

# Effect of routinely tailoring anti-hypertensive therapy to hemodynamic profile in primary care

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## ABSTRACT

**PURPOSE:** Controlling blood pressure (BP) reduces cardiovascular morbidity and mortality but is often not achieved in clinical practice. Tailoring therapy to an individual's hemodynamic profile using impedance cardiography (ICG) might attain efficient, effective BP control.

**METHODS:** An observational study of hypertensive patients managed by two large US primary care groups (PriMED and Premier) used therapeutic algorithms based on ICG-derived hemodynamics linked to clinical decision support tools to promote physician and patient engagement and medication adherence. The main outcome of interest was BP control according to contemporary (2014) guidelines (<140/<90 mmHg). A subset of PriMED patients was followed for six years, to evaluate clinical outcomes. Clinical information was extracted from electronic medical records.

**RESULTS:** Of 14,058 patients, median (interquartile range (IQR)) age was 62 (51 to 71) years, 50% were women, and initial systolic and diastolic BP were 152 (145-162) mmHg and 90 (80-98) mmHg. The hemodynamic profile was vasoconstriction for 6,609 (47%) patients, hyperdynamic for 3,365 (24%) and mixed for 4,084 (29%). For PriMED, 92% achieved BP control at the second follow-up visit. For Premier, 81% achieved control at second follow-up, and 91% by the fourth visit. Annual control rates thereafter for both groups ranged from 82% to 93%. For 2,955 patients continuously managed by PriMED between 2016-2022, annual rates of myocardial infarction and stroke were 0.30% and 0.43%.

**CONCLUSIONS:** Tailoring anti-hypertensive therapy according to hemodynamic profile in primary care is feasible, providing rapid and sustained BP control with low rates of myocardial infarction and stroke.

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## Introduction

Most people will develop hypertension, but the diagnosis is often missed and when diagnosed, blood pressure (BP) control is often poor.<sup>1</sup> Between 2017 and 2020, of 95 million US adults diagnosed with hypertension, only 56% achieved a BP of <140/90 mmHg and only 28% a BP <130/80 mmHg.<sup>2</sup> Consequently, hypertension continues to cause substantial disability and mortality. Improving the management of hypertension is an international healthcare imperative.<sup>3</sup>

Hypertension is fundamentally a hemodynamic problem, but current guidelines recommend medications based mainly on age, cardiovascular risk profile and end-organ damage, rather than on hemodynamics.<sup>3,4</sup> Hypertension is caused by a high peripheral vascular resistance or raised cardiac output or both. Giving beta-blockers to patients with a high peripheral vascular resistance may be ineffective or harmful. Similarly, vasodilators may be inappropriate for patients with a low peripheral resistance.

Hemodynamics can be measured non-invasively, quickly and inexpensively using impedance cardiography (ICG). Selecting the most appropriate anti-hypertensive therapy tailored to an individual's hemodynamic profile might reduce the number of medications and office visits required to control BP.

Over the last two decades, two groups of US primary care physicians have integrated ICG measurements into their routine workflow for hypertension to provide hemodynamically tailored treatment for >14,000 patients. We share their experience in the hope that it might stimulate interest in this approach to improving patient care.

## Methods

Between 2014 and 2024, patients with systolic BP  $\geq 140$  mmHg or diastolic BP  $\geq 90$  mmHg on repeated office measurements were enrolled in hypertension quality improvement programs of two large primary care groups in the USA; PriMED Physicians (Dayton, OH) and Premier Medical Associates (Pittsburgh, PA). Management involved the following steps (Fig. 1):

- For patients with elevated BP, repeated measurements were taken to confirm the diagnosis according to American Heart Association (AHA) guidelines<sup>4</sup>

- If either systolic BP was  $\geq 140$  mmHg or diastolic BP was  $\geq 90$  mmHg, the criteria used to define hypertension by the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) between 2014 and 2024<sup>5,6</sup>, hemodynamic profile was assessed using a commercially available ICG system (NICaS InnovaMed Sphere, Fall River MA).<sup>7,8</sup> This was done using two specialized electrodes applied wrist-to-ankle with the patient reclining (Fig. 1). Three consecutive 20-second recordings

were averaged. Height, weight and BP were entered manually to allow measurements to be indexed to body surface area (BSA). The ICG system calculates mean arterial pressure (MAP), cardiac output indexed to BSA (CI), cardiac power index (CPI), which is derived from CI and MAP and declines when heart function is impaired, total peripheral resistance indexed to BSA (TPRI), heart rate and total body water. Formulas for deriving these variables are provided in [Supplementary Table 1](#) (available online).

- Demographic and clinical data were obtained from primary care electronic medical records (EMR). Prescribing information was not made available for these analyses. Patients could already be receiving anti-hypertensive agents if, for instance, transferring from another clinical practitioner.

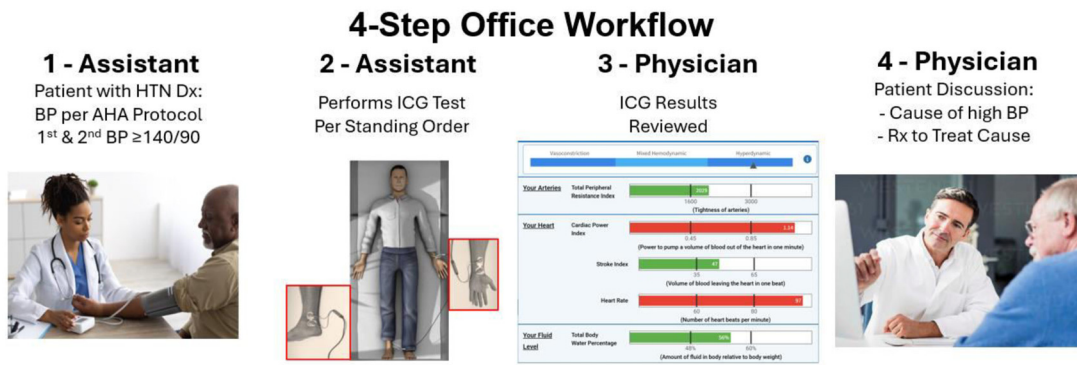
- Hemodynamic profiles were classified as:

- **Vasoconstriction**, defined as TPRI  $> 3000$  dynes\*sec/ $m^5*m^2$  and CPI  $< 0.85$  watts/ $m^2$ , indicating a relatively low CI for a given MAP.
- **Mixed Hemodynamic Profile**, TPRI generally  $\geq 3000$  dynes\*sec/ $m^5*m^2$  and CPI  $\geq 0.85$  watts/ $m^2$ , indicating a relatively preserved CI for a given MAP.
- **Hyperdynamic**, TPRI  $< 3000$  dynes\*sec/ $m^5*m^2$  and CPI  $> 0.85$  watts/ $m^2$ , driven either by a high heart rate or a high stroke volume, the amount of blood pumped out in a single heartbeat.

