# Supplementary Material

## Disrupted sleep patterns and atypical electroencephalograms in children admitted to the pediatric intensive care unit: an observational cohort study

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## Supplemental Methods

### A. Reference ranges

Literature sources for references range per parameter are specified across age categories in Table S1 on the next page. In children younger than one month, total sleep time (TST) and sleep efficiency reported by Daftary et al. were adjusted for the difference in measurement duration (i.e. TST divided by 0.6).(1) Sleep stage distributions for this age category were derived from the distribution of REM and NREM sleep of the youngest age category reported by Duenas-Meza et al.(2) For ages one to six months, TST reference ranges were obtained from Kato et al. who used the Rechtschaffen & Kales classification.(3) For ages six months to one year, TST ranges were interpolated between the 20 to 27 weeks group of Kato et al. and the one to two-year-old group of Scholle et al.(3, 4) For patients aged five years and older, 24-hour TST was compared to reference ranges for nighttime sleep only, assuming no habitual daytime sleep in this age category.

### B. Software and packages

We used python (version 3.11) with packages *os*, *pyedflib* (0.1.22), *datetime, pandas* (1.3.4), *math*, *numpy* (1.21.3), *matplotlib* (3.5.1) and a script based on *yasa* (0.6.2) for extraction and plotting of the hypnogram from the BrainRT export, and R (version 4.3.0), with packages *dplyr* (2.3.2), *ggplot2* (3.444.222), *ggsci* (3.0.0), *hms* (1.1.3), *openxlsx* (4.2.5.2), *readxl* (1.4.2) for the analyses.(5-13)

## Supplemental Tables

**Table S1. Reference ranges per parameter and age category**

| Age category | Source | Comment |
|---|---|---|
| *Total sleep time (TST)* | | |
| < 1 month | Daftary et al. | Corrected for difference in measurement duration |
| 1 – 6 months | Kato et al. | Rechtshaffen & Kales classification guidelines |
| 6 – 12 months | Kato et al., Scholle et al. | Interpolated between ages 20 – 27 weeks (Kato et al.) and 2 years (Scholle et al.) |
| ≥ 1 year | Scholle et al. | |
| *Sleep efficiency (SE)* | | |
| < 1 month | Daftary et al. | Corrected for difference in measurement duration |
| 1 – 12 months | Duenas-Mezas et al. | |
| ≥ 1 year | Scholle et al. | |
| *Sleep stage distributions (% REM, NREM, N1, N2, N3)* | | |
| < 1 month | Duenas-Mezas et al. | Derived from REM-NREM distributions of het youngest age category |
| 1 – 12 months | Duenas-Mezas et al. | Only REM-NREM distributions available |
| ≥ 1 year | Scholle et al. | |
| *Awakening index (AI)* | | |
| < 1 month | Daftary et al. | |
| 1 – 12 months | Unavailable | |
| ≥ 1 year | Scholle et al. | |
| *Sleep period duration (SPD)* | | |
| < 1 month | Unavailable | |
| 1 – 12 months | Unavailable | |
| ≥ 1 year | Scholle et al. | |

REM = rapid-eye movement; NREM = non-rapid eye movement; N1 – N3 = non-rapid eye movement stage 1 – 3

**Table S2. All sleep parameters of critically ill children compared to literature reference ranges**

| Participant | Age | 24h TST (min) | Nighttime TST (min) | Nighttime sleep (%) | REM (%TST) | NREM (%TST) | N1 (%TST) | N2 (%TST) | N3 (%TST) | SE (% SPT) | SPD (min) | AI (n/h) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0-1 months | *918* | 378 | *49.0* | 44.8 | 55.2 | 0.0 | 0.0 | 0.0 | 63.1 | *5.5* | 10.84 |
| 2 | 0-1 months | *984.5* | 413.5 | *49.5* | 17.9 | 82.1 | 0.0 | 0.0 | 0.0 | 69.0 | *263.0* | 0.49 |
| 3 | 0-1 months | *1230.5* | 545.5 | *49.4* | 37.5 | 62.5 | 0.0 | 0.0 | 0.0 | 91.0 | *14.4* | 4.18 |
| 4 | 0-1 months | *1018* | 534 | *50.9* | 0.7 | 99.3 | 0.0 | 0.0 | 0.0 | 89.9 | *23.9* | 2.51 |
| 5 | 0-1 months | *771.5* | 435 | *57.0* | 29.4 | 70.6 | 0.0 | 0.0 | 0.0 | 72.6 | *13.6* | 4.40 |
| 6 | 0-1 months | *700* | 393 | *51.1* | 30.8 | 69.2 | 0.0 | 0.0 | 0.0 | 65.6 | *6.8* | 8.81 |
| 7 | 1-2 months | *850* | 405 | *54.5* | 24.0 | 76.0 | 0.0 | 0.0 | 0.0 | 71.0 | *9.9* | *6.14* |
| 8 | 1-2 months | *474* | 357.5 | *65.8* | 36.1 | 63.9 | 0.0 | 0.0 | 0.0 | 60.1 | *3.8* | *15.70* |
| 9 | 1-2 months | *925.5* | 437 | *48.5* | 25.3 | 74.7 | 0.0 | 0.0 | 0.0 | 72.9 | *10.4* | *5.80* |
| 10 | 2-6 months | *599* | 260.5 | *50.6* | 18.2 | 81.8 | *0.0* | *0.0* | *0.0* | 43.5 | *9.1* | *6.68* |
| 11 | 2-6 months | *1176.5* | 543.5 | *50.6* | 8.5 | 91.5 | *0.0* | *0.0* | *0.0* | 91.0 | *28.2* | *2.14* |
| 12 | 2-6 months | *744.5* | 433 | *55.7* | 10.3 | 89.7 | *0.0* | *0.0* | *0.0* | 85.6 | *25.5* | *2.36* |
| 13 | 2-6 months | *829* | 385.5 | *49.4* | 8.7 | 91.3 | *0.0* | *0.0* | *0.0* | 64.3 | *10.5* | *5.82* |
| 14 | 2-6 months | *561* | 223.5 | *44.1* | 5.4 | 0.0 | *11.4* | *4.0* | *79.2* | 38.5 | *14.5* | *4.13* |
| 15 | 2-6 months | *1090.5* | 517 | *55.2* | 13.7 | 39.1 | *0.0* | *13.4* | *33.8* | 86.2 | *25.9* | *2.49* |
| 16 | 2-6 months | *239* | 83 | *29.2* | 0.0 | 100.0 | *0.0* | *0.0* | *0.0* | 14.1 | *4.9* | *12.29* |
| 17 | 6-12 months | *636* | 366.5 | *55.5* | 0.0 | 2.9 | *38.6* | *47.1* | *11.5* | 62.3 | *12.5* | *4.79* |
| 18 | 1-3 years | *1348* | 578.5 | *51.3* | 4.5 | 0.0 | 14.6 | 52.5 | 28.4 | 96.5 | 20.5 | 2.93 |
| 19 | 1-3 years | *842* | 459.5 | *56.5* | 11.3 | 0.0 | 16.2 | 53.2 | 19.3 | 77.4 | 15.3 | 4.20 |
| 20 | 5-9 years | 785.5 | 390 | 50.6 | 8.5 | 0.0 | 26.7 | 57.7 | 7.2 | 67.5 | 16.0 | 3.74 |
| 21 | 9-13 years | 592.5 | 342.5 | 59.0 | 0.0 | 0.0 | 42.2 | 54.2 | 3.6 | 57.1 | 18.6 | 3.37 |
| 22 | 13-18 years | 1094 | 552 | 50.3 | 0.0 | 73.9 | 0.0 | 21.8 | 4.3 | 92.1 | 90.1 | 0.72 |
| 23 | 13-18 years | 535.5 | 261 | 44.5 | 3.8 | 0.0 | 11.1 | 54.4 | 30.7 | 43.5 | 19.6 | 3.11 |
| 24 | 13-18 years | 617 | 323 | 56.4 | 0.0 | 0.0 | 46.1 | 50.6 | 3.3 | 53.9 | 9.8 | 6.10 |
| 25 | 13-18 years | 1167.5 | 575 | 51.8 | 0.0 | 100.0 | 0.0 | 0.0 | 0.0 | 95.9 | 57.6 | 1.04 |

