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# Neonatal heart rate variability: a contemporary scoping review of analysis methods and clinical applications

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## ABSTRACT

**Background** Neonatal heart rate variability (HRV) is widely used as a research tool. However, HRV calculation methods are highly variable making it difficult for comparisons between studies.

**Objectives** To describe the different types of investigations where neonatal HRV was used, study characteristics, and types of analyses performed.

**Eligibility criteria** Human neonates ≤1 month of corrected age.

**Sources of evidence** A protocol and search strategy of the literature was developed in collaboration with the McGill University Health Center's librarians and articles were obtained from searches in the Biosis, Cochrane, Embase, Medline and Web of Science databases published between 1 January 2000 and 1 July 2020.

**Charting methods** A single reviewer screened for eligibility and data were extracted from the included articles. Information collected included the study characteristics and population, type of HRV analysis used (time domain, frequency domain, non-linear, heart rate characteristics (HRC) parameters) and clinical applications (physiological and pathological conditions, responses to various stimuli and outcome prediction).

**Results** Of the 286 articles included, 171 (60%) were small single centre studies (sample size <50) performed on term infants (n=136). There were 138 different types of investigations reported: physiological investigations (n=162), responses to various stimuli (n=136), pathological conditions (n=109) and outcome predictor (n=30). Frequency domain analyses were used in 210 articles (73%), followed by time domain (n=139), non-linear methods (n=74) or HRC analyses (n=25). Additionally, over 60 different measures of HRV were reported; in the frequency domain analyses alone there were 29 different ranges used for the low frequency band and 46 for the high frequency band.

**Conclusions** Neonatal HRV has been used in diverse types of investigations with significant lack of consistency in analysis methods applied. Specific guidelines for HRV analyses in neonates are needed to allow for comparisons between studies.

## Strengths and limitations of this study

- ► This is a comprehensive scoping review describing all study characteristics and population details, heart rate variability (HRV) analysis methods and clinical applications of the neonatal HRV literature.
- ► The literature search strategy was developed in consultation with and performed by medical librarians.
- ► This review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Review guidelines for reporting items.
- ► This review does not include articles published prior to the year 2000.
- ► A single reviewer performed both the screening (SL) and data collection (SL or JL), though all questions or conflicts were discussed among all reviewers.

## INTRODUCTION

Heart rate variability (HRV) refers to the fluctuation of beat-to-beat intervals over time and is the result of the continuous counterbalancing input from the parasympathetic and sympathetic branches of the autonomic nervous system.[1] In neonates, a diversity of studies using HRV have been published during the last 20 years. HRV analyses were used in investigations of brain injuries,[2–5] response to pain,[6 7] effects of prenatal drug exposure[8 9] and to assess physiological maturation of preterm infants.[10–14] More recently the gradual integration of heart rate characteristics (HRC) monitoring (HeRO, Medical Predictive Science Corporation) into the neonatal intensive care unit (NICU) setting has also increased the use of neonatal HRV in clinical practice.

HRV indices can be processed in many different ways following three analysis approaches: time domain, frequency domain or non-linear methods.[1] Time domain methods use summary statistics of the normal-to-normal beat (NN) interval (or R-wave-to-R-wave (RR) intervals), such as the SD of NN intervals (SDNN). Frequency domain methods use spectral analyses to break down the RR interval time series into a distribution of the power as a function of frequency, which is then broken down into spectral ranges of interest. The third and more advanced type of HRV analysis is the non-linear method, which includes various measures of chaos, unpredictability and self-similarity, such as sample entropy (SampEn) and the detrended fluctuation analysis (DFA).[1]

In 1996, the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology published specific guidelines for processing of HRV indices in adults that became the gold standard.[15] Nevertheless, the majority of research projects did not strictly adhere to these standards.[16] Such standards are important for consistency in the literature so that results of studies may be compared and combined accurately. In neonates, there are no specific guidelines for processing of HRV indices. Thus, in order to understand the full extent of neonatal HRV analysis and its various applications, a scoping review was conducted. The aim was to provide an overview of the current studies and population characteristics, analysis methods used, and clinical research applications in which HRV has been used in the neonatal population.

## METHODS

### Protocol

A comprehensive protocol and search strategy of the literature was developed in collaboration with the McGill University Health Center's librarians. The study is reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for Scoping Reviews.

### Eligibility criteria

All articles that analysed human neonatal HRV were included. Articles were limited to the last 20 years (ie, from the year 2000 onwards) to review more contemporary research in neonatal HRV as methodologies and clinical care have evolved significantly making difficult to ascertain validity of studies performed and published more than 20 years ago. Articles in which human neonates of any gestational age (GA) and ≤1 month corrected age had HRV measured in at least five neonates were eligible. Articles performed in fetuses, animals, infants and children above 1 month corrected age, or adults were excluded. Other types of articles that analysed or discussed human neonatal HRV (reviews, case reports, commentaries, methodological papers, etc) were excluded from data collection. A tally of these different types of articles was maintained in order to understand the full degree to which neonatal HRV has been investigated or used.

### Information sources and search

The search was performed in Biosis, Cochrane, Embase, Medline and Web of Science databases and included articles of HRV in neonates in all languages, published between 1 January 2000 and 1 July 2020. The search was performed twice: first in October 2017, then updated again in July 2020. Details of the search strategy used for all databases is provided as online supplemental file 1.

### Selection of articles

After duplicate removal, all titles and abstracts were screened for inclusion by one reviewer (SL) based on the eligibility criteria. Full-text articles were then obtained and reviewed by two reviewers (SL or JL) to confirm eligibility and extract data.

### Data charting process

Two reviewers (SL or JL) extracted the data from the included articles using a predefined form which included the following sections and listed items below.

#### Study characteristics and population

##### *Study characteristics*

(a) Name of the journal, (b) region where the study was performed, (c) country where the study was performed, (d) type of study design and (e) single or multicentre.

##### *Population details*

(a) Sample size, (b) GA and birth weight (BW) categories based on the averages (or medians) of infants enrolled within the study (ie, not based on the study's inclusion criteria) and using the following definitions: term (≥37 weeks GA), preterm (<37 weeks GA), late preterm (LPT; 34–36$^6$ weeks GA), moderate preterm (MPT; 32–34$^6$ weeks GA), very preterm (28–31$^6$ weeks GA), extremely preterm (<28 weeks GA), normal BW (≥2500 g), low BW (<2500 g), very low BW (<1500 g) and extremely low BW (<1000 g).

#### HRV analysis methods

##### *Time domain parameters evaluated*

(a) SDNN: SD of normal-to-normal (NN) or R-wave-to-R-wave intervals, (b) CVNN: coefficient of variation of NN intervals, (c) SDANN: SD of the averages of NN intervals in all 5 min segments of the entire recording, (d) SDNNi: mean of the SDs of all NN intervals for all 5 min segments of the entire recording, (e) RMSSD: root mean square of the differences between adjacent NN intervals, (f) SDSD: SD of differences between adjacent NN intervals, (g) NN50/pNN50: pairs of adjacent NN intervals differing by more than 50 ms (count or per cent), (h) NNxx/pNNxx: pairs of adjacent NN intervals differing by a time other than 50 ms (count or per cent), (i) triangular index: total number of all NN intervals divided by the height of the histogram of all NN intervals, (j) TINN: baseline width of the minimum square difference triangular interpolation of the highest peak of the histogram of all NN intervals measured, (k) histogram analyses: includes measures of skew, kurtosis and so on and (l) other: any other time domain parameter not listed previously.[15]

##### *Frequency domain*

(a) Total power (TP), (b) ultra low frequency (ULF), (c) very low frequency (VLF), (d) low frequency (LF), (e) high frequency (HF), (f) LF/HF ratio and (g) other: any other frequency domain parameter not listed previously. Frequency ranges reported for each parameter were also collected.[15]

### *Non-linear*

(a) Poincaré plot analyses (SD1 and SD2), (b) alpha (α): exponent of the 1/f pattern (power spectral density), (c) DFA α1 (short-term exponent), (d) DFA α2 (long-term exponent), (e) approximate entropy (ApEn), (f) sample entropy (SampEn) and (g) other: any other non-linear parameter not listed previously.[17]

### *Heart rate characteristics*

Classified as its own category given its specific combination of HRV parameters, and the gradual integration of Heart Rate Observation System (HeRO) monitors (Medical Predictive Science Corporation, USA) providing these values into the NICU setting.

## HRV application: studies were classified into four major groups

### *Physiological conditions*

HRV measured under normal, healthy, physiological conditions. Includes: (a) normative: study provides data on normal or healthy infants either with the purpose of providing normative data or as controls, (b) sleep state: includes quiet sleep, active sleep, quiet awake and active awake statuses, (c) longitudinal: study provides longitudinal data (repeated measures, maturation, etc), (d) age or weight: study examines the effect of age or weight in a cross-sectional fashion, (e) feeding, (f) position: supine or prone, (g) tilt: study examines the effect of different degrees of bed inclination, (h) sex: male or female and (i) other: any other physiological application not listed previously.

### *Pathological conditions*

HRV measured in infants with certain conditions or diseases, including: (a) sepsis, (b) necrotising enterocolitis, (c) infection, (d) respiratory distress syndrome, (e) apnoea of prematurity (AOP), (f) extubation failure: peri-extubation measurements in relation to extubation outcome, (g) hypoxic ischaemic encephalopathy (HIE), (h) other brain injuries (eg, intraventricular haemorrhage, periventricular leukomalacia, etc), (i) seizures, (j) patent ductus arteriosus (PDA), (k) congenital heart disease or defects (CHD) (l) in-hospital mortality and (m) other (ie, any other condition or disease not listed previously).

### *Response to certain exposures, stimuli or external factors*

Includes: (a) pain, (b) medication, (c) sensory stimuli (light, sound or touch), (d) non-nutritive sucking (pacifiers), (e) kangaroo care (skin-to-skin), (f) sucrose, (g) procedures, (h) maternal factors and (i) other stimuli or responses not listed previously. Details regarding the types of medications, procedures and maternal factors were also collected.

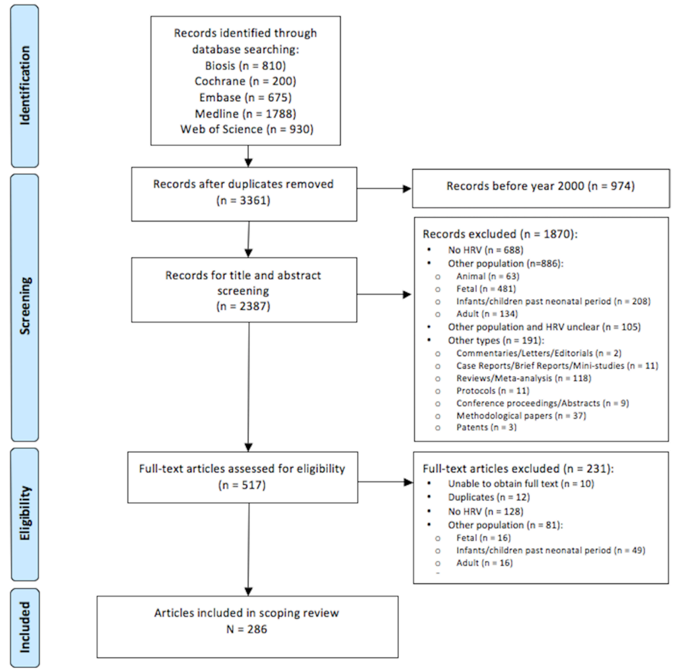


**Figure 1** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for record screening and inclusion. HRV, heart rate variability.

### *Outcome prediction*

HRV measured as predictor of outcomes during hospitalisation or beyond. Includes: (a) days on mechanical ventilation, (b) length of stay or postmenstrual age at discharge, (c) repeat hospitalisations, (d) neurodevelopmental impairment, (e) cerebral palsy, (f) behavioural or social assessments and (g) other: any other outcome not listed previously.

## Synthesis of results

Data were summarised descriptively using counts (n) and percentages (%), and presented as pie charts, bar graphs or tables. Years of publication were presented in 5-year bins to observe the overall trend of number of publications over time and minimise year-to-year fluctuations. References for the articles of population characteristics, HRV analysis methods, and HRV application groups are provided.

## Patient and public involvement

No patients were involved.

# RESULTS

## Selection of articles

Of the 3361 records identified, 286 articles were eligible and included for data collection; a PRISMA flow diagram of the screening process is provided as figure 1. A complete table (Microsoft Excel file) with each of the articles' data collection items is provided in the public repository Figshare, along with an EndNote file (X7, Clarivate Analytics, Philadelphia, Pennsylvania, USA)

Table 1 Top 10 journals publishing articles concerning neonatal heart rate variability

| Journal name | n (%) |
|---|---|
| *Early Human Development* | 26 (9.1) |
| *Pediatric Research* | 24 (8.4) |
| *Biology of the Neonate/Neonatology* | 11 (3.8) |
| *Acta Paediatrica* | 10 (3.5) |
| *Institute of Electrical and Electronics Engineers (IEEE)* | 10 (3.5) |
| *Journal of Perinatology* | 10 (3.5) |
| *Developmental Psychobiology* | 9 (3.1) |
| *Pediatrics* | 8 (2.8) |
| *Journal of Pediatrics* | 7 (2.4) |
| *Physiological Measurement* | 6 (2.1) |

with all references organised by each data collection item (figshare.com, DOI: 10.6084/m9.figshare.14750865).[18]

## Characteristics of included articles

Of the 286 articles included, 275 (96%) were published in English and the rest were in Russian (n=3), German (n=2), Chinese (n=2), Polish (n=1), French (n=1) and Japanese (n=1). Articles spanned 127 different journals, with the top 10 journals that most commonly published about HRV listed in table 1. Most articles were from North America (47%), primarily from the USA (41%) and Europe (32%) (figure 2). Since 2000, the number of publications in neonatal HRV has increased over time, most markedly in the last 5 years (figure 3). The type of study design was primarily observational (n=261; 91%), including case–control, prospective cohort and cross-sectional articles. There were 14 (4.9%) randomised controlled trials or crossover trials, and 11 (3.8%) retrospective or database articles. Most of the articles were single centre (n=251; 88%).