- Printed ICG reports, and subsequently a clinical decision support application integrated with patients' EMRs (MedsEngine—MedsEngine LLC, USA), were used to generate reports, including hemodynamic results and recommended therapy.
- The therapeutic goal was to achieve a BP of <140/<90 mmHg.<sup>9</sup> For vasoconstriction, angiotensin converting enzyme inhibitors (ACEi), angiotensin receptor blockers

## CLINICAL SIGNIFICANCE

- Hemodynamics were measured routinely using non-invasive impedance cardiography in 14,058 patients with hypertension in two large US primary care groups.
- Physicians were advised to choose therapy appropriate to hemodynamic profile; vasodilators for vasoconstriction (47% of patients); beta-blockers or non-dihydropyridine calcium channel blockers for hyperdynamic profiles (24% of patients); and vasodilating beta-blockers or non-dihydropyridine calcium channel blockers for mixed hemodynamic profiles.
- Tailoring treatment to hemodynamic profile was associated with rapid and sustained attainment of contemporary (2014) blood pressure targets and low rates of myocardial infarction and stroke.



**Fig. 1** Illustration of the workflow, including initial evaluation and confirmation of inadequate blood pressure control using a standard sphygmomanometer, triggering an evaluation by impedance cardiography (ICG) (usually wrist-to-ankle in a reclining position), physician review of the results and therapeutic recommendations followed by a discussion with the patient. ICG passes a low-magnitude, high-frequency current imperceptible to the patient between electrodes.<sup>7,8</sup> With each heartbeat, blood volume in the aorta, which has a low impedance, changes in proportion to stroke volume.

(ARB), dihydropyridine calcium channel blockers (dhCCB), and thiazides were recommended. For mixed hemodynamic profiles, vasodilating beta-blockers and non-dihydropyridine calcium channel blockers (non-dhCCB) were recommended. For hyperdynamic profiles, beta-blockers and non-dhCCB were recommended. The final clinical decision was made by the physician.

- Reports were shared with patients to illustrate the hemodynamic reason for their hypertension and why recommended medications were appropriate. Patients were encouraged to take BP measurements at home, to follow a “Dietary Approaches to Stop Hypertension” (DASH) diet and to make appropriate life-style modifications.<sup>10</sup>
- Rates of BP control were tracked using EMR. Patients were re-evaluated monthly until BP was at goal and then every six months. BP was also checked at office visits for any reason. ICG testing was repeated if BP  $\geq 140/90$  mmHg persisted or recurred, to determine whether to up-titrate an existing medication or add/change therapeutic classes.
- PriMED used the “Healthcare Effectiveness Data and Information Set” (HEDIS) to define BP control, which is the last BP measured in each year. Premier used the last BP in each month when measured, as required by one of their major insurance providers.

A subset of PriMED patients was followed continuously between 2016 and 2022 to assess longer-term BP control and outcomes, including myocardial infarction or stroke events, although information on deaths was not collected systematically.

## Statistics

Data are shown as median and quartiles for continuous data and as percentages for categorical data and compared across hemodynamic profiles using Kruskal-Wallis tests.

Categorical variables, including sex, race, age categories, and hemodynamic threshold indicators (e.g., systolic BP  $\geq 160$  mmHg), were reported as counts and percentages and compared across profiles using chi-square tests with  $2 \times 3$  contingency tables.

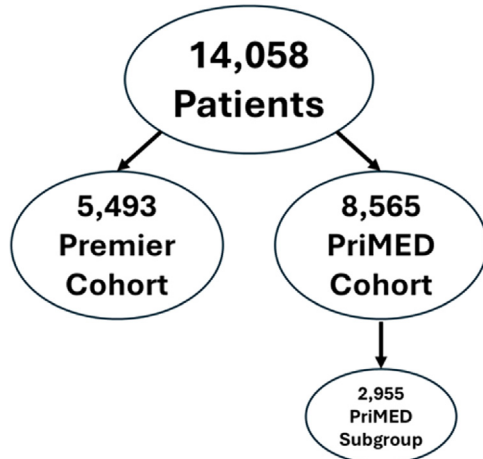
All *P* values correspond to global comparisons across the three hemodynamic profiles. Patient visits were tracked using primary care EMRs. Patients were censored at the time of the last entry into the EMR, which could include a BP visit, other chronic care visit, acute care visit, or wellness exam.

## Results

Altogether (Fig. 2), 14,058 patients (8,565 from PriMED and 5,493 from Premier) with hypertension were evaluated by ICG, of whom 28% were aged  $\geq 70$  years, 50% were women and 14% were Black (Table 1). At the first ICG assessment, median systolic and diastolic BP were respectively, 152 (145-162) mmHg and 90 (80-98) mmHg; 4,666 (33%) patients had a systolic BP  $\geq 160$  mmHg and 2,916 (21%) had a diastolic BP  $\geq 100$  mmHg. The hemodynamic profiles were vasoconstriction for 47% of patients, a mixed profile for 29% and a hyperdynamic profile for 24% (Fig. 3). Older patients, men, and Black patients had a higher proportion with vasoconstriction (Fig. 4). Although there were statistically significant differences in many characteristics among hemodynamic groups, these were small and not useful for imputing hemodynamic profile.

