Comparison of agreement between different measures of blood pressure in primary care and daytime ambulatory blood pressure

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Abstract

Objective To assess alternatives to measuring ambulatory pressure, which best predicts response to treatment and adverse outcome.
Setting Three general practices in England.
Design Validation study.
Participants Patients with newly diagnosed high or borderline high blood pressure; patients receiving treatment for hypertension but with poor control.
Main outcome measures Overall agreement with ambulatory pressure; prediction of high ambulatory pressure (>135/85 mm Hg) and treatment thresholds.
Results Readings made by doctors were much higher than ambulatory systolic pressure (difference 18.9 mm Hg, 95% confidence interval 16.1 to 21.7), as were recent readings made in the clinic outside research settings (19.9 mm Hg,17.6 to 22.1). This applied equally to treated patients with poor control (doctor *v* ambulatory 21.4 mm Hg, 17.3 to 25.4). Doctors' and recent clinic readings ranked systolic pressure poorly compared with ambulatory pressure and other measurements (doctor *r*=0.46; clinic 0.47; repeated readings by nurse 0.60; repeated self measurement 0.73; home readings 0.75) and were not specific at predicting high blood pressure (doctor 26%; recent clinic 15%; nurse 72%; patient in surgery 81%; home 60%), with poor likelihood ratios for a positive test (doctor 1.2; clinic 1.1; nurse 2.1, patient in surgery 4.7; home 2.2). Nor were doctor or recent clinic measures specific in predicting treatment thresholds.
Conclusion The "white coat" effect is important in diagnosing and assessing control of hypertension in primary care and is not a research artefact. If ambulatory or home measurements are not available, repeated measurements by the nurse or patient should result in considerably less unnecessary monitoring, initiation, or changing of treatment. It is time to stop using high blood pressure readings documented by general practitioners to make treatment decisions.

Introduction

Hypertension is perhaps the most common reason for initiation of lifelong drug treatment and ongoing management by doctors. Six prospective studies have shown that ambulatory blood pressures may be a much better predictor of target organ damage and subsequent adverse events than measurements made in a clinic.[1] As these results were found in research studies and mostly not in typical primary care settings, however, patients may have had a higher "alerting response" than in everyday settings with their family doctor or nurse. It is thus important to clarify whether the white coat effect applies equally outside a research study and in typical family practice settings.

Why is ambulatory monitoring not commonly used to make management decisions? The problem is not just extrapolating results from research or secondary care to routine settings but that clinic derived thresholds have been used in previous research to make treatment decisions. However, several lines of evidence show that patients with daytime ambulatory pressure lower than 135/85 mm Hg have a low risk of subsequent events.[2] An ambulatory pressure of 135/85 mm Hg thus represents good control and approximately corresponds to a clinic pressure of 140/90 mm Hg,[2] a generally accepted marker for control.[3] The threshold for diagnosis in the clinic is usually higher (>160/100 mm Hg for most patients),[4] so a higher ambulatory threshold of 145/95 mm Hg has been proposed.[5] Recent guidelines recommended ambulatory monitoring for both initial diagnosis and assessing control,[6] although few studies have looked at the assessment role in primary care. One trial in a mixed setting showed that management according to ambulatory pressure resulted in fewer visits, less use of drugs, and similar final blood pressures.[7] Further evidence is needed from typical primary care settings to explore the implications of using ambulatory pressures and other alternatives, both in the initiation of treatment and in monitoring control.

What about other alternatives? Preliminary evidence, mostly from other settings, indicates that measurements by a nurse or technician, repeated measurements, or home measurements may be closer to ambulatory pressure.[7–14] To our knowledge, no study in a typical primary care setting has compared these methods with ambulatory monitoring. Another alternative is self measurement by patients with equipment in the clinic, which to our knowledge has never been assessed.

We set out to assess the following in typical primary care settings. (1) The white coat effect in the broad group in which decisions are usually made on clinic readings (diagnosis and monitoring control). (2) The extent of the white coat effect as a research artefact. (3) The agreement—ranking, mean difference, and detection of high pressures—between ambulatory monitoring of blood pressure and the realistic alternatives (measurement by doctor or nurse, self measurement in surgery, home). (4) The potential implications of using alternative methods of blood pressure measurement in predicting treatment thresholds.