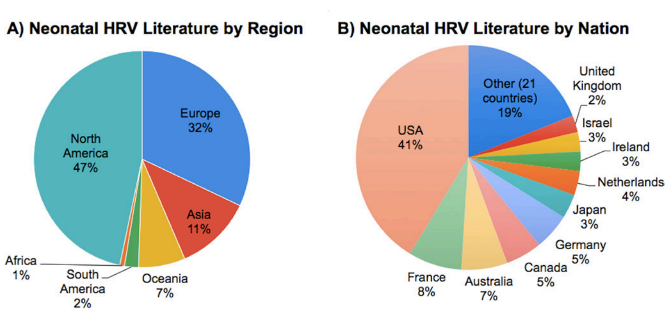


Figure 2 Distribution of neonatal heart rate variability literature by region and nation. (A) Distribution of articles published by region. (B) Distribution of articles published by nation. Other countries included Brazil (n=6), Italy (n=6), Belgium (n=5), Russia (n=5), Turkey (n=4), Switzerland (n=3), Croatia (n=3), Taiwan (n=2), Sweden (n=2), South Africa (n=2), Solvenia (n=2), Slovakia (n=2), Poland (n=2), China (n=2), Austria (n=2), Vietnam (n=1), Serbia (n=1), New Zealand (n=1), India (n=1), Greece (n=1) and Finland (n=1). HRV, heart rate variability.

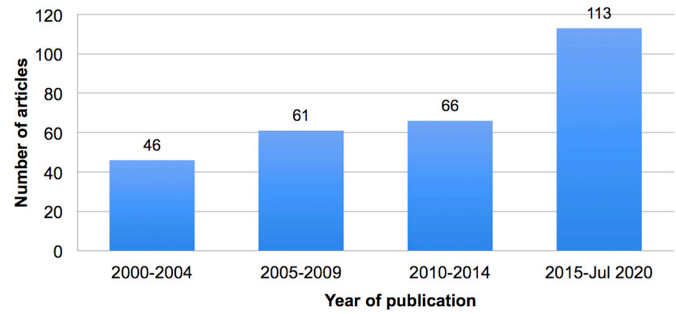


Figure 3 Distribution of studies published by 5-year intervals.

## Study population

Most articles enrolled a small number of infants (table 2). For the largest cohorts, n=6 articles enrolled >1000 patients, with n=3 (1%) between 1000 and 1999 and n=3 (1%) between 2000 and 2999. However, it should be noted that two of the three published articles that had between 2000 and 2999 infants recruited were analyses of the same large cohort study. Term infants with BW ≥2500 were the most common GA and BW categories studied (table 2). BW was more frequently omitted in articles than GA (n=46 vs n=11 not reported) and 18 articles (6.3%) reported including preterm patients, without specifying the ages (table 2).

## HRV analysis methods

The list of all HRV analysis methods and their references is provided as table 3.

### Time domain HRV

Time domain was the second most commonly employed type of HRV analysis (n=139; 48.6%), mostly by calculating SDNN (n=125; 43.7%) and RMSSD (n=83; 29.0%) (table 3). Some articles reported other time domain parameters (n=18), including: SDNN/SD delta NN,[19] log MSSD,[20] SDNN/RMSSD,[21] variance NN,[22] long-term variability,[23–25] short-term variability,[24 25] interval index,[24 25] differential index,[24 25] long-term irregularity,[24 25] expiration/inspiration ratio,[26] percentage of successive changes in NN intervals sustained over two consecutive increases and decreases,[27] temporally scaled SDNN,[28] temporally scaled CVNN,[28] log variance of heart rate,[29] IQRs,[30] per cent of NN intervals of transient decelerations,[31–35] SD of NN intervals of transient decelerations,[31–35] average acceleration and deceleration response[35] and an undefined variable 'X'.[36]

### Frequency domain HRV

Frequency domain was the most common type of HRV analysis used (n=210; 73.4%) (table 3). The most frequently used parameters were the LF (n=168; 58.7%), HF (n=188; 65.7%) and LF/HF ratio (n=117; 40.9%) (table 3). Many articles also reported other frequency domain parameters (n=41), including: mid-frequency (MF, reported at various ranges),[10 26 37–46] super HF,[47] ultra HF,[47] VLF/HF ratio,[28 48] MF/HF ratio,[26 40 41] LF/LF+VLF

Table 2 Study population characteristics

| | n (%) | References |
|---|---|---|
| Sample size | | |
| ≤20 | 63 (22.0) | 23 26 28 29 31 32 34 42–47 49 51–54 60 64 65 70 72 78 84 91 94 98 99 108–110 112 113 134 143 148 151 154 168 169 174–195 |
| 21–49 | 108 (37.8) | 9 20–22 24 25 35–39 41 50 57 59 63 66 67 71 73–75 81 82 85 87 90 92 93 101 103–106 111 118 120 125–128 138 142 147 149 150 152 153 155–158 160 161 167 196–248 |
| 50–99 | 57 (19.9) | 2 4 10 13 19 33 40 56 61 62 68 69 76 79 83 97 100 114 115 117 122 129 131 132 136 137 139 141 146 159 163 249–274 |
| 100–199 | 32 (11.2) | 48 55 77 80 88 89 95 96 102 107 116 121 123 130 133 144 162 165 275–288 |
| 200–499 | 12 (4.2) | 27 30 86 119 124 289–295 |
| ≥500 | 14 (4.9) | 58 135 140 145 164 166 296–303 |
| Gestational age category | | |
| Term (≥37 weeks) | 136 (47.6) | 2 4 9 10 13 19 20 23 26–28 30 37 38 40 46 49 50 52 53 55–57 59 60 62 65 69 75–79 81–83 85 86 88–92 94–96 99 102–104 106–108 111 115–118 121–123 127 128 130 136 137 139 141 142 144 151 152 158 162 168 169 174 176 186 188 189 193 194 196–198 202–206 208 209 213–215 219 221–223 228–230 232 234 237 240 241 244 247 249 253–255 258–260 265 266 268 270 274 275 279–281 285–291 294 295 303 |
| Preterm (<37 weeks) | 18 (6.3) | 10 13 22 30 47 49 102 113 114 141 187 203 208 218 234 241 252 257 |
| Late preterm (34–36$^6$ weeks) | 15 (5.2) | 62 67 71 80 89 95 110 129 134 202 245 266 275 294 295 |
| Moderate preterm (32–34$^6$ weeks) | 21 (7.3) | 29 41 54 64 80 84 101 109 115 133 157 200 201 204 216 239 271 273 296 297 299 |
| Very preterm (28–31$^6$ weeks) | 75 (26.2) | 21 24 25 31–34 36 39 48 51 61 70 80 87 93 98 108 120 131 132 135 136 143 145 146 153–156 159–161 163 165 167 178 182 185 192 195 202 204 207 210–212 220 224 226 227 231 233 235 236 238 242 243 246 248 250 258 261 264 265 269 272 276–278 282 283 292 298 300 |
| Extremely preterm (<28 weeks) | 42 (14.7) | 35 45 62 66 68 73 74 76 100 105 112 119 124–126 132 138 140 147–150 164 175 177 179–181 183 184 191 199 202 217 225 251 262 263 267 284 293 302 |
| Not reported | 11 (3.8) | 42–44 58 63 72 97 166 190 256 301 |
| Birth weight category | | |
| Normal (≥2500 g) | 117 (40.9) | 2 4 9 10 13 19 20 23 26 27 29 30 37 38 40 52 53 55–60 62 65 67 69 75 77–79 81–83 85 86 90–92 94–96 99 102–104 106–108 111 115–118 121–123 127–130 134 136 137 139 141 142 144 152 158 162 168 176 186 188 189 193 196–198 202 204–206 209 213 215 219 221–223 230 232 237 240 244 247 249 253 254 259 260 265 266 268 270 274 275 279–281 285–287 289 290 295 |
| LBW (<2500 g) | 49 (17.1) | 10 41 54 62 64 71 80 95 98 108–110 114 115 120 131–133 141 157 160 163 165 185 195 201 202 204 207 211 216 227 239 243 245 248 258 259 265 266 271 273 275 282 296–300 |
| VLBW (<1500 g) | 52 (18.2) | 13 32–36 39 45 48 51 61 70 80 84 93 102 113 124 135 136 143 146 153 154 156 159 161 166 178 180 182 192 200 204 212 218 220 224 231 235 246 250 261 264 267 269 272 276–278 283 292 |
| ELBW (<1000 g) | 42 (14.7) | 21 31 62 66 68 73 74 87 100 112 119 125 126 132 138 140 145 147–150 164 167 175 177 179 181 183 184 191 199 202 217 225 226 236 251 262 263 284 293 302 |
| Not reported | 46 (16.1) | 22 24 25 28 42–44 46 47 49 50 63 72 76 88 89 97 101 105 151 155 169 174 187 190 194 203 208 210 214 228 229 233 234 238 241 242 252 255–257 288 291 294 301 303 |

ELBW, extremely low birth weight; LBW, low birth weight; VLBW, very low birth weight.

ratio,[48] peak frequencies,[41 49] power in other sub-bands,[28] HF variability index,[50] beta (slope of VLF),[51] respiratory sinus arrhythmia,[22 47 52–60] vagal tone index,[61 62] area under the curve[50 63–65] and the Newborn Infant Parasympathetic Evaluation index.[36 64 66–71]

Among the frequency domain parameters, there were two different reported ranges used for ULF frequency band (upper border limit 0.003 (n=1), 0.0033 (n=2), not reported (n=2)), 13 different ranges for the VLF band, 29 different ranges used for the LF band and 46 different ranges used for the HF band (figure 4 and online supplemental file 2). The most common VLF and LF ranges were 0.003–0.04 Hz (n=8) and 0.04–0.15 Hz (n=60) (figure 4A and B), respectively, which follow the Task Force guidelines for adults.[15] For the HF range, the most common was 0.2–2 Hz (n=20), which is different from the Task Force guidelines range of 0.15–0.4 Hz (n=19) recommended for adults (figure 4C). Of the 210 articles using frequency domain analyses, only 17 (8.1%) articles

**Table 3** Heart rate variability analysis methods

| | N (%) | References |
|---|---|---|
| **Time domain** | **139 (48.6)** | |
| SDNN | 125 (43.7) | 4 9 19 21 22 24–28 30–37 40 41 43 44 51 53 73 75 82 84 86–93 97 101–105 107 108 114 116 121 122 127 128 130 134 137 139 141 143 146 148 149 152 153 156 158 161 167 169 175 179 182 187 189–191 193 195 196 198 203 205–207 209 211–213 215 221 222 224 226 229 231 234 235 239 243 244 246–248 250 251 253 255 259 261 266 267 270 272 273 275 279–281 284 285 287–289 294–296 298 303 |
| CVNN | 13 (4.5) | 26 28 30 40 43 44 46 109 110 149 176 213 242 |
| SDANN | 20 (7.0) | 9 24 25 44 86 90 91 101 114 123 130 141 175 187 190 193 253 259 261 275 |
| SDNNi | 14 (4.9) | 9 86 90 91 130 175 187 190 193 248 253 259 261 275 |
| RMSSD | 83 (29.0) | 9 21–28 30–36 40 53 86–93 101–105 107 108 114 116 121 122 128 130 134 137 141 148 149 152 158 161 175 182 187 189 190 195 203 206 212 213 215 222 224 226 229 231 235 238 239 243 247 248 250 253 259 261 267 273 275 279–281 289 294 295 303 |
| SDSD | 14 (4.9) | 19 22 28 107 116 122 127 148 149 152 187 190 209 224 |
| NN50 | 33 (11.5) | 9 30–32 40 86 87 90 91 95 103 107 128 134 139 141 148 149 191 195 203 205 206 215 239 243 247 253 259 261 270 273 275 |
| NNxx | 15 (5.2) | 9 22 28 36 40 84 86 107 161 190 195 206 213 235 259 |
| TINN | 7 (2.4) | 4 21 86 105 107 169 285 |
| Triangular index | 13 (4.5) | 9 24 25 36 86 95 101 107 190 253 259 261 290 |
| Histogram | 17 (5.9) | 21 35 43 44 46 77 86 92 97 105 167 212 226 251 278 296 298 |
| Other* | 18 (6.3) | 19–36 |
| **Frequency domain** | **210 (73.4)** | |
| Total power | 78 (27.3) | 9 13 20 26 28 30 36 38–41 43 44 46 53 54 74 79 86 87 95 96 99 107 111 116 120 123 125 126 129–131 134 136 141 144 148 149 151 152 155–157 176 180 186 188 195 201 202 204 206 208–210 212 213 216 218 223–226 232 233 241 247 249 253 258–260 265 275 281 286 289 |
| Ultra low frequency | 5 (1.7) | 86 141 253 259 275 |
| Very low frequency | 42 (14.7) | 4 9 21 28 45 48 86 102 105 111 120 130 134 141 148 149 152 155 161 169 176 186 190 191 195 202 208 213 222 225 231 235 244 248 253 258–260 275 281 285 291 |
| Low frequency | 168 (58.7) | 4 9 10 13 20 21 23–26 28 30 31 36–48 51 53 54 57 65 73–84 86–88 92 93 95 96 99 102–105 107 111–113 115 116 118 120 122 123 125–127 129–134 136–138 141 146–157 159 161 169 174 176 178–188 190–192 195 197 199–204 206–210 212 213 216 220–226 229–233 235 237 241 244 245 247–250 253 254 256 258–262 264 265 267 271 273 275–277 281 285 286 288 289 291 |
| High frequency | 188 (65.7) | 4 9 10 13 20 21 23–26 28 30 31 36–38 40–44 46–48 50 51 53 54 57 63–65 73–84 86–89 92 93 95 96 99 102–105 107 111–113 115–118 120 122 123 125–127 129–134 136–138 141 146–157 159 161 163 165 168 169 174 176–188 190–192 194 195 197 199–204 206–210 212–214 216 218–226 228–233 235–238 241 244 245 247–250 253 254 256–262 264 265 267 268 271 273 275–277 280–282 285 286 288 289 291 294 303 |
| LF/HF ratio | 117 (40.9) | 4 9 13 21 23 26 28 30 31 36–38 43 44 46 48 51 54 57 78 84 86 87 92 93 95 102 103 105 111 115 116 118 120 122 125 126 129–131 133 134 136–138 141 146 148 149 151–153 155–157 159–162 169 174 176 178 179 181 184–186 191 192 195 197 199 202 203 206 208 209 212 213 216 218–227 229–233 235 245 247 253 254 256 258 259 261 262 264 265 267 271 273 275–277 281 285 286 |
| Other* | 41 (14.3) | 22 26 28 30 36–71 |
| **Non-linear** | **74 (25.9)** | |
| Poincaré | 29 (10.1) | 28 30 36 84 86 87 92 93 95 102 103 105 107 149 152 158 161 190 191 194 213 222 231 236 243 246 247 267 273 |
| Alpha (α) | 4 (1.4) | 86 93 98 113 |
| DFA α1 | 28 (9.8) | 30 36 51 72–84 86 87 93 103 212 217 222 226 231 235 246 267 |
| DFA α2 | 25 (8.7) | 30 36 51 72–74 76–83 86 87 93 103 212 217 222 231 235 246 267 |
| ApEn | 19 (6.6) | 21 24 25 30 36 37 86 87 92 103 105 212 222 226 231 235 243 267 273 |
| SampEn | 22 (7.7) | 24 25 36 48 86–88 92 93 97 100 103 113 212 222 235 243 252 273 274 296 298 |
| Other* | 48 (16.8) | 21 24 25 28 30 36 37 43 44 46 48 72–107 240 |