All sleep characteristics (columns) of individual patients (rows, in order of increasing age) and the corresponding values which are either in range (black), below range (blue) or above range (red) with regard to reference ranges of healthy controls. Grey values represent values for which no valid reference range was found. All values except for 24h TST are calculated for nighttime only. The nighttime sleep proportion was corrected for the daytime and nighttime measurement duration. Up two months of age, we assumed differentiation of different NREM stages is not yet present in healthy children. AI = awakening index; NREM = non-rapid-eye-movement sleep (N); REM = rapid-eye-movement sleep; SE = Sleep efficiency; SPD = mean sleep period duration; SPT = sleep period time; TST = total sleep time

**Table S3. All mean sleep parameters in the SDB group compared to literature reference ranges**

| Age group | TST (min) | REM (%TST) | NREM (%TST) | N1 (%TST) | N2 (%TST) | N3 (%TST) | SE (% SPT) | SPD (min) | AI (n/h) |
|---|---|---|---|---|---|---|---|---|---|
| 0-2 months | 498.7 | 34.4 | 59.5 | *0.5* | *0.0* | *5.6* | 71.7 | *8.56* | 7.95 |
| 2-6 months | 524.6 | 32.0 | *20.1* | *5.4* | *14.0* | *28.5* | 81.7 | *22.89* | *3.29* |
| 6-12 months | 535.0 | 28.7 | *0.0* | *11.5* | *27.5* | *32.2* | 85.5 | *31.40* | *2.12* |
| 1-3 years | 493.3 | 22.6 | 0.0 | 15.1 | 28.9 | 33.4 | 83.9 | 42.04 | 1.88 |
| 3-5 years | 540.5 | 21.6 | 0.0 | 9.5 | 27.3 | 41.6 | 89.6 | 56.37 | 1.55 |
| 5-9 years | 507.0 | 21.5 | 0.0 | 9.0 | 35.6 | 33.9 | 86.0 | 61.70 | 1.69 |
| 9-13 years | 408.8 | 16.2 | 0.0 | 14.9 | 32.7 | 36.3 | 77.1 | 34.00 | 3.48 |
| 13-18 years | 412.7 | 17.9 | 0.0 | 13.2 | 38.0 | 30.8 | 82.2 | 28.41 | 2.97 |

All sleep characteristics (columns) per age category (rows, in order of increasing age) and the corresponding values which are either in range (black), below range (blue) or above range (red) with regard to reference ranges of healthy controls. Grey values represent values for which no valid reference range was found. AI = awakening index; NREM = non-rapid-eye-movement sleep (N); REM = rapid-eye-movement sleep; SDB = sleep disordered breathing; SE = Sleep efficiency; SPD = average sleep period duration; SPT = sleep period time; TST = total sleep time

