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Core outcome domains for chronic pain clinical trials: IMMPACT recommendations

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Abstract

Objective. To provide recommendations for the core outcome domains that should be *considered* by investigators conducting clinical trials of the efficacy and effectiveness of treatments for chronic pain. Development of a core set of outcome domains would facilitate comparison and pooling of data, encourage more complete reporting of outcomes, simplify the preparation and review of research proposals and manuscripts, and allow clinicians to make informed decisions regarding the risks and benefits of treatment.

Methods. Under the auspices of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), 27 specialists from academia, governmental agencies, and the pharmaceutical industry participated in a consensus meeting and identified core outcome domains that should be *considered* in clinical trials of treatments for chronic pain.

Conclusions. There was a consensus that chronic pain clinical trials should assess outcomes representing six core domains: (1) pain, (2) physical functioning, (3) emotional functioning, (4) participant ratings of improvement and satisfaction with treatment, (5) symptoms and

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adverse events, (6) participant disposition (e.g. adherence to the treatment regimen and reasons for premature withdrawal from the trial). Although consideration should be given to the assessment of each of these domains, there may be exceptions to the general recommendation to include all of these domains in chronic pain trials. When this occurs, the rationale for not including domains should be provided. It is not the intention of these recommendations that assessment of the core domains should be considered a *requirement* for approval of product applications by regulatory agencies or that a treatment must demonstrate statistically significant effects for all of the relevant core domains to establish evidence of its efficacy.

Keywords: Chronic pain; Clinical trials; Assessment; Outcomes; Quality of life; Physical functioning; Emotional functioning; Adverse events; Global ratings

1. Introduction

Variability among clinical trials in outcome assessments has impeded evaluations of the efficacy and effectiveness of treatments for chronic pain, and the use of different outcome domains precludes meaningful comparisons among studies. One way to facilitate such evaluations would be through the use of a standard set of outcome domains. Although investigators may wish to augment a core set of domains with others that are specific to the situation or treatment being studied, use of a core set of outcome variables among studies would permit comparisons among different samples, treatments, and settings.

Development of a core set of outcome domains and measurement procedures would facilitate comparison and pooling of data while leaving investigators free to augment the core set with others of their choice. In addition, a core set of domains would encourage more complete investigation and reporting of relevant outcomes, so that investigators do not simply present a single outcome while ignoring others. Another advantage is that it would encourage development of cooperative multicenter projects, in which different centers agree to assess the core domains, in addition to any measures selected to evaluate specific research questions. A standard set of outcome domains would simplify the process of designing and reviewing research proposals, manuscripts, and published articles. Finally, published results of clinical trials with common outcome domains will allow clinicians to make more informed clinical decisions for each patient regarding the optimal treatment, especially with respect to its risks and benefits. Once core outcome domains for clinical trials are identified, the next step would be to select measures that meet appropriate psychometric standards (i.e. reliability, validity, responsiveness, appropriate, normative data).

To address the identification of core outcome domains, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT, additional information concerning IMMPACT and its meetings can be found at immpact.org) convened a meeting to develop consensus recommendations for chronic pain clinical trials. There was agreement that the identification of specific measures would occur at a subsequent meeting. Other initiatives provide precedents for this undertaking, including Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT; Bellamy et al., 1997) and World Health Organization/International League of Associations for Rheumatology (WHO/ILARS; Brooks and Hochberg, 2001) in rheumatology, European Organization for Research and Treatment of Cancer (EORTC, Aaronson et al., 1993) and the Research Network of the European Association of Palliative Care (Caraceni et al., 2002) in oncology, and an international consortium of back pain researchers (Deyo et al., 1998). Although these other disease-specific initiatives were used to inform the discussion, the objective of the IMMPACT meeting was to develop a consensus on outcome domains that would transcend specific chronic pain syndromes. Our goal in this paper is to present the consensus recommendations from the first IMMPACT meeting for a core set of outcome domains that should be considered for all clinical trials of treatments for chronic pain.

2. Methods

2.1. Sponsorship

Abbott Laboratories, AstraZeneca, Elan Pharmaceuticals, Endo Pharmaceuticals Inc., GlaxoSmithKline, Novartis Pharmaceuticals, Ortho-McNeil Pharmaceutical Inc., Pfizer, and Purdue Pharma provided unrestricted educational grants to the University of Rochester Office of Professional Education to support a meeting and manuscript preparation.