For PriMED patients, 74% achieved BP control at the first follow-up visit and 92% by the second. Annual control rates, as defined by HEDIS, ranged from 91% to 93% between 2014 and 2023. For Premier patients, 62% achieved BP control at the first follow-up visit and 81%, 85%, and 91%, respectively, by the second, third and fourth visits. Control rates, as defined by end of month reporting, ranged from 82% to 90% between 2018 and 2023. A hyperdynamic profile required more follow-up visits to achieve

## Patient Populations



**Fig. 2** Diagram showing provenance of the various patient cohorts contributing to this analysis.

BP control ([Fig. 5](#)). Rates of BP control were approximately 90% for all racial groups.

A subset of 2,955 PriMED patients with hypertension was continuously followed between 2016-2022. This cohort had similar demographic and hemodynamic profiles as the overall population ([Supplementary Table 2](#); [Supplementary](#)

[Fig. 1](#)). BP was measured when patients came to the office for routine follow-up for hypertension, or any other clinical reason, and was <140/90 mmHg on 88% of 53,532 visits. Although more recent recommendations are to achieve a BP of <130/<80 mmHg, it was not the goal of this quality improvement program. Nonetheless, a systolic BP of <130 mmHg was reported on 45% of visits and a diastolic BP <80 mmHg on 50% of visits with both criteria met on 29% of visits.

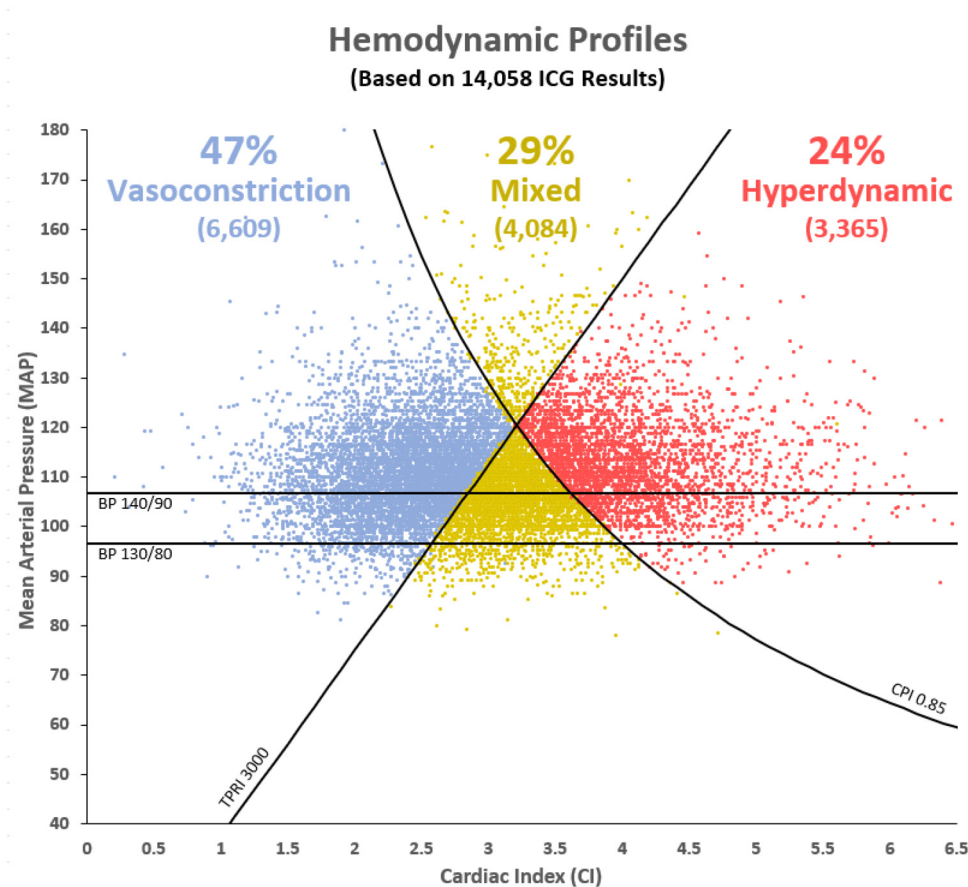
Altogether, 3,091 repeat ICGs were done on 1,482 patients in the PriMED subset, either because BP control was inadequate after the initial intervention or control was lost during follow-up. The hemodynamic profile was unchanged between the first and second ICG assessment in 51% of cases ([Supplementary Table 3](#)). Many patients switched to or from a mixed hemodynamic profile, 25% of patients switched from an initial hyperdynamic to a vasoconstriction profile, but only 10% of patients with vasoconstriction on the initial ICG had a hyperdynamic profile on the second ICG.

In the PriMED subset of patients with continuous long-term follow-up, annual rates for myocardial infarction and stroke were respectively 0.30 (95% CI 0.22 to 0.39) % and 0.43 (95% CI 0.34 to 0.54) %. Rates tended to be lower for those with a hyperdynamic profile ([Table 2](#)). Event rates compared favorably with those reported for the Systolic Blood Pressure Intervention Trial (SPRINT) that

**Table 1** Baseline characteristics classified by hemodynamic profile (data shown as numbers with percentage or median with quartiles).