## Supplemental Figures

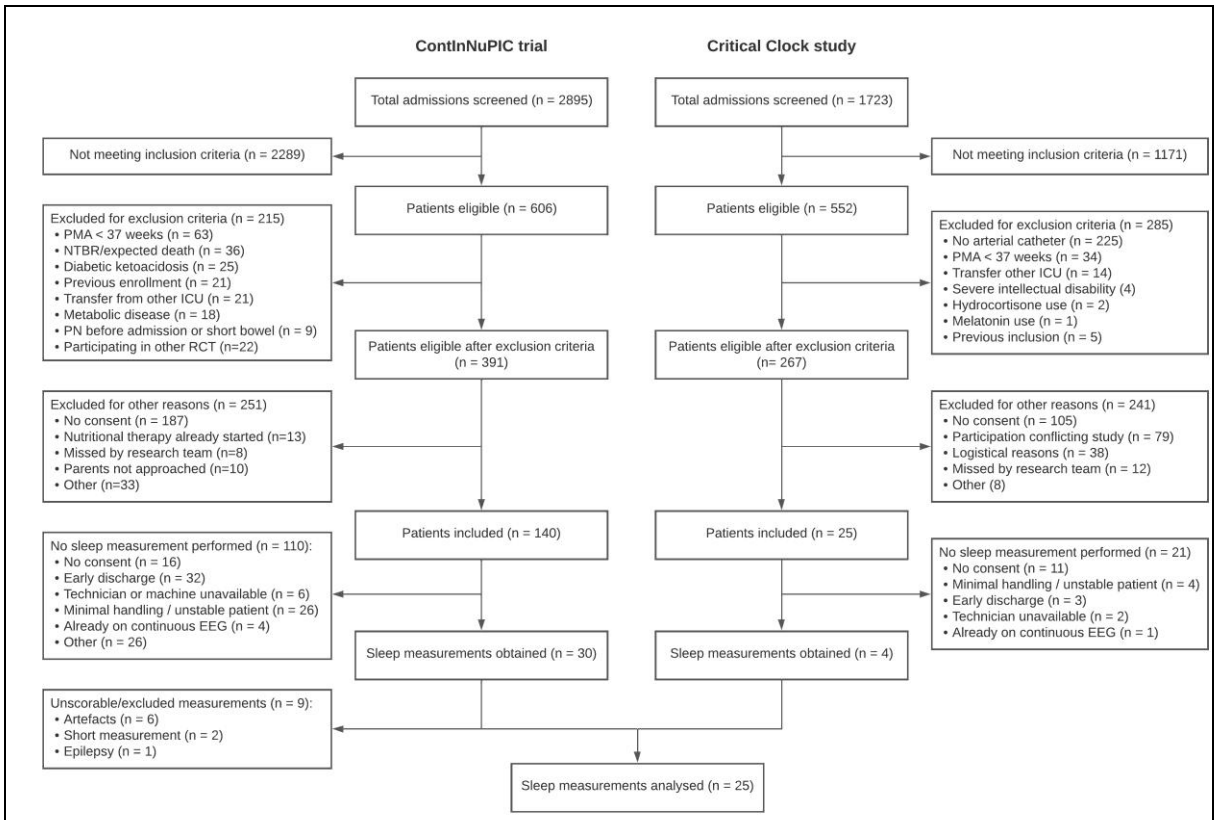
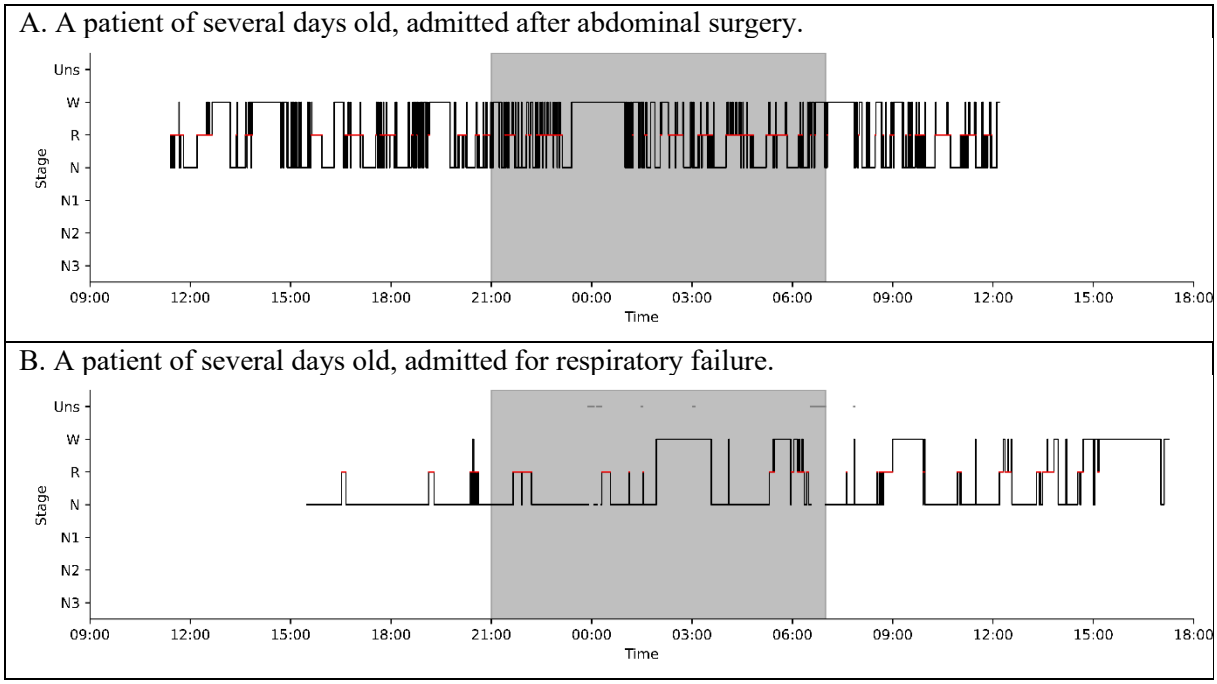
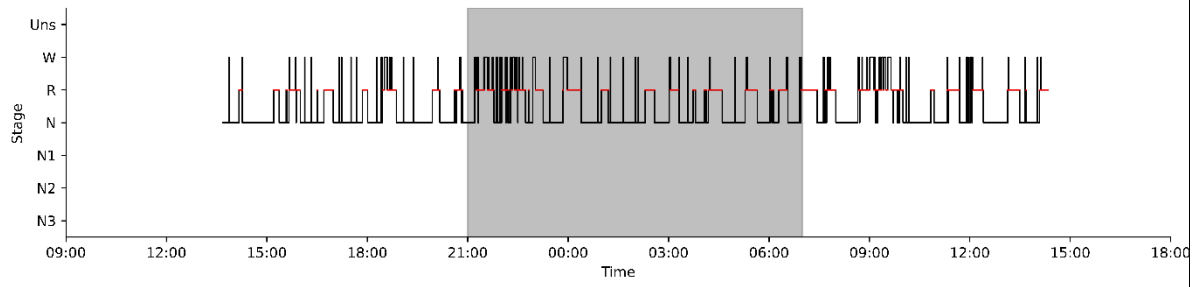


