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Predicting blood pressure outcomes using single-item physician-administered measures:

a retrospective pooled analysis of observational studies in Belgium

Abstract

Background
Patient adherence is often not monitored because existing methods of evaluating adherence are either burdensome or do not accurately predict treatment outcomes.

Aim
To examine whether two simple, single-item physician-administered measures of patient adherence to antihypertensive medication are predictive of blood pressure outcomes.

Design and setting
Retrospective database analysis of patients with hypertension treated in Belgian primary care.

Method
Using pooled data from five observational studies, a sample was identified of 9725 patients who were assessed using two single-item physician-administered measures of adherence to antihypertensive medication: the first item of the Basel Assessment of Adherence Scale (BAAS) and the Visual Analogue Scale (VAS). These two assessment tools were administered by GPs during regular appointments with patients. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and combined SBP/DBP were measured at baseline and at 90 days.

Results
BAAS-identified adherent patients achieved lower mean SBP and DBP compared with non-adherent patients at 90 days (P<0.001), and had odds ratios of achieving blood pressure control of 0.66 (95% confidence intervals (CI) = 0.61 to 0.73, P<0.001) for SBP, 0.69 (95% CI = 0.62 to 0.76, P<0.001) for DBP, and 0.65 (95% CI = 0.59 to 0.72, P<0.001) for combined SBP/DBP. For VAS-identified adherent patients, the odds ratios of achieving blood pressure control were 0.93 (95% CI = 0.86 to 1.00, P<0.001) for SBP, 0.79 (95% CI = 0.73 to 0.85, P<0.001) for DBP, and 0.91 (95% CI = 0.84 to 0.99, P<0.001) for combined SBP/DBP.

Conclusions
The first item of the BAAS and the VAS are independent predictors of blood pressure control. These methods can be integrated seamlessly into routine clinical practice by allowing GPs to quickly evaluate a patient's adherence and tailor treatment recommendations accordingly.

Keywords
hypertension; medication adherence; patient adherence; primary health care.

INTRODUCTION

Hypertension is a major risk factor for cardiovascular disease, as well as many other health conditions, and is prevalent both in the US and worldwide.[1,2] Despite the widespread availability and use of effective pharmacological treatments, only half of patients with hypertension, according to one study, achieve blood pressure control, defined as a systolic blood pressure (SBP) of <40 mmHg and diastolic blood pressure (DBP) of <90 mmHg.[3]

A major contributing factor to this poor outcome is patient non-adherence to prescribed therapies, as adherent patients are more than three times as likely as non-adherent patients to achieve blood pressure control.[4] Physicians and researchers have long relied on multiple-item patient-reported surveys to evaluate adherence and its effect on treatment outcomes. However, these surveys are time consuming and unreliable, as patients frequently overestimate their adherence.[5,6] Other strategies, such as pill counts and pharmacy refill rates, while showing some promise, still do not constitute a 'gold standard' for the evaluation of patient adherence.[7]

To better evaluate and understand adherence, healthcare providers require a tool that is reliable, easy to administer, and can be integrated seamlessly into routine clinical practice. This need is particularly acute in primary care settings, where clinicians typically work 50–60 hours per week in multiple roles.[8]

While past research has focused on multiple-item patient-rated surveys, this study used a large sample size to evaluate two single-item physician-administered tools for evaluating adherence: the first item of the Basel Assessment of Adherence Scale (BAAS) and the Visual Analogue Scale (VAS).

METHOD

Design and patients

Data were pooled from five prospective, multicentre, pharmaco-epidemiological studies in which patients with hypertension, for whom first-line treatment either failed or was not tolerated, were treated for 90 days with one of several valsartan formulations as second-line therapy.