|                                            | Overall             | Vasoconstriction    | Mixed               | Hyperdynamic        | P       |
|--------------------------------------------|---------------------|---------------------|---------------------|---------------------|---------|
| N=                                         | 14,058              | 6,609 (47%)         | 4,084 (29%)         | 3,365 (24%)         | n/a     |
| PriMED No. (%)                             | 8,565 (61%)         | 3,736 (44%)         | 2,416 (34%)         | 2,413 (20%)         | n/a     |
| Premier No. (%)                            | 5,493 (39%)         | 2,873 (52%)         | 1,668 (30%)         | 952 (17%)           | n/a     |
| Age (years)                                | 62 (51 to 71)       | 64 (53 to 74)       | 62 (51 to 71)       | 57 (46 to 66)       | <0.0001 |
| Age 18-49 years No. (%)                    | 3,367 (24%)         | 1,330 (20%)         | 915 (22%)           | 1,122 (33%)         | <0.0001 |
| Age 50-69 years No. (%)                    | 6,767 (48%)         | 3,041 (46%)         | 2,024 (50%)         | 1,702 (51%)         | <0.0001 |
| Age ≥70 years No. (%)                      | 3,924 (28%)         | 2,238 (34%)         | 1,145 (28%)         | 541 (16%)           | <0.0001 |
| Women No. (%)                              | 7,061 (50%)         | 3,176 (48%)         | 2,038 (50%)         | 1,847 (55%)         | <0.0001 |
| Men No. (%)                                | 6,997 (50%)         | 3,433 (52%)         | 2,046 (50%)         | 1,518 (45%)         | <0.0001 |
| White No. (%)                              | 11,225 (80%)        | 5,150 (78%)         | 3,342 (82%)         | 2,733 (81%)         | <0.0001 |
| Black No. (%)                              | 1,916 (17%)         | 1,066 (16%)         | 466 (11%)           | 384 (11%)           | <0.0001 |
| Asian No. (%)                              | 130 (1%)            | 53 (1%)             | 39 (1%)             | 38 (1%)             | 0.2638  |
| BMI (kg/m <sup>2</sup> )                   | 31.4 (27.4 to 36.4) | 30.8 (27.0 to 35.6) | 31.7 (27.6 to 37.0) | 32.3 (27.8 to 37.3) | <0.0001 |
| Baseline Blood Pressure & Hemodynamic Data |                     |                     |                     |                     |         |
| SBP (mmHg)                                 | 152 (145 to 162)    | 154 (146 to 162)    | 149 (143 to 158)    | 154 (146 to 163)    | <0.0001 |
| SBP ≥160 mmHg No. (%)                      | 4,666 (33%)         | 2,462 (37%)         | 892 (22%)           | 1,312 (39%)         | <0.0001 |
| ISH ≥140/<90 mmHg No. (%)                  | 6,700 (48%)         | 3,059 (46%)         | 2,551 (62%)         | 1,090 (32%)         | <0.0001 |
| DBP (mmHg)                                 | 90 (80 to 98)       | 90 (80 to 98)       | 84 (78 to 92)       | 92 (86 to 100)      | <0.0001 |
| DBP ≥100 mmHg No. (%)                      | 2,916 (21%)         | 1,357 (21%)         | 551 (13%)           | 1,008 (30%)         | <0.0001 |
| MAP (mmHg)                                 | 110 (104 to 116)    | 111 (105 to 117)    | 106 (101 to 111)    | 113 (107 to 119)    | <0.0001 |
| Heart Rate (bpm)                           | 73 (65 to 83)       | 67 (61 to 76)       | 74 (68 to 82)       | 84 (77 to 92)       | <0.0001 |
| Cardiac Index (L/min/m <sup>2</sup> )      | 2.9 (2.4 to 3.5)    | 2.4 (2.1 to 2.7)    | 3.2 (3.0 to 3.4)    | 4.0 (3.7 to 4.3)    | <0.0001 |
| Total Body Water (%)                       | 47% (41 to 54)      | 48% (41 to 54)      | 47% (41 to 53)      | 46% (41 to 53)      | <0.0001 |

#BMI = body mass index using the Mosteller Formula. SBP = systolic blood pressure. DBP = diastolic blood pressure. ISH = isolated systolic hypertension; MAP = mean arterial pressure.



**Fig. 3** Distribution of patients stratified by hemodynamic profile for the PriMED and Premier cohorts combined before treatment optimisation. The target systolic and diastolic blood pressures were <140 mmHg and <90 mmHg respectively with, ideally, the patient also being in the hemodynamic target zone. The line drawn at a blood pressure of 140/90 mmHg reflects a mean arterial pressure of 107 mmHg and 130/80 mmHg a mean arterial pressure of 97 mmHg. Patients with an isolated systolic or isolated diastolic hypertension can have a mean arterial pressure less than these thresholds (e.g. 145/70 mmHg is a mean arterial pressure of 95 mmHg resulting in some patients with hypertension appearing in the hemodynamic target zone. These patients are still recommended for treatment of hypertension based on hemodynamic profile. The hemodynamic target zone is smaller if the aim is to control blood pressure to <130/<80 mmHg.

compared treatment to systolic BP targets of <140 mmHg to <120 mmHg.<sup>11</sup> SPRINT enrolled people aged  $\geq 50$  years, >90% of whom were receiving anti-hypertensive therapy at baseline, who had a systolic BP between 130 mmHg and 180 mmHg (baseline BP 140/78 mmHg) but, unlike in the PriMED cohort, SPRINT excluded patients with diabetes or a prior stroke.<sup>11</sup> For those assigned to a target systolic BP of <140 mmHg, SPRINT reported annual rates of 0.78% for myocardial infarction and 0.47% for stroke; for those assigned to a target systolic BP of <120 mmHg, annual rates were 0.65% and 0.41% respectively. For patients in the PriMED cohort who met the SPRINT inclusion criteria, the annual rates of

myocardial infarction and stroke were respectively 0.31 (95% CI 0.20 to 0.46) % and 0.43 (95% CI 0.29 to 0.60) %.

## Discussion

Over the last 20 years, several small, randomized trials conducted in specialized hypertension clinics have investigated the use of ICG for managing resistant hypertension with mixed success.<sup>8,12–19</sup> Observational studies in nephrology services,<sup>20</sup> hemodialysis,<sup>21</sup> and antenatal services<sup>22</sup> all suggest a potential value of ICG for managing hypertension. This analysis demonstrates the feasibility of integrating hemodynamic information into the routine management of

**All Ages**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 6,609     | 47%  |
| Mixed Hemodynamic   | 4,084     | 29%  |
| Hyperdynamic        | 3,365     | 24%  |
| Totals              | 14,058    | 100% |

**Ages 18-49**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 1,330     | 40%  |
| Mixed Hemodynamic   | 915       | 27%  |
| Hyperdynamic        | 1,122     | 33%  |
| Totals              | 3,367     | 100% |

**Ages 50-69**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 3,041     | 45%  |
| Mixed Hemodynamic   | 2,024     | 30%  |
| Hyperdynamic        | 1,702     | 25%  |
| Totals              | 6,767     | 100% |

**Ages ≥70**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 2,238     | 57%  |
| Mixed Hemodynamic   | 1,145     | 29%  |
| Hyperdynamic        | 541       | 14%  |
| Totals              | 3,924     | 100% |

**Men**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 3,433     | 49%  |
| Mixed Hemodynamic   | 2,046     | 29%  |
| Hyperdynamic        | 1,518     | 22%  |
| Totals              | 6,997     | 100% |