2.2. Procedure

A meeting consisting of 27 people representing academia, governmental agencies, and the pharmaceutical industry was held on November 1–2, 2002. The participants attending the meeting were selected to represent health care disciplines that cover chronic pain broadly defined and included anesthesiology, biostatistics, clinical pharmacology, epidemiology, geriatrics, internal medicine, neurology, nursing, oncology, pediatric pain, physical medicine and rehabilitation, psychology, and rheumatology; all have research, clinical, or administrative expertise relevant to evaluating chronic pain treatment outcomes. In addition, representatives from the pharmaceutical industry who are engaged in chronic pain clinical trials and an attorney were included to provide specific expertise.

The process of the consensus meeting was semi-structured, with the first two authors leading discussions. Prior to the meeting, all participants were provided copies of a recent edited volume on pain assessment (Turk and Melzack, 2001), as well as four published clinical trials that are representative of chronic pain trials. Outcomes included in these studies were used to illustrate the diversity of domains examined in recent trials. The list of various domains generated by the participants was discussed and consensus was reached based on the results of the discussion and a formal vote.

The first two authors facilitated the consensus meeting and prepared the first draft of this paper. They were responsible for revising the manuscript and integrating the comments of the other authors. All authors reviewed the final draft and endorsed its publication.

3. General issues

To demonstrate the benefits of treatment, investigators must decide the appropriate endpoints for establishing both the statistical significance and the clinical importance of the effects of treatment. In a clinical trial of a treatment for chronic pain, pain reduction and safety are necessary outcome variables but they may not be sufficient for a comprehensive evaluation of the overall benefit or harm of treatment (Dionne and Witter, 2003). The complexity of chronic pain and its negative impact on diverse aspects of function is well established (e.g. Melzack and Wall, 1982). Thus, evaluation of the effectiveness of any treatment for chronic pain requires consideration of the assessment of multiple outcome domains to adequately characterize the impact of the intervention. Adverse events resulting from the treatment might outweigh the benefits of pain reduction, and pain reduction alone does not guarantee that physical or emotional functioning will improve.

The domains of importance in a clinical trial should match the purpose of the study, measure positive and negative outcomes of treatment, and be appropriate for the chronic pain syndrome studied and the specific characteristics of the sample (e.g. geriatric participants). Central issues involve the identification of outcome domains that are clinically meaningful and for which there are measures that are responsive and provide a comprehensive yet efficient evaluation of treatment response (Bellamy et al., 1997; Revicki and Ehreth, 1997).

4. Core outcome domains for chronic pain clinical trials

The authors recommend that each of the six core outcome domains listed in Table 1 should be *considered* in the design of all clinical trials of the efficacy and effectiveness of treatments for chronic pain. If one or more of these domains is not included in such a chronic pain clinical trial, the reasons for the exclusion should be justified a priori. Importantly, it is not the intention of these recommendations that assessment of these core domains should be considered a requirement for the approval of product applications by regulatory agencies or that a treatment must demonstrate statistically significant effects for all of the core domains to establish evidence of its efficacy. Rather, these recommendations are presented in an effort to promote collection and publication of standardized outcomes, which will allow for improved evidence-based comparisons and meta-analyses of chronic pain treatments. As noted above, there will be clinical trials in which these core assessment domains will require modification, for example, clinical trials in individuals with mild pain (in whom the impact of treatment on physical function and emotional distress may be less relevant than it is in patients with moderate or severe pain), single-dose studies in participants with a chronic pain syndrome, and clinical trials in the cognitively impaired and in infants and children.

Table 1
Core domains for clinical trials of chronic pain treatment efficacy and effectiveness

Pain
Physical functioning
Emotional functioning
Participant ratings of global improvement
Symptoms and adverse events
Participant disposition (including adherence to the treatment regimen and reasons for premature withdrawal from the trial)

Our recommendations are most applicable to clinical trials of treatments for chronic pain designed to evaluate efficacy or effectiveness, for example, what are termed Phase III and IV trials within the regulatory context (United States Department of Health and Human Services, 1997). These recommendations are made with the assumption that clinical trials will be conducted according to the principles of good clinical practice presented in the E6 Good Clinical Practice Consolidated Guidance of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (United States Department of Health and Human Services, 1996).

4.1. Pain

There are several dimensions of pain that can be assessed in a clinical trial (e.g. intensity, location, specific descriptors and qualities). Most chronic pain clinical trials will also assess pain history, but these variables are more likely to be considered baseline characteristics or covariates.

