PAIN MEASUREMENT TOOLS AND METHODS, AMBULATORY BLOOD PRESSURE MONITORING AND QUESTIONNAIRES IN CLINICAL RESEARCH- OVERVIEW

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ABSTRACT

An Expert Working to review the status of the use of pain measurement tools (PMTs), Ambulatory blood pressure monitoring (ABPM) and Questionnaires in Clinical Research. The present work recommends that standardized methods should be applied for the use of PMTs in research. Unidimensional pain measurement tools (PMTs) and multidimensional pain measurement tools (PMTs) designed to assess pain, the McGill Pain Questionnaire and Brief Pain Inventory are valid in many multilingual versions.

The diagnosis and management of hypertension is based on blood pressure (BP) measurements taken by doctors or nurses with conventional sphygmomanometers. Asking the patient to take their own BP at home has been sporadically reported for many years, but the potential value of patient home measurement has been overshadowed by the development of continuous ambulatory BP monitoring.

Ambulatory blood pressure monitoring have been shown to improve the management of hypertension. Twenty practices were asked to monitor hypertensive patients, in particular those about to start drug treatment and those who were poorly controlled.

A good questionnaire design for a clinical trial will minimize bias and maximize precision in the estimates of treatment effect within budget. The mode of administration can also impact on the cost, quality and completeness of data collected. There is good evidence for design features that improve data completeness but further research is required to evaluate strategies in clinical trials. Theory-based guidelines for style, appearance, and layout of self-administered questionnaires have been proposed.

KEYWORDS: pain measurement tools (PMTs), Ambulatory blood pressure monitoring (ABPM), Questionnaire design, Mode of administration, Guidelines.

1. PAIN MEASUREMENT TOOLS AND METHODS

1.1 INTRODUCTION

Pain is a complex and subjective experience that poses a number of measurement challenges. However, in the current culture of evidence-based medicine, it is important that clinicians and researchers utilize sensitive and accurate pain outcome measures. Currently, there exists no valid and reliable method of objectively quantifying an individual's experience of pain. Therefore, we rely mainly on self-report measures to determine the impact of pain. Despite the challenges that pain measurement presents, a number of tools and approaches can be employed to collect useful pain estimates.[1]

Interpretation of research data requires that the data be valid and recorded in an interpretable format. In clinical studies on pain, valid and reliable outcomes should be used. Furthermore, in order to compare data between studies, a standardization of outcomes, namely, pain measures, will increase the validity of the comparisons.[2]

Success in meeting this challenge requires delineation of the scope of the problem, characterization of the pain syndromes, determination of optimal therapeutic strategies, identification of barriers to implementation of effective strategies, determination of strategies to overcome these obstructions, and the monitoring of outcomes for purposes of continual quality improvement.

Many approaches to the measurement of pain attributes have evolved over the past four decades. Some of them have been applied to cancer pain and palliative care, but the selection and application of these approaches in palliative care has often been capricious and idiosyncratic.[3]

No valid instrument is applicable at the moment for the assessment of pain in the cognitively impaired. A behavioral scale has been recently designed for pain assessment in the cognitively impaired patient and its validation is ongoing.[4-6]

1.2 DESCRIPTION OF PAIN MEASUREMENT TOOLS (PMTS)

Because resources and time are always limited, we are forced to make decisions on which outcomes to include in our measurements. In some cases, a simple measure of pain intensity may be the most logical primary outcome variable. In other cases, a general indicator of work or social functioning may be more clinically relevant. Pain clinicians will recognize cases in which an individual is profoundly disabled by seemingly low pain intensity, and cases in which an individual maintains a productive and fulfilling lifestyle despite reporting a high degree of pain. Some interventions may have little impact on pain intensity scores, but may benefit mood, motivation, and functioning.

Therefore, one of the most important decisions to make in testing a new treatment is determining what outcomes are most clinically relevant. We now review a few of the available pain outcome measures, which range from simple and narrowly defined, to large and multidimensional. Each has its proper place in measuring pain outcomes. We also refer readers to the IMMPACT recommendation on a core set of outcome measures.[7-10]

1.2.1 UNIDIMENSIONAL PAIN MEASUREMENT TOOLS

Three types of unidimensional pain measurement tools are considered,

- Visual analogue scales (VAS),
- Categorical verbal rating scales (VRS), and
- Categorical numerical rating scales (NRS).