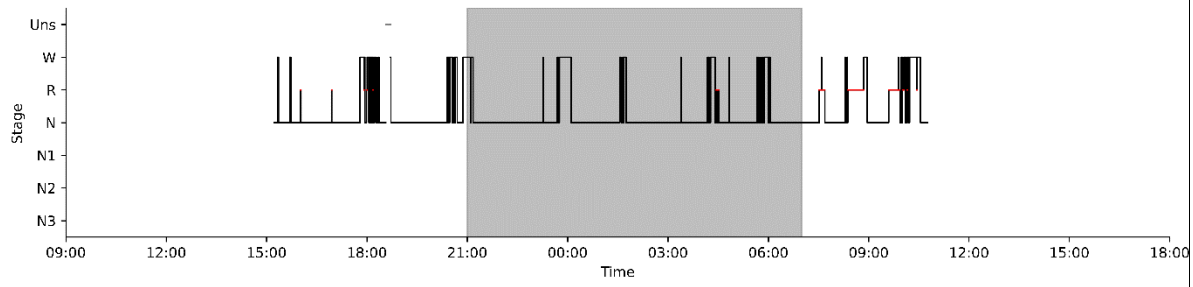

**Figure S1. Flow chart of patient inclusion and exclusion.** In this study, patients from two trials were included, the ContInNuPIC trial and Critical Clock study, with each their respective in- and exclusion crtieria as depicted in the figure. PMA: post-menstrual age; NTBR: do not resuscitate; ICU: intensive care unit.



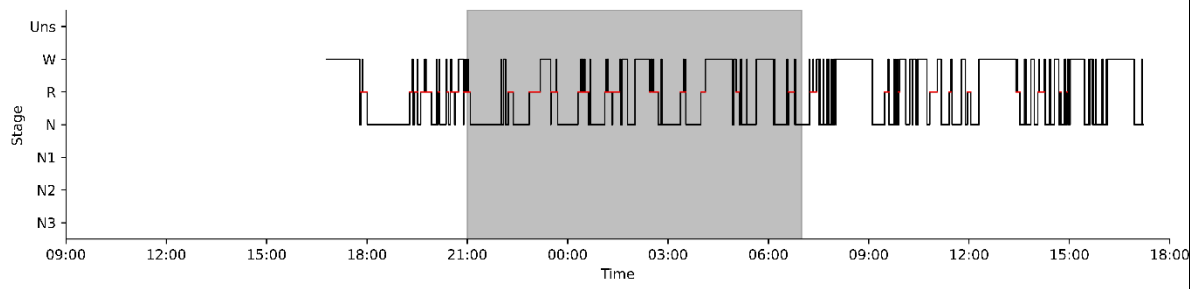
C. A patient of one week old, admitted for respiratory failure and asphyxia.



