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A METHOD FOR RESEARCH PROGRAMMING IN THE FIELD OF EVIDENCE-BASED MEDICINE

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Abstract

Objective: This paper presents the method we used in programming research on the efficacy of therapeutic interventions for nine chronic benign pain disorders.

Methods: We started with an inventory to identify commonly applied interventions. For these interventions we searched the literature to identify gaps in evidence. First, we searched for recent reviews, of which we assessed the methodologic quality. If only reviews of poor or moderate quality were found, a new systematic review was recommended. When we found no recent reviews, we searched for randomized controlled trials (RCTs). If there was insufficient or inconsistent evidence, the performance of a new RCT was advised. This structured procedure resulted in a list with topics for which new systematic reviews were recommended and topics for which new RCTs were needed. These lists were the starting points for priority setting by four Centers for Pain Management and Research. All members of the centers were asked to state the priority of each topic. The resulting hierarchy of topics for their own center was discussed in a meeting in each center, giving participants the opportunity to elucidate their views and considerations.

Results: The final result was a robust priority list for the need of research (systematic reviews and RCTs) on chronic benign pain syndromes.

Discussion: The strength and weaknesses of this approach are discussed. This method of priority setting is by no means restricted to treatments for chronic pain; it is also a useful approach for programming research to enable evidence-based medicine in other fields of interest.

Keywords: Research programming, Evidence-based medicine, Chronic benign pain, Systematic review, Randomized clinical trial

Evidence-based medicine is an internationally shared ideal in modern health care, and an impressive amount of research is focused on providing the evidence at issue (4;6). Given the limited resources available, research funding agencies must set priorities in this field

of applied research. Identification of gaps in the evidence is the first step in this process of research programming, followed by the setting of priorities for research (7;12).

Identifying gaps in knowledge translates into the question of whether there is already sufficient evidence on a specific topic. A survey among researchers or practitioners who are active in the field at issue might identify the white spots. However, researchers often have a too narrow view and tend to formulate detailed questions in their own area of research. This mechanism hampers the identification of topics on which research is almost completely lacking. A survey among practitioners in the field at issue may be more fruitful. They encounter problems for which evidence is lacking, and these might be identified in this way. Practitioners may have a more realistic and broader view on the (prevalence of) problems in their field than researchers. However, a disadvantage of a survey among practitioners is that they may be only partially aware of the available evidence. An alternative method to identify the gaps in evidence on medical interventions is searching the literature. This method can be standardized and is reproducible, and therefore more objective. A disadvantage is that also white spots, which are irrelevant for medical practice, will be identified in this way.

For the process of research programming, or setting priorities with regard to identified gaps in the evidence, several strategies are available. The nominal group technique consists of discussions among a group of experts in the field of interest, who deliberate on priorities, using arguments and considerations, with the aim of convincing each other (5). A second method is the Delphi technique (11;16), in which the participants do not discuss these issues directly with each other. They each list their priorities, accompanied by their arguments and considerations, after which these lists are distributed among all group members. In the next step, the participants have the opportunity to react to each other's views and arguments, and to reconsider their opinions. These feedback rounds and new priority rounds may continue until no new information or ideas are put forward and individual priorities remain stable. The choice of the participants in the priority-setting process is crucial and unavoidably affects the outcome, since all participants have their own expertise, preferences, and (hidden) agendas.

Funded by the Dutch Organisation for Scientific Research, a study was performed to investigate the need for research on the effectiveness of therapeutic interventions for a number of chronic benign pain syndromes. The first aim of the study was to screen the literature for evidence on the effectiveness of interventions for chronic benign pain disorders that are commonly applied in the Netherlands, resulting in lists of interventions for which effectiveness or noneffectiveness has been proven, and lists of interventions for which either new systematic reviews or new effect studies are needed. The second aim was to set research priorities with regard to these topics. This paper describes the methodology used and discusses the strengths and weaknesses of the approach.

