

THE AUTOMATIC PATIENT SYMPTOM MONITOR (APSM): A VOICE MAIL SYSTEM FOR CLINICAL RESEARCH

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ABSTRACT

*Double-blind clinical trials become very tedious when symptoms are measured rather than objective laboratory and physical parameters. The standard "diary card" method is labor intensive for patients and impractical to use for more than a few weeks. In chronic relapsing disorders it would be far better for patients to record symptoms one or more times per day, at defined times, for weeks, months or even years. The Automatic Patient Symptom Monitor (APSM) is a voice processing system designed to achieve this goal. APSM calls patients at home every night, addresses each patient by name and then asks a set of questions which patients answer by pressing the touch tone keys on their telephone. APSM enters data into a computer database file which can be easily retrieved by investigators, even by modem. In a pilot study, patients with telephones easily learned how to use APSM. They were given therapy for a gastric infection (*H.pylori*) and were monitored by APSM until follow-up one month after completing treatment. Eight of nine patients recorded valid data on >80% of study days. In all cases, APSM data matched the patient's own impression of whether they were better, the same, or worse. With one exception, APSM assessment correlated with microbiologic data obtained post therapy i.e. when the gastric infection had been eradicated, patients felt better ($p < 0.047$). Long term clinical monitoring with APSM may decrease clinical trial time and improve the statistical power of double blind studies.*

INTRODUCTION

In order to introduce new therapies into the United States, investigators must be able to demonstrate safety and efficacy in double-blind controlled studies. Such trials are straightforward when the goal of therapy is easily measured; for example blood pressure lowering effect or peptic ulcer healing. However, some disorders are very difficult to study because there are no objective physical signs or abnormal laboratory parameters to measure during therapy. Examples of such disorders are non-ulcer dyspepsia,

irritable bowel, migraine and fibromyalgia. These syndromes are of unknown etiology, produce few objective physical signs or abnormal laboratory tests, and run a chronic, relapsing, unpredictable course.

To measure a therapeutic effect in such poorly understood disorders, a daily symptom assessment over many months would be ideal. Daily diary cards are used in most clinical studies, but diaries are very tedious for the patients and labor intensive for study nurses. In addition, patients who are poorly educated often have problems filling out diary cards so that another family member is sometimes required. Finally, retrieving, editing and entering untidy diary card data into the study database often causes several weeks delay after a patient has completed the study.

The only alternatives to frequent diary cards are weekly or monthly patient interviews. Periodic interviews may be colored by the patient's condition on the interview day rather than reflect an average over a time interval. Some therapeutic trials may also be difficult to blind if the investigators have frequent interviews with patients.

Because the above methods of patient monitoring have so many limitations, investigators must increase recruitment into clinical trials to overcome loss of statistical power introduced by variability of data and scarcity of observation points for each patient. This serves to increase the expense and delay the outcome of clinical trials. Ultimately, the public must pay back these extra costs as increased drug prices or delayed access to a new useful remedy.

In order to solve some of the above problems we attempted to construct a hardware and software package which could remotely monitor patient symptoms in clinical trials. We have called this system the Automatic Patient Symptom Monitor (APSM).

PATIENTS AND METHODS

System Design:

Essential features necessary for use by patients were *user friendliness*, ruggedness, simplicity, brevity, accuracy, and flexibility. For study nurses and study monitors APSM required telephone messaging, remote access, activity reporting and simple new-patient setup. For drug companies, statisticians and data processing personnel, APSM required flexible output format and remote access without interrupting the system. For researchers APSM needed to be inexpensive.

Hardware:

The APSM system was initially based on a 286 computer with 1 megabyte of ram and a 40 megabyte hard disc running under DOS 5.0. APSM also runs in a multitasking environment under Windows™ but requires at least a 486SX with 4 Mb ram to operate efficiently. The telephone interface was achieved with a Dialogic two line voice processing board. This board performs simultaneous inbound and outbound calls. A 9600 baud data modem was added which could receive inbound calls on the second (outbound) voice line as shown in Figure 1.

Software:

The two software components of APSM are the database and the voice processor. The database was programmed in the Clipper™ language with interface modules in Turbo C™. The software is modular so that it can run in less than 512k of ram. The voice system database interface was programmed in a proprietary macro language appropriate to the hardware. The APSM program is protected with a hardware lock.

Prototype software was continually upgraded during the first year of operation. The program currently has the following specifications.

Patient Interface:

APSM calls patients at the time of day they specify, usually between 4PM and 11:30PM.

Patients are addressed by their usual name. For example; "Hello, this is the University of Virginia call-

ing for Mary Johnson, please press 1 to confirm you are on the line."

If the patient is not home, APSM will call back at intervals during the next hour before canceling the call. If the call is intermittent, such as once per week or once per month, APSM will call back each day for three days or until an answer is received.