Methods

Setting

Eight doctors and three practice nurses from three varied practices (deprived urban, cathedral city, market town), each serving 8000 patients, agreed to participate. The doctors and nurses had not previously been involved in research on hypertension. Practice nurses were trained to use the 24 hour monitor and to follow the protocol of measurements.

Participants

Two hundred patients in whom management changes were being considered on the basis of clinic readings participated in the study. Participants were in two categories: newly diagnosed or borderline hypertension (three clinic readings of systolic blood pressure >140 mm Hg or diastolic pressure >90 mm Hg),[4] or established hypertension (three clinic readings >160/100 mm Hg) being treated but with poor control (>140/90 mm Hg).[3]

Most participants were referred opportunistically by doctors; nine eligible patients declined to participate. In one practice some patients were also invited on the basis of high readings documented in the notes.

Equipment

We used the UA-751421 semiautomated device and the OMRON HEM 705CP for measurements by a nurse and home readings by patients.[15 16] For 24 hour readings we used the TM-2421,[17] which is a later, better validated version of the extensively used and validated TM-2420. We also assessed the calibrated mercury sphygmomanometers in current use by the practices. Large cuffs were used where appropriate.

Sample size

Assuming that 50% of patients have high systolic ambulatory pressure and that other methods can detect this with a sensitivity and specificity of 70%, with a 95% confidence interval around this estimate of 20% (plus or minus 10%), then we needed 180 participants.

Blood pressure measurements

The order of measurement reflected the way measurements might be used in practice. Firstly, two measurements were made by the nurse (two visits). The nurse took readings with two types of device three times each, sequentially at every visit, after the patient had been seated for five minutes: a calibrated mercury sphygmomanometer and a validated, calibrated semiautomated cuff oscillometric device. The nurse alternated the two devices and the arm used; which device was used first was randomised. Secondly, the patient carried out self measurement in the surgery (the last 70 patients were invited; 59 came once and 52 twice). A room was provided for the patients to come and take three measurements with the semiautomated device, having previously been instructed by the nurse. Thirdly, 24 hour ambulatory measurement readings were taken at half hourly intervals during the day (0700-2300) and hourly at night (2300-0700). Fourthly, patients took readings at home using semiautomated machines. Patients took four readings a day (two in the morning and two in the evening) on successive days until 14 readings had been taken (which enabled cross validation with the machines' 14 reading memory). Fifthly, after all the other measurements had been carried out, the doctor measured blood pressure with a calibrated mercury sphygmomanometer three times sequentially after the patient had been seated for five minutes.

We randomised the order of home and ambulatory measurements. For the first 130 patients ambulatory or home monitoring took place between the first and second visit to the nurse, with the other measurement (whichever of home and ambulatory had not been done) after the second visit. To estimate whether the fall in blood pressure between the two nurse visits was due to habituation to the intervening ambulatory or home measurements, for the last 70 patients both the home and ambulatory measurements took place after both nurse visits and self measurement in the surgery.

We also recorded up to three recent measurements made in the clinic and recorded in the notes before participation in the study. By their nature, these readings were not controlled in terms of a study protocol, and most readings were made by doctors in the weeks immediately before the study.

Data entry and analysis

We used SPSS and Stata for Windows to set up and analyse the database. We assessed whether the readings were significantly different by using repeated measures analysis of variance and the Bonferroni correction for retrospective comparisons. We made several comparisons of each "test" method and ambulatory monitoring: mean difference (standard deviation; 95% confidence intervals); rank correlation from the Bland Altman plot (plot of the difference between measurements against the mean); rank correlation from a simple scatter plot to document how each test method ranked the blood pressures and thus the risk due to blood pressure; the sensitivity, specificity, and likelihood ratios for a positive and negative test, for predicting high blood pressure and treatment thresholds.

Results

Sample

Of the 200 participants, 107 (54%) were women, 63/194 (33%) were over the age of 65, 96 had newly diagnosed high or borderline high blood pressure (systolic pressure 161 (SD 16) mm Hg; diastolic pressure 95 (9) mm Hg), and 104 were treated but had poor control (systolic pressure 163 (16) mm Hg; diastolic pressure 94 (9) mm Hg). Six patients did not have ambulatory readings (withdrawn or cuff uncomfortable); 173 patients had a complete set of all readings.