Continued


Latremouille S, *et al*. *BMJ Open* 2021;**11**:e055209. doi:10.1136/bmjopen-2021-055209

**Table 3** Continued

| | N (%) | References |
|---|---|---|
| **Heart rate characteristics** | **25** (8.7) | 2 100 119 124 135 140 142 145 164 166 251 263 269 272 283 284 292 293 296–302 |

*Others are described in detail within the manuscript text (with references).
ApEn, approximate entropy; CVNN, coefficient of variation of NN intervals; DFA, detrended fluctuation analysis; LF/HF ratio, low frequency/high frequency ratio; NN, normal-to-normal beat intervals; NN50, pairs of adjacent NN intervals differing by more than 50 ms (count or per cent); NNxx, pairs of adjacent NN intervals differing by a time other than 50 ms (count or per cent); SampEn, sample entropy; SDANN, SD of the averages of NN intervals in all 5 min segments of the entire recording; SDNN, standard deviation of NN intervals; SDNNi, mean of the SDs of all NN intervals for all 5 min segments of the entire recording; SDSD, SD of differences between adjacent NN intervals; TINN, triangular interpolation of NN intervals.

had both their LF and HF ranges following the Task Force guidelines. Nine of these articles also included VLF measures, of which seven also matched the Task Force guidelines for VLF ranges, while the other two used the slightly altered range of 0.0033–0.04 Hz.[15] A summary of the number of articles adhering to the frequency ranges from the Task Force guidelines is provided as table 4. A few articles reported using an individualised approach to determine the range for each patient, often by taking into consideration the breathing frequency: fully individualised range (n=8) and upper limit individualised (n=3) (figure 4C).

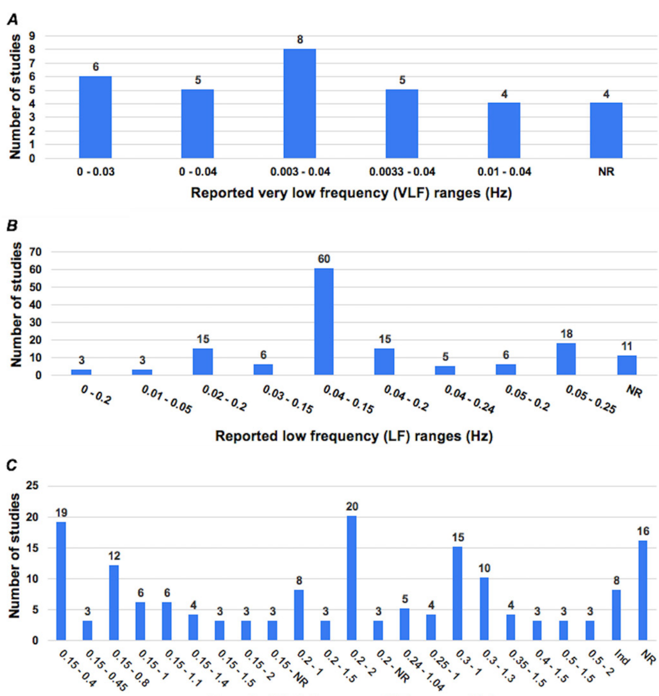


**Figure 4** Reported very low frequency, low frequency and high frequency ranges for the articles using frequency domain analysis. (A) Reported very low frequency (VLF) ranges with n≥3 articles using each range. (B) Reported low frequency (LF) ranges with n≥3 articles using each range. (C) Reported high frequency (HF) ranges with n≥3 articles using each range. All ranges excluded from the figure (n≤2 articles) can be found in online supplemental file 2. Ind, individualised; NR, not reported.

### Non-linear HRV

A total of 74 articles reported using non-linear HRV analysis (table 3). The parameters used were evenly distributed between the Poincaré plot analyses (n=29; 10.1%), DFA α1 (n=28; 9.8%) and α2 (n=25; 8.7%), approximate entropy (n=19; 6.6%) and sample entropy (n=22; 7.7%). Most frequently, however, articles reported using some other non-linear parameters (n=48; 16.8%) (table 3) such as: DFA RMS1 and/or RMS2,[72–83] Shannon entropy,[28 36 43 44 46 84–87] other entropies,[25 28 48 84 86–89] deceleration/acceleration capacity[24 25 86 90–93] and numerous (n=26) other combinations of measures, indices, exponents and dimensions of various chaos, fractality, sample asymmetry, correlations and graphical analyses.[21 28 30 36 37 48 72 84–87 93–107]

### Heart rate characteristics

N=25 articles reported using HRC (table 3). Most of them (n=20) come from within the same group of researchers. However, since 2016, other groups have begun using HRC.

## HRV applications

The list of all HRV applications and their references is provided as table 5.

### Physiological condition

N=162 articles (56.6%) included some form of physiological application of HRV (table 5). The most common form was the use of longitudinal design or repeated measures (n=80). There were 14 articles that examined HRV in relation to 13 other types of normal physiological application or parameters: QT interval,[108] EEG bursts,[109 110] respiration,[33 47 111 112] heart rate,[33] blood pressure,[111 112] oxygen saturation,[111] fetal HRV,[113] movements,[114] crying frequency,[115] body fat percentage,[116] ethnicity,[117] height-for-age ratio[118] and the Neonatal Behavior Assessment Scale.[62]

### Pathological conditions

N=109 articles included an investigation of a specific condition or disease. The list of the conditions studied and their references is provided as table 5. The most commonly studied conditions were sepsis (n=20) and HIE (n=19) (table 5). There were 37 articles that examined 27 other conditions: cardiorespiratory events,[30 119 120] abnormal

Table 4 Articles using frequency domain analyses that follow the Task Force guideline's frequency ranges

| Frequency range | Task Force ranges[15] | Number of articles following Task Force ranges |
|---|---|---|
| VLF | 0.003–0.04 Hz | 8/210 (3.8%) |
| LF | 0.04–0.15 Hz | 60/210 (28.6%) |
| HF | 0.15–0.4 Hz | 18/210 (8.5%) |
| LF+HF | 0.04–0.15 and 0.15–0.4 Hz | 17/210 (8.1%) |
| VLF+LF+HF | 0.003–0.04, 0.04–0.15 and 0.15–0.4 Hz | 7/210 (3.3%) |

Data reported as n/N (%), where N=number of articles using frequency domain analyses (N=210).
HF, high frequency; LF, low frequency; VLF, very low frequency.

fetal status,[107 121–123] unplanned intubation,[124] hypotension,[21 105 125] abnormal polysomnography,[101 126] neonatal abstinence syndrome,[56 127 128] Transport Risk Index of Physiologic Stability score,[29 129] hyperbilirubinaemia,[104 128 130] Score for Neonatal Acute Physiology score,[131 132] delivery complications,[107 123] clinical course score,[21 105] risk of neurodevelopmental impairment,[133] gastro-oesophageal reflux disease,[134] bronchopulmonary dysplasia,[135] inflammatory cytokines,[81] fetal growth restriction,[136] cardiovascular development,[137] APGAR score (newborn health assessment of Appearance, Pulse, Grimace, Activity, and Respiration),[137] retinopathy of prematurity,[138] intrathoracic masses,[139] stroke,[78] antibiotic use,[140] non-benign tachyarrhythmia,[141] death/disability score,[142] T-wave alternans,[143] epigenetic ageing[144] and Clinical Risk Index for Babies (CRIB) score.[45 125]

### Response

N=136 articles investigated HRV in response to certain stimuli. The list of the responses studied and their references is shown in table 5. The most common stimuli studied were response to pain (n=32), followed by light, sound or touch (n=22) and procedures (n=22; table 5). There were 11 different medication or medication groups, 9 different procedures, and 21 different maternal factors studied; a list of these 3 subgroups and their references is provided as table 6. There were 38 articles examining 17 other stimuli: respiratory support,[112 145–151] delivery mode,[20 69 77 121–123 137] phototherapy,[104 128 146 152] consoling devices,[32 34 59 153 154] electromagnetic field,[155 156] stress,[48 118 157] cocoon/swaddle,[64 158] transport,[129] hypoxic hypercapnia,[23] feeding protocol,[159] environmental tobacco smoke,[55] caregiving,[160] incubator temperature,[161] non-invasive electrical stimulation at acupuncture points,[162] CRIB versus incubator,[156] self-consoling behaviour[157] and family nurture intervention.[163]

### Outcome prediction

N=30 articles examined HRV in relation to long-term outcomes at discharge and beyond. The list of outcomes studied and their references is provided as table 5. The most common outcome examined was neurodevelopmental impairment (n=12) (table 5). There were 11 articles that included 9 other outcome measures: days on antibiotics,[119 164] days on oxygen,[137 165] days off mechanical ventilation,[166] days alive,[166] death,[4 167] feeding skill or type of feeding at discharge,[157 168] abnormal polysomnography,[101] 'unfavourable' outcome (multifactorial)[169] and cardiovascular development (echocardiography and blood pressure measurements).[137]

## DISCUSSION

### Study and population characteristics

In the last 20 years, there has been an increasing interest in neonatal HRV, with a notable increase from 2017 onward. Indeed, in this scoping review, we also found 118 review articles that mentioned neonatal HRV, further pointing to its potential usefulness as a clinical tool. Interestingly, the majority of published articles were single-centre investigations that enrolled a small number of infants (<50). It is possible that sample sizes may increase over time as a consequence of advances in monitoring technology and in-hospital data storage systems, which will allow access to ECG signals recorded during hospital stay rather than performing separate signal collection for specific research projects.

There were notably fewer articles in MPT and LPT infants than in the other GA groups despite the fact that these infants account for the majority of preterm infants admitted to the NICUs.[170] These patients still encounter a variety of clinical issues such as respiratory problems requiring different types of respiratory support, feeding and thermoregulation difficulties, and prolonged hospitalisation.[171 172] This is a population where further HRV studies may show clinical benefit.

### HRV analysis methods

A large variety of HRV analyses methods were noted. This review identified 37 additional parameters used for HRV analysis, primarily within the non-linear analyses. Furthermore, the 46 different frequency ranges reported for the HF frequency domain parameter demonstrates how a single HRV parameter can have multiple definitions. Few articles fully adhered to the Task Force guidelines for the frequency domain ranges; however, guidelines for the adult population may not be appropriate for use in neonates given the differences in respiratory and heart rates.[173] Moreover, this review did not collect certain aspects and details concerning ECG signal or HRV analysis, such as the duration of the ECG segment and handling of artefacts, which can also vary between studies