It has often been assumed that chronic pain is highly associated with alterations in emotional and physical functioning and that reduction in pain will inevitably lead to improvement in function and satisfaction with treatment. This is not necessarily the case, and in many studies, pain and functioning are only modestly related. Moreover,

changes in pain severity may have only a variable relationship with participants' ratings of improvement and satisfaction (Dougados et al., 2002; Farrar et al., 2001; Dawson et al., 2002). Such data indicate that even though pain is typically considered the primary outcome in evaluating pain treatments, it is important to consider other outcomes in clinical trials.

4.2. Physical functioning

In addition to relieving clinical symptoms and prolonging survival, the objectives of health care intervention include improvement of functioning (Revicki et al., 2000). Thus, there is a need to assess multiple domains of functioning, including behavior, mood, and satisfaction (Ware, 1984; Revicki, 1993). *Quality of life* (QOL) is a term that refers to how a person feels and how he or she functions in daily life. Concerns with the all-encompassing nature of QOL in the evaluation of treatment outcomes have led a number of investigators to use a more circumscribed construct, *health-related quality of life* (HRQOL). HRQOL refers to those domains that are specifically related to health and that can be potentially influenced by the healthcare system (Varni et al., 1999; Seid et al., 2000). HRQOL outcomes are especially important for evaluating the impact of treatment on chronic diseases for which cure is not possible and therapy may be prolonged. Moreover, especially when treatment extends over long periods, it is critical to examine whether the benefits of symptom reduction are compromised by reductions in QOL resulting from adverse effects of treatment.

Several authors have argued that the assessment of QOL and HRQOL is problematic because of the lack of clear definitions and shared theoretical frameworks, which makes it difficult to determine whether a given scale is a valid measure (Faden and LePlege, 1992; Cella and Bonomi, 1995). The consensus of the authors is that two central components of existing HRQOL instruments, physical functioning and emotional functioning, are core domains that should be considered in all clinical trials of chronic pain treatments. This recommendation is supported by the results of studies in which exploratory and confirmatory factor analyses were used to identify the variables needed to comprehensively assess chronic pain participants, which suggested that three relatively independent domains—pain severity, physical functioning, and emotional functioning—are required to capture the multidimensionality of the pain experience (Mikail et al., 1993; De Gagné et al., 1995; Holroyd et al., 1999).

Measures of physical functioning evaluate diverse aspects of a participant's life, including the ability to carry out such daily activities as household chores, walking, work, travel, and self-care, as well as strength and endurance. A major decision to be made in assessing the impact of a treatment on physical functioning involves whether a generic or a disease-specific measure will be used (Stucki et al., 1995; Garratt et al., 2001). Disease-specific measures are designed to evaluate the impact of a specific condition (e.g. ability to wear clothing in participants with postherpetic neuralgia). Such specific effects of a disorder may not be assessed by a generic measure, and disease-specific measures may therefore be more likely to reveal clinically important improvement or deterioration in function that is a consequence of treatment. In addition, responses on disease-specific measures will generally not reflect the effects of co-morbid conditions on physical functioning, which may confound the interpretation of change occurring over the course of a trial when generic measures are used. Generic measures, however, make it possible to compare the physical functioning associated with a given disorder and its treatment with those of different conditions (Dworkin et al., 2001). Thus, the use of disease-specific and generic measures in combination facilitates the achievement of both sets of objectives (Patrick and Deyo, 1989).

Different levels of analysis can be used to conceptualize the core outcome domain of physical functioning. For example, activities of daily living such as performing self-care behaviors (e.g. bathing and dressing) can be distinguished from social-role functioning. The consensus of the meeting was that these two levels of activities should be differentiated with activities of daily living being more fundamental than engaging in social activities. Consequently, there was agreement that the effect of the treatment on the ability of the participant to perform specific physical tasks or the reduction in the interference of the pain in the participant's ability to engage in routine, daily physical activities should be treated as a core domain, whereas the impact of treatment on alteration in social functioning was considered a supplemental domain.