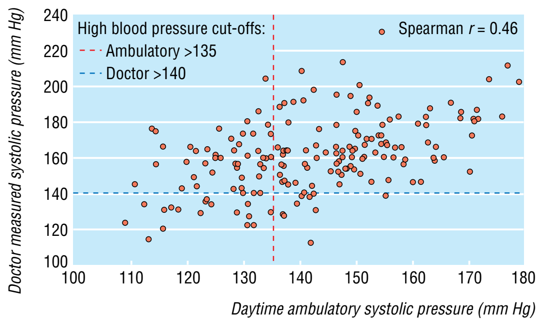

Fig 1 Scatter plot of systolic pressure measured by doctor against daytime ambulatory systolic pressure. On the basis of the cut-off points indicated, doctors' readings have a sensitivity of 91.2%, a specificity of 25.8%, and likelihood ratios of 1.2 for a positive test and 0.33 for a negative test

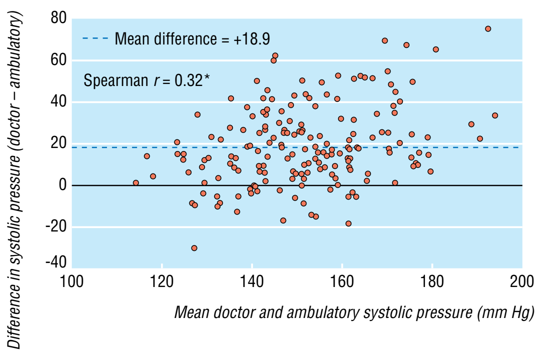

Fig 2 Bland Altman plot of difference between doctors' readings and ambulatory systolic pressure against mean systolic pressure. *Positive rank correlation: difference increases as blood pressure increases

Preliminary analysis: are different readings significantly different?

Repeated measures analysis of variance (excluding self measurement by patients in the surgery, owing to the small numbers) showed that measurements of systolic pressure were not equivalent (F=63.1, $P<0.001$). Post hoc tests showed that all the means differed significantly from ambulatory pressure and from each other, except readings by the doctor and recent clinic readings (which did not differ significantly from each other) and home readings and the second measurement by the nurse (which did not differ significantly from each other). Significant differences also existed between measures of diastolic blood pressure (F=74.4, $P<0.001$). In post hoc analysis diastolic ambulatory pressure differed significantly from all other measures, and readings by the doctors and clinic readings differed significantly from all other measures but not from each other.

Estimating agreement: main results

Figures 1 and 2 illustrate the results in tables 1, 2 and 3 graphically by taking data from the first line of tables 1 and 2. Overall agreement for systolic pressure is illustrated by the scatter plot (fig 1), with a moderate rank correlation (r=0.46); the cut-off points show that readings by the doctor are reasonably sensitive in detecting high ambulatory pressure, but poorly specific. The Bland Altman plot (fig 2) is summarised by the mean difference (the readings by the doctor on average exceed ambulatory pressure by 18.9 mm Hg) and the positive rank correlation (Spearman's r=0.32). Thus the difference between readings by the doctor and ambulatory pressure increases as the blood pressure increases.

Readings made by the doctor were much higher than systolic ambulatory pressure (difference=18.9 mm Hg, 95% confidence interval 16.1 to 21.7), as were recent clinic readings not made in a research study (19.9 mm Hg, 17.6 to 22.1). The white coat effect applied equally for patients on established treatment with poor control (readings by doctor *v* ambulatory pressure, difference=21.4 mm Hg, 17.3 to 25.4). For most methods the difference from ambulatory monitoring increased with blood pressure (a positive correlation on the Bland Altman plots, see table 1). Readings by the doctor and in the clinic also ranked systolic ambulatory pressure poorly compared with other methods (table 1). Most methods were sensitive in predicting high systolic ambulatory pressure (all sensitivity >75%), but readings by the doctor and recent clinic readings were not specific, with poor like-

Table 1 Overall agreement of different measures with mean daytime ambulatory readings (mean difference, rank correlation, and rank correlation from Bland Altman plot)