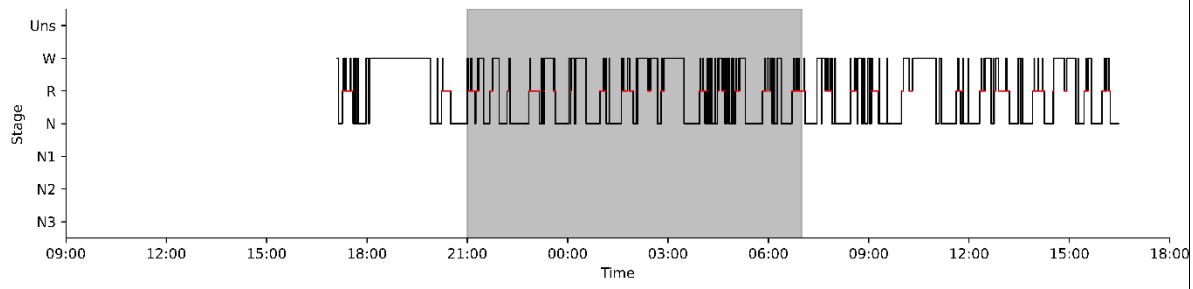

D. A patient of one week old, admitted for a metabolic condition.



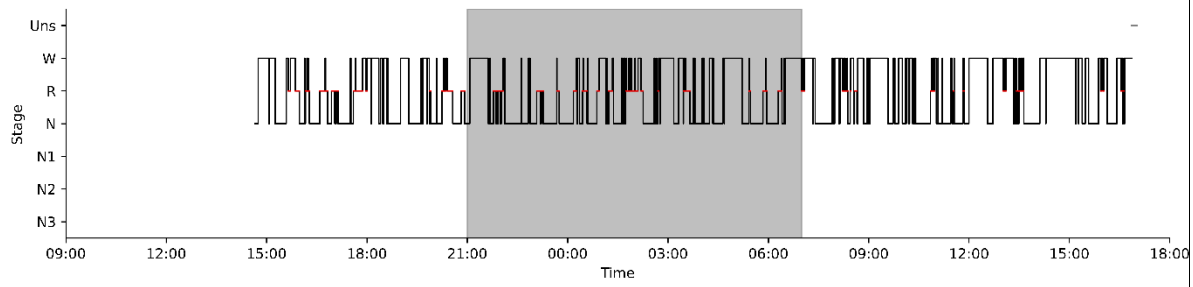

E. A patient of one week old, admitted for congenital heart disease.



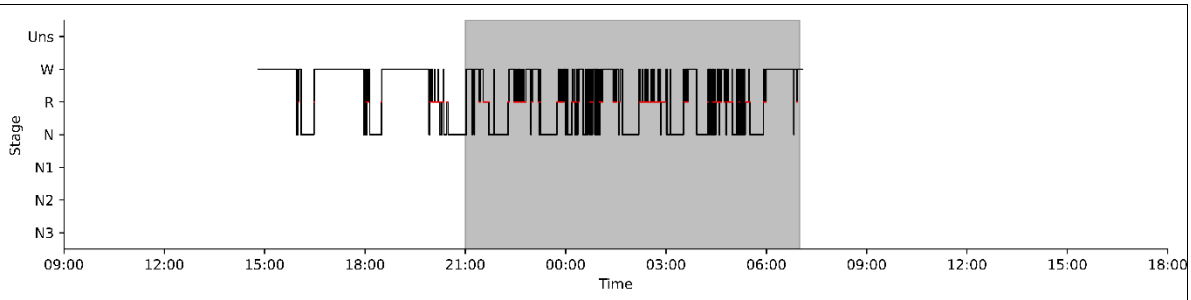

F. A patient of several weeks old, admitted for congenital heart disease.



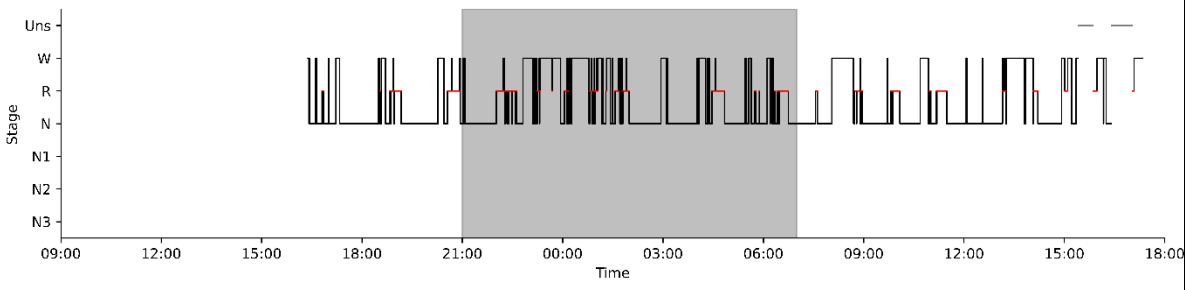

G. A patient of one month old, admitted for a neuromuscular disease.



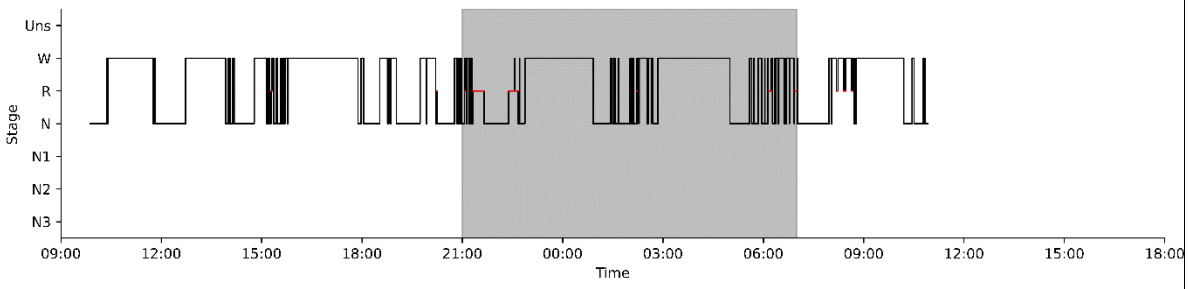

H. A patient of one month old, admitted for respiratory failure



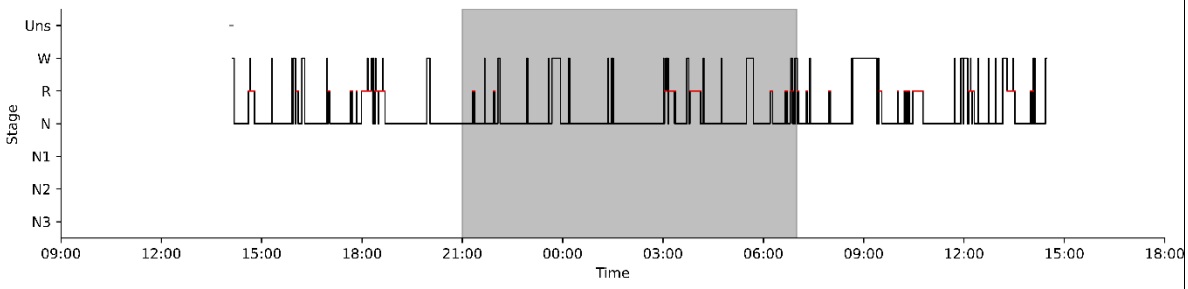

I. A patient of one month old, admitted for respiratory failure



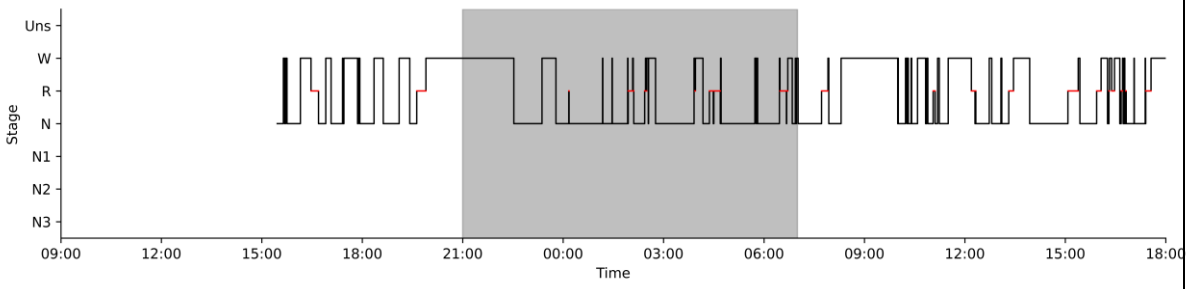