METHODS

Identification of Topics

In consultation with the committee that granted the funding, the following chronic benign pain syndromes were chosen: migraine, cluster headache, tension headache, back pain, neck pain, shoulder pain, fibromyalgia, stump and phantom limb pain, and irritable bowel syndrome. In order to assess which therapeutic interventions are commonly used in the Netherlands, a survey was conducted among all medical and related disciplines that play a role in the treatment of patients with one of the abovementioned syndromes. Candidate interventions were classified and listed on the basis of currently used textbooks and discussion with experts. A total of 8,947 questionnaires, stratified according to disciplines and pain syndromes, were distributed to 5,000 medical professionals (13 different disciplines). The average response rate was 40.6% and varied per discipline (Table 1). Each professional had to state whether he/she applied a specific intervention: never (<1%), sometimes

Table 1. Number of Questionnaires Returned by Each Discipline and Response Rate

Discipline	Number of questionnaires sent	Response rate
General practitioners	1,347	38.0%
Physiotherapists	1,200	47.6%
Chiropractors	731	54.8%
Psychologists	1,352	26.1%
Gastroenterologists	150	57.3%
Rheumatologists	456	55.3%
Rehabilitation doctors in hospitals	755	57.5%
Rehabilitation doctors in rehabilitation centers	120	63.3%
Neurologists	1,049	32.3%
Neurosurgeons	285	34.4%
Orthopedic surgeons	450	40.7%
Anesthesiologists	900	30.0%
Surgeons	150	37.3%

(1–25%), regularly (26–74%), frequently (75–99%), or always (>99%) for patients with pain syndrome at issue. Referral to other care providers was also labeled as an intervention. Commonly applied interventions were defined as interventions that were applied regularly, often, or always (26–100%) by at least 50% of the general practitioners. For other disciplines, commonly applied interventions were defined in the same way, but only if more than 50% of the general practitioners referred patients to these disciplines at least regularly.

Subsequently, an extensive literature search was carried out to examine the level of evidence for the effectiveness of those commonly applied interventions. The search strategy for systematic reviews developed by Boynton et al. (2) was used and MeSH terms were added for the nine syndromes. A search was made using MEDLINE, EMBASE, and PSYCHLIT from 1966 to mid-1999, and the Cochrane Library (4) was searched for reviews until the end of 2000. In addition, references of the retrieved relevant publications were checked. The search was restricted to recent reviews (published in 1990 or later). The Cochrane Library was also checked for protocols submitted for reviews in preparation. All reviews on the nine syndromes were retrieved from the literature and checked to ensure that the commonly applied interventions identified by the survey were included. The methodologic quality of the relevant reviews was assessed independently by HCWV and RJPMS according to the method developed by Assendelft et al. (1) on a 0–100 point scale. Consensus on discrepancies was reached during subsequent discussion.

If reviews of reasonable (60–79 points) to good quality (≥ 80 points) were found, their conclusions (effective, not effective, inconclusive) were adopted. If only reviews of poor or moderate quality were found, a new systematic review was recommended. If no recent reviews of a specific topic were found, a search was made for randomized controlled trials (RCTs), using the strategy recommended by the Cochrane Collaboration (3). If there were more than five RCTs in the computerized databases mentioned above, a systematic review was recommended. If there were five RCTs or less, the following data were extracted from the abstract: the design (parallel or a crossover study), the sample size, whether the trial was really randomized, whether it was blinded, which interventions were compared, and the conclusions. If the conclusions were inconsistent, a new RCT was recommended. If the results appeared to be consistent, it was advised that the evidence of (in)effectiveness should be studied in detail in order to decide on the level of evidence. When the evidence from a small number of studies is convincing, it should be incorporated in a clinical guideline. A decision tree was used for this purpose for each intervention-syndrome combination (topic) (Figure 1). This resulted in a list of topics for the nine chronic benign pain syndromes for which systematic reviews were recommended and a list of topics for which new RCTs were needed.