Table 5 Neonatal heart rate variability applications

| | n (%) | References |
|---|---|---|
| **Physiological conditions** | **162 (56.6)** | |
| Normative | 48 (16.8) | 13 30 33 40 41 47 60 76 86 88–93 107 113 117 118 130 131 141 160 163 178 193 195 208 210 213 215 218 223 229 232 233 243 247 248 253 264–266 271 274 294 295 303 |
| Sleep state | 49 (17.1) | 10 11 13 19 24 27 30 37 38 48 53 62 84 88 94 99 101 115 125 126 134 136 158 160 161 163 174 176 181 188 189 195 205 211 213 220 223 232–235 250 264 265 271 275 288 294 295 303 |
| Longitudinal | 80 (28.0) | 2 13 19 20 25 30 33 35 39 48 51 53 54 56 60–62 65 72 80 86 88 90 91 93 94 96 98 104 107 114 117–119 125 126 128 129 136 138 140 142 145 147 150 152 158 160 163 168 177 192–194 198 200 207 208 218 221 223 227–229 232 233 243 244 247 248 256 257 260 265 279 291 293 295 296 303 |
| Age or weight | 49 (17.1) | 10 13 19 21 25 33 40 41 62 73 76 89 93 95 98 102 107 111 113 115 116 118 122 125 132 134 137 141 181 183 202–204 208 241 243 250 258 259 265 266 271 274 275 280 294–296 303 |
| Feeding | 16 (5.6) | 117 120 127 159 168 182 183 194 207 214 221 228 236 280–282 |
| Position | 13 (4.5) | 19 23–25 111 146 182 201 205 211 232 233 273 |
| Tilt | 7 (2.4) | 96 111 197 200 209 223 303 |
| Sex | 6 (2.1) | 33 55 73 86 111 151 |
| Other* | 14 (4.9) | 33 47 62 108–118 |
| **Pathological conditions** | **109 (38.1)** | |
| Sepsis | 20 (7.0) | 35 92 97 100 119 126 135 164 166 191 212 251 252 278 292 296 298–300 302 |
| NEC | 7 (2.4) | 74 76 119 131 135 263 302 |
| Infection | 8 (2.8) | 76 119 137 145 186 283 298 301 |
| RDS | 2 (0.7) | 39 139 |
| AOP | 1 (0.3) | 231 |
| Extubation failure | 7 (2.4) | 87 140 148 149 225 269 284 |
| HIE | 19 (6.6) | 2 4 28 52 65 72 75 81–83 142 151 169 190 219 230 237 244 285 |
| Other brain injury | 7 (2.4) | 135 175 199 210 217 242 293 |
| Seizures | 6 (2.1) | 28 42–44 46 241 |
| PDA | 2 (0.7) | 73 224 |
| CHD | 8 (2.8) | 79 194 206 214 221 228 256 275 |
| In-hospital mortality | 9 (3.1) | 26 65 72 135 164 166 293 297 298 |
| Other* | 37 (12.9) | 21 29 30 45 56 78 81 101 104 105 107 119–144 |
| **Responses** | **136 (47.6)** | |
| Pain | 32 (11.2) | 36 48 50 57 59 63 64 67 69 71 85 103 106 132 133 150 153 154 162 185 199 220 222 240 249 254 260 262 268 276 277 281 |
| Medication | 18 (6.3) | 2 4 70 73 78 125 128 132 146 180 192 196 203 231 246 249 267 284 |
| Light, sound or touch | 22 (7.7) | 22 29 64 68 146 153–155 160 184 187 227 238 239 245 255 257 262 264 273 281 282 |
| NNS | 5 (1.7) | 49 127 232 233 281 |
| Kangaroo care | 13 (4.5) | 31–34 61 66 165 179 185 188 194 220 264 |
| Sucrose | 3 (1.0) | 59 162 281 |
| Procedure | 22 (7.7) | 2 26 50 65 67 72 82 117 119 125 146 168 169 196 214 221 226 260 261 267 272 285 |
| Maternal | 30 (10.5) | 9 27 37–39 55–58 60 117 122 126–128 137 193 197 209 216 229 235 254 255 270 282 286 287 289 290 |
| Other* | 38 (13.3) | 20 23 32 34 48 55 59 64 69 77 104 112 118 121–123 128 129 137 145–163 |
| **Outcome prediction** | **30 (10.5)** | |
| NDI | 12 (4.2) | 4 57 58 65 72 100 114 126 167 175 190 293 |
| Cerebral palsy | 5 (1.7) | 4 100 114 126 175 |
| LOS or GA at discharge | 5 (1.7) | 129 164 165 175 256 |

Continued

**Table 5** Continued

| | n (%) | References |
|---|---|---|
| Repeat hospitalisations | 1 (0.3) | 175 |
| Behaviour or social | 6 (2.1) | 62 177 207 228 279 282 |
| Days on MV | 4 (1.4) | 129 132 164 165 |
| Other | 11 (3.8) | 4 101 119 137 157 164–169 |

*Others are described in detail within the manuscript text (with references).
AOP, apnoea of prematurity; CHD, congenital heart defects or disease; GA, gestational age; HIE, hypoxic ischaemic encephalopathy; LOS, length of stay; MV, mechanical ventilation; NDI, neurodevelopmental impairment; NEC, necrotising enterocolitis; NNS, non-nutritive sucking (eg, pacifier); PDA, patent ductus arteriosus; RDS, respiratory distress syndrome; SIDS, sudden infant death syndrome.

but is not often clearly reported. As a result, the methodological variation and lack of consensus in neonatal HRV analysis makes synthesis and comparisons between investigations very difficult, if not impossible. As a result, analysis of neonatal HRV data have been limited to simplified interpretations of trends or shifts in HRV before and after any intervention or condition.

## HRV applications

Neonatal HRV was used in numerous clinical applications well over the 34 different applications prespecified in this review. Including the applications listed within the 'other' categories, as well as the subgroups of responses to medications, procedures and maternal factors, a total of 138 clinical applications have been identified in this

**Table 6** Detailed types of medications, procedures and maternal factors within the responses category of heart rate variability applications

| Response subgroup | n | References | Response subgroup | n | References |
|---|---|---|---|---|---|
| Medications (n=18) | | | Maternal factors (n=30) | | |
| Vasoactives | 3 | 73 125 180 | Smoke | 9 | 27 55 56 58 126 137 197 216 235 |
| Phenobarbital | 3 | 2 4 78 | Cocaine | 8 | 37 38 56 58 128 209 289 290 |
| Morphine | 3 | 4 128 132 | Opioids | 4 | 56 58 127 128 |
| Caffeine | 3 | 146 231 246 | Depression | 2 | 117 255 |
| Thiopental | 1 | 196 | SSRI | 2 | 56 254 |
| EMLA | 1 | 249 | Alcohol | 3 | 27 57 58 |
| Cisapride | 1 | 203 | Other drugs | 4 | 56 58 289 290 |
| Aminophylline | 1 | 192 | Diabetes | 3 | 122 270 287 |
| Corticosteroids | 2 | 73 284 | Glycaemic index | 1 | 122 |
| Ibuprofen | 1 | 267 | Fatty acid status | 1 | 193 |
| Surfactant | 1 | 70 | Low SES | 2 | 117 282 |
| Procedures (n=22) | | | Benzodiazepines | 1 | 254 |
| Therapeutic hypothermia | 6 | 2 65 72 82 169 285 | Magnesium sulfate | 1 | 39 |
| Intubation | 2 | 146 196 | Ritodrine | 1 | 39 |
| Surgery | 7 | 50 117 119 168 214 221 260 | Life stressors | 1 | 117 |
| Immunisation | 2 | 226 267 | Antenatal steroids | 2 | 9 137 |
| ECMO | 1 | 26 | Hypertension | 1 | 137 |
| UVC | 1 | 261 | PET | 1 | 137 |
| IAC | 1 | 125 | Cardioresp. Phys. | 1 | 60 |
| Chest tube insertion | 1 | 67 | Aerobic exercise | 1 | 229 |
| Transfusion | 1 | 272 | Maternal diet | 1 | 286 |

Cardioresp Phys, cardiorespiratory physiolog; ECMO, extracorporeal membrane oxygenation; IAC, indwelling arterial catheter; PET, pre-eclampsia toxaemia; SES, socioeconomic status; SSRI, selective serotonin reuptake inhibitor; UVC, umbilical venous catheter.


Latremouille S, et al. BMJ Open 2021;11:e055209. doi:10.1136/bmjopen-2021-055209

Table 7 Suggested reporting items for neonatal HRV

| | Reporting item | Details |
|---|---|---|
| Methodology | | |
| ECG | Acquisition | Describe the acquisition set-up, including devices and software used, sampling frequency, sleep state and positioning of the newborn, and details of the period during which ECG is recorded (eg, 1 hour prior to extubation, immediately after feeding, etc). |
| | Segment | Describe the segment length used to calculate HRV and methods used to select the segment (if any). |
| | Handling | Describe any filtering applied to the ECG or artefact removal methods, including any software used. |
| HRV | R-wave identification | Describe the algorithms or software used to identify beats (R-waves). |
| | Handling | Describe any filtering, selection or artefact removal methods applied to the RR intervals, including any software used. |
| | Parameters | Describe all HRV parameters calculated with definitions and methods for obtaining the values, with references where appropriate and including any software used. Report all frequency domain ranges. |
| Results | Demographics | Report the baseline demographics of all patients and subgroups of patients where HRV was investigated, including weights, gestational ages and day of life. |
| | Reporting | Report all values for all HRV parameters calculated, regardless of statistical significance. |

HRV, heart rate variability.

review. The articles evaluating physiological conditions and responses to stimuli articles should be particularly useful in highlighting certain considerations when planning a research study. It is encouraging that many studies used a longitudinal or repeated measures design, as this allows each patient to act as their own control which is important in the absence of established normative data. The context within these designs is key in interpreting, for example, in which state or condition is the newborn stressed versus relaxed, or the system's balanced versus disorganised and dysfunctional. It is important that future research also consider performing similar and multiple HRV measures, with the goal of quantitatively combining the results of several investigations. Furthermore, this review highlights areas where more in-depth reviews and larger scale studies could be worth pursuing such as AOP and various long-term outcomes.

### Harmonising neonatal HRV

Until a consensus is reached and a guideline is made available, neonatal HRV will continue to have varied methodologies, with simplified interpretability and limited meta-analytic potential. Without the ability to combine results from multiple studies, establishing normative data within this population is not possible. While waiting for an established neonatal HRV methodology to be recommended, we provide a table of suggested reporting items for all studies of neonatal HRV (table 7). Consistency in reporting will ensure, at least, that methodologies can be adequately compared, which will in turn allow certain studies with matching methodologies to be compared and combined. Indeed, with the ever-expanding capabilities of storing large amounts of data, such as the ECGs used for HRV analysis, it may be possible to re-analyse past datasets while applying a newly standardised methodology.

### Limitations

This scoping review has some limitations. First, with the intent of keeping the review contemporary, we did not include articles published before 2000. Second, a single reviewer performed both the screening and data collection, but any questions or conflicts were discussed among all reviewers. Third, as previously mentioned, additional details concerning ECG signal or HRV analysis (eg, duration of the ECG segment and handling of artefacts) were not collected since they are not clearly reported in a number of publications. However, this review provides an updated and comprehensive view on neonatal HRV that can be used as reference for future investigations.

## CONCLUSION

This scoping review highlights the growing interest in neonatal HRV, with numerous applications being investigated. Most importantly, it reveals the lack of consistency in calculating and reporting HRV, likely due to the lack of consensus and published guidelines for neonatal HRV. Future investigations will benefit from a consensus guideline for neonatal HRV, and this review may help in the planning of that.

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## REFERENCES

1 Kamath MV, Watanabe MA, Upton A. *Heart rate variability (HRV) signal analysis: clinical applications*. Boca Raton, Florida: CRC Press, 2012.
2 Vergales B, Zanelli S, Matsumoto J, *et al*. Depressed heart rate variability is associated with abnormal EEG, MRI, and death in neonates with hypoxic ischemic encephalopathy. *Am J Perinatol* 2014;31:855–62.
3 Matić V, Cherian PJ, Widjaja D. *Heart rate variability in newborns with hypoxic brain injury*. Oxygen Transport to Tissue XXXV: Springer, 2013: 43–8.
4 Goulding RM, Stevenson NJ, Murray DM, *et al*. Heart rate variability in hypoxic ischemic encephalopathy: correlation with EEG grade and 2-y neurodevelopmental outcome. *Pediatr Res* 2015;77:681–7.
5 Goulding RM, Stevenson NJ, Murray DM, *et al*. Heart rate variability in hypoxic ischemic encephalopathy during therapeutic hypothermia. *Pediatr Res* 2017;81:609–15.
6 Weissman A, Zimmer EZ, Aranovitch M, *et al*. Heart rate dynamics during acute pain in newborns. *Pflugers Arch - Eur J Physiol* 2012;464:593–9.
7 Cong X, Cusson RM, Walsh S, *et al*. Effects of skin-to-skin contact on autonomic pain responses in preterm infants. *J Pain* 2012;13:636–45.
8 Hambleton MT, Reynolds EW, Sithisarn T, *et al*. Autonomic nervous system function following prenatal opiate exposure. *Frontiers in Pediatrics* 2013;1.
9 Schäffer L, Burkhardt T, Tomaske M, *et al*. Effect of antenatal betamethasone administration on neonatal cardiac autonomic balance. *Pediatr Res* 2010;68:286–91.
10 Eiselt M, Zwiener U, Witte H. Influence of prematurity and extrauterine development on the sleep state dependent heart rate patterns. *Somnologie* 2002;6:116–23.
11 Fyfe K, Odoi A, Yiallourou S. Parasympathetic activity is reduced during sleep in very preterm infants. *J Paediatr Child Health* 2014;50:48.
12 Witcombe N, Yiallourou S, Sands S. Maturation of autonomic nervous system activity during sleep: effects of preterm birth. *Sleep Biol Rhythms* 2009;7:A60–1.
13 Yiallourou SR, Witcombe NB, Sands SA, *et al*. The development of autonomic cardiovascular control is altered by preterm birth. *Early Hum Dev* 2013;89:145–52.
14 De Rogalski Landrot I, Roche F, Pichot V, *et al*. Autonomic nervous system activity in premature and full-term infants from theoretical term to 7 years. *Autonomic Neuroscience* 2007;136:105–9.
15 Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task force of the European Society of cardiology and the North American Society of pacing and electrophysiology. *Circulation* 1996;93:1043–65.
16 Nunan D, Sandercock GRH, Brodie DA. A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing Clin Electrophysiol* 2010;33:1407–17.
17 Sassi R, Cerutti S, Lombardi F, *et al*. Advances in heart rate variability signal analysis: joint position statement by the e-Cardiology ESC Working group and the European heart rhythm association co-endorsed by the Asia Pacific heart rhythm Society. *Europace* 2015;17:1341–53.
18 Latremouille S, Lam J, Shalish W. Datasets (EndNote and Excel) for "Neonatal heart rate variability: a contemporary scoping review of analysis methods and clinical applications". *Figshare Digital Repository* 2021.
19 Galland BC, Taylor BJ, Bolton DPG, *et al*. Heart rate variability and cardiac reflexes in small for gestational age infants. *J Appl Physiol* 2006;100:933–9.
20 Kozar M, Tonhajzerova I, Mestanik M, *et al*. Heart rate variability in healthy term newborns is related to delivery mode: a prospective observational study. *BMC Pregnancy Childbirth* 2018;18:264.
21 Semenova O, Carra G, Lightbody G, *et al*. Prediction of short-term health outcomes in preterm neonates from heart-rate variability and blood pressure using boosted decision trees. *Comput Methods Programs Biomed* 2019;180:104996.
22 Djordjevic D, Linderkamp O, Brussau J. Interrelation between well-being of the mother and heart rate variability of her preterm infant]. *Prax Kinderpsychol Kinderpsychiatr* 2007;56:852–69.
23 Naidoo M, Colditz PB, Browne CA, *et al*. Cardiac responses to mild hypoxic hypercapnia in newborn babies: no effect of sleep position. *J Paediatr Child Health* 2000;36:462–5.
24 Lucchini M, Signorini MG, Fifer WP, *et al*. Multi-Parametric heart rate analysis in premature babies exposed to sudden infant death syndrome. *Annu Int Conf IEEE Eng Med Biol Soc* 2014;2014:6389–92.
25 Lucchini M, Fifer WP, Sahni R, *et al*. Novel heart rate parameters for the assessment of autonomic nervous system function in premature infants. *Physiol Meas* 2016;37:1436–46.
26 Longin E, Schaible T, Demirakca S, *et al*. Heart rate variability during extracorporeal membrane oxygenation and recovery in severe neonatal disease. *Early Hum Dev* 2006;82:135–42.
27 Fifer WP, Fingers ST, Youngman M, *et al*. Effects of alcohol and smoking during pregnancy on infant autonomic control. *Dev Psychobiol* 2009;51:234–42.
28 Doyle OM, Temko A, Marnane W, *et al*. Heart rate based automatic seizure detection in the newborn. *Med Eng Phys* 2010;32:829–39.
29 Karlsson B-M, Lindkvist M, Lindkvist M, *et al*. Sound and vibration: effects on infants' heart rate and heart rate variability during neonatal transport. *Acta Paediatr* 2012;101:148–54.
30 Lewicke A, Corwin M, Schuckers M, *et al*. Analysis of heart rate variability for predicting cardiorespiratory events in infants. *Biomed Signal Process Control* 2012;7:325–32.
31 Kommers DR, Joshi R, van Pul C, *et al*. Features of heart rate variability capture regulatory changes during kangaroo care in preterm infants. *J Pediatr* 2017;182:92–8.
32 Kommers D, Joshi R, Pul Cvan, *et al*. Unlike kangaroo care, mechanically simulated kangaroo care does not change heart rate variability in preterm neonates. *Early Hum Dev* 2018;121:27–32.
33 Joshi R, Kommers D, Guo C, *et al*. Statistical modeling of heart rate variability to unravel the factors affecting autonomic regulation in preterm infants. *Sci Rep* 2019;9:7691.
34 Kommers DR, Joshi R, van Pul C, *et al*. Changes in autonomic regulation due to kangaroo care remain unaffected by using a swaddling device. *Acta Paediatr* 2019;108:258–65.
35 Joshi R, Kommers D, Oosterwijk L, *et al*. Predicting neonatal sepsis using features of heart rate variability, respiratory characteristics, and ECG-Derived estimates of infant motion. *IEEE J Biomed Health Inform* 2020;24:681–92.