J. A patient of 2 months old, admitted for a cardiac disease.



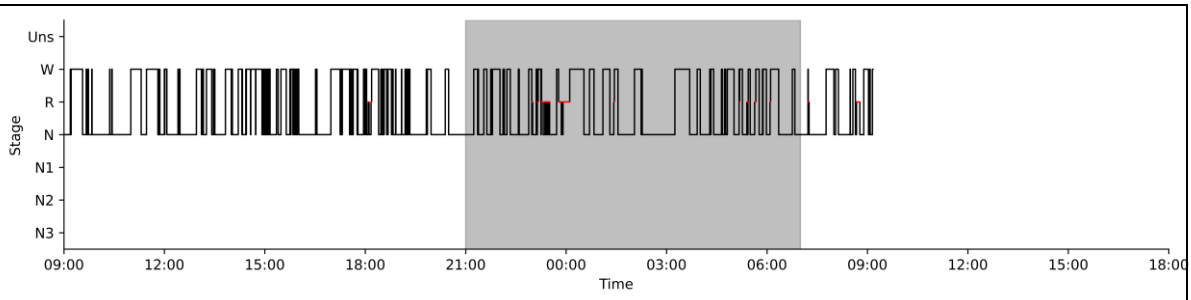

K. A patient of 2 months old, admitted with a severe infection.



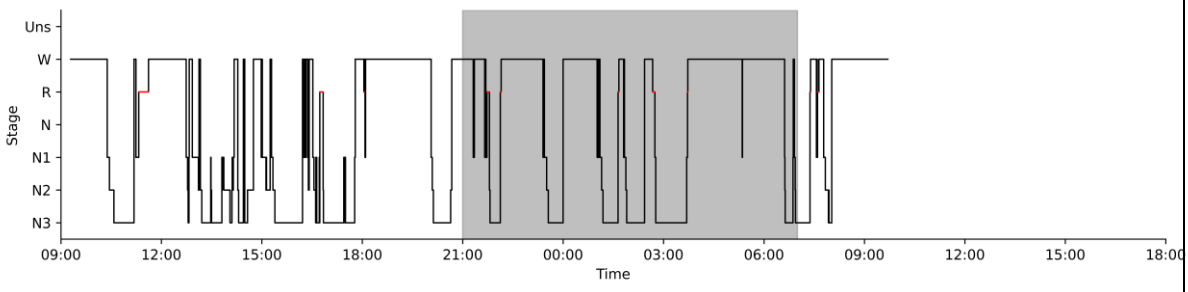

L. A patient of 2 months old, admitted with respiratory failure and a neurological condition.



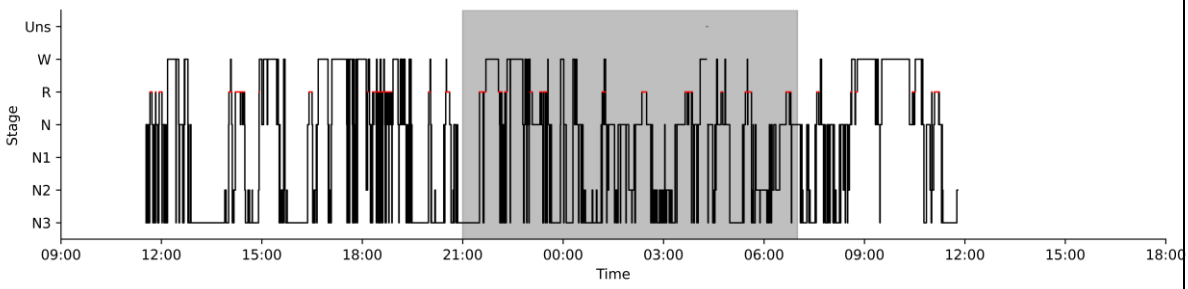

M. A patient of several months old, admitted after cardiac surgery.



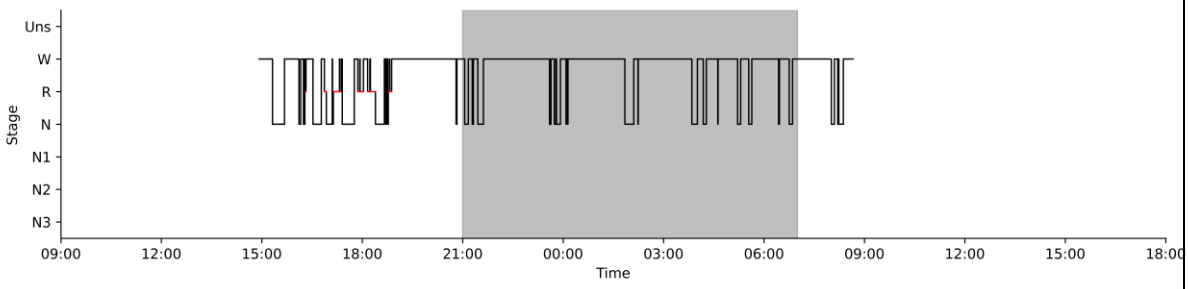

N. A patient of several months old, admitted after cardiac surgery.



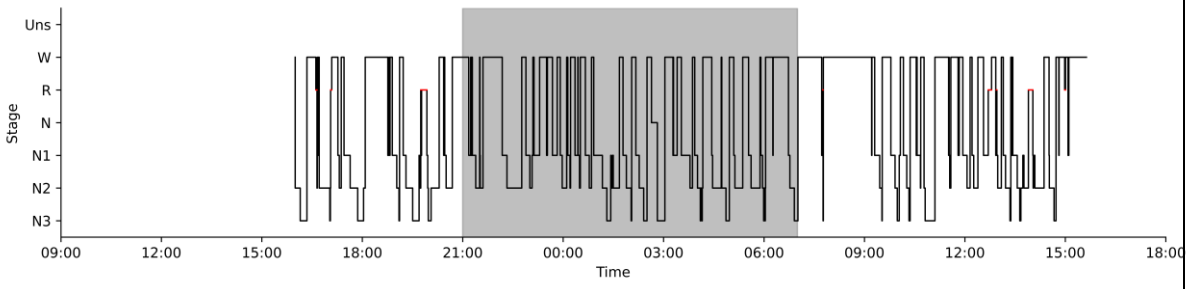

O. A patient of several months old, admitted for congenital heart disease.



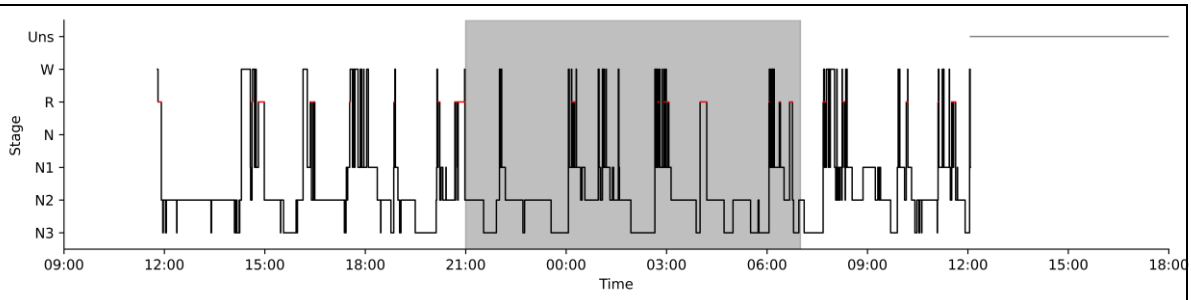

P. A patient of several months old, admitted after cardiac surgery.