	Systolic pressure				Diastolic pressure			
	Mean difference (95% CI)	Standard deviation	Scatter plot *r*	Bland Altman plot* *r*	Mean difference (95% CI)	Standard deviation	Scatter plot *r*	Bland Altman plot* *r*
Doctor (n=179)	18.9 (16.1 to 21.7)	19.0	0.46	0.32	11.4 (9.7 to 13.0)	11.2	0.42	0.13
Nurse 1—mercury (n=194)	9.0 (6.8 to 11.3)	16.1	0.48	0.15	9.8 (8.4 to 11.1)	9.7	0.52	0.01†
Nurse 1—oscillometric (n=185)	7.6 (5.3 to 9.8)	15.6	0.52	0.20	10.0 (8.5 to 11.5)	10.3	0.50	0.12†
Nurse 2—mercury (n=193)	5.2 (2.9 to 7.5)	16.2	0.60	0.27	8.3 (7.0 to 9.6)	9.3	0.58	0.09†
Nurse 2—oscillometric (n=190)	3.9 (1.8 to 6.1)	15.2	0.63	0.31	7.9 (6.6 to 9.3)	9.6	0.58	0.14
Self measurement in surgery 1 (n=59)	9.8 (5.9 to 13.0)	15.0	0.63	0.24†	12.9 (10.4 to 15.4)	9.7	0.62	0.14†
Self measurement in surgery 2 (n=52)	7.4 (3.9 to 10.9)	12.5	0.73	0.30	10.6 (8.1 to 13.2)	9.2	0.64	0.18†
Home measurement (n=190)	4.6 (2.7 to 6.4)	12.8	0.75	0.33	6.4 (5.0 to 7.8)	9.8	0.52	0.05†
Last three clinic measurements (n=182)	19.9 (17.6 to 22.1)	15.5	0.47	0.06†	12.6 (11.3 to 13.9)	8.8	0.55	–0.16

*Bland Altman plot (difference plotted against mean) assesses whether mean difference is a fair summary over the range of measurement. Rank correlation summarises whether difference changes with measurement level (0=no change; positive correlation=difference increases with higher pressures; negative correlation=difference decreases with higher pressures).
†Not significant. All other rank correlations were significant at P<0.05.

Table 2 Sensitivity, specificity, and likelihood ratios for a positive and negative test of different measures in predicting high mean daytime ambulatory pressure (>135/85 mm Hg)

	Systolic pressure				Diastolic pressure			
	Sensitivity (%)	Specificity (%)	Likelihood ratio (positive)	Likelihood ratio (negative)	Sensitivity (%)	Specificity (%)	Likelihood ratio (positive)	Likelihood ratio (negative)
Doctor	91.2	25.8	1.2	0.33	85.3	47.7	1.6	0.31
Nurse 1—mercury	83.3	41.2	1.4	0.41	85.3	47.1	1.6	0.31
Nurse 1—oscillometric	79.7	50.7	1.6	0.40	76.1	56.1	1.7	0.43
Nurse 2—mercury	80.8	61.8	2.1	0.31	82.7	58.5	2.0	0.30
Nurse 2—oscillometric	76.4	71.6	2.7	0.33	79.7	61.2	2.1	0.33
Self measurement in surgery 1	92.7	50.0	1.9	0.15	90.9	48.6	1.8	0.19
Self measurement in surgery 2	88.9	81.3	4.7	0.14	100	60.6	2.5	–
Home measurement	87.0	59.7	2.2	0.22	89.0	52.6	1.9	0.21
Last three clinic measurements	97.5	14.5	1.1	0.17	90.0	34.8	1.4	0.29

Cut-off points used to define high blood pressure: home and ambulatory measurements >135/85 mm Hg (chosen as all patients with pressures above 135/85 mm Hg need treatment, change in treatment, or further monitoring[2,6]; for this comparison we assumed that home measurements were similar to ambulatory readings[14]—that is, that >135/85 also represented higher readings[2]); clinic measurements >140/90 mm Hg (we used this cut-off point on the basis of previous consensus for all measurements in the surgery—that is, by doctor, nurse, or self measurement[3]).