4.3. Emotional functioning

The results of numerous studies suggest that chronic pain is often associated with emotional distress, particularly depression, anxiety, anger, and irritability (e.g. Fernandez and Turk, 1995; Banks and Kerns, 1996; Robinson and Riley, 1999). Emotional functioning as reflected in emotional distress, is not intended to be synonymous with a psychiatric diagnosis or disorder, but is rather meant to refer to distressed mood more generally. The consensus of the participants was that the assessment of emotional functioning should be considered a core outcome in chronic pain clinical trials. Although it is difficult to interpret changes in emotional functioning because of the many factors that contribute, this domain is central in people's assessments of their well-being and satisfaction with life and the authors recommend that it should be considered a core outcome domain in clinical trials of treatments for chronic pain.

4.4. Participant ratings of global improvement and satisfaction with treatment

Assessments of individual outcome domains such as pain and physical and emotional functioning may not adequately characterize the participant's expectations about the treatment, overall assessment of treatment, and the meaningfulness to the participant of any improvement (or worsening). Global evaluations by participants in clinical trials of the benefits of treatment reflect not only the magnitude of the changes in these outcomes and feelings about treatment delivery, but also the personal importance that these outcomes have for participants. Such perceptions of the importance of treatment-associated changes often differ considerably from those of health care professionals (Lipton and Stewart, 1999), and the value and significance of therapeutic changes differ greatly among participants and are important determinants of their treatment satisfaction.

The use of participants' overall evaluation of treatment in clinical trials is controversial. A substantial amount of confusion about this group of outcomes is generated by vastly different meaning applied to terms such as 'patient satisfaction' and 'impression of change'. In addition, many such assessments are based on rating a single item, and it is not possible to establish the internal consistency of one rating. In addition, global impressions of improvement may fail to detect important changes (e.g. Just et al., 1999). Furthermore, the judgment of change requires participants to assess both their present and initial state and then perform what may be an unreliable mental subtraction; because participants may be unable to recall their initial state, their ratings may be based on an 'implicit theory' of change beginning with their present state and working backward (Ross, 1989). However, if a treatment is associated with severe adverse effects, the participant may not need to remember baseline pain to rate satisfaction with treatment. In addition to problems of memory recall, participants' global impressions may be influenced by systematic biases such as the desire to please health care providers (e.g. demand characteristics). Participants' efforts to comply with their perceptions of provider expectations might also contribute to global judgments beyond the actual balancing of perceived benefits against accompanying negative effects. Despite the necessity for care in the use of participant global assessments, the results of recent research provide support for their validity (e.g. Fischer et al., 1999; Collins et al., 2001; Farrar et al., 2001).

Ultimately, participants decide whether the positive attributes of a treatment outweigh its negative aspects, and this is an important determinant of whether they adhere to and continue with treatment. Willingness to continue with the treatment regimen may be viewed as a gross indication of participant satisfaction. A more systematic approach is to ask participants to rate their degree of satisfaction. Such ratings permit a range of satisfaction beyond the dichotomous behavior of withdrawal from a protocol. Participant ratings of improvement and satisfaction with treatment provide unique information in outcomes assessment in clinical trials because they may allow an integration of the benefits of treatment and adverse events and other costs from within the participant's personal perspective. The authors therefore recommend that at least one rating of global improvement should be considered for inclusion in all chronic pain clinical trials, but must be carefully constructed to capture the relevant data.

4.5. Symptoms and adverse events

Many participants will experience symptoms and adverse events associated with their illness and pharmacologic treatment. The importance of monitoring adverse events has long been recognized as an essential component of all therapeutic clinical trials (Anderson and Testa, 1994). Therapies, such as the drugs that relieve pain, have a variety of effects, and these cannot only cause discomfort but also may potentially impair physical and emotional function and exacerbate co-morbid symptoms, which thereby may potentially offset the therapeutic benefit (Croog et al., 1986). Max and Laska (1991) have noted that common analgesic adverse events (e.g. gastrointestinal distress, sedation, depression) can limit the dosage that can be realistically prescribed. Moreover, side effect burden plays an important role in treatment adherence (Anderson et al., 1999). Participants may view adverse events as sufficiently noxious to discontinue treatment or limit dosage, and the overall benefit of treatment may therefore be reduced. A major challenge in developing analgesic drugs is determining an optimal dosage (i.e. one that minimizes adverse events and maximizes pain relief and functional improvement).