All of these approaches are commonly used to measure pain intensity and are well validated in the cancer population.[11]

VAS, VRS, and NRS are also commonly used to measure pain relief. The VAS has been studied and is often considered an ideal scale, because it is continuous, approximates a ratio scale, and is more independent from language than verbal scales (although the choice of the extreme anchor words or end-phrases can be relevant).On the other hand, its validity more strongly depends on the appropriateness of administration method and of the instructions given to the study subjects.[12-15]It is, therefore, more difficult to use than other scales.

Evidence suggests that numeric rating scales are easier to apply and are associated with better compliance than the VAS. Based on the available evidence, the use of a standard 0-10 numeric rating scale and 100-mm horizontal visual analogue scale can be recommended.[16] although these are typically administered with pen and paper; other valid approaches include the use of touch screens for VAS and NRS, sliding scales, and verbally administered numeric rating scales.

For purposes of intervention studies, both pain intensity and pain relief can be measured. Pain relief can be measured by asking the patients to compare pain now with previous pain experiences.

Pain relief measurement validity is limited to short-term intervention studies (24 hours or less); in chronic studies, its validity has been seriously questioned and the construct underlying its meaning in descriptive studies is uncertain.[17]

1.2.2 MULTIDIMENSIONAL PAIN MEASURING TOOLS

Three multidimensional scales are considered,

- the McGill Pain Questionnaire,
- the Brief Pain Inventory, and the
- Memorial Pain Assessment Card.

Although recognizing that other instruments exist or are under study, the Expert Working Group recommends the use of the Short form of the Brief Pain Inventory or the McGill Pain Questionnaire.

The Brief Pain Inventory (BPI) is a simple and easy to administer tool that provides information about the history, intensity, location, and quality of pain. Numeric scales (range 0 to 10) indicate the intensity of pain in general, at its worst, at its least, and right now. A percentage scale quantifies relief from current therapies. A figure representing the body is provided for the patient to shade the area corresponding to his or her pain.[18-20]

The McGill Pain Questionnaire (MPQ) is a self-administered questionnaire that provides global scores and subscales scores that reflect the sensory, affective, and evaluative dimensions of pain. It has been validated in cancer pain.

A short form of the MPQ (SF-MPQ) was developed for use in research settings. The SF-MPQ consists of 15 representative words from the sensory (n _11) and affective (*n*_4) categories of MPQ. The Present Pain Index, verbal rating scale, and visual analogue scale (VAS) measuring pain intensity is included.

The 15 words are scored using a 4-point verbal rating scale, ranging from none, mild, moderate, to severe pain. The SF-MPQ correlates highly with the MPQ. Whereas the MPQ is available in many languages, the SF-MPQ is not.[22-25]

1.3 PHYSICAL METHODS USED IN PAIN MEASUREMENTS

A large number of techniques for pain threshold determination have been described. The painful stimuli used in these methods fall into several categories:

CHEMICAL STIMULI: Several alkaline and acid solutions, amines and peptides have been used. They are generally ineffective when use, don't intact skin and therefore methods of applying these substances intraepidermally, intradermally, intramuscularly and at the exposed base of a blister have been used. Problems include the inability to repeat the test frequently due to accumulation of the chemical, measurement of the concentration of the substance within the tissue, and determination of the precise site of action.[26]

THERMAL STIMULI: Thermal stimulation is favored by most investigators as the most adequate for pain threshold determination studies. Radiant heat has been widely used since the popularization of the method by Hardy et al.(1940). However, potential tissue damage is associated with repetitive stimulation of the same point of the skin and there is not a strict linear relationship between the intensity of the stimulus and the heat delivered to the skin. This is probably related to regional blood flow and can introduce errors in the measurement. A recent improvement in this field has been the introduction of infrared laser beam stimulation. This method shortens the exposure time required for thermal noxious stimulation to a few milliseconds, avoiding co-activation of non-noxious thermoreceptors.[27]

Conducted heat for noxious thermal stimulation does not have the specificity of radiant. Heat methods due to simultaneous activation of mechanoreceptors. Recently, a method for Routine

clinical practice using a mode has been developed by Fruhstorfer et al. (1976). It is a rapid and repeatable method that can be used on any part of the body surface.