**Women**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 3,176     | 45%  |
| Mixed Hemodynamic   | 2,038     | 29%  |
| Hyperdynamic        | 1,847     | 26%  |
| Totals              | 7,061     | 100% |

**Black**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 1,066     | 56%  |
| Mixed Hemodynamic   | 466       | 24%  |
| Hyperdynamic        | 384       | 20%  |
| Totals              | 1,916     | 100% |

**Non-Black**

| Hemodynamic Profile | ICG Count | %    |
|---------------------|-----------|------|
| Vasoconstriction    | 5,543     | 46%  |
| Mixed Hemodynamic   | 3,618     | 30%  |
| Hyperdynamic        | 2,981     | 24%  |
| Totals              | 12,142    | 100% |

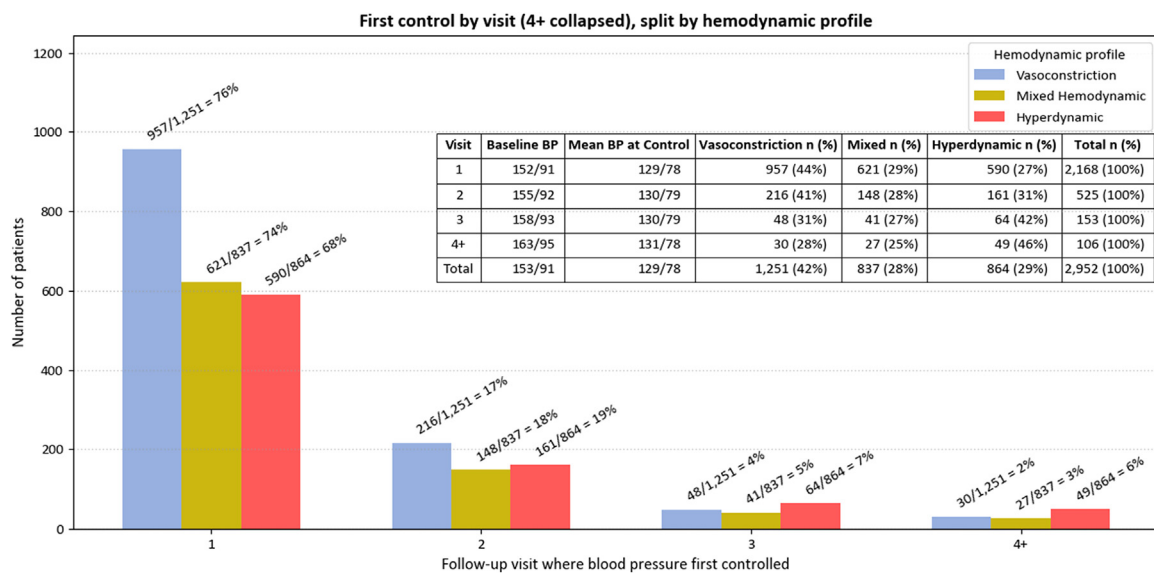
**Fig. 4** Proportion of patients with each hemodynamic profile stratified by age, sex and race.

hypertension in primary care and shows that tailoring treatment according to hemodynamic profile is associated with rapid and sustained BP control, regardless of age, sex or race. Hemodynamic profile might also predict the risk of future cardiovascular events. In the current analysis, patients with hypertension due to vasoconstriction tended to have higher rates of myocardial infarction and stroke compared to those with a hyperdynamic profile.

Current guidelines classify hypertension by measurements of systolic and diastolic BP, cardiovascular risk profile and evidence of end-organ damage. Indeed, recent guidelines on hypertension do not mention hemodynamic profiling.<sup>3,4</sup> Managing a heterogeneous hemodynamic problem with a homogenous therapeutic strategy is unlikely to lead to optimal results. Simply adding more anti-

hypertensive treatments might eventually achieve BP targets. However, polypharmacy increases side effects and costs and reduces adherence. It may also lead to patients being labelled as having resistant hypertension, rather than recognizing that their therapy does not match their hemodynamic profile. A low-cost, widely applicable method of assessing hemodynamic profile opens new opportunities for understanding the pathophysiology of hypertension and its treatment. Sharing hemodynamic information with patients and tailoring therapy accordingly is a logical approach to managing hypertension that, in this large observational experience in primary care, led to high rates of BP control.

An increase in peripheral vascular resistance alone was present in about half of all patients, although a further 29% had a mixture of both vasoconstriction and increased



**Fig. 5** Number of visits required to achieve blood pressure control (<140/<90 mmHg) according to hemodynamic profile at baseline in the PriMED cohort.

cardiac output. An ICG study from China that enrolled 17,112 patients with a systolic BP >140 mmHg also found that >70% had a raised vascular resistance with a normal or low cardiac output.<sup>23–25</sup> Similarly, a study from the United Kingdom of 1,483 people with newly diagnosed hypertension found that vasoconstriction was the predominant hemodynamic profile in middle-aged and older patients.<sup>26</sup>

For patients with vasoconstriction, treatment with agents that have vasodilator properties, such as ARB and dh-CCB, is appropriate. A higher proportion of older patients, men, and those of Black race had hypertension due to raised vascular resistance, but prediction of hemodynamic profile based on these features was not reliable. For approximately a quarter of patients, the main finding was a raised cardiac output with normal vascular resistance, for which beta-1 selective blockers or non-dhCCBs seem hemodynamically appropriate.

In our two large cohorts of patients with hypertension managed in primary care, 85–92% of patients achieved and maintained a BP of <140/<90 mmHg over many years, the BP targets recommended in guidelines published in 2014.<sup>9</sup> Many patients achieved target BP goals after a single hemodynamic assessment, and the great majority after only two visits. Systolic BP <130 mmHg and diastolic BP <80 mmHg, recommended targets in recently updated guidelines on hypertension, were achieved on about 50% of visits. An ICG assessment takes little more time than measuring BP itself. Reducing the number of visits and time to attain BP control could reduce workload, improve efficiency and effectiveness of care, and should reduce overall costs.