Hypertension was defined as SBP of at ≥140 mmHg (≥130 mmHg for patients with concomitant diabetes) and/or DBP of ≥90 mmHg (≥80 mmHg for patients with concomitant diabetes).[9] The five studies had

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How this fits in

Patient adherence to medication regimens is a critical component of achieving positive treatment outcomes. Despite this, patient adherence is often not monitored because existing methods of evaluating adherence are either overly time consuming or do not accurately predict treatment outcomes. This study demonstrates that two simple single-item physician-administered methods of evaluating adherence are predictive of blood pressure after 90 days of antihypertensive therapy. The incorporation of these tools into clinical practice could improve treatment outcomes by allowing physicians to better monitor adherence and encourage patients to more closely follow treatment.

a similar design and included a baseline assessment at the time valsartan treatment was initiated and at a follow-up assessment 90 days later.[10] These were observational studies and all data were collected from routine clinical practice. The common methodology of these studies has been described in detail elsewhere;[10] however, essential elements are summarised in Table 1.

The pooled data set included a total of 9725 patients. Adherence data were available for 9394 patients and these patients constituted the sample for the analysis reported here. While a database was initially consulted that included seven valsartan studies and a total of 17 516 patients, two studies were omitted because they did not contain patient adherence data. All patients provided informed consent, and ethical approvals were obtained from appropriate committees.

Measures

At both baseline and 90-day follow-up, SBP and DBP were measured three times in a sitting position with an oscillometric device at 1–2 minute intervals. The mean of these three measurements was reported. Physicians also collected data on patient adherence using the four-item BAAS and the VAS. Other demographic and clinical data were collected at baseline. Due to small disparities across the five studies in terms of these data, as well as the research interests, the only variable linked with blood pressure outcome at 90 days was adherence status.

Basel Assessment of Adherence Scale. The BAAS[11,12] is an adherence questionnaire that instructs clinicians to ask patients four questions, of which the first one is of interest to this study's hypothesis. This first item asks, 'Do you recall *not* having taken your medication some time in the past 4 weeks?' and offers six possible responses: 'No', 'Once in past 4 weeks', 'Once every 2 weeks', 'Once weekly', 'More than once/week but not daily', and 'Daily', respectively. For this analysis, those who responded 'No' were considered to be adherent, while those who chose any of the other five responses were considered to be non-adherent.

Visual Analogue Scale. Physicians also completed a VAS. This item instructed physicians to 'Place a mark [X] on the line below at the point indicating your impression of this patient's overall compliance with their antihypertensive medication in the past 4 weeks'. The horizontal line on which physicians placed their marks was anchored by 0% (no medication taken in the past month) and 100% (every single dose was taken in the past month), with demarcations provided for every 10th percentile. VAS scores were converted to a dichotomous response in order to categorise patients as adherent (VAS score of ≥80%) or non-adherent (VAS score <80%).[13,14] The questionnaire did not instruct clinicians to ask any particular questions to determine a VAS score and instead rely on their clinical impression.

Statistics

A two-tailed *t*-test was conducted to determine whether mean blood pressure values were different for adherent and non-adherent patients, as classified by the first item of the BAAS, and to determine whether mean blood pressure values were significantly different between patients above and below the 80% cut-off of VAS score. Logistic regression analysis was performed to estimate the odds of blood pressure control of adherent patients according to each measure. Additionally, the cumulative incidence function of blood pressure control was calculated as a function of VAS score. Statistical significance was indicated by a *P*-value of <0.05. Data were analysed using Stata (version 11).

RESULTS

Table 1 summarises the key characteristics of the five studies. At baseline, 40.8% of patients had blood pressure in the high normal range (SBP 130–139 mmHg and/or DBP 85–89 mmHg), 31.4% had Grade 1