ELECTRICAL STIMULI: Electrical stimuli are widely used in experimental pain research. Usually a Square wave pulse or train of pulses is delivered to the skin. The current applied may vary considerably as a result of changes in the electrical resistance of the skin unless a device to Maintain a constant current is incorporated.[28]

MECHANICAL STIMULI: Compression of skin, tendons and underlying bone structures by means of a calibrated device is the commonly used method. The rate of application of the pressure is an important factor and should be taken into account in the experimental design. Differences in tissue compliance affect the distribution of the applied force and can be another source of variation.[29]

1.4 PRINCIPLES IN THE APPLICATION OF PAIN

Several principles are relevant when incorporating a PMT into the methodology of a descriptive or interventional study.

APPROPRIATENESS: The selected tool must be appropriate to the study design and the intended study population.[30]

FREQUENCY OF APPLICATION: The frequency of pain measurement must be relevant to the research question to be addressed and the study population. It must be practical and not excessive burdensome.

DATA COLLECTION: Data should be collected in a standardized format, which is applied identically to all participating patients.[32]

The procedure should be documented as part of the study protocol. Where the patient population is heterogeneous and comprises sub populations that require different measurement approaches, contingencies for the application of differing methods of group specific data collections should be documented. However, in general, it is not recommended that different measurement approaches be applied sub populations in the same study.[33-34]

2. AMBULATORY BLOOD PRESSURE MONITORING (ABPM)

2.1 INTRODUCTION

The diagnosis and management of hypertension is based on blood pressure (BP) measurements taken by doctors or nurses with conventional sphygmomanometers. Asking the patient to take their own BP at home has been sporadically reported for many years,[35-39] but the potential value of patient home measurement has been overshadowed by the development of continuous ambulatory BP monitoring.[40]

Home BP monitoring is recommended in some national[41] and local guidelines (Burns-Cox, personal communication, 1998) as an adjunct to the diagnosis and management of hypertension because it has been shown to diagnose sustained 'white coathypertension' (WCH)[42,43] improve patient compliance with follow- up and medication, help in the management of poor BP control[44] and drug side-effects, and reduce prescribing costs. It has not been widely used in the United Kingdom because it has required patient training in the use of mercury or aneroid sphygmomanometers and because of doubts about the accuracy of
Patient measurements.

Now that accurate, reliable, and inexpensive semi-automatic monitors are available and have been validated, home monitoring has become feasible. We saw the need to establish the feasibility of home BP monitoring in the diagnosis of sustained WCH and assess its acceptability to doctors, nurses, and patients. This study therefore investigated the use and acceptability of home monitoring and estimated the incidence of WCH as diagnosed in a primary care setting.[46]

2.2 METHOD

Local practices were offered participation in the study and the 20 who agreed were offered a monitor in exchange for data on its use. Each practice was provided with an Omron 705CP monitor, which enabled the storage of up to 14 measurements within its mechanism and a print out of these with mean values. They were asked to monitor new hypertensive patients before starting drug treatment (the 'untreated' group), those who were poorly controlled before increasing or changing their medication (the 'uncontrolled' group), and others whom they thought might benefit.

Details of prior BP measurements, medication, and cardiovascular risk were requested, and nurses were asked to brief patients to take the patients' BP 14 times over five days, recording the figures automatically in the device and on a written chart. Patients completed a simple questionnaire on acceptability. Doctors and nurses detailed their experiences and opinions during the study. Focus groups with patients and with doctors and nurses were held.[47]

Guidelines on monitoring and using the results were provided for practices. We used the British Hypertension Society Guidelines on the criteria for the diagnosis (≥160/100) and control (<160/90) of hypertension12 using clinic readings. Home BP levels are known to be similar to those of daytime ambulatory monitoring, 13 and we defined the normal as a mean home BP of <150/95 for untreated cases and <150/85 for those poorly controlled. Mean home levels could be compared with clinic readings by adding the correction factors of 10 mmHg to the mean home systolic and five to the mean home diastolic as discussed below.