36 Cremillieux C, Makhlouf A, Pichot V, *et al*. Objective assessment of induced acute pain in neonatology with the newborn infant parasympathetic evaluation index. *European Journal of Pain* 2018;22:1071–9.
37 Garde S, Regalado MG, Schechtman VL, *et al*. Nonlinear dynamics of heart rate variability in cocaine-exposed neonates during sleep. *Am J Physiol Heart Circ Physiol* 2001;280:H2920–8.
38 Regalado MG, Schechtman VL, Khoo MC, *et al*. Spectral analysis of heart rate variability and respiration during sleep in cocaine-exposed neonates. *Clin Physiol* 2001;21:428–36.
39 Rantone TH, Grönlund JU, Jalonen JO, *et al*. Comparison of the effects of antenatal magnesium sulphate and ritodrine exposure on circulatory adaptation in preterm infants. *Clin Physiol Funct Imaging* 2002;22:13–17.
40 Longin E, Schaible T, Lenz T, *et al*. Short term heart rate variability in healthy neonates: normative data and physiological observations. *Early Hum Dev* 2005;81:663–71.
41 Longin E, Gerstner T, Schaible T, *et al*. Maturation of the autonomic nervous system: differences in heart rate variability in premature vs. term infants. *J Perinat Med* 2006;34:303–8.
42 Malarvili MB, Mesbah M, Boashash B. Time-frequency analysis of heart rate variability for neonatal seizure detection. *EURASIP J Adv Signal Process* 2007;2007.
43 Malarvili MB, Mesbah M. Combining newborn EEG and HRV information for automatic seizure detection. *Annu Int Conf IEEE Eng Med Biol Soc* 2008;2008:4756–9.
44 Malarvili MB, Mesbah M. Newborn seizure detection based on heart rate variability. *IEEE Trans Biomed Eng* 2009;56:2594–603.
45 Zhang Y, Chan GSH, Tracy MB, *et al*. Spectral analysis of systemic and cerebral cardiovascular variabilities in preterm infants: relationship with clinical risk index for babies (CRIB). *Physiol Meas* 2011;32:1913–28.
46 Mesbah M, Balakrishnan M, Colditz PB, *et al*. Automatic seizure detection based on the combination of newborn multi-channel EEG and HRV information. *EURASIP J Adv Signal Process* 2012;2012.
47 Indic P, Salisbury E, Paydarfar D, *et al*. Interaction between heart rate variability and respiration in preterm infants. *Comput Cardiol* 2008;35:57–60.
48 Lavanga M, Smets L, Bollen B, *et al*. A perinatal stress calculator for the neonatal intensive care unit: an unobtrusive approach. *Physiol Meas* 2020;41:10.
49 Morren G, Van Huffel S, Helon I, *et al*. Effects of non-nutritive sucking on heart rate, respiration and oxygenation: a model-based signal processing approach. *Comp Biochem Physiol A Mol Integr Physiol* 2002;132:97–106.
50 Faye PM, De Jonckheere J, Logier R, *et al*. Newborn infant pain assessment using heart rate variability analysis. *Clin J Pain* 2010;26:777–82.
51 Nakamura T, Horio H, Miyashita S, *et al*. Identification of development and autonomic nerve activity from heart rate variability in preterm infants. *Biosystems* 2005;79:117–24.
52 Anninos P, Anastasiadis PG, Kotini A, *et al*. Neonatal magnetocardiography and Fourier spectral analysis. *Clin Exp Obstet Gynecol* 2001;28:249–52.
53 Patzak A, Mrowka R, Springer S. Heart rate variability in the paediatric sleep laboratory - Recommendations for measurement and analysis. German]. *Somnologie* 2002;6:39–50.
54 Hata T, Matsuura H, Miyata M, *et al*. Autonomic modulation of sinus and atrioventricular nodes in premature low-birth-weight infants. *Pacing Clin Electrophysiol* 2005;28 Suppl 1:S288–91.
55 Schuetze P, Eiden RD. The association between maternal smoking and secondhand exposure and autonomic functioning at 2–4 weeks of age. *Infant Behav and Development* 2006;29:32–43.
56 Jansson LM, DiPietro JA, Elko A, *et al*. Infant autonomic functioning and neonatal abstinence syndrome. *Drug Alcohol Depend* 2010;109:198–204.
57 Oberlander TF, Jacobson SW, Weinberg J, *et al*. Prenatal alcohol exposure alters biobehavioral reactivity to pain in newborns. *Alcohol Clin Exp Res* 2010;34:681–92.
58 Conradt E, Sheinkopf SJ, Lester BM, *et al*. Prenatal substance exposure: neurobiologic organization at 1 month. *J Pediatr* 2013;163:989–94.
59 Gray L, Garza E, Zageris D, *et al*. Sucrose and warmth for analgesia in healthy newborns: an RCT. *Pediatrics* 2015;135:e607–14.
60 Van Puyvelde M, Loots G, Meys J, *et al*. Whose clock makes yours tick? how maternal cardiorespiratory physiology influences newborns' heart rate variability. *Biol Psychol* 2015;108:132–41.
61 Feldman R, Eidelman AI. Skin-to-skin contact (kangaroo care) accelerates autonomic and neurobehavioural maturation in preterm infants. *Dev Med Child Neurol* 2003;45:274–81.
62 Feldman R. From biological rhythms to social rhythms: physiological precursors of mother-infant synchrony. *Dev Psychol* 2006;42:175–88.
63 De Jonckheere J, Rakza T, Logier R, *et al*. Heart rate variability analysis for newborn infants prolonged pain assessment. *Annu Int Conf IEEE Eng Med Biol Soc* 2011;2011:7747–50.
64 Alexandre C, De Jonckheere J, Rakza T, *et al*. [Impact of cocooning and maternal voice on the autonomic nervous system activity in the premature newborn infant]. *Arch Pediatr* 2013;20:963–8.
65 Massaro AN, Govindan RB, Al-Shargabi T, *et al*. Heart rate variability in encephalopathic newborns during and after therapeutic hypothermia. *J Perinatol* 2014;34:836–41.
66 Butruille L, Blouin A, De Jonckheere J, *et al*. Impact of skin-to-skin contact on the autonomic nervous system in the preterm infant and his mother. *Infant Behav Dev* 2017;49:83–6.
67 Buyuktiryaki M, Uras N, Okur N, *et al*. Evaluation of prolonged pain in preterm infants with pneumothorax using heart rate variability analysis and EDIN (Échelle Douleur Inconfort Nouveau-Né, neonatal pain and discomfort scale) scores. *Korean J Pediatr* 2018;61:322–6.
68 Gautheyrou L, Durand S, Jourdes E, *et al*. Facilitated tucking during early neonatologist-performed echocardiography in very preterm neonates. *Acta Paediatr* 2018;107:2079–85.
69 Rakza T, Butruille L, Thirel L, *et al*. Short-Term impact of assisted deliveries: evaluation based on behavioral pain scoring and heart rate variability. *Clin J Pain* 2018;34:445–9.
70 Okur N, Uras N, Buyuktiryaki M, *et al*. Neonatal pain and heart rate variability in preterm infants treated with surfactant: a pilot study. *Arch Argent Pediatr* 2019;117:397.
71 Walas W, Latka-Grot J, Maroszyńska I, *et al*. Newborn infant parasympathetic evaluation index for the assessment of procedural pain in Nonanesthetized infants: a multicenter pilot study. *Am J Perinatol* 2021;38:10.
72 Govindan RB, Massaro AN, Al-Shargabi T, *et al*. Detrended fluctuation analysis of non-stationary cardiac beat-to-beat interval of sick infants. *EPL* 2014;108:40005.
73 Andescavage NN, Metzler M, Govindan V, *et al*. The impact of surgical patent ductus arteriosus closure on autonomic function in premature infants. *Am J Perinatol* 2017;34:874–8.
74 Al-Shargabi T, Reich D, Govindan R, *et al*. Changes in autonomic tone in premature infants developing necrotizing enterocolitis. *Am J Perinatol* 2018;35:1079–86.
75 Campbell H, Govindan RB, Kota S, *et al*. Autonomic dysfunction in neonates with hypoxic ischemic encephalopathy undergoing therapeutic hypothermia impairs physiological responses to routine care events. *J Pediatr* 2018;196:38–44.
76 Mulkey SB, Kota S, Swisher CB, *et al*. Autonomic nervous system depression at term in neurologically normal premature infants. *Early Hum Dev* 2018;123:11–16.
77 Mulkey SB, Kota S, Govindan RB. The effect of labor and delivery mode on electrocortical and brainstem autonomic function during neonatal transition. *Sci* 2019;9:11020.
78 Reich DA, Govindan RB, Whitehead MT, *et al*. The effect of unilateral stroke on autonomic function in the term newborn. *Pediatr Res* 2019;85:830–4.
79 Mulkey SB, Govindan R, Metzler M, *et al*. Heart rate variability is depressed in the early transitional period for newborns with complex congenital heart disease. *Clin Auton Res* 2020;30:165–72.
80 Mulkey SB, Govindan RB, Hitchings L, *et al*. Autonomic nervous system maturation in the premature extrauterine milieu. *Pediatr Res* 2021;89:863–8.
81 Al-Shargabi T, Govindan RB, Dave R, *et al*. Inflammatory cytokine response and reduced heart rate variability in newborns with hypoxic-ischemic encephalopathy. *J Perinatol* 2017;37:668–72.
82 Massaro AN, Campbell HE, Metzler M, *et al*. Effect of temperature on heart rate variability in neonatal ICU patients with hypoxic-ischemic encephalopathy. *Pediatric Critical Care Medicine* 2017;18:349–54.
83 Metzler M, Govindan R, Al-Shargabi T, *et al*. Pattern of brain injury and depressed heart rate variability in newborns with hypoxic ischemic encephalopathy. *Pediatr Res* 2017;82:438–43.
84 Reulecke S, Schulz S, Voss A. Autonomic regulation during quiet and active sleep states in very preterm neonates. *Front Physiol* 2012;3:61.
85 Šapina M, Karmakar CK, Kramarić K, *et al*. Multi-lag tone-entropy in neonatal stress. *J R Soc Interface* 2018;15:20180420.
86 Patural H, Pichot V, Flori S, *et al*. Autonomic maturation from birth to 2 years: normative values. *Heliyon* 2019;5:e01300.
87 Silva MGF, Gregório ML, de Godoy MF. Does heart rate variability improve prediction of failed extubation in preterm infants? *J Perinat Med* 2019;47:252–7.

