with Guidelines treatment
C: Non-concordant with Guidelines treatment
O: CDID–related Intensive Care Unit admission, CDID–related mortality, 30-day survival, 30-day all-cause-mortality.

Primary objective 2.
P: All cases with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, blood leucocyte count < 15 x 10^9/L, creatinine serum level ≤ 133 µmol/L, and concordant also non-concordant treatment
I: Concordant with Guidelines treatment
C: Non-concordant with Guidelines treatment
O: CDID–related Intensive Care Unit admission, CDID–related mortality

Primary objective 3.

P: Cases with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, blood leucocyte count ≥ 15 x 10^9/L, creatinine serum level > 133 µmol/L, and concordant also non-concordant treatment
I: Concordant enteral vancomycin treatment (Group V)
C: Non-concordant enteral metronidazole treatment (Group M)
O: Treatment failure (refractory CDID)

Primary objective 4.

P: Patients with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, and non-concordant enteral metronidazole treatment (Group M)
I: Blood leucocyte count ≥ 15 x 10^9/L, **and** creatinine serum level > 133 µmol/L
C: Blood leucocyte count ≥ 15 x 10^9/L, **or** creatinine serum level > 133 µmol/L
O: CDID–related Intensive Care Unit admission, CDID–related mortality

Secondary objective 1.

P: Patients with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, severe also non-severe CDID, and concordant treatment
I: CCI score ≥ 5
C: CCI score < 5
O: 30-day survival, 30-day all-cause mortality

Secondary objective 2.

P: Patients with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, severe also non-severe CDID, and concordant treatment
I: Continuation of concomitant antibiotics
C: Discontinuation of concomitant antibiotics
O: 30-day survival, 30-day all-cause mortality

Secondary objective 3.

P: Patients with diarrhea, confirmed *C. difficile* A and/or B toxins in stools, severe also non-severe CDID, and concordant also non-concordant treatment
I: The use of CDID precipitating broad-spectrum antibiotics also vancomycin for primary CDID treatment in 2011-2016 (Group 1)
C: The use of CDID precipitating broad-spectrum antibiotics also vancomycin for primary CDID treatment in 2017-2020 (Group 2)
O: Rate of CDID