Sustained WCH was diagnosed if clinic levels were hypertensive but corrected mean home levels were normal.14 We advised that patients with WCH, mild to moderate clinic levels, and no evidence of cardiovascular damage or major risk factors could be treated by non-drug strategies and observation with further home monitoring.[48]

2.3 RESULTS

The practices' age–sex distributions, their setting, their teaching status, and their socioeconomic profiles varied considerably, but these were not associated with any differences in monitor use.

There were 81 full-time equivalent doctors, a total list size of 142 000, a mean of 7200 patients per practice, and 1760 per doctor. Most practices quickly developed a waiting list for monitoring And five were lent second monitors by the project. Others purchased one so that, within a few months of the beginning of the investigation, 12 practices had more than one monitor.

THE PATIENTS

A total of 672 patients were offered monitoring. One refused and a further 11 were excluded from the analyses; three because they provided no monitor readings, two where the practices did not provide records of clinic BP measurements and a further six because of unacceptable readings. Of the 660 remaining, 236 (36%) were new patients, 258 (39%) were poorly controlled, and 166 (25%) were monitored for other reasons (Table 1).

This latter group was mainly borderline cases not fulfilling the study criteria for hypertension or poor control, while three were pregnant and several others were monitored for undocumented reasons. Twenty-nine (4.4%) of the total had diabetes and 45 (7%) had a history of cardiovascular disease.

Table 1. Numbers of patients monitored by age and sex.

	Age group (years)						
	<40	40–49	50–59	60–69	70–79	>80	Total
Male	27	65	80	70	28	5	275
Female	39	67	110	106	60	6	385
Total	66	132	190	176	88	8	660
Percentage of those monitored	10%	20%	29%	27%	13%	1	100%
Per 1000 of total population	3	6	10	12	8	1	5

MONITOR USE

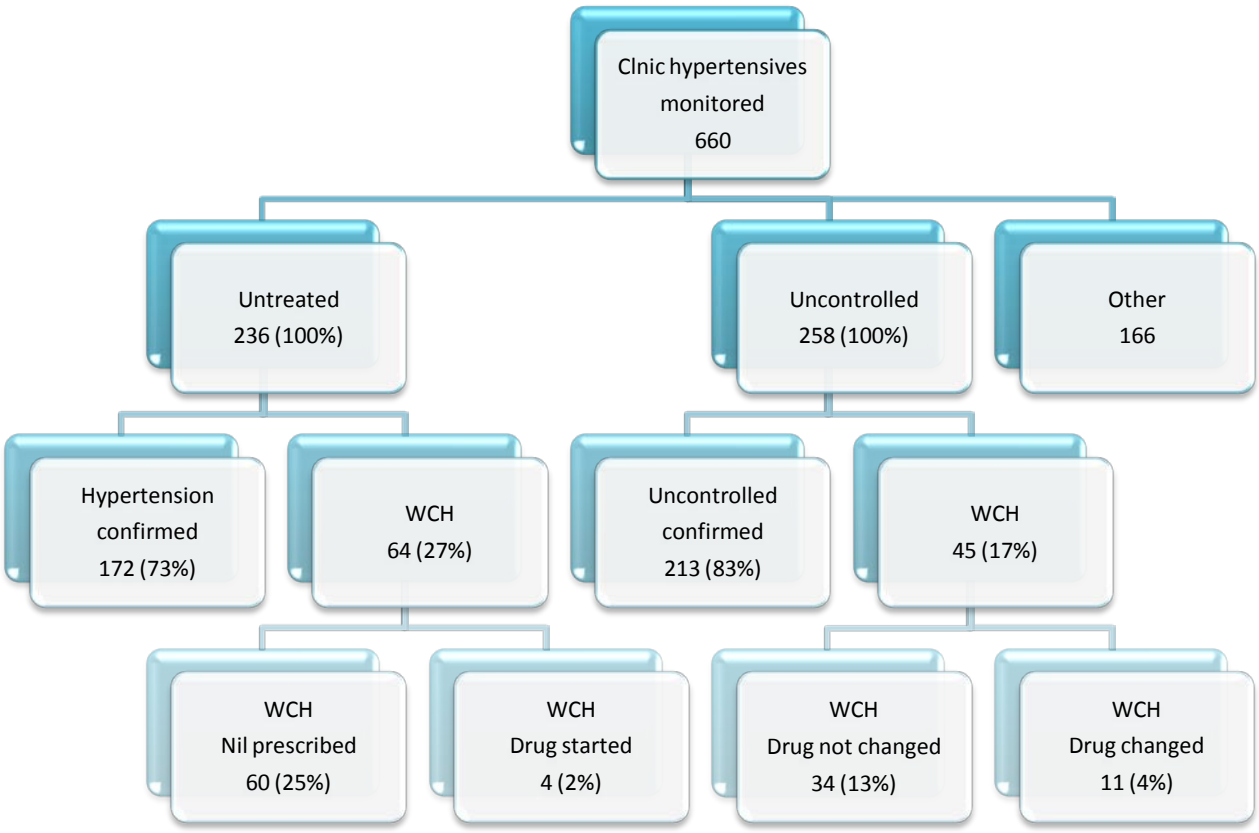
The 37 monitors in use for a period between six and 12 months had only minor technical problems. Two reported faulty printers; one of which was resolved by correcting the paper feed and the other was replaced by the supplier. The standard cuff containing a bladder measuring 23.5 cm by 12 cm was supplied, and this was found to be too short for a few patients with very fat arms.