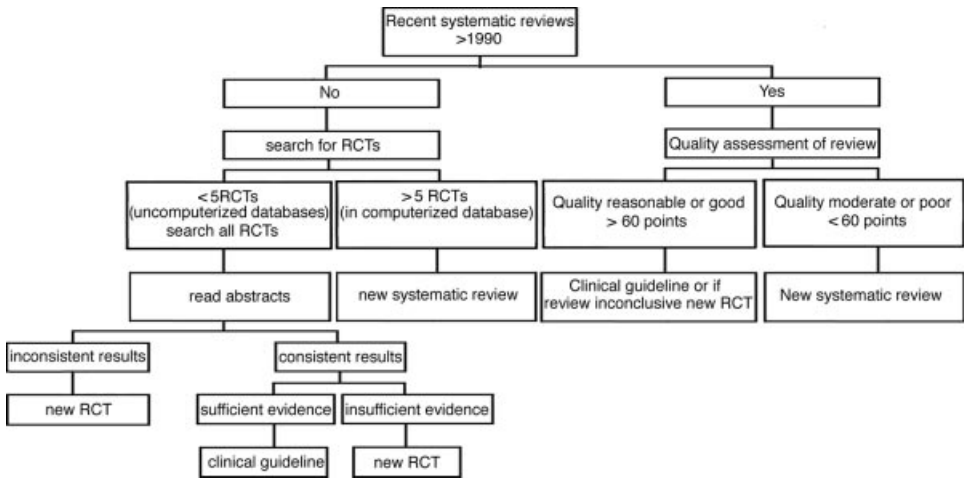


Figure 1. Decision tree to decide about the need for a new systematic review or the need for a new RCT for each topic.

Process of Priority Setting

The next challenge was to set priorities within these two lists of topics. In the Netherlands, there are four Centers for Pain Management and Research. The most important disciplines involved in the treatment of chronic pain are represented in these centers, and they are familiar with a multidisciplinary approach. For that reason these centers were chosen to perform the priority setting, based on a combination of a Delphi method and a nominal group technique. All members of the Centers for Pain Management and Research received the results of the literature search. This consisted of an overview of the number and quality of reviews found and an overview of RCTs if no recent reviews were found, resulting in a list of topics (intervention-syndrome combinations) for which systematic reviews were needed and a list of topics indicated for new RCTs. For each topic the members had to state independently whether it had, in their opinion, either no, low, or high priority. They were also asked to indicate which considerations played a role in their assessment. To help them in this process, a number of potential considerations were suggested (Table 2).

Table 2. Possible Considerations To Be Used in Priority Setting

Considerations

- Prevalence of the syndrome
- Impact of the syndrome on the patient
- Impact of the syndrome on society
- Costs of treatment
- Preference for simple methods of treatment above more advanced ones
- Impact of the treatment on the patient
- Availability of a clinical guideline
- Frequency of use of the treatment
- Applicability for one of the pain syndromes or for chronic pain in general
- Likelihood of positive outcome with the treatment
- Feasibility of new research
- Availability of grants for new research
- Relationship of the treatment with the cause or mechanism of the disorder
- Others

For each of the four centers a summary priority score was calculated for each topic. For this purpose, no priority was graded as 0, low priority as 1, and high priority as 2. Adding up these scores for all members in a center for each topic resulted in hierarchical list according to priority of topics per center. This can be considered as the Delphi aspect of the procedure, in which all members gave their opinions without being influenced by others. A meeting was then organized in each center, in which the nominal group technique was applied. In these meetings the hierarchical list of their own center was discussed and reconsidered. A listing of considerations mentioned by each individual member was used as a guide during the discussion about each topic. Overall lists of priorities, both before and after the discussion, were constructed by adding up the rankings in the centers. A more detailed description of this approach can be found in the research reports (in Dutch) (8;9;10).

RESULTS

Identification of Topics

A total number of 85 interventions appeared to be commonly applied: 9 for migraine, 9 for cluster headache, 8 for tension headache, 11 for back pain, 9 for neck pain, 14 for shoulder pain, 9 for fibromyalgia, 8 for stump and phantom limb pain, and 8 for irritable bowel syndrome (the most current treatments are listed in Appendix 1). For 42 topics, no recent reviews were found. For the remaining 43 topics, 65 published reviews were found and, according to the Cochrane Library (4), two reviews (for four topics) were in preparation (9). Twenty-nine published reviews (45%) were of reasonable quality (60–79 points), but only five (8%) reviews were considered to be of good quality (≥ 80 points). Many of these 34 reviews concluded that from the present evidence, no decision could be made with regard to the effectiveness or noneffectiveness of the intervention under study, thus indicating the need for new RCTs. For only five topics was the effectiveness shown in a systematic review of reasonable to good quality. They concerned spasmolytics for the treatment of irritable bowel syndrome and sumatriptan for the treatment of migraine, although for the latter it was stated that the optimal method of administration needs further study (13;14;15). For back pain there was evidence of the effectiveness of behavioral programs and back schools (the latter only in an occupational setting) (4). Exercise therapy was found to be more effective than a wait and see policy by the general practitioner, but not more effective than other physiotherapeutic treatments (4). Thirty-one reviews (48%) were of poor or moderate quality. As ample RCTs have been carried out in most cases, new systematic reviews on these topics were recommended. RCTs were sought for the 42 topics for which no recent reviews were found. These topics mainly pertained to fields in which not many RCTs had been performed. For no topics were the results of the RCTs consistent. A new RCT was therefore recommended for all these topics.