After pressing 1, patients choose to answer questions in English or a second language. Thus APSM can be used throughout the United States without modification.

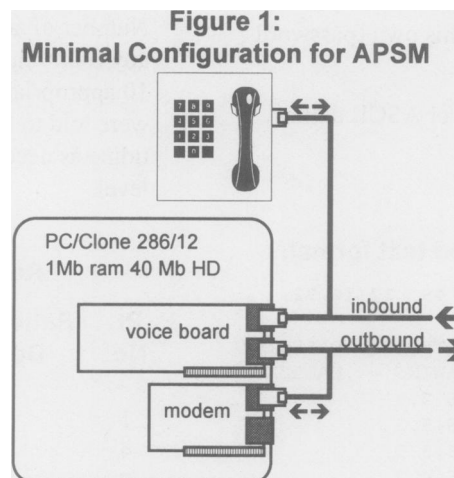
If patients are out of town they can access APSM by calling an 800 number. When receiving an inbound call, APSM allows anyone to leave a voice message. If the patient selects the option to answer a questionnaire, APSM first asks for the social security number. When the patient types in a valid social security number APSM gives a personal greeting "Hello *Mary Johnson*. You should now answer the questions by pressing the keys on your telephone, and you can leave a message at the end."

To allow rapid data entry, patients answer questions by pressing touch tone keys on their telephone. Key-press immediately causes APSM to skip to the next question thus allowing patients to speed up data entry as they gain experience.

Appropriate questions are asked for each patient. For example, a patient who has nausea but no heartburn would not be asked about heartburn symptoms. This serves to speed up calls because unnecessary questions are omitted from each patient's uniquely configured questionnaire.

Symptoms are scored on a digital analog scale. APSM prompts patients with acceptable ranges. For example; "How bad was your heartburn over the past 24 hours, answer on a scale of 0 up to 5." The actual scale used can be varied for each question. If necessary, a 100 point linear analog scale can be measured by the patient and keyed into APSM.

When a patient keys in an incorrect value, APSM immediately detects the error. For example; "I'm sorry, your answer was out of range. Please try again."



Messages from the investigator can be relayed to patients using APSM. Usually the message is played to the patients before APSM asks the questions.

At the end of each questionnaire, patients can record a voice message. These messages are collected and relayed to the investigator at home. Each patient may have a different investigator to whom messages are forwarded. Investigators may delete messages after they have been heard. APSM will leave messages on the investigator's answering machine if he is not home but in this case the message also remains on APSM until deleted by the investigator.

Investigator Interface:

Investigators each have a unique mailbox which allows them to retrieve voice messages from their patients.

Investigators may access their patients' data remotely by modem.

Each investigator can only access his own (password protected) patient data files.

Data output can be in DBF format or ASCII delimited text as in Figure 2.