A feature of modern semi-automatic sphygmomanometers is that mechanical problems, rather than causing inaccurate readings, produce an 'error' reading, and patients were asked to record these on their chart. The commonest, 'cuff over-inflation', is often a result of the cuff being too loosely applied. The total of58 error readings recorded represented less than 1% of the 9240BP measurements taken, and no patients had more than two. Occasional unexpectedly high readings occurred for no obvious reason, but a second attempt usually gave a reading in the expected range. However, six patients produced records with consistently exceptionally high values, which we were unable to explain and which were excluded from our analysis. In these cases, practices used office values for management decisions.

OUTCOME OF MONITORING

Where WCH was diagnosed, no change in drug status was made for 60 (94%) out of 64 untreated patients and 34 (76%) out of 45of the uncontrolled patients (Figure 1).

(Figure 1): ***Outcome of monitoring***



PATIENT ACCEPTABILITY

Practices asked patients to record BP measurements using the 'memory' button on the machine and on a chart. Twenty-three patients (3.5%) had problems with the memory button and a further Two (0.3%) had difficulty in reading the figures on the monitor. Nine (1.4%) had difficulty in entering figures on the chart. A total of 14 entries (the maximum number that the memory will Store) were requested, and we found that chart records were more complete than those in the memory. Of chart entries, 533 (81%) patients made all 14 entries and only 11 (1.7%) made less than10, whereas, of memory entries, 501 (76%) made 14 and 75(11%) made less than 10. Using both machine and chart entries, 98% of patients produced 10 or more recordings.

A focus group highlighted the interest and enthusiasm that patients had for monitor use, their views on anxiety and BP variability, difficulties making recordings at work, and the importance of help from the practice nurses. Two hundred and one (30%) patients said that cuff inflation was comfortable, 349(53%) said it was uncomfortable, and 90 (14%) said that it was very

uncomfortable or painful. Forty-one (6%) patients said that monitoring interfered with normal living; most of these having found that it was inconvenient to take a BP reading while at work.

DOCTOR AND NURSE QUESTIONNAIRES

Seventy-one questionnaires were returned from 15 practices: 49from doctors and 22 from nurses. Seventy responders said that monitoring had improved patient management, and other replies expressed satisfaction and interest. The median reported number of monitors needed per practice was 2.6.

MONITOR VALIDATION

Periodic checks are advised in recent American guidelines,[6] and the European Union is expected to introduce regulations concerning annual checks on medical instruments. Checks by practice enurses were made in this study using 'Y-tubes' to connect a mercury sphygmomanometer in parallel with their monitor and take 10 random readings. Of the 40 mean systolic and diastolic figures received, 32 were within less than 2 mmHg, four within 3mmHg and four between 3 and 5 mmHg.

3. QUESTIONNAIRES IN CLINICLA RESEARCH

Much of the data in clinical research is gathered using questionnaires or interviews.
The validity of the results depends on the quality of these instruments. Poorly designed questions can result in poor data quality. Critical to improve our understanding of the inherent flaws of Survey questions.