Table 1. Patient and study characteristics

Study characteristics	ADVANCE[a]	INSIST[16]	eNOVA[a]	BSCORE[17]	EXCELLENT[18]	Total
Year initiated	2005	2006	2006	2008	2008	
Number of patients	1899	703	275	3389	3459	9725
Number of physicians	602	308	284	354	698	2246
Patient characteristics						**Weighted average**
Mean age, years (±SD)	63.3 ± 2.3	63.9 ± 11.4	62.1 ± 12.0	63.8 ± 11.9	63.8 ± 11.7	63.7 ± 11.9
Male sex, %	50.9	49.4	51.7	53.8	54.8	53.2
Ethnicity: white, %	98.9	98.0	99.5	n/a	—	—
Diabetes mellitus, %	1.9	30.0	9.3	23.7	26.9	22.0
Angina, %	14.6	10.9	11.6	—	—	—
Myocardial infarction, %	7.4	8.2	7.1	8.3	8.8	8.6
Congestive heart failure, %	4.0	2.3	3.5	—	4.1	—
Current smoker, %	21.6	17.5	20.6	—	—	—
Renal impairment, %	3.7	1.2	1.7	—	—	—
Metabolic syndrome, %	25.9	26.8	24.8	—	—	—
Valsartan formulations						
80 mg	✓		✓	✓		
160 mg	✓		✓	✓		
80 mg/12.5 mg HCTZ	✓		✓	✓		
160 mg/12.5 mg HCTZ	✓		✓	✓		
160 mg/25 mg HCTZ	✓	✓		✓		
80 mg/5 mg amlodipine					✓	
160 mg/5 mg amlodipine					✓	
160 mg/10 mg amlodipine					✓	

HCTZ = hydrochlorothiazide. [a]Novartis data on file (unpublished).

hypertension (SBP 140–159 mmHg and/or DBP 90–99 mmHg), and 26.8% had Grade 2 hypertension (SBP 160–179 mmHg and/or DBP 100–109 mmHg), according to guidelines published by the European Society of Hypertension and the European Society of Cardiology.[15]

As previously mentioned, patients were recruited to receive valsartan due to a lack of adequate results with other antihypertensive drugs. At the time of study initiation, 78.4% of patients had uncontrolled blood pressure despite prior treatment with other antihypertensive therapies, 8.5% had controlled blood pressure but did not tolerate other antihypertensive therapies, and 13.2% had uncontrolled blood pressure and did not tolerate prior antihypertensive therapies; 66.5% were taking more than one medication.

Using the first item of the BAAS, 74.6% of patients were classified as adherent and 25.4% were classified as non-adherent. As shown in Table 2, BAAS-classified adherent patients achieved significantly lower mean SBP and DBP measures (135.6 mmHg and 81.0 mmHg, respectively) following treatment than did those who were non-adherent (138.6 mmHg and 83.0 mmHg, respectively) ($P<0.001$). These non-adherence means were weighted based on the number of responses to each of the five non-adherent answers. The means of each of the five non-adherent responses are included in Table 2, and suggest that more frequent non-adherence is associated with poorer blood pressure outcomes. Of BAAS-classified adherent patients, 37.6% achieved SBP control (SBP <140 mmHg or <130 mmHg with concomitant diabetes), 53.4% achieved DBP control (DBP <90 mmHg or <80 mmHg with concomitant diabetes), and 33.6% achieved combined SBP/DBP control at

Table 2. Blood pressure at 90 days by adherence category as assessed using BAAS query

In the past 4 weeks, do you recall *not* having taken your antihypertensive medication sometimes?

			Systolic blood pressure		Diastolic blood pressure	
	N	%	Mean ± SD, mmHg	*P*-value	Mean ± SD, mmHg	*P*-value
No	7008	74.6	135.6 ± 11.0	<0.001[a]	81.0 ± 7.0	<0.001[a]
Yes	2386	25.4	138.6 ± 12.0	[a]	83.0 ± 8.0	[a]
A	1003	10.7	137.1 ± 10.6		82.5 ± 7.0	
B	847	9.0	137.9 ± 11.1		82.5 ± 7.5	
C	315	3.4	141.1 ± 13.3		83.9 ± 8.4	
D	191	2.0	144.9 ± 16.1		84.6 ± 9.0	
E	30	0.3	148.9 ± 14.9		88.3 ± 8.0	

[a]Represents a comparison between adherent patients (those who answered 'No') and non-adherent patients (those who answered A: 'Once in past 4 weeks', B: 'Once every 2 weeks', C: 'Once weekly', D: 'More than once/week but not daily', or E: 'Daily'). The adherent patients are classified in the 'No' category and non-adherent patients are grouped into the 'Yes' category.

