# Beyond CRP: FeNO and RDW as Complementary Biomarkers Linking Sleep Health and Inflammation

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## Abstract

**Background**
Poor sleep contributes to chronic inflammation, increasing long-term disease risk. Prior studies have primarily relied on C-reactive protein (CRP), offering a limited view of inflammatory activity.
This research introduces two additional biomarkers:

- **Fractional exhaled nitric oxide (FeNO):** reflects airway inflammation
- **Red blood cell distribution width (RDW):** indicates oxidative stress–related inflammation

**Objective**
To investigate how poor sleep contributes to chronic inflammation by incorporating multiple bio-markers beyond C-reactive protein (CRP).
**Challenges**
Overreliance on single inflammatory markers (CRP).
Incomplete understanding of distinct inflammation pathways.

## Literature Review Procedure

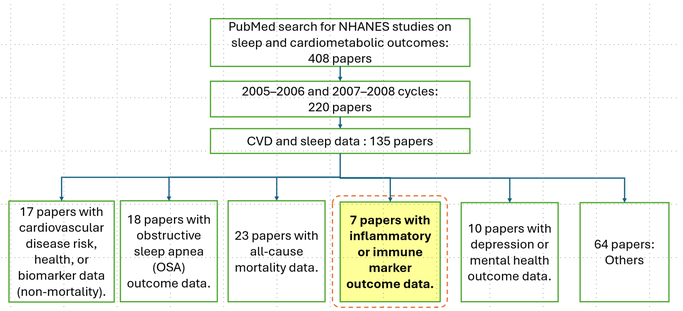


**Figure 1**: Overview of the literature review steps used to identify studies connecting sleep health with inflammation and cardiometabolic outcomes

## Research Gap

| | CRP | RDW | FENO |
|---|---|---|---|
| Sleep Quality | **[1, 2, 3]** | - | - |
| Sleep Duration | **[2, 4]** | **[4]** | **[5]** |
| Sleep Disorder | **[4, 4]** | **[4]** | - |

**Figure 2**: Identified gaps in current research papers regarding additional biomarkers

## Data Description

| Category | Variable |
|---|---|
| Sleep Quality | Frequency of trouble falling asleep<br>Frequency of waking during the night<br>Frequency of waking too early in morning<br>Frequency of feeling unrested during the day<br>Frequency of feeling overly sleepy during the day<br>Frequency of not getting enough sleep<br>Frequency of leg jerks while sleeping<br>Frequency of legs cramping while sleeping |
| Sleep Duration | Sleep Hours – Spline<br>Sleep Hours |
| Sleep Disorder | Trouble Sleeping<br>Sleep Disorder<br>Sleep Apnea<br>Insomnia<br>Restless Legs<br>Other Disorders |
| Outcomes | Red Cell Distribution (%)<br>C-Reactive Protein (>1 mg/dL = elevated)<br>Mean, 2 reproducible FENO measures (ppb) |
| Covariates | Age<br>Gender<br>BMI<br>Pregnancy Status |

**Figure 3**: Sleep, health, and demographic data were grouped into categories (e.g., sleep quality, duration, disorders, inflammation markers). Sleep-related questions were combined into a single Sleep Quality score: “Often” = poor, “Sometimes” = moderate, others = good.

## Method

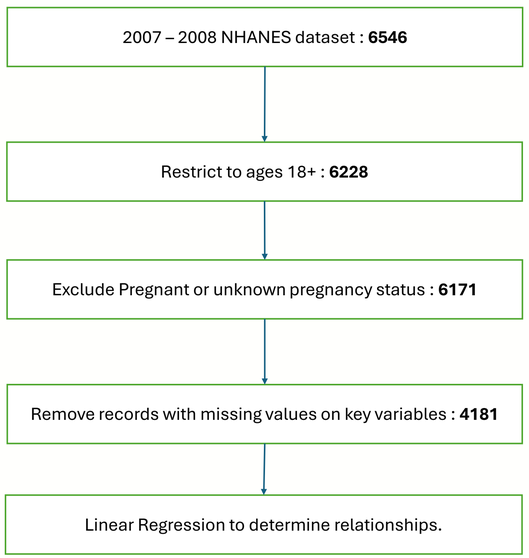


**Figure 4**: Data Pre-Processing Flowchart

## Results

| | β | P-value |
|---|---|---|
| Sleep Quality: Moderate vs Good | 0.0306 | 0.4722 |
| Sleep Quality: Poor vs Good | 0.1090 | 0.0139* |
| Sleep Hours (continuous) | 0.0087 | 0.0553 |
| Short Sleep (<6 h) vs Normal | 0.1415 | 0.0033** |
| Long Sleep (>8 h) vs Normal | 0.2085 | 0.0046** |
| Sleep Disorder | −0.0919 | 0.3580 |

**Figure 5**: Poor sleep quality was linked with higher levels of CRP (log-transformed), indicating greater overall inflammation.

| | β | P-value |
|---|---|---|
| Sleep Quality: Moderate vs Good | 0.0014 | 0.9589 |
| Sleep Quality: Poor vs Good | 0.1409 | <0.001*** |
| Sleep Hours (continuous) | 0.0019 | 0.5221 |
| Short Sleep (<6 h) vs Normal | 0.1022 | 0.001*** |
| Long Sleep (>8 h) vs Normal | 0.0661 | 0.165 |
| Sleep Disorder | 0.0944 | 0.0272* |

**Figure 6**: Poor or short sleep and reported sleep disorders were tied to higher FeNO (log-transformed), reflecting elevated airway inflammation.

| | β | P-value |
|---|---|---|
| Sleep Quality: Moderate vs Good | 0.0502 | 0.2358 |
| Sleep Quality: Poor vs Good | 0.0786 | 0.0743 |
| Sleep Hours (continuous) | 0.0037 | 0.4145 |
| Short Sleep (<6 h) vs Normal | 0.1781 | <0.001*** |
| Long Sleep (>8 h) vs Normal | 0.2162 | 0.0031** |
| Sleep Disorder | 0.1247 | 0.0574 |

**Figure 7:** Sleep duration was associated with higher Red Cell Distribution Width (RDW), suggesting increased systemic inflammation with abnormal sleep length.

**Asterisks indicate significance levels**

| | |
|---|---|
| p ≤ 0.05 | * Significant |
| p ≤ 0.01 | ** Very Significant |
| p ≤ 0.001 | *** Highly Significant |

## Conclusion

- This study examined links between **sleep quality, sleep duration, and sleep disorders** with **inflammation markers**.
- **Poor sleep quality** and **abnormal sleep duration** (<6h or >8h) were significantly associated with **higher C-reactive protein (CRP)**, indicating greater overall inflammation.
- **Sleep disorders** showed **no significant association with CRP**, suggesting CRP alone does not capture inflammation from sleep disorders.
- **Additional biomarkers** revealed stronger associations:
  - **Red Cell Distribution Width (RDW):** Elevated with sleep disorders and short sleep, indicating systemic inflammation.
  - **Fractional exhaled nitric oxide (FeNO):** Higher in poor or abnormal sleep, reflecting airway inflammation.
- Combining **CRP, RDW, and FeNO** provides a more comprehensive view of **sleep-related inflammation**, showing more consistent patterns than CRP alone.

## References

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