To assess the empirical evidence for how questionnaire length and other design features might influence data completeness in a clinical trial; a systematic review of randomized controlled trials (RCTs) was conducted, and has recently been updated. The strategies found to be effective in increasing response to postal and electronic questionnaires are summarized in the section on increasing data completeness below.

Clinical trial investigators have also relied on principles of questionnaire design that do not have an established empirical basis, but which are nonetheless considered to present 'good practice', based on expert opinion. The section on questionnaire development below includes some of that advice and presents general guidelines for questionnaire development which may help investigators who are about to design a questionnaire for a clinical trial.

3.1 REGULATORY GUIDELINES

The International Conference on Harmonization (ICH) of technical requirements for registration of pharmaceuticals for human use states:

'The collection of data and transfer of data from the investigator to the sponsor can take place through a variety of media, including paper case record forms, remote site monitoring systems, medical computer systems and electronic transfer. Whatever data capture instrument is used, the form and content of the information collected should be in full accordance with the protocol and should be established in advance of the conduct of the clinical trial. It should focus on the data necessary to implement the planned analysis, including the context information (such as timing assessments relative to dosing) necessary to confirm protocol compliance or identify important protocol deviations. 'Missing values' should be distinguishable from the 'value zero' or 'characteristic absent'.

This suggests that the choice of variables that are to be measured by the questionnaire (or case report form) is constrained by the trial protocol, but that the mode of data collection is not. The trial protocol is unlikely, however, to list all of the variables that may be required to evaluate the safety of the experimental treatment. The choice of variables to assess safety will depend on the possible consequences of treatment, on current knowledge of possible adverse effects of related treatments, and on the duration of the trial. In drug trials there may be many possible reactions due to the pharmacodynamics properties of the drug.

The Council for International Organizations of Medical Sciences (CIOMS) advises that: 'Safety data that cannot be categorized and succinctly collected in predefined data fields should be recorded in the comment section of the case report form when deemed important in the clinical judgment of the investigator'.

3.2 DESIGNING A QUESTIONNAIRE

- Requires development of a set of questions used to obtain clinically and statistically useful information from an individual.

- Difficult for several reasons

    - Each question must provide a valid and reliable measure.
    - The questions must clearly communicate the research intention to the respondent.
    - The questions must be assembled into a logical, clear instrument that flows naturally and will keep the respondent sufficiently interested to continue cooperation.

Good questionnaires are difficult to construct. Bad questionnaires are difficult to analyze

.

- Start early and plan for plenty of time.
    - More challenging and time-consuming than you think.
    - Time spent =Quality of questionnaire.
    - Wrong approach:
    - A questionnaire is finished when time runs out, not necessarily when it is the best it can be.

3.3 THREE DISTINCT PHASES

- Initial questionnaire planning.

- Development of specific questions.
- Final construction of the data collection instrument as a whole.

3.3.1 INITIAL QUESTIONNAIRE PLANNING

Prior to writing any questions:

- Define the problem and specific aim(s) of the study, including the population of interest.
- Make a detailed list of the information to be collected and concepts to be measured.
    - Don't forget about demographics and possible inclusion/exclusion criteria to define the target population.
    - Formulate a statistical analysis plan that outlines how every item will be analyzed.
    - Helpful to list the role of each item (predictor, outcome, or confounder) in addressing each specific aim.
    - Useful to think ahead to the reporting of results (i.e., sketch out the final results tables).
    - Review the literature and collect any existing measures, related surveys, and/or data collection instruments that might have measured similar concepts.
    - Saves development time and allows comparison with other studies if used appropriately.
    - Ideal to use existing instruments without modification.
    - Existing instruments may not be entirely appropriate for the question or the population, or may be too long; may be necessary to delete, change, or add a few items.
    - Direct comparison with other studies may no longer be possible if original instrument has been modified.

3.3.2 DEVELOPMENT OF SPECIFIC QUESTIONS

- First goal: Shorten the set of questions.
    - Questions not essential to addressing the specific aim(s) increase the amount of effort involved in entering, cleaning, and analyzing the data.
    - Decrease the overall quality and productivity of the study.
    - Every item in the questionnaire must be a meaningful contribution to the intended analyses.
    - Compare the draft questions to the survey objectives to ensure that the right types of questions (e.g., knowledge) are being asked for a given topic.
    - Resist the temptation to include additional questions or measures or just in case" they might produce interesting data.

