$Table \ S7. \ Total \ ICU \ cost \ differences \ between \ the \ study \ treatment \ groups \ in \ the \ different \ sensitivity \ analyses \ (S1-S8), \ based \ on \ MIDEX$ 

| Sensitivity analysis of MIDEX: dexmedetomidine vs. midazolam  | Difference in mean costs, € | Difference in median costs, € |
|---|-----------------------------|-------------------------------|
| S1. Standard sedative set to cost zero  | - 2,467                     | - 3,466                       |
| S2. Dexmedetomidine cost increased to €22 per 200 mcg (€0.11 per 1 mcg)   | - 2,476                     | - 3,557                       |
| S3. Cost of a NIV day (24 hr) decreased to € 1,390  | - 2,519                     | - 3,557                       |
| S4. Cost of a NIV day (24 hr) increased to €1,850   | - 2,541                     | - 3,573                       |
| S5. Patients with observed data available from all three time periods (without any censoring or imputations)                    | - 3,900                     | - 3,675                       |
| S6. MIDEX patients of those 18 study centers, from which routine ICU costs were available. N (dexmedetomidine):63; propofol: 58 | - 907                       | - 3,351                       |
| S7a. TISS-based total ICU costs, at unit cost €40 per TISS point  | - 2,444                     | - 2,364                       |
| S7b. TISS-based total ICU costs, at unit cost of €50 per TISS point   | -3,105                      | -2,972                        |
| S8a. Only declining, direct variable daily costs included, assuming they represent 25% of the total ICU costs                   | -483                        | -704                          |
| S8b. Only the periodically declining, direct variable costs considered, assuming they represent 50% of the total ICU costs      | -1,167                      | -1,772                        |

NIV= non-invasive ventilation, TISS= Therapeutic Intervention Scoring System

Table~S8.~Total~ICU~cost~differences~between~the~study~treatment~groups~in~the~different~sensitivity~analyses~(S1-S8),~based~on~PRODEX

| Sensitivity analysis of PRODEX: dexmedetomidine vs. propofol   | Difference in mean costs, € | Difference in median costs, € |
|--|-----------------------------|-------------------------------|
| S1. Standard sedative set to cost zero   | - 606                       | - 1,265                       |
| S2. Dexmedetomidine cost €22 per 200 mcg (€0.11 per 1 mcg)   | - 668                       | - 1,234                       |
| S3. Cost of a NIV day decreased to €1,390 per 24 hours   | - 1,022                     | - 1,266                       |
| S4. Cost of a NIV day increased to €1,850 per 24 hours   | - 1,614                     | - 2,552                       |
| S5. Patients with observed data available from all three time periods (without any censoring or imputations)                       | - 2,486                     | - 1,182                       |
| S6. PRODEX patients of those 18 study centers, from which routine ICU costs were available. N (dexmedetomidine):108; propofol: 110 | - 2,571                     | - 2,207                       |
| S7a. TISS-based total ICU costs, at unit cost of €40 per TISS point  | - 517                       | - 781                         |
| S7b. TISS-based total ICU costs, at unit cost of €50 per TISS point  | -700                        | -1,089                        |
| S8a. Only the declining, direct variable daily costs included, assuming they represent 25% of the total ICU costs                  | -25                         | -660                          |
| S8b. Only declining, direct variable daily costs included, assuming they represent 50% of the total ICU costs                      | -266                        | -1,550                        |

NIV= non-invasive ventilation, TISS= Therapeutic Intervention Scoring System