

# Visit-to-Visit Blood Pressure Variability in Cardiovascular Disease

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**Abstract:** Visit-to-visit blood pressure variability (BPV) is associated with cardiovascular disease (CVD), independently of mean blood pressure (BP). However, in real world clinical practice, this phenomenon is frequently considered as random fluctuation. This review aimed to investigate the differences among studies investigating visit-to-visit BPV and CVD using electronic health record (EHR) and clinical trial data. Our review suggests that BP values in clinical trial data are derived using a stricter protocol compared to EHR data. Furthermore, there was no consensus on metrics used in estimation of BPV.

**Keywords:** blood pressure variability, electronic health record, clinical trial data

## 1. Introduction

BPV is an independent risk factor of CVD (1–5). However, BPV at serial clinic visits are frequently considered as random fluctuations (6). BPV from EHR are considered as data that are collected with varying reliability compared to BPV data from clinical trials. Although previous studies analyzing BPV from EHR suggest strong association with CVD (2,3), BPV application in real-world clinical practice is still challenging. Therefore, this review aimed to explain the differences among studies investigating visit-to-visit BPV and CVD using EHR and clinical trial data.

## 2. Methods

Relevant studies were extracted from PubMed Central, EMBASE, and CINAHL published between 2014–2022 with the following keywords (‘blood pressure variability’ OR ‘blood pressure fluctuation’ OR ‘long term blood pressure variability’) AND (‘cardiovascular disease’ OR ‘myocardial infarction’ OR ‘heart failure’ OR ‘atrial fibrillation’ OR ‘cerebrovascular disease’ OR ‘peripheral artery disease’).

## 3. Results

Studies investigating the association between visit-to-visit BPV and CVD have been conducted using different data sources such as clinical trial, claim, and electronic health record data. BP values in clinical trial data are derived using a stricter protocol of BP measurement compared to EHR data. Clinical trial investigators provide training on BP

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measurement and standardized tools to minimize observer bias in BP measurements. Conversely, in EHR data observer bias cannot be avoided.

#### 4. Discussion

Multiple BP measurements are essential in BPV estimation, a previous study suggested a minimum of six BP readings for estimation of visit-to-visit BPV (7). Post hoc analysis of clinical trial data utilized 3-5 BP readings for visit-to-visit BPV analysis (1,4,5). However, BPV estimation from EHR data used more BP measurements than that from clinical trial data. Previous studies using EHR applied at least 5 BP measurements (2,3). The optimal duration of follow-up for CVD risk investigation is still unclear. BPV studies using clinical trial data has shorter outcome follow up duration compared to EHR.

Our review also identified that there is no consensus on metrics used in estimation of visit-to-visit BPV. Standard deviation (SD) is the most used BPV metric in studies using EHR or clinical trial data. Average real value (ARV) weights the between-reading time intervals and takes the order of the BP measurements into account. Variability independent of mean (VIM) is another BPV metric that is uncorrelated with mean values. It has been suggested that VIM can be utilized in real-world clinical settings and is robust to the lower fidelity of BP measurements recorded outside of clinical trials (8).

#### 5. Conclusions

In summary, studies investigating the association of BPV and CVD using clinical trial data have stricter protocols in obtaining BP measurements compared to studies using EHR data. There is also no consensus on the BPV metric among these studies.

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