Based on the decision tree, a list was made of topics for which systematic reviews were needed (number of topics = 16), and a list of topics indicated for new RCTs (number of topics = 60). For topics for which systematic reviews are already under way in the Cochrane Collaboration ($n = 4$), no advice was given pending the outcome of these reviews. Together with the five topics for which effectiveness was shown, advice could be given on all 85 topics under consideration.

Process of Priority Setting

The four Centers for Pain Management and Research had a total of 29 members and included 5 neurologists, 4 anesthesiologists, 2 general practitioners, 4 psychologists, 7 physical therapists, 2 rehabilitation physicians, 2 epidemiologists, a nurse, an occupational physician and a geriatrician. Twenty-two members (76%) returned the questionnaire containing the individual priority scores. Unfortunately, some members did not state their priority for all

Table 3. Ranking of Topics for Systematic Reviews Before and After Discussion in the Centers for Pain Management and Research

Pain syndrome	Intervention	Ranking before discussion	Ranking after discussion
Tension headache	Respondent therapy	1	1
Tension headache	Cognitive therapy	2	2
Primary fibromyalgia	Fitness/aerobics	3	3
Migraine	Cognitive-behavioral therapy	6	4
Primary fibromyalgia	Tricyclic antidepressive	4	5
Irritable bowel syndrome	Brans and fibers	5	6
Primary fibromyalgia	NSAIDs	7	7
Irritable bowel syndrome	Bulk-increasing laxative	— ^a	8
Migraine	Beta-blockers (prophylaxis)	8	9
Migraine	5HT ₁ -antagonists	— ^a	10

Abbreviation: NSAIDs-nonsteroidal anti-inflammatory drugs; 5HT₁-antagonists-S-hydroxy-tryptophane,-antagonists.

^aNot in top 10, but ranking between 11–15.

Table 4. Ranking of Topics for RCTs Before and After Discussion in the Centers for Pain Management and Research

Pain syndrome	Intervention	Ranking before discussion	Ranking after discussion
Neck pain	Active exercise therapy	4	1
Neck pain	Cognitive therapy	1–2	2
Primary fibromyalgia	Active exercise therapy	3	3
Shoulder pain	Active exercise therapy	1–2	4
Neck pain	Cervical facet denervation	— ^a	5
Neck pain	Relaxation exercises	6	6
Neck pain	Cervical epidural therapy	— ^a	7
Tension headache	Active exercise therapy	9–10	8
Primary fibromyalgia	Cognitive behavioral therapy	5	9
Irritable bowel syndrome	Cognitive behavioral therapy	7	10

^aNot in top 10, but ranking between 11–15.

interventions, because they doubted whether they were able to assess some interventions adequately. Three of the four centers were visited. One center was not able to plan a meeting in time because too many members were absent during the study period. In the other three centers, during a 2-hour meeting the members reached consensus on the priority of the topics, for both systematic reviews and RCTs. There was an animated discussion in which all members made an active contribution. The possible considerations for priority setting (Table 2) were found to be very useful in the discussion. No attempt was made to quantify the impact of these considerations, so their role remains informal.

The results of the settings and before and after discussions in three centers are presented in Table 3 for systematic reviews and in Table 4 for RCTs. Priority rankings before and after discussions seem to be very similar. Nine and seven items of the top 10 overlap for systematic reviews and RCTs, respectively, and the interventions with the highest priority are high on both lists. The ranking based on the individual priority setting in the fourth center, where no group discussion took place, was similar to the other centers (data not shown).

DISCUSSION

Setting priorities of research obviously involves many subjective decisions. This study only attempts to make some of these decisions transparent and explicit. A first subjective

decision was the choice of the nine chronic benign pain syndromes. This choice was made in collaboration with the committee that granted the funding. Subsequently, it was decided to limit the priority setting to interventions that were commonly applied in the Netherlands. This increased the societal relevance of the study, but might imply that interventions that are effective but not yet commonly applied were missed.

The decision tree used to indicate for each topic the need for new systematic reviews or the need for new RCTs contains many arbitrary decisions (e.g., what is a recent review, what is a review of acceptable quality, and what is the minimal number of available RCTs to recommend a new systematic reviews?). The decision tree was easy to follow for each topic.