The onset of new diseases and initiation of new treatments during a clinical trial complicates assessments of symptoms and adverse events. When initiated during a trial, concomitant treatments (e.g. drugs, physical therapy, psychological therapy, nerve blocks) are often protocol violations. Participant disease is a baseline characteristic or covariate when present at the beginning of a trial but is an adverse event when it emerges or worsens. The risk of addiction has attracted considerable attention in the evaluation of analgesic drugs. Addiction is a neurobiologic disease, and if it occurs during a trial it should be considered an adverse event but when it is present at the beginning of a trial it is a baseline characteristic. As a caution, we note that addiction is not the same as physical dependence or tolerance. Physical dependence is a pharmacologic consequence of a drug characterized by the occurrence of a withdrawal syndrome following abrupt discontinuation of the substance or the administration of an antagonist. Tolerance refers to a physiologic state in which increased dosages of a substance are required to sustained a desired effect.

Assessment of the percentages of participants experiencing adverse events based on passive capture is standard in clinical trials; however, assessments of their severity and

importance to participants are much less common, although this may provide valuable information (Katz, 2002). The authors recommend that the prospective assessment of symptoms present at the onset of a trial and symptoms and adverse events that emerge during the trial is a core outcome domain that should be included in all chronic pain clinical trials, and that the strategy used to assess these events should include participant ratings of their presence, severity, change, and importance.

4.6. Participant disposition

Following the recommendations of the CONSORT statement (Consolidated Standards of Reporting Trials guidelines, CONSORT; Begg et al., 1996; Moher et al., 2001), all participants screened for a clinical trial should be carefully described with respect to the proportion who are ultimately enrolled, and why those who were not enrolled were not. Detailed information should be provided regarding the extent and reasons for treatment non-adherence, prohibited concomitant medications and all other protocol deviations that may impact the interpretation of the trial results, treatment modification, premature participant withdrawal from the trial, and loss to follow-up. Investigators should report the number of withdrawals related to each of the symptoms and adverse events identified in each of the treatment groups. This detailed characterization of participant disposition is the sixth core domain that should be assessed in all clinical trials of chronic pain treatment.

To be effective, a treatment must have a beneficial effect on the symptom or disease being treated and the participant must adhere to the treatment regimen (Turk and Rudy, 1991). The most potent analgesic may demonstrate less than its potential benefit if participants in a clinical trial fail to use the medication in the manner prescribed, are unable to tolerate a fully effective dose, or drop out of the trial due to unacceptable adverse events or inadequate pain relief. Furthermore, the benefit of the treatment being studied may be obscured if participants receive any treatments that are not allowed in the protocol.

The dosage and duration of all treatments received by participants during the clinical trial must be recorded, not only the treatment being investigated, but also all concomitant treatments. Treatments initiated during the trial often reflect inadequate pain relief or the presence of distressing or uncontrolled adverse events (the use of rescue medications and changes in concomitant medication use may be justifiable as pain outcome measures when specified in the protocol). Assessments of the use of rescue and prohibited medications and alterations in prescribed treatment due to adverse events and symptoms must be considered in evaluating the results of chronic pain clinical trials.

To evaluate whether side effects or other factors have compromised the double-blind in a clinical trial, it is important to assess subjects' and investigators' guesses of which treatment was administered. The reasons for the specific guesses should also be assessed, because these can have different implications for interpretation of the results, for example, unblinding occurring because of the effectiveness of the active treatment or because of its side effects (Moscucci et al., 1987).

Table 2
Supplemental domains for chronic pain clinical trials

Role functioning (i.e. work and educational activities)
Interpersonal functioning (i.e. relationships and activities with family, friends, and others)
Pharmacoeconomic measures and health care utilization
Biological markers (e.g. assessments based on quantitative sensory testing, imaging, genetic markers, pharmacogenomics, and punch skin biopsy)
Coping
Clinician or surrogate ratings of global improvement
Neuropsychological assessments of cognitive and motor function
Suffering and other end-of-life issues

5. Supplemental outcome domains

There are many other outcome domains that can be considered in the design of pain clinical trials depending on the specific research question. Supplemental assessment domains may be included in a clinical trial without a hypothesis that they will change and without the trial having adequate power to test the hypothesis that they will respond to treatment. Table 2 contains a list of eight supplemental outcome domains that might be considered in the design of chronic pain clinical trials.

6. Conclusions

The core outcome domains specified in these IMMPACT consensus recommendations—pain, physical functioning, emotional functioning, participant ratings of global improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition—are generally consistent with the recommendations for arthritis clinical trials from OMERACT-III (Bellamy et al., 1997) and WHO/ILARS (Brooks and Hochberg, 2001). Pain, physical function, participant global assessment, and imaging studies are the core outcome domains specified in the OMERACT guidelines, and the first three of these domains are included in the present recommendations.