Table 3 Sensitivity, specificity, and likelihood ratios for a positive and negative test of different measures in predicting ambulatory pressure treatment thresholds

	Systolic pressure				Diastolic pressure			
	Sensitivity (%)	Specificity (%)	Likelihood ratio (positive)	Likelihood ratio (negative)	Sensitivity (%)	Specificity (%)	Likelihood ratio (positive)	Likelihood ratio (negative)
Doctor	83.7	50.7	1.7	0.32	79.5	63.0	2.1	0.33
Nurse 1—mercury	67.9	67.1	2.1	0.48	75.0	33.6	2.2	0.38
Nurse 1—oscillometric	69.9	73.2	2.6	0.41	68.1	69.6	2.2	0.46
Nurse 2—mercury	66.7	75.3	2.7	0.44	79.2	74.5	3.1	0.28
Nurse 2—oscillometric	58.5	83.3	3.5	0.50	80.9	76.9	3.5	0.25
Self measurement in surgery 1	77.1	58.3	1.8	0.39	100	65.1	2.9	–
Self measurement in surgery 2	80.0	90.9	8.8	0.22	92.3	74.4	3.6	0.10
Home measurement	84.1	68.7	2.7	0.23	80.4	70.6	2.7	0.28
Last three clinic measurements	85.8	43.4	1.5	0.33	84.8	58.8	2.1	0.26

Thresholds at which drug treatment for high blood pressure would be started or changed: ambulatory readings—previous recommendations suggested that in patients with newly diagnosed or borderline hypertension ambulatory readings or home readings of >145/95 mm Hg would indicate a need for treatment,[5] and at >135/85 mm Hg poor control would warrant changing treatment for established hypertension[2,5]; clinic readings (by doctor, nurse, or self measurement in the surgery)—in patients with newly diagnosed hypertension drug treatment would be started at >160/100 mm Hg,[4] and poor control would warrant a change in treatment for established hypertension at >140/90 mm Hg.[3]

lihood ratios (table 2). Nor were readings by the doctor or recent clinic readings specific in predicting ambulatory systolic treatment thresholds, having poor likelihood ratios (table 3). Measurement by the doctor and recent clinic readings performed slightly better for diastolic pressures than for systolic pressures, although other methods still performed better, with higher likelihood ratios for a positive test.

Reliability of ambulatory pressure

Five consecutive patients had ambulatory monitoring repeated after two weeks, which showed good agreement (r=0.86 for daytime systolic pressure, r=0.84 for 24 hour systolic pressure; mean differences −2.2 (SD 5.9) mm Hg and −3 (4.8) mm Hg). This confirms previous evidence about the reliability of ambulatory pressure.[18]

Attenuation of white coat effect with visits to nurse

The fall in blood pressure between the two visits to the nurse was even greater for the last 70 patients, in whom no intervening measurements occurred. For these 70 patients the difference between ambulatory systolic pressure and measurements taken by the nurse was 11 mm Hg for the first visit and 2.8 mm Hg for the second visit.

Patient documentation at home compared with semiautomated sphygmomanometer memory

Agreement existed for consecutive patients between the 14 readings documented by patients and the machine memory for both systolic pressure (n=21; r=0.97; mean difference 3.5 (SD 9.3) mm Hg) and diastolic pressure (r=0.85; mean difference 1.4 (6.0) mm Hg). The differences between readings recorded by the patient and the machine reflect the fact that "practice" readings or readings taken at other times of day (for example, during work) were also recorded by the machine.

Discussion

Limitations of the study

Routine equipment—The agreement with ambulatory pressure was similar when routine equipment was used and when well validated equipment was used. Thus the main limitation of measurement in routine clinic settings is not the type of sphygmomanometer used.

Varied sample—We used patients with newly diagnosed hypertension and patients with poorly controlled hypertension, but this reflected recent guidance.[6] Furthermore, the subgroups (newly diagnosed and established hypertension) had very similar blood pressures.

Arbitrary cut-off points to define potential management decisions—Exact management thresholds will always be debated. Nevertheless, agreement exists that poor control in clinic readings for most patients is >140/90 mm Hg,[3] and that for ambulatory readings ≤135/85 mm Hg represents good control (although patients with additional risk factors may need tighter control).[2 5 6] There is also agreement that patients with clinic pressures of >160/100 mm Hg need drug treatment to be started,[4] but debate continues about the threshold for ambulatory pressure. We used a level defined by previous recommendations (>145/95 mm Hg, which corresponds approximately to the 160/100 mm Hg for clinic pressures).[5] Other authors have suggested using a similar criterion by adding 10 mm Hg systolic and 5 mm Hg diastolic to home or ambulatory pressures to provide "equivalent" clinic readings to inform decision making.[14] The poor specificity and likelihood ratios of readings by the doctor and in the clinic with either a single cut-off point for high pressure or different cut-off points for treatment suggests that the particular thresholds chosen do not alter the inferences from the study.