Table 3. Blood pressure at 90 days by adherence category as assessed using VAS

			Systolic blood pressure		Diastolic blood pressure	
	N	%	Mean ± SD, mmHg	*P*-value	Mean ± SD, mmHg	*P*-value
≥80%	7606	81.0	135.0 ± 11.0	<0.001[a]	81.2 ± 7.4	<0.001[a]
<80%	1788	19.0	139.5 ± 13.5	[a]	82.9 ± 8.2	[a]

[a]t = –14.6152, P<0.001. VAS = visual analogue scale.

Table 4. VAS score and probability of reaching combined SBP/DBP control blood pressure at 90 days

VAS score	Probability, %	95% CI
70	74.4	72.3 to 76.4
75	78.2	75.9 to 80.4
80	83.5	81.0 to 85.9
85	84.0	81.3 to 86.5
90	84.9	81.7 to 87.1
95	93.1	89.5 to 95.8

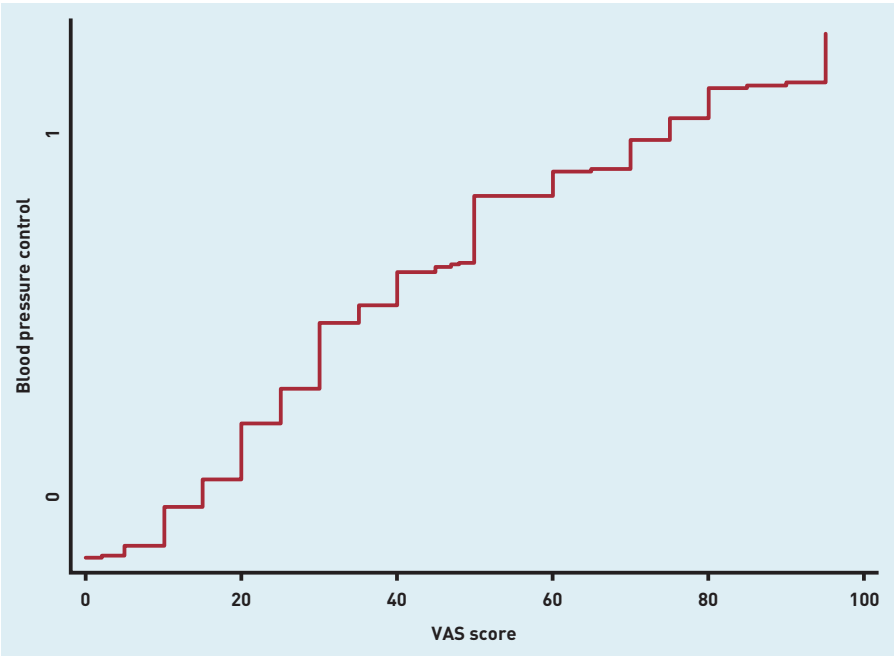
DBP = diastolic blood pressure. SBP = diastolic blood pressure. VAS = visual analogue scale.

90 days, with odds ratios for SBP of 0.66 (95% confidence intervals [CI] = 0.61 to 0.73, *P*<0.001), for DBP of 0.69 (95% CI = 0.62 to 0.76, *P*<0.001), and for SBP/DBP of 0.65 (95% CI = 0.59 to 0.72, *P*<0.001). Of BAAS-identified non-adherent patients, only 10.2% achieved SBP control, 16.0% achieved DBP control, and 8.8% achieved combined SBP/DBP control at 90 days.

Using the VAS, 81.0% of patients were classified as adherent according to the VAS (score of ≥80) and 19.0% were classified as non-adherent (VAS score <80). As shown in Table 3, VAS-classified adherent patients achieved significantly lower mean SBP and DBP measures (135.0 mmHg and 81.2 mmHg, respectively) following treatment than did those who were non-adherent (139.5 mmHg and 82.9 mmHg, respectively) (*P*<0.001). Of VAS-classified adherent patients, 40.1% reached SBP control, 57.7% reached DBP control, and 36.1% reached combined SBP/DBP control, with odds ratios of 0.93 (95% CI = 0.86 to 1.00, *P*<0.001) for SBP, 0.79 (95% CI = 0.73 to 0.85, *P*<0.001) for DBP, and 0.91 (95% CI = 0.84 to 0.99, *P*<0.001) for combined SBP/DBP. For VAS-identified non-adherent patients, only 7.3% reached SBP control, 11.7% reached DBP control, and 6.3% reached combined SBP/DBP.