The objective of the first IMMPACT consensus meeting was to establish recommendations for clinical trials of chronic pain treatment. Imaging studies were not considered because they have limited relevance to the assessment of outcome in many chronic pain syndromes. In addition to the three domains that overlap with the OMERACT guidelines, the authors consider emotional functioning a core outcome domain because of its well-established and clinically important relationships with chronic pain. Symptoms and

adverse events have been included as a core domain to emphasize that comprehensive assessment of the health burdens that often accompany treatment is necessary to achieve the key purpose of clinical trials—assessment of the risk-benefit balance. The recommendation that participant disposition is a core outcome domain is consistent with the CONSORT guidelines (Begg et al., 1996; Moher et al., 2001), although we have emphasized that reports of participant disposition should be accompanied by detailed explanations of withdrawals, non-adherence, and protocol violations.

A legitimate concern for any clinical trial is participant burden. Assessment of the six core domains will inevitably require more effort from participants than simply assessing pain reduction as the sole end-point of importance. However, it is important to emphasize that there are reasonably brief measures available that are capable of capturing the domains described above. Attention toward identifying measures that have demonstrated appropriate psychometric properties with the least participant burden will be the focus of the second IMMPACT consensus recommendations. Those who are designing clinical trials for chronic pain will need to balance the importance of assessing the core domains against the added participant burden.

The authors believe that investigators designing and conducting clinical trials of chronic pain treatment efficacy and effectiveness should consider each of the six core domains listed in Table 1 and discussed in this paper. It is important to emphasize, however, that we are not suggesting that positive results must be obtained for all of the core domains for the treatment to be deemed efficacious. Also we would like to emphasize the word considered. These core domains should be considered and are not mandatory because it is possible that there are specific trials for which one or more of these domains might not be relevant. In such instances, our recommendation is that investigators should acknowledge that they have considered each outcome domain and provide the rationale when they decide not to include assessment of a particular domain. Of course, there are many supplemental outcome domains that can be included in a chronic pain clinical trial (see Table 2), and we expect that the core outcome domains will be supplemented by assessment of additional domains that are required to evaluate a specific treatment (or that the investigator wishes to include for exploratory purposes).

Numerous outcome measures related to the recommended core domains have appeared in the research literature (e.g. Benzon et al., 1994; McDowell and Newell, 1996; Turk and Melzack, 2001). Selection of specific measures of each of the core and supplemental outcome domains from the many available should be based on reliability, validity, responsiveness to change, feasibility and practicality within the clinical trial setting (e.g. participant and investigator burden, need for special training), availability of normative data and linguistically and culturally validated versions, mode of administration, and appropriateness to study objectives and the participant population and treatment being investigated (Dworkin et al., 2001). Future IMMPACT recommendations will focus on identifying specific measures within the six core outcome domains that have the most favorable characteristics and the widest range of applicability, methods for determining the clinical importance to patients of changes in these measures, and strategies for selecting primary endpoints and combining multiple endpoints in assessments of treatment efficacy and effectiveness. The use of standard outcome assessments has the potential to greatly enhance the validity, comparability, and clinical applicability of clinical trials of chronic pain treatments.

Academic, health care, and pharmaceutical industry investigators who conduct clinical trials, the government and private organizations that provide funding for many such studies, and the government regulatory agencies that review this research and ultimately approve new therapies for the public all share a commitment to identifying treatments for chronic pain that are more effective and have fewer adverse effects than those currently available. These different groups, however, sometimes have different goals, contrasting ideologies, and separate constituencies with particular interests in clinical trials. Although unsystematic efforts to bring these different individuals together have occurred in various medical specialties, much more can and should be done to enhance mutual understanding and promote creativity in the development and investigation of improved treatment approaches (Klein et al., 2002). The authors hope that IMMPACT and the recommendations made in this paper will provide an example of the value of such collaborative efforts among academia, government, and industry. The ultimate goal of such efforts should be to advance the science of chronic pain clinical trials and thereby provide improved treatments for patients suffering from chronic pain.

7. Disclaimer

The views expressed in this paper are those of the authors. No official endorsement by the US Department of Veterans Affairs, US Food and Drug Administration, US National Institutes of Health, or any of the pharmaceutical companies that provided unrestricted educational grants to the University of Rochester Office of Professional Education should be inferred.

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