- Second goal: Refine the remaining questions.
    - Every word in a question can influence the validity and Reproducibility of the responses.
    - Iterative cycles of review and revision.
        - Refine and clarify the research objectives.
        - Focus the concepts included in the survey.
    - Target:

- Terms and concepts should be familiar and easy to understand.
- Cues and ordering of questions should serve to stimulate recall.
- Ordering and format of questions should be unbiased and balanced.

➢ Terms and concepts should be familiar and easy to understand.
- Questions should be simple, be free of ambiguity, and encourage accurate and honest responses without embarrassing or offending the respondent.
    - Clarity: specific and concrete wording.
    - "How much exercise do you usually get?" vs. \During a typical week, how many hours do you spend exercising (e.g., vigorous walking or sports)?"
    - Simplicity: short non-technical words and simple grammar.
        - "Over-the-counter medications" vs. \Drugs you can buy without a doctor's prescription".
    - Neutrality: avoid "loaded" words and stereotypes.
        - "During the last month, how often did you drink too much Alcohol?" vs. during the last month, how often did you drink? More than five drinks in one day?"

➢ Cues and ordering of questions should serve to stimulate recall.
- Respondents often asked to recall and access information from memory.
    - Problems: asked to recall too much information or asked to recall information from too far in memory.
    - Regarding behavior, interested in the average or the extremes?
- Steps that can help the respondent's memory search:
    - Ask a short series of related questions.
    - Provide an anchor for the reference period of time frame.
        - Goal: To ask about the shortest recent segment of time that accurately represents the characteristic over the whole period of interest for the research question.
        - Example: "During the last 7 days, how many beers did you have?"
    - Keep recall to a minimum and focus on the recent past.

3.3.3 ASSEMBLING THE FINAL QUESTIONNAIRE

➢ Objective: Fit the items together in a meaningful way so that the entire questionnaire is unified.
- Order of sections of questions and order of questions within sections.
- Question and response formats.
- Skip patterns/Branching questions.

➢ Also need to consider mode of administration.
- Self-administered questionnaire, face-to-face interview, telephone interview, or computer-assisted approaches?
- For self-administered questionnaires, give to respondents in person or administer through the mail, by email, or via a Website?

3.4 MODE OF ADMINISTRATION

- Self-administered questionnaires:
  - More economical, more readily standardized, and the added privacy can enhance the validity of responses.
  - No middle-man bias (no verbal or visual clues from an interviewer to inuence the respondent); more uniform.

- Interviews:
  - Can ensure more complete responses and enhance validity through improved understanding.
  - May be necessary when participants will have variable ability to read and understand questions.
  - Requires substantial training and practice of interviewers.

- Self-administered questionnaires vs. interviews
  - Both susceptible to errors caused by imperfect memory.
  - Both affected by the respondent's tendency to give socially acceptable answers, although not necessarily to the same degree.

- Another decision to make: software.
  - Software to aid creation/formatting, administration (e.g., create Web site), and/or data collection/entry.
  - An option: REDCap Survey.
    - Go to www.mc.vanderbilt.edu.
    - Click on “StarBRITE" link under “For Employees" area.
    - Login with your VUnetID and password.
    - Click on the “Data Management" tab.

4. CONCLUSIONS

Despite the difficulty inherent to measuring pain, there are a number of accepted tools for tracking pain-related treatment outcomes. The proper use of these tools can allow clinicians and researchers to demonstrate both statistically and clinically significant treatment effects. These instruments range from quick, one-item assessments of pain intensity, to long surveys that tap into multiple dimensions of the pain experience and overall functioning.

As with the use of continuous ambulatory monitoring, it is necessary to establish arbitrary levels of the normal BP, and this we did on the best available evidence. Having done so, we then adopted the use of correction factors as a practical guide to diagnosis.

A good questionnaire design for a clinical trial will minimize bias and maximize precision in the estimates of treatment effect within budget. Attempts to collect more data than will be analyzed may risk reducing recruitment and increasing losses to follow-up. Questionnaire design still does remain as much an art as a science, but the evidence base for improving the quality and completeness of data collection in clinical trials is growing.

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