Table 4 shows the probability of achieving combined SBP/DBP control using responses from the VAS. Patients with higher VAS scores have significantly higher probabilities of achieving combined SBP/DBP control at 90 days. In Figure 1, the y-axis represents the probability of reaching blood pressure control. The area closer to zero represents uncontrolled combined SBP/DBP (SBP >140 mmHg or >130 mmHg with concomitant diabetes, and DBP >90 mmHg or >80 mmHg with concomitant diabetes), and the area closer to one represents controlled SBP/DBP (SBP <140 mmHg or <130 mmHg with concomitant diabetes, and DBP <90 mmHg or <80 mmHg with concomitant diabetes).

Figure 1. Relationship between VAS score and combined SBP/DBP control.
VAS = visual analogue scale.



DISCUSSION

Summary

Despite the availability of safe and efficacious pharmacological treatments for hypertension, a large percentage of patients with hypertension do not achieve blood pressure control.[19–21] This efficacy–effectiveness gap may be caused in part by poor patient adherence.[22] The current study, by evaluating 9725 patients from five observational valsartan studies, supports this claim by demonstrating that medication adherence, as measured by two simple single-item physician-administered queries, is positively correlated with systolic, diastolic, and overall blood pressure control.

These findings support two methods that can be seamlessly integrated into physicians' encounters with patients. While this study does not explicitly statistically compare these methods with each other, both the BAAS and VAS methods were found to be predictive of SBP, DBP, and SBP/DBP control, with odds ratios of similar orders of magnitude (considering they are in the less than 1.00 tail of the respective odds ratios).

Strengths and limitations

A strength of this study is that, to the authors' knowledge, it is the first to evaluate the ability of these two single-item physician-administered methods of measuring adherence to predict patient outcomes. These items are of particular interest to physicians because they can be easily integrated into routine clinical practice. Another strength is that this study uses a large observational pool of patient

data collected in real-life settings, which may increase the reproducibility of the findings.

The decision to include these five studies was a pragmatic one. The database analysed was a pooled data set of the databases of seven valsartan studies that employed a similar design; however, adherence data were only available for five studies. The authors recognise the risk of bias and selectivity; on the other hand, the pooling provided access to a large and therefore statistically more stable sample.

Nevertheless, a potential limitation of this study is that it included data from one European country (Belgium), and multi-country data would be needed to generalise the findings to other populations. Accordingly, future research on this topic should include more diverse patient and physician populations.

Another limitation is that the protocols for the studies used in this pooled analysis did not specify when the VAS was to be completed. The authors assume that in most cases this was done after the patient encounter when the physician was completing the case record form for the patient's visit. This might bias the results, certainly at the 90-day mark but also at the enrolment visit (as valsartan-centric regimens are initiated because prior line of treatment was not effective or not tolerated).

Furthermore, because patients have been shown to be more adherent during the initial phase of treatment with a new therapy,[13] future research should include patients at different stages of treatment. Another problem with measuring adherence is the vulnerability of measurements to the Hawthorne effect, that is, a change in patient behaviour as a result of being monitored in a study. This effect may be particularly common when the patient is familiar with the methods being used to measure adherence or anticipates negative consequences resulting from non-adherence.

A number of confounding variables, including age and sex of patient, salt intake, polypharmacy, and coexisting conditions, may influence blood pressure outcomes; therefore, future research is needed to validate adherence generally and these two adherence measures specifically as predictors of blood pressure outcome. However, because the tools evaluated in this study can be easily integrated into practice and because the adherence measures obtained using them are associated with blood pressure outcomes, they may be valuable components of clinical practice.