**Figure 2:
Example of ASCII delimited text format.**

```
SMITH, JOANNE, 123456789, F, 49, 12/14/92,
APSM DIARY COMPARISON, ,
Time, CallDate, SrvDate, NIGHTPAIN, DAYPAIN
, HEARTBURN, STOMCHPAIN, GNAWING, NAUSEA
19:32,12/1/92,12/1/92,3,5,2,5,2,4
19:31,12/2/92,12/2/92,3,5,3,5,5,3
19:30,12/3/92,12/3/92,5,5,2,5,3,1
20:36,12/4/92,12/4/92,4,4,2,5,4,2
21:00,12/5/92,12/5/92,3,2,0,3,3,0
21:00,12/6/92,12/6/92,3,5,3,5,5,1
21:00,12/7/92,12/7/92,3,1,1,4,4,0
21:00,12/8/92,12/8/92,2,3,0,4,4,0
21:09,12/9/92,12/9/92,2,4,0,4,3,2
21:26,12/10/92,12/10/92,1,4,0,3,0,1
21:00,12/11/92,12/11/92,2,4,1,3,1,3
21:01,12/12/92,12/12/92,2,3,0,3,1,2
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The ASCII format can immediately be taken up by spreadsheet and graphics programs and charted as shown in Figure 3.

Many different questionnaires can be run (for different investigators) at the same time.

Unlimited calling patterns are possible. For example, daily, several per day, once per week, once per month, seven days per month, seven days every three months, daily for one month then once per week for one year, etc.

A maximally configured APSM system can handle 500 patients and 500 questions.

Up to 4 voice boards (16 telephone lines) can be used in one PC. In this case 300 calls could be made per hour. A minimal system can make and/or receive 50 calls per hour.

APSM is configured to restart after power failures. With screen saver and password protection the system cannot be tampered with or altered except by approved personnel.

Evaluation Study:

Patients selected for the study were persons with stable chronic dyspepsia who underwent therapy with antibiotics for *Helicobacter pylori* gastritis [1]. A master questionnaire for dyspepsia was constructed and recorded in APSM. Answers were on a digital analog scale of 0 (none), 1 (minimal), 2 (mild), 3 (moderate), 4 (severe) and 5 (very severe/maximal). Number of antacid tablets and/or acid-reducing therapy (ranitidine) was also asked. For each patient, 5-10 appropriate questions were selected. Patients were told to take their antacid medication and ranitidine as necessary to reduce symptoms to a tolerable level.

**Table 1:
Results of APSM Pilot Study.**

Pt. No.	Patient's Opinion: Better, Same, Worse	APSM Result	Follow up Test
1	B	B	Neg.
4	B	B	Neg.
7	B	B	Neg.
8	B	B	Neg.
9	B	B	Neg.
6	S	S (21d)	Pos.
2	S	S	Pos.
3	S	S	Pos.
5	S	S	Neg.

After explaining the study to the patient, a 15 minute training session was performed via a speakerphone using a dummy social security number (123456789). Data from new patients were examined 48 hours later and the patient was called to check that no problems had developed. After that time APSM called patients daily for at least 60 days allowing for a 14 day baseline period, a 14 day treatment (with antibiotics) period and a 30 day follow-up period.

One month after therapy, patients were seen in the outpatient clinic. At that visit they were asked

whether or not they had improved. Patients then underwent a microbiologic test to determine whether or not the gastric infection had been eradicated.

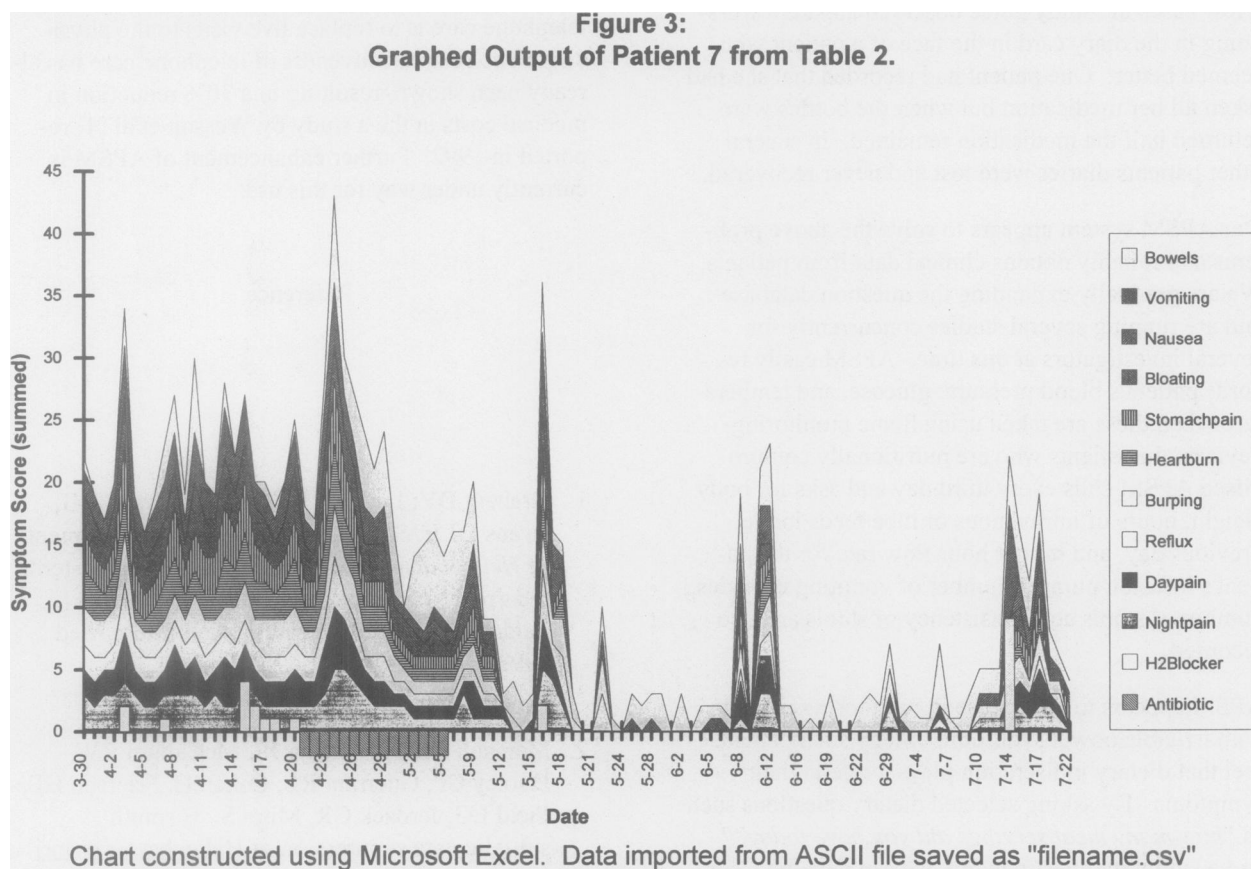
RESULTS:

Of twelve consecutive patients, two could not be included in the study because they did not have a telephone line at home. Ten therefore took part. One of these patients was admitted to another hospital after one week and could not complete the study. Outcome of the other nine patients is shown in Table 1. Patient 6 did not take medication as instructed and did not fully understand the study so calls were ter-

In all patients studied, APSM graphs concurred with the patient's impression of whether or not improvement had occurred, i.e. clinical success or failure of the therapy (shown in Table 1). The APSM graph from patient 7 of Table 1 is illustrated in Figure 2. This patient had reduced scores in all parameters with a significant improvement over baseline ($p < 0.001$ Student's t test). It can be seen from the graph that a point assessment on date 7-14 would have led to the erroneous conclusion that the patient was unchanged from baseline. In fact, she reported great improvement as shown by area under the curve post therapy.

Although the numbers are small, APSM results also

Figure 3:
Graphed Output of Patient 7 from Table 2.



minated after only 21 days.