88 Lucchini M, Pini N, Fifer WP, *et al*. Entropy information of cardiorespiratory dynamics in neonates during sleep. *Entropy* 2017;19:225.
89 Lucchini M, Burtchen N, Fifer WP, *et al*. Multi-Parametric cardiorespiratory analysis in late-preterm, early-term, and full-term infants at birth. *Med Biol Eng Comput* 2019;57:99–106.
90 Makarov LM, Komoliatova VN, Zeval'd SV, *et al*. [Holter monitoring in healthy children during first days of life]. *Kardiologiia* 2009;49:27–30.
91 Makarov L, Komoliatova V, Zevald S, *et al*. Qt dynamicity, microvolt T-wave alternans, and heart rate variability during 24-hour ambulatory electrocardiogram monitoring in the healthy newborn of first to fourth day of life. *J Electrocardiol* 2010;43:8–14.
92 Nguyen N, Vandenbroucke L, Hernández A, *et al*. Early-Onset neonatal sepsis is associated with a high heart rate during automatically selected stationary periods. *Acta Paediatr* 2017;106:749–54.
93 Nguyen Phuc Thu T, Hernández AI, Costet N, *et al*. Improving methodology in heart rate variability analysis for the premature infants: impact of the time length. *PLoS One* 2019;14:e0220692.
94 Mrowka R, Patzak A, Persson PB. The complexity of heart rate in its postnatal development: the role of sleep stages and age in the development of heart rate control complexity. *IEEE Engineering in Medicine and Biology Magazine* 2001;20:88–91.
95 Shiraishi M, Miyake Y, Yamamoto T. The development of heart rate control in healthy infants. *Nichidai Igaku Zasshi* 2001;60:450–8.
96 Tsoy EG, Igisheva LN, Galeev AR. Cardiac rhythm variability in adaptive processes estimation in neonates. *Pediatriya* 2003;1:23–7.
97 Cao H, Lake DE, Griffin MP, *et al*. Increased nonstationarity of neonatal heart rate before the clinical diagnosis of sepsis. *Ann Biomed Eng* 2004;32:233–44.
98 Nakamura T, Horio H, Chiba Y. Local holder exponent analysis of heart rate variability in preterm infants. *IEEE Trans Biomed Eng* 2006;53:83–8.
99 Frasch MG, Zwiener U, Hoyer D, *et al*. Autonomic organization of respirocardial function in healthy human neonates in quiet and active sleep. *Early Hum Dev* 2007;83:269–77.
100 Addison K, Griffin MP, Moorman JR, *et al*. Heart rate characteristics and neurodevelopmental outcome in very low birth weight infants. *J Perinatol* 2009;29:750–6.
101 Vandeput S, Naulaers G, Daniels H, *et al*. Heart rate variability during REM and non-REM sleep in preterm neonates with and without abnormal cardiorespiratory events. *Early Hum Dev* 2009;85:665–71.
102 Selig FA, Tonolli ER, Silva EV. Heart rate variability in preterm and term neonates. *Arq Bras Cardiol* 2011;96:443–9.
103 Zeng C, Jiang Q-Y, Chen C-Y. Application of heart rate variability analysis to pain detection for newborns. *Wlxb* 2014;63:208704.
104 Uhrikova Z, Zibolen M, Javorka K, *et al*. Hyperbilirubinemia and phototherapy in newborns: effects on cardiac autonomic control. *Early Hum Dev* 2015;91:351–6.
105 Semenova O, Carra G, Lightbody G. Heart rate variability during periods of low blood pressure as a predictor of short-term outcome in Preterms. *Conf Proc IEEE Eng Med Biol Soc* 2018;2018:5614–517.
106 Kramarić K, Šapina M, Garcin M, *et al*. Heart rate asymmetry as a new marker for neonatal stress. *Biomed Signal Process Control* 2019;47:219–23.
107 Oliveira V, von Rosenberg W, Montaldo P, *et al*. Early postnatal heart rate variability in healthy newborn infants. *Front Physiol* 2019;10:922.
108 Pladys P, Senhadji L, Blanche PM, *et al*. Beat-To-Beat analysis of the relation between RT and Rr intervals in newborns. *J Perinatol* 2003;23:212–7.
109 Pfurtscheller K, Müller-Putz GR, Urlesberger B, *et al*. Synchronous occurrence of EEG bursts and heart rate acceleration in preterm infants. *Brain and Development* 2005;27:558–63.
110 Pfurtscheller K, Müller-Putz GR, Urlesberger B, *et al*. Relationship between slow-wave EEG bursts and heart rate changes in preterm infants. *Neurosci Lett* 2005;385:126–30.
111 Fister P, Nolimal M, Lenasi H, *et al*. The effect of sleeping position on heart rate variability in newborns. *BMC Pediatr* 2020;20:156.
112 Rassi D, Mishin A, Zhuravlev YE, *et al*. Time domain correlation analysis of heart rate variability in preterm neonates. *Early Hum Dev* 2005;81:341–50.
113 Padhye NS, Verklan M, Brazdeikis A, *et al*. A comparison of fetal and neonatal heart rate variability at similar post-menstrual ages. *Annu Int Conf IEEE Eng Med Biol Soc* 2008;2008:2801–4.
114 Dimitrijević L, Bjelaković B, Čolović H, *et al*. Assessment of general movements and heart rate variability in prediction of neurodevelopmental outcome in preterm infants. *Early Hum Dev* 2016;99:7–12.
115 Shinya Y, Kawai M, Niwa F, *et al*. Associations between respiratory arrhythmia and fundamental frequency of spontaneous crying in preterm and term infants at term-equivalent age. *Dev Psychobiol* 2016;58:724–33.
116 Dissanayake HU, McMullan RL, Kong Y, *et al*. Body fatness and cardiovascular health in newborn infants. *J Clin Med* 2018;7:11.
117 Jacob S, Byrne M, Keenan K. Neonatal physiological regulation is associated with perinatal factors: a study of neonates born to healthy African American women living in poverty. *Infant Ment Health J* 2009;30:82–94.
118 Hashiguchi K, Kuriyama N, Koyama T, *et al*. Validity of stress assessment using heart-rate variability in newborns. *Pediatr Int* 2020;62:694–700.
119 Sullivan BA, Grice SM, Lake DE, *et al*. Infection and other clinical correlates of abnormal heart rate characteristics in preterm infants. *J Pediatr* 2014;164:775–80.
120 Veerappan S, Rosen H, Craelius W, *et al*. Spectral analysis of heart rate variability in premature infants with feeding bradycardia. *Pediatr Res* 2000;47:659–62.
121 Moehler E, Poustka L, Resch F. Vacuum extraction and autonomic balance in human infants. *J Perinat Med* 2007;35:347–9.
122 Russell NE, Higgins MF, Kinsley BF, *et al*. Heart rate variability in neonates of type 1 diabetic pregnancy. *Early Hum Dev* 2016;92:51–5.
123 Sheen T-C, Lu M-H, Lee M-Y, *et al*. Nonreassuring fetal heart rate decreases heart rate variability in newborn infants. *Ann Noninvasive Electrocardiol* 2014;19:273–8.
124 Clark MT, Vergales BD, Paget-Brown AO, *et al*. Predictive monitoring for respiratory decompensation leading to urgent unplanned intubation in the neonatal intensive care unit. *Pediatr Res* 2013;73:104–10.
125 Golder V, Hepponstall M, Yiallourou SR, *et al*. Autonomic cardiovascular control in hypotensive critically ill preterm infants is impaired during the first days of life. *Early Hum Dev* 2013;89:419–23.
126 Thiriez G, Mougey C, Vermeylen D, *et al*. Altered autonomic control in preterm newborns with impaired neurological outcomes. *Clin Auton Res* 2015;25:233–42.
127 Hambleton MT, Reynolds EW, Sithisarn T, *et al*. Autonomic nervous system function following prenatal opiate exposure. *Front Pediatr* 2013;1:27.
128 Nagiub M, Alton K, Avula V, *et al*. Heart rate variability evaluation in the assessment and management of in-utero drug-exposed infants. *SAGE Open Med* 2014;2:205031211455652.
129 Snedec N, Simoncic M, Klemenc M, *et al*. Heart rate variability of transported critically ill neonates. *Eur J Pediatr* 2013;172:1565–71.
130 Özdemir R, Olukman Özgür, Karadeniz C, *et al*. Effect of unconjugated hyperbilirubinemia on neonatal autonomic functions: evaluation by heart rate variability. *The Journal of Maternal-Fetal & Neonatal Medicine* 2018;31:2763–9.
131 Doheny KK, Palmer C, Browning KN, *et al*. Diminished vagal tone is a predictive biomarker of necrotizing enterocolitis-risk in preterm infants. *Neurogastroenterol Motil* 2014;26:832–40.
132 Grunau RE, Holsti L, Haley DW, *et al*. Neonatal procedural pain exposure predicts lower cortisol and behavioral reactivity in preterm infants in the NICU. *Pain* 2005;113:293–300.
133 Stevens B, McGrath P, Gibbins S, *et al*. Determining behavioural and physiological responses to pain in infants at risk for neurological impairment. *Pain* 2007;127:94–102.
134 Djeddi D-D, Kongolo G, Stéphan-Blanchard E, *et al*. Involvement of autonomic nervous activity changes in gastroesophageal reflux in neonates during sleep and wakefulness. *PLoS One* 2013;8:e83464.
135 Sullivan BA, McClure C, Hicks J, *et al*. Early Heart Rate Characteristics Predict Death and Morbidities in Preterm Infants. *J Pediatr* 2016;174:57–62.
136 Cohen E, Wong FY, Wallace EM, *et al*. Fetal-growth-restricted preterm infants display compromised autonomic cardiovascular control on the first postnatal day but not during infancy. *Pediatr Res* 2017;82:474–82.
137 CYL A, Lewandowski AJ, Oster J. Neonatal autonomic function after pregnancy complications and early cardiovascular development. *Pediatr Res* 2018;84:85–91.
138 Hussein MA, Deng N, Rusin C, *et al*. Heart rate variability changes and its association with the development of severe retinopathy of prematurity. *J Aapos* 2018;22:371–5.
139 Schierz IAM, Giuffrè M, Piro E, *et al*. Clinical cardiac assessment in newborns with prenatally diagnosed intrathoracic masses. *Ital J Pediatr* 2018;44:98.