Order of measurements—Recent measurements in the clinic (that is, historic measurements) were very similar to measurements by the doctor (the last recorded in the study). Furthermore, the drop between the two measurements by the nurse for the first 130 patients could not be explained by the intervening home or 24 hour measurements, as a similar or greater effect was seen in the last 70 patients, for whom there were no intervening measurements. Thus the differences between measurements are likely to be due not to effects of order or time but to the different alerting responses for different measurements.

The white coat effect—artefact of setting, sample, or research studies?

The estimates of the white coat effect in this study are similar to those in previous work, mostly not from typical primary care settings.[8–14] This was true for both patients with newly diagnosed hypertension and those with established hypertension, and for both measurements taken as part of the study and recent measurements documented in the clinical notes. Thus the white coat effect observed in the major prognostic studies to date is not likely to be an artefact of other settings or of research studies and applies equally to new diagnosis and assessment of control.

Although debate continues about just how benign white coat hypertension is,[19] such studies have been criticised as some have not measured the white coat effect in a standard way.[20] Prospective studies indicate that patients with white coat hypertension are at considerably reduced risk compared with those with higher ambulatory pressures and that treatment modifies blood pressure and outcomes only in patients with high ambulatory blood pressure.[2 7 19] The overzealous initiation and maintenance of treatment for white coat hypertension represents an enormous opportunity cost for health professionals and for patients, in addition to the associated iatrogenesis—particularly unnecessary anxiety[21] and side effects.[22 23]

What is already known on this topic

Prospective studies indicate that ambulatory blood pressure is a much better predictor of adverse outcome and response to treatment than readings made by a doctor

Preliminary evidence suggests that measurements by doctors are likely to be higher than those made by nurses, technicians, or patients

No study has compared all the available measures in a typical primary care setting with ambulatory blood pressure in patients with newly diagnosed and established hypertension

What this study adds

The white coat effect associated with measurements by doctors is not an artefact of research studies; it applies equally in primary care and for both initial diagnosis and assessment of control

If ambulatory measurement is not possible, repeated measurement by a nurse or by the patient will result in much less unnecessary treatment or change in treatment for high blood pressure

Are the alternatives to measurements by a doctor better?

Evidence exists from prospective studies about the relation between ambulatory blood pressure and outcome.[1] Nevertheless, ambulatory monitoring equipment is expensive (the machine used in this study cost £2000), and as approximately half of all patients with hypertension are poorly controlled each practice would need several machines to cope with the workload. Although more automated downloading of results should potentially reduce costs, staff costs (setting up, reviewing, downloading, printing) are also currently high, meaning that costs are not reduced overall.[7]

Measurement by a nurse—This study shows that repeated readings by a nurse in primary care provide a better assessment than readings by doctors, supporting research from other settings.[10] However, staff costs are similar to those for ambulatory monitoring.[7]

Home measurement—This study confirms that patients can accurately measure and record their blood pressure themselves at home,[10 14 24] with great potential advantages of lower equipment and staff costs compared with ambulatory pressure. Although ambulatory monitoring can assess night time dipping and hence help with diagnosis of secondary hypertension, this can only be securely diagnosed by investigation (renal function tests, ultrasonography, electrolytes, vanillylmandelic acid).

Self measurement by patients in the clinic—Self measurement by patients in the clinic may provide similar levels of overall agreement with ambulatory pressure to home measurement. The advantages are that practice staff are available for questions and that equipment costs are minimal (one machine can be kept in the practice, rather than several machines being lent out). The disadvantages are that more visits to the clinic are needed than for home readings and that suitable rooms have to be made available. The estimates from this study are also less precise and need confirmation (only 52 of the 70 patients invited completed both measurements).

Conclusion

The "white coat" effect is important in diagnosing and assessing control of hypertension in primary care and is not a research artefact. If ambulatory or home measurements are not available, repeated measurements by a nurse or the patient should result in considerably less unnecessary monitoring, initiation, and changing of treatment. It is time to stop using high blood pressure readings documented by general practitioners to make decisions about treatment.

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