Comparison with existing literature

Previous studies have also demonstrated a relationship between adherence and blood pressure control. For example, one meta-analysis found that 26% more patients experienced a positive outcome by adhering than not adhering to antihypertensive therapy. This same study found the odds of responding to treatment to be 3.44 times higher in adherent than in non-adherent patients.[4] Nevertheless, many of these studies had small sample sizes and/or employed complex and time-consuming patient-reported questionnaires, most of which are not useful in primary healthcare settings because of physician and patient time constraints. Moreover, patient-reported data are unreliable, as patients tend to overestimate their adherence.[5] For these reasons, this study evaluated two single-item physician-administered tools that are easy to administer and can be completed in minimal time.

The first item of the BAAS is a relatively simple and time-efficient method of assessing adherence. The VAS is another simple method that quickly and accurately assesses a physician's impression of a patient's adherence, a finding echoed by Kalichman *et al*'s study of patients with HIV.[23] While patients responded to the first item of the BAAS, the authors consider the query to be a physician-administered tool because a physician was present, asked the question, and recorded a response. This approach is distinct from surveys in which patients respond independently to questions regarding their adherence, and most research on the unreliability of patient-reported adherence data focuses on these types of independently completed surveys. Furthermore, the first item of the BAAS is a 'Yes/No' question and patients are less likely to lie when asked yes or no questions than when asked more specific questions with a range of responses. While the BAAS traditionally includes four items, this study found that the first question alone: 'Do you recall not having taken your medication some time in the past 4 weeks?' proved to be an independent predictor of blood pressure control, demonstrating a relationship between adherence and effective therapeutic result. Omitting the BAAS's other three questions, which were frequently left unanswered in the five valsartan studies, makes this tool even simpler and easier to administer.

The question of how to best evaluate patient adherence remains open, as no 'gold standard' measure currently exists. Recent research has found no association,

for example, between electronic monitoring of the opening of medicine containers and blood pressure outcome.[24,25] Other methods to assess adherence, such as patient-reported questionnaires, have been shown to be either unreliable or overly time consuming. On the other hand, patient interview methods have been shown to inspire patients to be an active part of treatment decisions, helping to increase adherence.[26] Therefore, methods that involve patients but leave survey administration to physicians, as is the case in the two tools under investigation in this study, are preferable.

Implications for research and practice

Adherence to treatments generally, and to medications in particular, will remain a major concern of health providers, leading researchers to pursue the goal of identifying a gold standard of measuring adherence. However, the argument has been made in the adherence literature that there may not be a gold standard of measurement.[7] Electronic monitoring devices, for instance, only record openings and closings, not actual ingestion. More recent technologies of biosensors embedded in pills (for example, the Proteus® system) may record ingestion but user concerns about privacy have been considerable. Last, it is impractical, in research and in clinical practice, to order assays of metabolites to verify intake.

Therefore, while it is acknowledged that both the BAAS and VAS methods could introduce bias, the authors argue that, despite not providing an exact estimate of each patient's 'true' adherence, they do allow a patient to admit they have missed pills and allow a clinician to provide a rating of his or her impression of the patient's adherence behaviour. Based on the data, the authors would argue that either single-item measure, whether patient admission (through the first item of the BAAS) or clinician impression (through the VAS), might be sufficient because they are predictive of actual blood pressure control. They are also likely to promote discussion and to improve physician–patient communication.

To promote successful therapeutic results, research is still needed to identify tools for measuring adherence that are practical and useful in clinical settings, and to identify the patient-related, physician-related, and treatment-related determinants of adherence.

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Ethical approval

All of the constituent studies were approved by ethical committees. Secondary analysis is exempt from ethics review.

Provenance

Freely submitted: externally peer reviewed.

Competing interests

Ivo Abraham, Kris Denhaerynck, and Karen MacDonald are employees of Matrix45. Lorenzo Villa and Diana Sun were interns at Matrix45. Matrix45 was contracted by Novartis to conduct the individual studies from which the data were pooled for the analyses reported in this article. The present analyses were performed *pro bono* by Matrix45 and without contract or compensation. By company policy, employees of Matrix45 cannot hold equity in client organisations or perform services for these clients independently. Matrix45 provides similar services to other biopharmaceutical companies. Stefaan Vancayzeele, Heidi Brié, Ann Aerts, and Christine Hermans are employees of Novartis. Michael Levengood has no competing interests to declare.

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