140 Chakraborty M, Watkins WJ, Tansey K, *et al*. Predicting extubation outcomes using the heart rate characteristics index in preterm infants: a cohort study. *Eur Respir J* 2020;56:1901755.
141 Yan X-T, Bo T, Wang C, *et al*. [Heart rate variability in neonates with non-benign tachyarrhythmia]. *Zhongguo Dang Dai Er Ke Za Zhi* 2019;21:474–8.
142 Kayton A, DeGrazia M, Sharpe E. Correlation between heart rate characteristic index score and severity of brain injury in neonates with hypoxic-ischemic encephalopathy. *Adv Neonat Care* 2020:27:27.
143 Marcantoni I, Sbrollini A, Agostinelli G, *et al*. T-Wave alternans in Nonpathological preterm infants. *Ann Noninvasive Electrocardiol* 2020;25:e12745.
144 Phang M, Ross J, Raythatha JH, *et al*. Epigenetic aging in newborns: role of maternal diet. *Am J Clin Nutr* 2020;111:555–61.
145 Weitkamp J-H, Aschner JL, Carlo WA, *et al*. Meningitis, urinary tract, and bloodstream infections in very low birth weight infants enrolled in a heart rate characteristics monitoring trial. *Pediatr Res* 2020;87:1226–30.
146 Aita M, Johnston C, Goulet C, *et al*. Intervention minimizing preterm infants' exposure to NICU light and noise. *Clin Nurs Res* 2013;22:337–58.
147 Khattak AZ, Padhye NS, Williams AL, *et al*. Longitudinal assessment of heart rate variability in very low birth weight infants during their NICU stay. *Early Hum Dev* 2007;83:361–6.
148 Latremouille S, Al-Jabri A, Lamer P, *et al*. Heart rate variability in extremely preterm infants receiving nasal CPAP and Non-Synchronized noninvasive ventilation immediately after extubation. *Respir Care* 2018;63:62–9.
149 Latremouille S, Shalish W, Kanbar L, *et al*. The effects of nasal continuous positive airway pressure and high flow nasal cannula on heart rate variability in extremely preterm infants after extubation: a randomized crossover trial. *Pediatr Pulmonol* 2019;54:788–96.
150 Padhye NS, Williams AL, Khattak AZ, *et al*. Heart rate variability in response to pain stimulus in VLBW infants followed longitudinally during NICU stay. *Dev Psychobiol* 2009;51:638–49.
151 Yasova Barbeau D, Krueger C, Huene M, *et al*. Heart rate variability and inflammatory markers in neonates with hypoxic-ischemic encephalopathy. *Physiol Rep* 2019;7:e14110.
152 Weissman A, Berkowitz E, Smolkin T, *et al*. Effect of phototherapy on neonatal heart rate variability and complexity. *Neonatology* 2009;95:41–6.
153 Holsti L, MacLean K, Oberlander T, *et al*. Calmer: a robot for managing acute pain effectively in preterm infants in the neonatal intensive care unit. *Pain Rep* 2019;4:e727.
154 Williams N, MacLean K, Guan L, *et al*. Pilot testing a robot for reducing pain in hospitalized preterm infants. *OTJR* 2019;39:108–15.
155 Bellieni CV, Acampa M, Maffei M, *et al*. Electromagnetic fields produced by incubators influence heart rate variability in newborns. *Arch Dis Child Fetal Neonatal Ed* 2008;93:F298–301.
156 Passi R, Doheny KK, Gordin Y, *et al*. Electrical grounding improves vagal tone in preterm infants. *Neonatology* 2017;112:187–92.
157 Gardner FC, Adkins CS, Hart SE, *et al*. Preterm stress behaviors, autonomic indices, and maternal perceptions of infant colic. *Adv Neonatal Care* 2018;18:49–57.
158 Richardson HL, Walker AM, Horne RSC. Influence of swaddling experience on spontaneous arousal patterns and autonomic control in sleeping infants. *J Pediatr* 2010;157:85–91.
159 McCain GC, Fuller EO, Gartside PS. Heart rate variability and feeding bradycardia in healthy preterm infants during transition from gavage to oral feeding. *Newborn and Infant Nursing Reviews* 2005;5:124–32.
160 Smith SL, Haley S, Slater H, *et al*. Heart rate variability during caregiving and sleep after massage therapy in preterm infants. *Early Hum Dev* 2013;89:525–9.
161 Stéphan-Blanchard E, Chardon K, Léké A, *et al*. Heart rate variability in sleeping preterm neonates exposed to cool and warm thermal conditions. *PLoS One* 2013;8:e68211.
162 Mitchell AJ, Hall RW, Golianu B, *et al*. Does noninvasive electrical stimulation of acupuncture points reduce heelstick pain in neonates? *Acta Paediatr* 2016;105:1434–9.
163 Porges SW, Davila MI, Lewis GF, *et al*. Autonomic regulation of preterm infants is enhanced by family nurture intervention. *Dev Psychobiol* 2019;61:942–52.
164 Fairchild KD, Schelonka RL, Kaufman DA, *et al*. Septicemia mortality reduction in neonates in a heart rate characteristics monitoring trial. *Pediatr Res* 2013;74:570–5.
165 Marvin M, Gardner F, Sarsfield K, *et al*. Increased frequency of Skin-to-Skin contact is associated with enhanced vagal tone and improved health outcomes in preterm neonates. *Am J Perinatol* 2019;36:505–10.
166 Lake DE, Fairchild KD, Moorman JR. Complex signals bioinformatics: evaluation of heart rate characteristics monitoring as a novel risk marker for neonatal sepsis. *J Clin Monit Comput* 2014;28:329–39.
167 Lloyd RO, O'Toole JM, Livingstone V, *et al*. Predicting 2-y outcome in preterm infants using early multimodal physiological monitoring. *Pediatr Res* 2016;80:382–8.
168 Harrison TM. Trajectories of parasympathetic nervous system function before, during, and after feeding in infants with transposition of the great arteries. *Nurs Res* 2011;60:S15–27.
169 Vesoulis ZA, Rao R, Trivedi SB, *et al*. The effect of therapeutic hypothermia on heart rate variability. *J Perinatol* 2017;37:679–83.
170 Canadian Neonatal Network. The Canadian neonatal network annual report 2017, 2017. Available: http://www.canadianneonatalnetwork.org/Portal/LinkClick.aspx?fileticket=XhPMIxFgc2M%3d&tabid=39
171 Ramachandrappa A, Jain L. Health issues of the late preterm infant. *Pediatr Clin North Am* 2009;56:565–77.
172 Altman M, Vanpée M, Cnattingius S, *et al*. Neonatal morbidity in moderately preterm infants: a Swedish national population-based study. *J Pediatr* 2011;158:239–44.
173 Rosenstock EG, Cassuto Y, Zmora E. Heart rate variability in the neonate and infant: analytical methods, physiological and clinical observations. *Acta Paediatr* 1999;88:477–82.
174 Goto K, Sato K, Izumi T. Sleep stage transition and changes in autonomic function in newborn infants. *Psychiatry Clin Neurosci* 2000;54:303–4.
175 Hanna BD, Nelson MN, White-Traut RC, *et al*. Heart rate variability in preterm brain-injured and very-low-birth-weight infants. *Biol Neonate* 2000;77:147–55.
176 Rosen H, Craelius W, Curcie D, *et al*. Spectral analysis of heart variability in the newborn infant. *Biol Neonate* 2000;77:224–9.
177 Doussard-Roosevelt JA, McClenny BD, Porges SW. Neonatal cardiac vagal tone and school-age developmental outcome in very low birth weight infants. *Dev Psychobiol* 2001;38:56–66.
178 Andriessen P, Koolen AMP, Berendsen RCM, *et al*. Cardiovascular fluctuations and transfer function analysis in stable preterm infants. *Pediatr Res* 2003;53:89–97.
179 Smith SL. Heart period variability of intubated very-low-birth-weight infants during incubator care and maternal holding. *Am J Crit Care* 2003;12:54–64.
180 Andriessen P, Janssen BJA, Berendsen RCM, *et al*. Cardiovascular autonomic regulation in preterm infants: the effect of atropine. *Pediatr Res* 2004;56:939–46.
181 Smith SL, Doig AK, Dudley WN. Characteristics of heart period variability in intubated very low birth weight infants with respiratory disease. *Neonatology* 2004;86:269–74.
182 Fifer WP, Myers MM, Sahni R. Interactions between sleeping position and feeding on cardiorespiratory activity in preterm infants. *Dev Psychobiol* 2005;47:288–96.
183 Smith SL, Doig AK, Dudley WN. Impaired parasympathetic response to feeding in ventilated preterm babies. *Arch Dis Child Fetal Neonatal Ed* 2005;90:F505–8.
184 Whitley JA, Rich BL. A double-blind randomized controlled pilot trial examining the safety and efficacy of therapeutic touch in premature infants. *Adv Neonat Care* 2008;8:315–33.
185 Cong X, Ludington-Hoe SM, McCain G, *et al*. Kangaroo care modifies preterm infant heart rate variability in response to heel stick pain: pilot study. *Early Hum Dev* 2009;85:561–7.
186 Stock C, Teyssier G, Pichot V, *et al*. Autonomic dysfunction with early respiratory syncytial virus-related infection. *Autonomic Neuroscience* 2010;156:90–5.
187 Indic P, Bloch-Salisbury E, Bednarek F, *et al*. Assessment of cardio-respiratory interactions in preterm infants by bivariate autoregressive modeling and surrogate data analysis. *Early Hum Dev* 2011;87:477–87.
188 Morgan BE, Horn AR, Bergman NJ. Should neonates sleep alone? *Biol Psychiatry* 2011;70:817–25.
189 Leeuwen PV, Geue D, Lange S, *et al*. Relation between neonatal behavioral states and heart rate variability. *Biomedical Engineering Biomedizinische Technik* 2012;57.
190 Matić V, Cherian PJ, Widjaja D, *et al*. Heart rate variability in newborns with hypoxic brain injury. *Adv Exp Med Biol* 2013;789:43–8.
191 Bohanon FJ, Mrazek AA, Shabana MT, *et al*. Heart rate variability analysis is more sensitive at identifying neonatal sepsis than conventional vital signs. *The American Journal of Surgery* 2015;210:661–7.

192 Maeda T, Inoue M, Sekiguchi K, *et al*. Aminophylline-associated irritable behaviour in preterm neonates. *Early Hum Dev* 2016;99:37–41.
193 Drewery ML, Gaitán AV, Spedale SB, *et al*. Maternal n-6 and n-3 fatty acid status during pregnancy is related to infant heart rate and heart rate variability: an exploratory study. *Prostaglandins Leukot Essent Fatty Acids* 2017;126:117–25.
194 Harrison TM, Brown R. Autonomic nervous system function after a Skin-to-Skin contact intervention in infants with congenital heart disease. *J Cardiovasc Nurs* 2017;32:E1–13.
195 Werth J, Long X, Zwartkruis-Pelgrim E, *et al*. Unobtrusive assessment of neonatal sleep state based on heart rate variability retrieved from electrocardiography used for regular patient monitoring. *Early Hum Dev* 2017;113:18.
196 Bhutada A, Sahni R, Rastogi S, *et al*. Randomised controlled trial of thiopental for intubation in neonates. *Arch Dis Child Fetal Neonatal Ed* 2000;82:F34–7.
197 Browne CA, Colditz PB, Dunster KR. Infant autonomic function is altered by maternal smoking during pregnancy. *Early Hum Dev* 2000;59:209–18.
198 DiPietro JA, Costigan KA, Pressman EK, *et al*. Antenatal origins of individual differences in heart rate. *Dev Psychobiol* 2000;37:221–8.
199 Oberlander TF, Grunau RE, Fitzgerald C, *et al*. Does Parenchymal Brain Injury Affect Biobehavioral Pain Responses in Very Low Birth Weight Infants at 32 Weeks' Postconceptional Age? *Pediatrics* 2002;110:570–6.
200 Schrod L, Walter J. Effect of head-up body tilt position on autonomic function and cerebral oxygenation in preterm infants. *Biol Neonate* 2002;81:255–9.
201 Jean-Louis M, Anwar M, Rosen Har'el, *et al*. Power spectral analysis of heart rate in relation to sleep position. *Biol Neonate* 2004;86:81–4.
202 Patural H, Barthelemy JC, Pichot V, *et al*. Birth prematurity determines prolonged autonomic nervous system immaturity. *Clin Auton Res* 2004;14:391–5.
203 Zamora SA, Belli DC, Friedli B, *et al*. 24-Hour electrocardiogram before and during cisapride treatment in neonates and infants. *Biol Neonate* 2004;85:229–36.
204 Andriessen P, Oetomo SB, Peters C, *et al*. Baroreceptor reflex sensitivity in human neonates: the effect of postmenstrual age. *J Physiol* 2005;568:333–41.
205 Gabai N, Cohen A, Mahagney A, *et al*. Arterial blood flow and autonomic function in full-term infants. *Clin Physiol Funct Imaging* 2006;26:127–31.
206 Polson JW, McCallion N, Waki H, *et al*. Evidence for cardiovascular autonomic dysfunction in neonates with coarctation of the aorta. *Circulation* 2006;113:2844–50.
207 Brown L. Heart rate variability in premature infants during feeding. *Biol Res Nurs* 2007;8:283–93.
208 De Rogalski Landrot I, Roche F, Pichot V, *et al*. Autonomic nervous system activity in premature and full-term infants from theoretical term to 7 years. *Auton Neurosci* 2007;136:105–9.
209 John V, Dai H, Talati A, *et al*. Autonomic alterations in cocaine-exposed neonates following orthostatic stress. *Pediatr Res* 2007;61:251–6.
210 Krueger CA, Gyland EA, Theriaque DW. Neonatal heart rate variability and intraventricular hemorrhage: a case study. *Pediatr Nurs* 2008;34:401–4.
211 Ammari A, Schulze KF, Ohira-Kist K, *et al*. Effects of body position on thermal, cardiorespiratory and metabolic activity in low birth weight infants. *Early Hum Dev* 2009;85:497–501.
212 Beuchée A, Carrault G, Bansard JY, *et al*. Uncorrelated randomness of the heart rate is associated with sepsis in sick premature infants. *Neonatology* 2009;96:109–14.
213 Doyle OM, Korotchikova I, Lightbody G, *et al*. Heart rate variability during sleep in healthy term newborns in the early postnatal period. *Physiol Meas* 2009;30:847–60.
214 Harrison TM. Effect of maternal behavior on regulation during feeding in healthy infants and infants with transposition. *J Obstet Gynecol Neonatal Nurs* 2009;38:504–13.
215 Korableva NN, Korablev VA, Tretyakov EN. Holter ECG monitoring combined with record of pneumogram in early neonatal period. *Pediatriya* 2009;88:43–8.
216 Thiriez G, Bouhaddi M, Mourot L, *et al*. Heart rate variability in preterm infants and maternal smoking during pregnancy. *Clin Auton Res* 2009;19:149–56.
217 Tuzcu V, Nas S, Ulusar U, *et al*. Altered heart rhythm dynamics in very low birth weight infants with impending intraventricular hemorrhage. *Pediatrics* 2009;123:810–5.
218 Krueger C, van Oostrom JH, Shuster J. A longitudinal description of heart rate variability in 28—34-Week-Old preterm infants. *Biol Res Nurs* 2010;11:261–8.
219 Aliefendioğlu D, Doğru T, Albayrak M, *et al*. Heart rate variability in neonates with hypoxic ischemic encephalopathy. *Indian J Pediatr* 2012;79:1468–72.
220 Cong X, Cusson RM, Walsh S, *et al*. Effects of skin-to-skin contact on autonomic pain responses in preterm infants. *J Pain* 2012;13:636–45.
221 Harrison TM, Brown RL. Autonomic nervous system function in infants with transposition of the great arteries. *Biol Res Nurs* 2012;14:257–68.
222 Weissman A, Zimmer EZ, Aranovitch M, *et al*. Heart rate dynamics during acute pain in newborns. *Pflugers Arch* 2012;464:593–9.
223 Yiallourou SR, Sands SA, Walker AM, *et al*. Maturation of heart rate and blood pressure variability during sleep in term-born infants. *Sleep* 2012;35:177–86.
224 Goudjil S, Imestouren F, Chazal C, *et al*. Patent ductus arteriosus in preterm infants is associated with cardiac autonomic alteration and predominant parasympathetic stimulation. *Early Hum Dev* 2013;89:631–4.
225 Kaczmarek J, Chawla S, Marchica C, *et al*. Heart rate variability and extubation readiness in extremely preterm infants. *Neonatology* 2013;104:42–8.
226 Mialet-Marty T, Beuchée A, Ben Jmaa W, *et al*. Possible predictors of cardiorespiratory events after immunization in preterm neonates. *Neonatology* 2013;104:151–5.
227 Smith SL, Lux R, Haley S, *et al*. The effect of massage on heart rate variability in preterm infants. *J Perinatol* 2013;33:59–64.
228 Harrison TM, Ferree A. Maternal-Infant interaction and autonomic function in healthy infants and infants with transposition of the great arteries. *Res Nurs Health* 2014;37:490–503.
229 May LE, Scholtz SA, Suminski R, *et al*. Aerobic exercise during pregnancy influences infant heart rate variability at one month of age. *Early Hum Dev* 2014;90:33–8.
230 Schneebaum Sender N, Govindan RB, Sulemanji M, *et al*. Effects of regional brain injury on the newborn autonomic nervous system. *Early Hum Dev* 2014;90:893–6.
231 Ulanovsky I, Haleluya NS, Blazer S, *et al*. The effects of caffeine on heart rate variability in newborns with apnea of prematurity. *J Perinatol* 2014;34:620–3.
232 Yiallourou SR, Poole H, Prathivadi P, *et al*. The effects of dummy/pacifier use on infant blood pressure and autonomic activity during sleep. *Sleep Med* 2014;15:1508–16.
233 Horne RSC, Fyfe KL, Odoi A, *et al*. Dummy/pacifier use in preterm infants increases blood pressure and improves heart rate control. *Pediatr Res* 2016;79:325–32.
234 Isler JR, Thai T, Myers MM, *et al*. An automated method for coding sleep states in human infants based on respiratory rate variability. *Dev Psychobiol* 2016;58:1108–15.
235 Stéphan-Blanchard E, Chardon K, Djeddi D-D, *et al*. The dynamics of cardiac autonomic control in sleeping preterm neonates exposed in utero to smoking. *Clin Neurophysiol* 2016;127:2871–7.
236 Pados BF, Thoyre SM, Knafl GJ, *et al*. Heart rate variability as a feeding intervention outcome measure in the preterm infant. *Adv Neonat Care* 2017;17:E10–20.
237 Schneebaum Sender N, Govindan RB, Whitehead MT, *et al*. Cerebral modulation of the autonomic nervous system in term infants. *J Perinatol* 2017;37:558–62.
238 Parga JJ, Bhatt RR, Kesavan K, *et al*. A prospective observational cohort study of exposure to womb-like sounds to stabilize breathing and cardiovascular patterns in preterm neonates. *J Matern Fetal Neonatal Med* 2018;31:2245–51.
239 Ranger A, Helmert E, Bott TS, *et al*. Physiological and emotional effects of pentatonic live music played for preterm neonates and their mothers in the newborn intensive care unit: a randomized controlled trial. *Complement Ther Med* 2018;41:240–6.
240 Šapina M, Kośmider M, Kramarić K, *et al*. Asymmetric detrended fluctuation analysis in neonatal stress. *Physiol Meas* 2018;39:085006.
241 Statello R, Carnevali L, Alinovi D, *et al*. Heart rate variability in neonatal patients with seizures. *Clinical Neurophysiology* 2018;129:2534–40.
242 Chiarelli AM, Mahmoudzadeh M, Low KA, *et al*. Assessment of cerebrovascular development and intraventricular hemorrhages in preterm infants with optical measures of the brain arterial pulse wave. *J Cereb Blood Flow Metab* 2019;39:466–80.
243 de Souza Filho LFM, de Oliveira JCM, Ribeiro MKA, *et al*. Evaluation of the autonomic nervous system by analysis of heart rate variability in the preterm infants. *BMC Cardiovasc Disord* 2019;19:198.