In the USA, the annual cost associated with high BP was estimated to be >\$200 billion in 2019<sup>27</sup>, reflecting the high prevalence of hypertension, the costs of medical care (about \$3,000 annually per patient) and the consequences of

serious adverse events. The proposed reimbursement cost for an ICG is about \$35. If patients require, on average, one or two tests per year, this appears to be an attractive option to enhance the effective use of low-cost generic anti-hypertensive medicines.<sup>28,29</sup>

The high rate of successful BP control may reflect factors additional to prescribing tailored anti-hypertensive therapy. Physicians may become more knowledgeable and motivated to achieving BP control leading to decreased therapeutic inertia. Similarly, patients may become more engaged in managing their BP, thereby becoming more adherent to therapy. The visual presentation of results (Fig. 1) may help impress upon both the patient and physician that hypertension is a serious problem not to be taken lightly, encouraging them to attain better BP control. Determining why measuring hemodynamics improves control of BP requires further research, including randomized trials. Nonetheless, a simple, low-cost-per-test intervention that enables such a large proportion of patients with hypertension to achieve treatments goals should not be ignored.

Patients in the PriMED long-term cohort had low rates of cardiovascular events compared to rates reported in the SPRINT trial. This is remarkable because SPRINT excluded patients with diabetes, prior stroke, other co-morbidities, and had a substantially lower baseline systolic BP than in the PriMED cohort. For these reasons, and the extra care that patients receive in trials, the event rates in SPRINT are almost certainly lower than in routine clinical practice. Also, in the PriMED cohort, event rates were lower for those with a hyperdynamic profile. Whether this reflects a more benign form of hypertension, or greater prescription of beta-blockers and non-dhCCB is unclear.<sup>30,31</sup>

There are several limitations to this analysis. This was an observational study. BP may have declined either due to a

**Table 2** Clinical profile and rates of myocardial and stroke (first events) in the systolic blood pressure intervention trial (SPRINT) compared to the PriMED cohort, overall and in the subset fulfilling SPRINT inclusion criteria (aged  $\geq 50$  years, no diabetes or prior stroke & systolic BP  $< 180$  mmHg).

|                                            | N =   | Age           | Women | Smokers |       | CVD | DM  | Baseline<br>SBP/DBP | Patient-Years<br>Follow-up <sup>#</sup> | Myocardial<br>Infarction<br>Patients | Stroke<br>Patients | Annual rate of<br>myocardial infarction<br>Percent per year (first event only) | Annual rate of stroke |
|--------------------------------------------|-------|---------------|-------|---------|-------|-----|-----|---------------------|-----------------------------------------|--------------------------------------|--------------------|--------------------------------------------------------------------------------|-----------------------|
|                                            |       |               |       | Curr.   | Prev  |     |     |                     |                                         |                                      |                    |                                                                                |                       |
| SPRINT<br>(which excluded diabetes)        |       |               |       |         |       |     |     |                     |                                         |                                      |                    |                                                                                |                       |
| Standard                                   | 4,683 | 68            | 35%   | 13%     | 43%   | 17% | 0%  | 140/78              | 15,300 <sup>#</sup>                     | 116                                  | 97                 | 0.78                                                                           | 0.47                  |
| Intensive                                  | 4,678 | 68            | 36%   | 14%     | 42%   | 17% | 0%  | 140/78              | 15,300 <sup>#</sup>                     | 70                                   | 62                 | 0.65                                                                           | 0.41                  |
|                                            |       |               |       | Curr.   | Prev. |     |     |                     | Patient-Years<br>Follow-up <sup>*</sup> |                                      |                    | Percent per year (first events)<br>with 95% confidence intervals               |                       |
| PriMED long-term cohort<br>(no exclusions) | 2,955 | 60 (50 to 69) | 50%   | 7%      | 34%   | 18% | 30% | 150/92              | 17,282                                  | 51                                   | 74                 | 0.30 (0.22 to 0.39)                                                            | 0.43 (0.34 to 0.54)   |
| Vasoconstriction                           | 1,252 | 62 (52 to 70) | 47%   | 7%      | 36%   | 21% | 30% | 152/92              | 7,139                                   | 23                                   | 34                 | 0.32 (0.20 to 0.48)                                                            | 0.48 (0.33 to 0.67)   |
| Mixed Profile                              | 837   | 61 (50 to 69) | 48%   | 7%      | 35%   | 19% | 32% | 146/88              | 4,983                                   | 20                                   | 21                 | 0.40 (0.25 to 0.62)                                                            | 0.42 (0.26 to 0.64)   |
| Hyperdynamic                               | 866   | 57 (47 to 66) | 55%   | 8%      | 32%   | 11% | 28% | 152/94              | 5,160                                   | 8                                    | 19                 | 0.16 (0.07 to 0.31)                                                            | 0.37 (0.22 to 0.58)   |
| PriMED SPRINT-like<br>patients             | 1,361 | 63 (57 to 70) | 53%   | 6%      | 35%   | 15% | 0%  | 152/90              | 7,812                                   | 24                                   | 33                 | 0.31 (0.20 to 0.46)                                                            | 0.43 (0.29 to 0.60)   |

<sup>#</sup>for the SPRINT trial, follow-up was censored on the date of the first event, as reported by investigators, and estimated to the nearest 100 years.

<sup>\*</sup>patient-years of follow-up censored for the first myocardial infarction or end of follow-up. CVD = prior history of cardiovascular disease; DM = diabetes mellitus; SBP/DBP = systolic and diastolic blood pressure. Curr. = current. Prev. = previous.

"placebo" effect or improved adherence to existing therapy. We did not test the effects of individual classes of anti-hypertensive agents on hemodynamic profile or BP. Randomized trials comparing the effects of anti-hypertensive agents on BP according to hemodynamic profile should be done.<sup>17</sup> We used only one ICG system and do not know whether other systems would achieve similar results. We used contemporary AAFP and ACP targets for BP control <140/<90 mmHg. Fewer patients achieved revised targets of <130/<80 mmHg but the proportion might have increased had it been our goal. A BP goal of <130/80 will require greater effort and/or a fresh approach, which ICG, an existing FDA approved non-invasive, hyper-scalable, and inexpensive tool, could help achieve. We used total peripheral resistance rather than systemic vascular resistance because we had no reliable method of assessing right atrial pressure. Most patients probably had normal right atrial pressures. Non-invasive methods of assessing right atrial pressure exist but would add complexity.<sup>32</sup> Reliable data on mortality was not available for the PriMED long-term cohort.