The decision to involve members of the Centers for Pain Management and Research in the study was also subjective. There are only four such centers in the Netherlands, which made it feasible to invite them all to participate. These centers have ample experience with the multidisciplinary treatment of patients with pain. This decision turned out to be a fruitful one. As expected, the members had a broad view with regard to the treatment of chronic pain, although some of them were reluctant to assess interventions applied by other disciplines. Two physical therapists and two psychologists refrained from setting priorities for some of the interventions applied by other disciplines. On the other hand, in the opinion of the authors, none of the participants tended to favor their own discipline.

In the priority-setting process, a combination of a Delphi method and a nominal group technique was used. The advantage of this procedure was that every member had input in the process, first by contributing to the overview of the individual priorities that formed the starting point of the discussion in their center, and then by contributing to the discussion within their center. It seems to be easier to explain one's priorities and to defend them than to introduce them to a group in which the opinions differ. Different opinions about the priority of an intervention could often be traced back to different views on why a topic is important. This facilitated the discussion and increased the acceptance of arguments put forth by other members.

The priorities before and after the discussion were compared (Tables 2 and 3), but it is difficult to draw a conclusion from this comparison. If the results had been very similar, the joint discussion within the Centers for Pain Management and Research would not have been necessary. If the results had been very different, one would doubt whether all members were really convinced and question the influence of prestige and authority.

This method of programming research is certainly applicable in the field of applied research, but not if the objective is to search for promising innovative approaches. If the field can be clearly demarcated, a literature search can be used to identify white spots. These white spots provide a clear and explicit starting point for priority setting. The combination of a Delphi method and a nominal group technique seemed to result in a robust hierarchy of topics. The explicit statement of individual considerations was found to be very useful in the group discussions on priorities. The study also demonstrated that in the field of chronic benign pain syndromes, evidence-based medicine is currently only an ambitious ideal, as convincing evidence could only be found for 5 of 85 commonly applied interventions. This situation will possibly change now that the Cochrane Collaboration and other organizations are stimulating the performance of high-quality reviews for the purpose of evidence-based medicine.

In conclusion, departing from the view that the evidence of effectiveness of regularly applied interventions for important chronic benign pain syndromes should be available, the strength of this method for research programming is that it can identify the relevant research questions. Using individual priority setting and group discussions appears to be an efficient and feasible method for priority setting. This approach is by no means restricted to interventions for chronic pain syndromes; it is also useful for programming research to enable evidence-based medicine in other fields of interest.

POLICY IMPLICATIONS

Research programming within the field of evidence-based medicine requires the identification of topics with paucity of evidence for efficacy. The presented method, including a structured but global literature review followed by priority setting by experts in the field, suits this purpose very well.

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APPENDIX 1

Frequently Used Treatments for the Various Chronic Benign Pain Syndromes

All syndromes^a:

- Education, instruction, advice, and psychosocial care^b

- Analgesics
- Nonsteroid anti-inflammatory drugs (NSAIDs)

Migraine

- Beta-blockers
- Anti-emetics
- 5-HT-antagonists

Cluster headache

- 5-HT-antagonists^b

Tension headache

- Stopping pain medication^b
- Massage^c
- Active exercise therapy^c

Back pain

- Active exercise therapy^{c,d,e,f}
- Passive exercise therapy^c
- Massage^{c,d}
- Mobilization and manipulations^d

Neck pain

- Active exercise therapy^{c,d,e,f}
- Passive exercise therapy^c
- Massage^{c,d}

Shoulder pain

- Rest^b
- Active exercise therapy^c
- Passive exercise therapy^c
- Massage^{b,c}

Fibromyalgia

- Active exercise therapy^{b,c}
- Massage^{b,c}

Stump and phantom limb pain

- Nerve blocks^{b,g}
- Transcutaneous electrical nerve stimulation (TENS)^{b,g}

Irritable bowel syndrome

- Adaptation of the diet (increasing fiber and fluid intake^b, no coffee^b)
- Spasmolytic
- Laxative

^aThese treatments are prescribed regularly for all chronic benign pain syndromes, except that analgesics and NSAIDs are not regularly prescribed for irritable bowel syndrome.

^bNo recent review available.

^cBy a physical therapist (PT).

^dBy a manual therapist.

^eBy a Menseidieck therapist.

^fBy a Cesar therapist.

^gBy an anesthesiologist.

When no superscripts are added, it refers to treatment by a general practitioner.