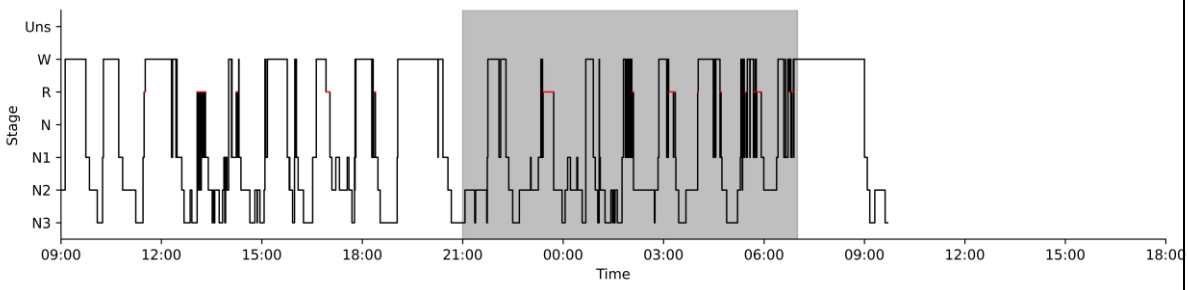

Q. A patient of six to twelve months old, admitted after cardiac surgery.



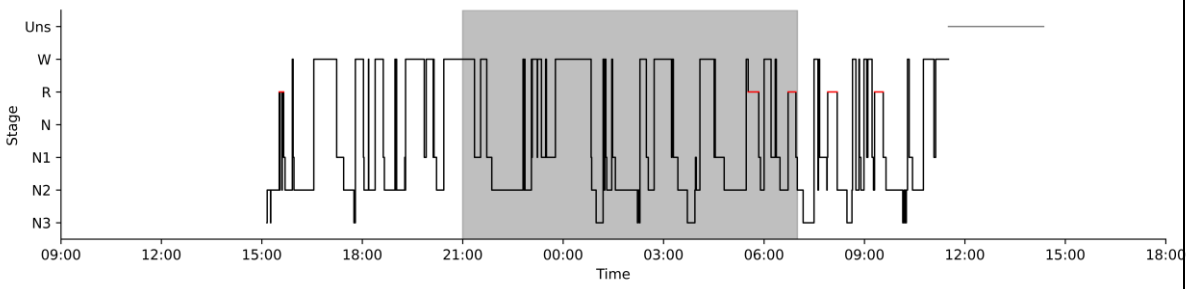

R. A patient of one year old, admitted for respiratory failure.



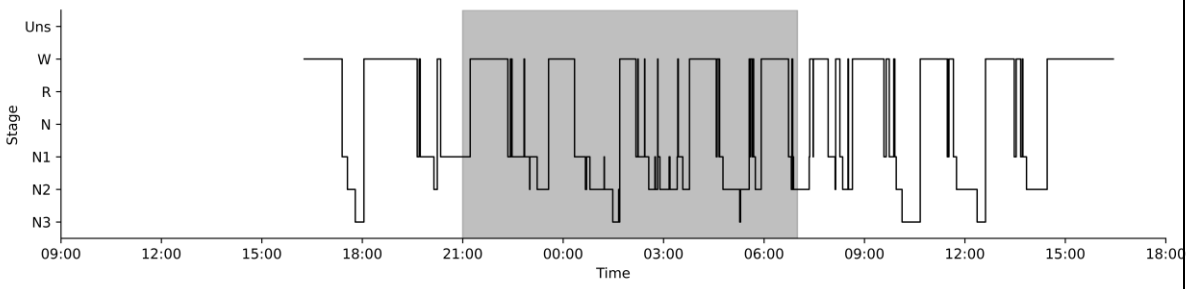

S. A patient of one year old, admitted for respiratory failure.



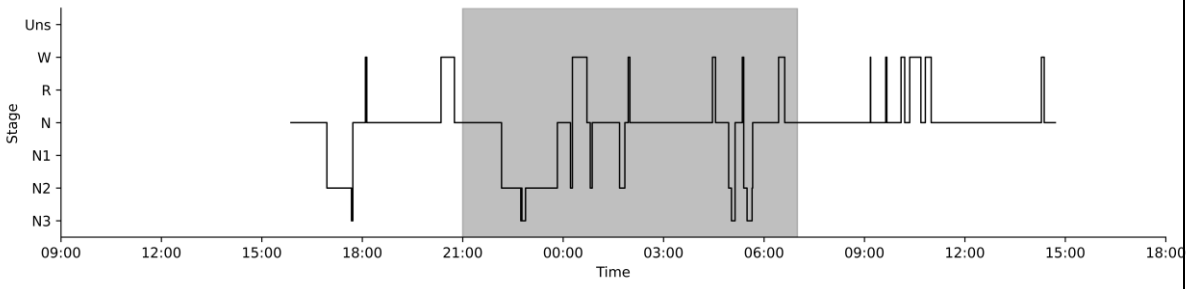

T. A patient of 5-9 years old, suffering from a malignancy.



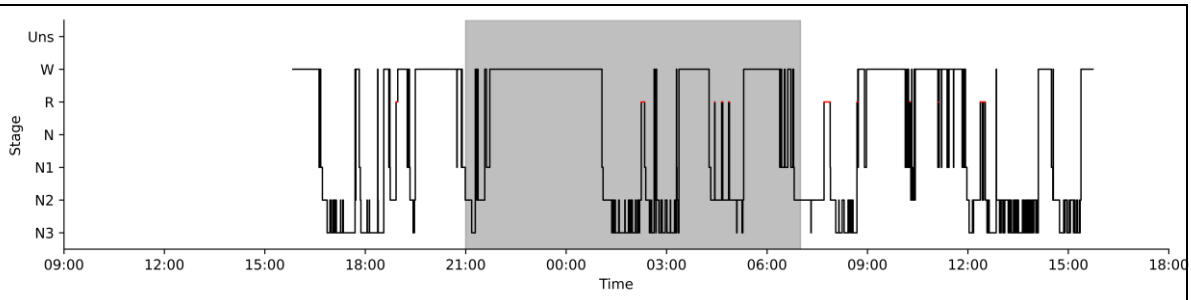

U. A patient of 9-13 years old, suffering from a severe infection.



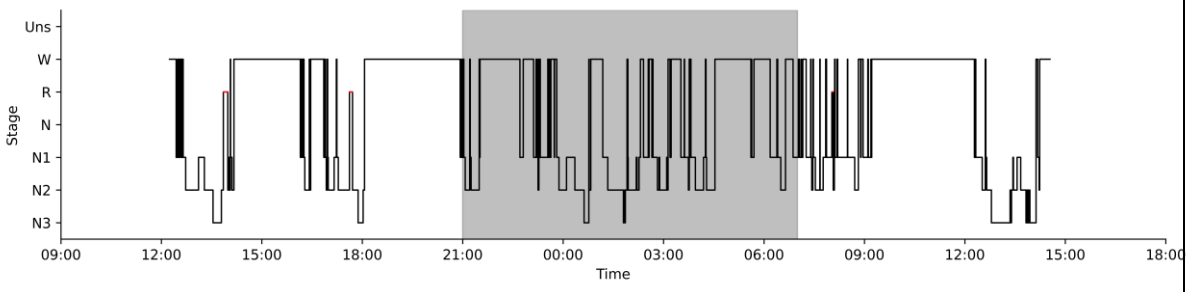

V. A patient of 13-18 years old, suffering from a neurological condition.