In conclusion, routine use of ICG in primary care to enable hemodynamic tailoring of therapy for hypertension is associated with a high proportion of patients achieving and sustaining long-term BP control. This success contrasts with decades of poor BP control that revised guideline targets will make even more difficult to achieve. The value of hemodynamic monitoring in primary care should be assessed in pragmatic randomized trials. In the absence of randomized trials, implementation studies at scale with robust audit might determine whether a hemodynamic ICG strategy increases the proportion of patients achieving contemporary BP targets. Trials of ICG's utility for the investigation of novel anti-hypertensive therapies are also warranted.

## Declarations of interest

Cleland reports grants from British Heart Foundation, grants and personal fees from Bayer, Bristol Myers Squibb, CSL-Vifor and Pharmacosmos, grants and stock options from Viscardia, personal fees from Abbott, Astra-Zeneca, Biopeutics, Holosis, Idorsia, Medtronic, Vectorious, personal fees and non-financial support from Boehringer-Ingelheim and NI Medical, non-financial support from Corvia, stock options from HeartFelt.

Romer is Chief Medical Officer of MedsEngine, LLC

Kaiser is Chief Technology Officer of MedsEngine, LLC

Gearhardt is Chief Executive Officer of MedsEngine, LLC

Froehlich is President of PriMED Physicians

Perez MD is Chief Medical Officer of PriMED Physicians

Colangelo reports no conflicts of interest.

Hirsch is Chief Executive Officer of InnovaMed Sphere

Granov is Chief Operations officer of InnovaMed Sphere

Moshkovitz reports no conflicts of interest.

Michael Bottorff reports no conflicts of interest.

Casey reports no conflicts of interest.

Sobotka reports no conflicts of interest.

Viera reports no conflicts of interest.

Vered is Medical Director of InnovaMed Sphere

## Contributions and access to data

Kaiser analyzed the data; other authors were able to access data if they wished through him.

Cleland with Romer wrote the first draft of the text, which was reviewed and commented on by all other authors. Kaiser and Romer were predominantly responsible for generation of figures.

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## SUPPLEMENTARY DATA

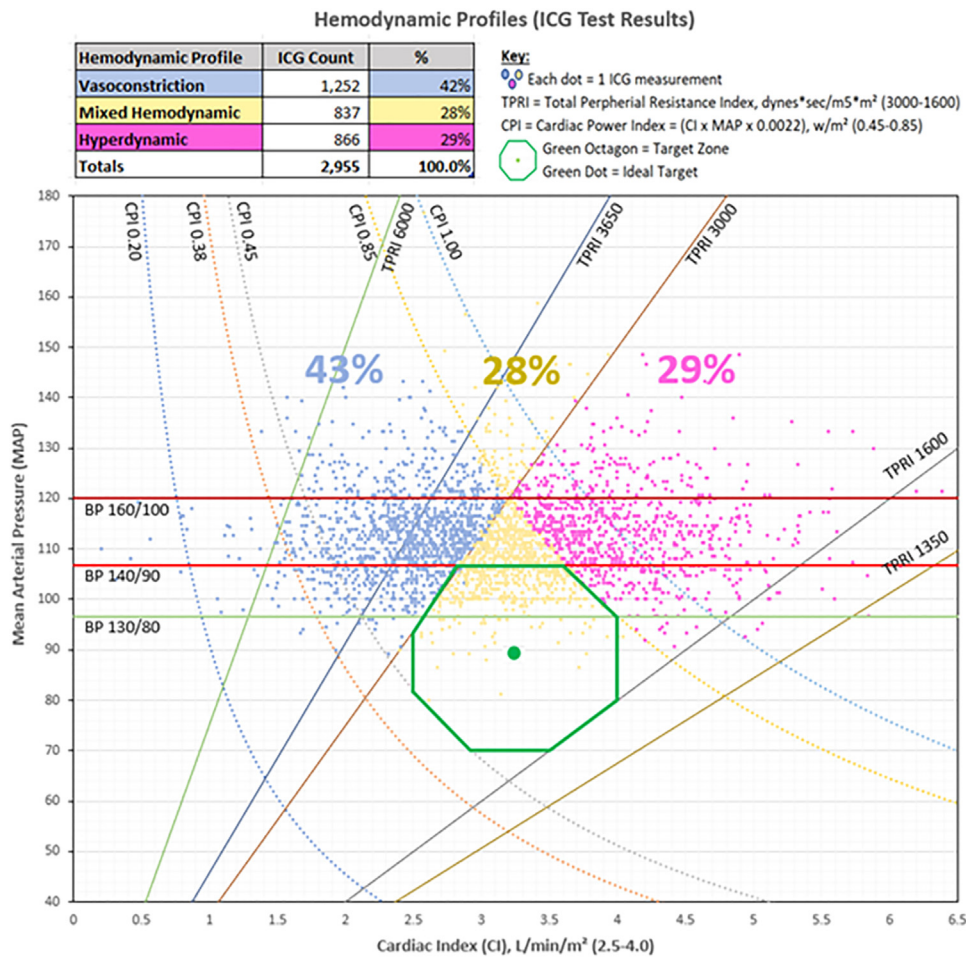
Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amjmed.2026.07.001>.