244 Govindan RB, Massaro A, Vezina G, *et al*. Identifying an optimal epoch length for spectral analysis of heart rate of critically-ill infants. *Comput Biol Med* 2019;113:103391.
245 Hasegawa Y, Hoshiyama M. Effect of environmental music on autonomic function in infants in intensive and growing care units. *J Neonatal Perinatal Med* 2019;13:395–401.
246 Huvanandana J, Thamrin C, McEwan AL, *et al*. Cardiovascular impact of intravenous caffeine in preterm infants. *Acta Paediatr* 2019;108:423–9.
247 Shayani LA, da Cruz CJ, Porto LGG, *et al*. Cardiac autonomic function in the first hours of postnatal life: an observational cross-sectional study in term neonates. *Pediatr Cardiol* 2019;40:1703–8.
248 Israeli-Mendlovic H, Mendlovic J, Zuk L, *et al*. Reproducibility of 24-h heart rate variability measures in preterm infants born at 28–32 weeks of gestation. *Early Hum Dev* 2020;148:105117.
249 Lindh V, Wiklund U, Håkansson S. Assessment of the effect of EMLA® during venipuncture in the newborn by analysis of heart rate variability. *Pain* 2000;86:247–54.
250 Sahni R, Schulze KF, Kashyap S, *et al*. Maturational changes in heart rate and heart rate variability in low birth weight infants. *Dev Psychobiol* 2000;37:73–81.
251 Griffin MP, Moorman JR. Toward the early diagnosis of neonatal sepsis and sepsis-like illness using novel heart rate analysis. *Pediatrics* 2001;107:97–104.
252 Lake DE, Richman JS, Griffin MP, *et al*. Sample entropy analysis of neonatal heart rate variability. *Am J Physiol Regul Integr Comp Physiol* 2002;283:R789–97.
253 Mehta SK, Super DM, Connuck D, *et al*. Heart rate variability in healthy newborn infants. *Am J Cardiol* 2002;89:50–3.
254 Oberlander TF, Eckstein Grunau R, Fitzgerald C, *et al*. Prolonged prenatal psychotropic medication exposure alters neonatal acute pain response. *Pediatr Res* 2002;51:443–53.
255 Hernandez-Reif M, Diego M, Field T. Instrumental and vocal music effects on EEG and EKG in neonates of depressed and non-depressed mothers. *Infant Behavior and Development* 2006;29:518–25.
256 Kaltman JR, Hanna BD, Gallagher PR, *et al*. Heart rate variability following neonatal heart surgery for complex congenital heart disease. *Pacing and Clinical Electrophysiology* 2006;29:471–8.
257 Diego MA, Field T, Hernandez-Reif M, *et al*. Preterm infant massage elicits consistent increases in vagal activity and gastric motility that are associated with greater weight gain. *Acta Paediatr* 2007;96:1588–91.
258 Patural H, Pichot V, Jaziri F, *et al*. Autonomic cardiac control of very preterm newborns: a prolonged dysfunction. *Early Hum Dev* 2008;84:681–7.
259 Schäffer L, Burkhardt T, Müller-Vizentini D, *et al*. Cardiac autonomic balance in small-for-gestational-age neonates. *Am J Physiol Heart Circ Physiol* 2008;294:H884–90.
260 Franck LS, Ridout D, Howard R, *et al*. A comparison of pain measures in newborn infants after cardiac surgery. *Pain* 2011;152:1758–65.
261 Babaoglu K, Seringec M, Altun G. Effects of umbilical venous catheters on arrhythmia and heart rate variability in premature newborns. *Turk Pediatri Arsivi* 2013;48:131–7.
262 Johnston C, Campbell-Yeo M, Rich B, *et al*. Therapeutic touch is not therapeutic for procedural pain in very preterm neonates: a randomized trial. *Clin J Pain* 2013;29:824–9.
263 Stone ML, Tatum PM, Weitkamp J-H, *et al*. Abnormal heart rate characteristics before clinical diagnosis of necrotizing enterocolitis. *J Perinatol* 2013;33:847–50.
264 Arnon S, Diamant C, Bauer S, *et al*. Maternal singing during kangaroo care led to autonomic stability in preterm infants and reduced maternal anxiety. *Acta Paediatr* 2014;103:1039–44.
265 Fyfe KL, Yiallourou SR, Wong FY, *et al*. The effect of gestational age at birth on post-term maturation of heart rate variability. *Sleep* 2015;38:1635–44.
266 Wang Y-L, Kuo H-C, Wang L-Y, *et al*. Design of wireless multi-parameter monitoring system for oral feeding of premature infants. *Med Biol Eng Comput* 2016;54:1061–9.
267 Jmaa WB, Hernandez AI, Sutherland MR. Cardio-Respiratory events and inflammatory response after primary immunization in preterm infants. *Pediatric Infectious Disease Journal* 2017;36:988–94.
268 Jones L, Fabrizi L, Laudiano-Dray M, *et al*. Nociceptive cortical activity is dissociated from nociceptive behavior in newborn human infants under stress. *Curr Biol* 2017;27:3846–51.
269 Goel N, Chakraborty M, Watkins WJ, *et al*. Predicting extubation Outcomes-A model incorporating heart rate characteristics index. *J Pediatr* 2018;195:53–8.
270 Schierz IAM, Pinello G, Piro E, *et al*. Transitional hemodynamics in infants of diabetic mothers by targeted neonatal echocardiography, electrocardiography and peripheral flow study. *J Matern Fetal Neonatal Med* 2018;31:1578–85.
271 Takatani T, Takahashi Y, Yoshida R, *et al*. Relationship between frequency spectrum of heart rate variability and autonomic nervous activities during sleep in newborns. *Brain Dev* 2018;40:165–71.
272 Weaver B, Guerreso K, Conner EA, *et al*. Hemodynamics and perfusion in premature infants during transfusion. *AACN Adv Crit Care* 2018;29:126–37.
273 Gomes ELdeFD, Santos CMD, Santos AdaCS, *et al*. Autonomic responses of premature newborns to body position and environmental noise in the neonatal intensive care unit. *Rev Bras Ter Intensiva* 2019;31:296–302.
274 Porto DC, Sande LS, Perrone ACB, *et al*. The entropy of Rr intervals is associated to gestational age in full-term newborns with adequate weight for gestational age. *J Matern Fetal Neonatal Med* 2021;34:1–6.
275 Wnuk W. [Heart rate variability in healthy newborns and in newborns with congenital heart defect]. *Roczniki Pomorskiej Akademii Medycznej w Szczecinie* 2000;46:151–64.
276 Grunau RE, Oberlander TF, Whitfield MF, *et al*. Demographic and Therapeutic Determinants of Pain Reactivity in Very Low Birth Weight Neonates at 32 Weeks' Postconceptional Age. *Pediatrics* 2001;107:105–12.
277 Morison SJ, Grunau RE, Oberlander TF, *et al*. Relations between behavioral and cardiac autonomic reactivity to acute pain in preterm neonates. *Clin J Pain* 2001;17:350–8.
278 Kovatchev BP, Farhy LS, Cao H, *et al*. Sample asymmetry analysis of heart rate characteristics with application to neonatal sepsis and systemic inflammatory response syndrome. *Pediatr Res* 2003;54:892–8.
279 Moehler E, Kagan J, Parzer P, *et al*. Relation of behavioral inhibition to neonatal and infant cardiac activity, reactivity and habituation. *Pers Individ Dif* 2006;41:1349–58.
280 Cohen M, Brown DR, Myers MM. Cardiorespiratory measures before and after feeding challenge in term infants are related to birth weight. *Acta Paediatr* 2009;98:1183–8.
281 Weissman A, Aranovitch M, Blazer S, *et al*. Heel-lancing in newborns: behavioral and spectral analysis assessment of pain control methods. *Pediatrics* 2009;124:e921–6.
282 Poehlmann J, Schwichtenberg AJM, Bolt DM, *et al*. Infant physiological regulation and maternal risks as predictors of dyadic interaction trajectories in families with a preterm infant. *Dev Psychol* 2011;47:91–105.
283 Raynor LL, Saucerman JJ, Akinola MO, *et al*. Cytokine screening identifies NICU patients with gram-negative bacteremia. *Pediatr Res* 2012;71:261–6.
284 Alonzo CJ, Fairchild KD. Dexamethasone effect on heart rate variability in preterm infants on mechanical ventilation. *J Neonatal Perinatal Med* 2017;10:425–30.
285 Goulding RM, Stevenson NJ, Murray DM, *et al*. Heart rate variability in hypoxic ischemic encephalopathy during therapeutic hypothermia. *Pediatr Res* 2017;81:609–15.
286 Mckenzie K, Dissanayake H, McMullan R, *et al*. Quantity and quality of carbohydrate intake during pregnancy, newborn body fatness and cardiac autonomic control: conferred cardiovascular risk? *Nutrients* 2017;9:19.
287 Schierz IAM, Pinello G, Piro E, *et al*. Transitional hemodynamics in infants of diabetic mothers by targeted neonatal echocardiography, electrocardiography and peripheral flow study. *J Matern Fetal Neonatal Med* 2018;31:1578–85.
288 Pini N, Lucchini M, Fifer WP, *et al*. A point process framework for the characterization of sleep states in early infancy. *Annu Int Conf IEEE Eng Med Biol Soc* 2019;2019:3645–8.
289 Mehta SK, Super DM, Salvator A, *et al*. Heart rate variability in cocaine-exposed newborn infants. *Am Heart J* 2001;142:828–32.
290 Mehta SK, Super DM, Salvator A, *et al*. Heart rate variability by triangular index in infants exposed prenatally to cocaine. *Ann Noninvasive Electrocardiol* 2002;7:374–8.
291 Evsiukova IN, Kondrat'eva MV, Medvenskaia VV, *et al*. [Central hemodynamic parameters and cardiointervalogram features in infants during early postnatal adaptation]. *Fiziol Cheloveka* 2004;30:545–50.
292 Griffin MP, Lake DE, O'Shea TM, *et al*. Heart rate characteristics and clinical signs in neonatal sepsis. *Pediatr Res* 2007;61:222–7.
293 Fairchild KD, Sinkin RA, Davalian F, *et al*. Abnormal heart rate characteristics are associated with abnormal neuroimaging and outcomes in extremely low birth weight infants. *J Perinatol* 2014;34:375–9.
294 Lucchini M, Pini N, Fifer WP, *et al*. Characterization of cardiorespiratory phase synchronization and directionality in late premature and full term infants. *Physiol Meas* 2018;39:11.

295 Burtchen N, Myers MM, Lucchini M, *et al*. Autonomic signatures of late preterm, early term, and full term neonates during early postnatal life. *Early Hum Dev* 2019;137:104817.
296 Griffin MP, O'Shea TM, Bissonette EA, *et al*. Abnormal heart rate characteristics preceding neonatal sepsis and sepsis-like illness. *Pediatr Res* 2003;53:920–6.
297 Griffin MP, O'Shea TM, Bissonette EA, *et al*. Abnormal heart rate characteristics are associated with neonatal mortality. *Pediatr Res* 2004;55:782–8.
298 Griffin MP, Lake DE, Bissonette EA, *et al*. Heart rate characteristics: novel physiomarkers to predict neonatal infection and death. *Pediatrics* 2005;116:1070–4.
299 Griffin MP, Lake DE, Moorman JR. Heart rate characteristics and laboratory tests in neonatal sepsis. *Pediatrics* 2005;115:937–41.
300 Xiao Y, Griffin MP, Lake DE, *et al*. Nearest-Neighbor and logistic regression analyses of clinical and heart rate characteristics in the early diagnosis of neonatal sepsis. *Med Decis Making* 2010;30:258–66.
301 Coggins SA, Weitkamp J-H, Grunwald L, *et al*. Heart rate characteristic index monitoring for bloodstream infection in an NICU: a 3-year experience. *Arch Dis Child Fetal Neonatal Ed* 2016;101:F329–32.
302 Fairchild KD, Lake DE, Kattwinkel J, *et al*. Vital signs and their cross-correlation in sepsis and NEC: a study of 1,065 very-low-birth-weight infants in two NICUs. *Pediatr Res* 2017;81:315–21.
303 Myers MM, Elliott AJ, Odendaal HJ, *et al*. Cardiorespiratory physiology in the safe passage study: protocol, methods and normative values in unexposed infants. *Acta Paediatr* 2017;106:1260–72.