W. A patient of 13-18 years old with a severe infection, after resuscitation.




X. A 13-18 year old, suffering from a neuromuscular disease.




Y. A 13-18 year old, suffering from a severe infection

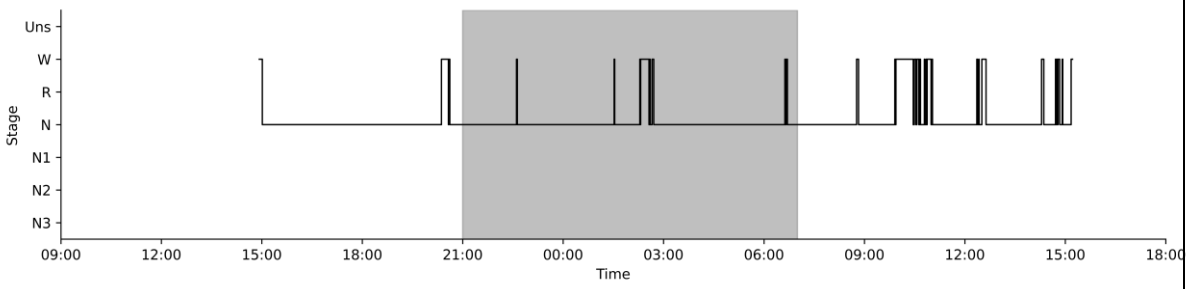



**Figure S1. Hypnograms of all critically ill patients.** Hypnograms of all included critically ill patients are shown. The grey section reflects the nighttime as used in calculating sleep characteristics, i.e. 21:00 to 7:00. Limited clinical information is provided to ensure patients' privacy. N, N1, N2, N3: non-rapid-eye-movement sleep, unspecified and stages 1, 2 and 3; R: rapid-eye-movement sleep; Uns: unscored (e.g., due to artifacts); W: wake

## References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