**Supplementary Table 1** Hemodynamic formulas and their interpretation.

| Measurement                              | Formulas for Calculation           | Comments                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|------------------------------------------|------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mean Arterial Pressure (MAP)             | Diastolic BP + (Pulse Pressure/3)  | Pulse Pressure = Systolic - Diastolic BP                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Cardiac Index (CI)                       | Cardiac Output / Body Surface Area | A low CPI reflects the inability of the heart to maintain CI for a given MAP, indicating cardiac dysfunction that may progress, or have already progressed, to heart failure.<br><br>A low CPI may be due to a normal or high MAP associated with a low CI, or a low MAP associated with an apparently normal CI.<br><br>A low CPI due to a high MAP with a low CI suggests hypertensive heart disease that may progress, or have already progressed, to heart failure. |
| Cardiac Power Index (CPI)                | (CI x MAP)/451                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Total Peripheral Resistance Index (TPRI) | (MAP - Mean Venous Pressure) / CI  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
|                                          |                                    | TPRI reflects the resistance to cardiac output, which depends mainly on arteriolar tone and to a lesser extent on blood viscosity and venous pressure. In the absence of heart failure mean venous pressure is usually <5 mmHg and is usually ignored.                                                                                                                                                                                                                  |

**Supplementary Table 2** Baseline characteristics classified by hemodynamic profile (data shown as numbers with percentage or median with quartiles) for the PriMed patient subset with long-term follow-up

|                                            | Overall             | Vasoconstriction    | Mixed               | Hyperdynamic        | P       |
|--------------------------------------------|---------------------|---------------------|---------------------|---------------------|---------|
| PriMED (n/% by row)                        | 2,955               | 1,252 (42%)         | 837 (28%)           | 866 (29%)           | n/a     |
| Age (years)                                | 60 (50 to 69)       | 62 (52 to 70)       | 61 (50 to 69)       | 57 (47.3 to 66)     | <0.0001 |
| Age (years)                                |                     |                     |                     |                     |         |
| Age 18-49 years No. (%)                    | 739 (25%)           | 268 (21%)           | 206 (25%)           | 265 (31%)           | <0.0001 |
| Age 50-69 years No. (%)                    | 1,595 (54%)         | 674 (54%)           | 451 (54%)           | 470 (54%)           | 0.9784  |
| Age ≥70 years No. (%)                      | 621 (21%)           | 310 (25%)           | 180 (22%)           | 131 (15%)           | <0.0001 |
| Women No. (%)                              | 1,475 (50%)         | 591 (47%)           | 405 (48%)           | 479 (55%)           | 0.0007  |
| Men No. (%)                                | 1,480 (50%)         | 661 (53%)           | 432 (52%)           | 387 (45%)           | 0.0007  |
| White No. (%)                              | 2,293 (78%)         | 942 (75%)           | 660 (79%)           | 691 (80%)           | n/a     |
| Black No. (%)                              | 430 (15%)           | 223 (18%)           | 109 (13%)           | 98 (11%)            | <0.0001 |
| Asian No. (%)                              | 26 (1%)             | 7 (1%)              | 5 (1%)              | 14 (2%)             | n/a     |
| Current Smokers (n/%)                      | 209 (7%)            | 82 (7%)             | 59 (7%)             | 68 (8%)             | 0.5162  |
| Former Smokers (n/%)                       | 1,015 (34%)         | 450 (36%)           | 290 (35%)           | 275 (32%)           | 0.1336  |
| Diabetes (n/%)                             | 885 (30%)           | 378 (30%)           | 268 (32%)           | 239 (28%)           | 0.1336  |
| Coronary artery disease (n/%)              | 453 (15%)           | 235 (19%)           | 135 (16%)           | 83 (10%)            | <0.0001 |
| BMI (kg/m <sup>2</sup> )                   | 31.4 (27.6 to 36.2) | 31.1 (27.2 to 35.5) | 31.5 (27.9 to 36.8) | 31.8 (27.6 to 36.6) | 0.0785  |
| Baseline Blood Pressure & Hemodynamic Data |                     |                     |                     |                     |         |
| SBP (mmHg)                                 | 150 (144 to 160)    | 152 (146 to 160)    | 146 (140 to 156)    | 152 (146 to 162)    | <0.0001 |
| SBP ≥160 mmHg No. (%)                      | 915 (31%)           | 439 (35%)           | 161 (19%)           | 315 (36%)           | <0.0001 |
| ISH ≥140/<90 mmHg No. (%)                  | 1,038 (35%)         | 377 (30%)           | 425 (51%)           | 236 (27%)           | <0.0001 |
| DBP (mmHg)                                 | 92 (84 to 100)      | 92 (86 to 100)      | 88 (80 to 94)       | 94 (88 to 100)      | <0.0001 |
| DBP ≥100 mmHg No. (%)                      | 756 (26%)           | 348 (28%)           | 131 (16%)           | 277 (32%)           | <0.0001 |
| MAP (mmHg)                                 | 111 (106 to 117)    | 113 (108 to 118)    | 107 (103 to 112)    | 113 (108 to 119)    | <0.0001 |
| Heart Rate (bpm)                           | 74 (66 to 83)       | 68 (61 to 76)       | 74 (67 to 82)       | 83 (77 to 92)       | <0.0001 |
| Cardiac Index (L/min/m <sup>2</sup> )      | 3.1 (2.6 to 3.6)    | 2.5 (2.2 to 2.7)    | 3.2 (3.0 to 3.4)    | 4.0 (3.7 to 4.4)    | <0.0001 |



**Supplementary Fig. 1** Distribution of patients stratified by hemodynamic profile for the subset of the PriMED cohort with complete follow-up. Patients with a isolated systolic or isolated diastolic hypertension may have a mean arterial pressure <106.7 mmHg resulting in some being in the provisional target zone.

**Supplementary Table 3** Differences in hemodynamic classification between a 1<sup>st</sup> and 2<sup>nd</sup> ICG reading in patients who had more than one record.

| 1 <sup>st</sup> ICG→<br>2 <sup>nd</sup> ICG↓ | All Patients | Vasoconstriction               | Mixed Hemodynamic              | Hyperdynamic                   |
|----------------------------------------------|--------------|--------------------------------|--------------------------------|--------------------------------|
|                                              | 1482         | 571 (39%)                      | 428 (29%)                      | 483 (33%)                      |
| Vasoconstriction                             | 680 (46%)    | Profile Unchanged<br>377 (66%) | 180 (42%)                      | 123 (25%)#                     |
| Mixed Hemodynamic                            | 413 (28%)    | 136 (24%)                      | Profile Unchanged<br>147 (34%) | 130 (27%)                      |
| Hyperdynamic                                 | 389 (26%)    | 58 (10%)#                      | 101 (24%)                      | Profile Unchanged<br>230 (48%) |

Note that changes in medication, which were not made available for this analysis, will have occurred between readings and that there was not set timing between readings, which occurred a median of 17 (IQR 4 to 41) months apart