Four of the nine patients lived outside Virginia. None of the patients were reimbursed but seven of them were monitored by APSM for more than three months, and one of them for 12 months. Two patients requested that APSM cease after three months, in the other seven patients APSM was ceased at the discretion of the investigator. One of the patients did not have a touch tone telephone so it was supplied by the investigator.

correlated with the result of antibiotic therapy. As control group we used patients with failed eradication. In patients who experienced eradication of *H. pylori* (and presumed healing of gastritis), APSM recorded improvement over baseline ($p = 0.047$, Fishers exact test, data from patient 6 included).

DISCUSSION:

The development of APSM followed a very frustrating clinical trial involving patients with non-ulcer dyspepsia (NUD). In brief, NUD represents a syndrome in which patients have ulcer-like symptoms but in whom no peptic ulcer can be found at endo-

scopy. These patients have a variable response to acid reducing medications and often pursue a diagnosis for many years. Double blind trials of therapy have failed to show a benefit over placebo for acid reducing drugs such as cimetidine, or from antacids.

In our study, patients with gastritis caused by *H.pylori* were given Pepto-Bismol, an agent which inhibits the bacterium and heals gastritis [2]. No significant clinical benefit was seen in the study even though the gastritis healed with therapy. In retrospect we realized that some of the patients had not understood the diary card well enough and may have been scoring with an inverted scale on some days. In a few cases the study nurse observed apparent worsening in the diary card in the face of a patient who seemed better. One patient had recorded that she had taken all her medication but when the bottles were returned half the medication remained. In several other patients diaries were lost and never recovered.

Our APSM system appears to solve the above problems and reliably obtains clinical data from patients. We are gradually expanding the question database and are running several studies concurrently for several investigators at this time. APSM easily records patient's blood pressure, glucose, and temperature when these are taken using home monitoring devices. In patients who are nutritionally compromised APSM calls every third day and asks for body weight, hours of intravenous or tube feeds in the previous day, and ml per hour flow rate for the patient's infusion pump. Number of vomiting episodes, number of stools and consistency of stools are also recorded.

APSM appears to have a use in monitoring patients with irritable bowel syndrome. Many such patients feel that dietary indiscretion plays a role in their symptoms. By asking selected dietary questions such as "how many meat servings did you have today?" and a symptom questionnaire, we can develop a correlation matrix to study the relationship between diet and symptoms. Then, if a therapeutic trial is performed, clinical response can be seen in the APSM output. This detailed information may save patients from taking expensive medication which is otherwise useless.

We have now been using APSM for over one year. As Patel and Babbs have stated [3], telephone monitoring of patient parameters is a useful means of unobtrusively obtaining clinical data. Patel's patients entered weight and cardiology parameters in order for the investigators to monitor their medical condi-

tion at home. While Patel's system had many of the features we describe, it was not designed specifically for clinical trials and apparently did not have the security coded investigator access to database files. However, Patel's system did offer a graphical output which could be faxed to the patient's physician.

APSM is versatile enough to be used in routine practice as well as in clinical trial settings. The voice-mail feature is especially liked by patients who can leave messages for medication refills or drug side effects. With this feature, plus 3 day call back ability, APSM is ideally suited to replace nursing calls if telephone care is to replace live visits to the physician. The cost-effectiveness of telephone care has already been shown, resulting in a 30% reduction in medical costs in the a study by Wesson et al [4] reported in 1992. Further enhancement of APSM is currently under way for this use.

Reference

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4. Wasson J, Gaudette C, Whaley F, Sauvigne A, Baribeau P, Welch HG. Telephone care as a substitute for routine clinic follow-up. JAMA 1992; 267: 1788-93.