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Measurement Methods of Drug Consumption as a Secondary Judgment Criterion for Clinical Trials in Chronic Rheumatic Diseases

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Drug consumption is sometimes used as a secondary judgment criterion for clinical trials. Many measurement methods are available to quantify drug consumption. Several methods were applied in a rheumatic disease trial involving 121 patients with chronic low back pain who lived around Saint-Nectaire, France, and who participated in the trial from April to November 1993 to determine an easily used and practical measurement method to detect a significant drug consumption change over time. Analgesic and nonsteroidal antiinflammatory drugs (NSAIDs) were classified according to the anatomical therapeutic chemical classification. Consumption was quantified on a weekly basis in number of tablets (method 1), unit of defined daily dose (method 2), milligrams of active principle (method 3), and NSAID equivalence score (method 4). These methods were applied in a randomized clinical trial of spa therapy on sufferers of chronic low back pain. An analysis of variance with repeated measures showed a significant difference in drug consumption between treatment and control groups detected by all methods, except for the NSAID consumption measured with method 3. The comparison of each method by the relative efficiency index indicated that method 1 had a greater sensitivity for detecting changes of drug consumption. Tablet count appears to be a more sensitive and more practical method for detecting a drug consumption change in clinical trials. *Am J Epidemiol* 1997;145:826–33.

clinical trials; drug therapy; evaluation studies; methods

Measurement of drug consumption is sometimes used as a primary or secondary judgment criterion for controlled clinical trials to assess the effects of a therapeutic intervention (1–4). The question is whether it is possible to reduce symptomatic treatments after commencement of an effective long-term treatment (5, 6). Such studies have been based on the following postulate: A reduction of drug consumption is a reflection of the improvement of the disease, of the reduction of symptoms, and of a subsequent decrease in need of symptomatic treatments. Particularly in chronic rheumatic diseases, some authors have measured drug consumption (analgesic and nonsteroidal antiinflammatory) over time in clinical trials testing symptomatic slow-acting drugs for osteoarthritis. In osteoarthritis of the knee, authors have observed a reduction of drug consumption with a simultaneous improvement in patients' pain-function index (5).

Many measurement methods have been used to quantify drug consumption (7–12). These have included the measurement of tablets, defined daily dose and derived methods, milligrams of active principle, or equivalent doses of nonsteroidal antiinflammatory drugs (NSAIDs) related to unit of time. These different measurement methods are not mutually transposable, and the lack of uniformity of measurement methods sometimes makes the comparison of results from different studies difficult. As of this writing, even if some authors have acknowledged these problems (2, 9), no study has attempted to resolve them in any specific way.

Herein, different measurement methods of drug consumption were applied in a controlled clinical trial in which the consumption (analgesics and NSAIDs) was a secondary judgment criterion. The aim of this study was to compare different measurement methods to determine an easily used and practical method for detecting a significant drug consumption change over time.

MATERIALS AND METHODS

Presentation of measurement methods of drug consumption

Classification framework for analgesic and antiinflammatory drugs. Analgesic and antiinflammatory

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Abbreviations: ATC, anatomical therapeutic chemical; DDD, defined daily dose; NSAID, nonsteroidal antiinflammatory drug; SRM, standardized response mean.

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drugs are often used as symptomatic treatments in chronic rheumatic diseases. The polymorphism of these two drug classes leads to their division into several subclasses, as is found in the European drug or anatomical therapeutic chemical (ATC) classification (11). This classification is recommended by the World Health Organization to be used in drug utilization studies, and it has therefore been adopted in North America as well as in many European countries. It is based on a system of hierarchical coding with five levels. The first level (i.e., one letter) symbolizes the anatomical main classes (14 in total). The second level (i.e., two numbers) and the third level (i.e., one letter) symbolize, respectively, the main therapeutic classes and the therapeutic subclasses. The fourth level (i.e., one letter) represents the therapeutic and chemical subclasses. The fifth level (i.e., two numbers) represents the chemical substances that comprise the proprietary drugs.

In this classification system, the main therapeutic class of antiinflammatory and antirheumatic products is divided into three therapeutic subclasses: 1) antiinflammatory and antirheumatic nonsteroid products including butylpyrazolidines, oxicams, propionic acid derivatives, fenamates, and other antiinflammatory and antirheumatic nonsteroid products; 2) antiinflammatory and antirheumatic agents in combination with corticosteroids or other antiinflammatory and antirheumatic agents; and 3) specific antirheumatic agents.

The main therapeutic class of analgesics is divided into two therapeutic subclasses: 1) opioids, and 2) other analgesics and antipyretics including salicylic acid and derivatives, pyrazolones, anilides, and other analgesics and antipyretics. We used this ATC classification framework to categorize the description of drug consumption.

Description of measurement methods of drug consumption. In this study, the following four methods, calculable at the individual level, were compared:

First method. Drug consumption was quantified in number of tablets taken per week in every main therapeutic class (i.e., antiinflammatory and antirheumatic products and analgesics).

Second method. Drug consumption was quantified in unit of defined daily dose (DDD). Initially, this measurement method had been devised by the World Health Organization drug utilization research group to allow comparisons of drug consumption over time, in space, and in terms of morbidity and economics at the country level (11). For each active principle, the drug utilization research group has defined a daily dose, which is the assumed average dose per day for the drugs used for its primary indication in adults. The DDD has therefore been a basic measurement unit for each active principle, and it has been used particularly for the economic measure of the drug consumption of a population or country where it has been applied to individuals. Drug consumption was quantified in units of DDD taken per week, and the calculation of individual consumption was made as follows: $\sum_1^7$ (number of mg of active principle/DDD in mg) $\times$ (number of days of drugs intake per week) = number of DDD units taken per week.

Third method. Drug consumption was quantified in milligrams of active principle taken per week. This corresponded to the sum of active principles in a given main therapeutic class.

Fourth method. Drug consumption was quantified in an equivalence score. This measurement method has been developed only for NSAIDs as the result of an agreement among several rheumatologists (12). These physicians established an equivalence score for various NSAIDs in an effort to limit the difficulties of therapeutic evaluation resulting from the great number of NSAIDs. The score was proportional to the amount of drug consumption, and the equivalent score of 10 was arbitrarily allocated to the following doses of drugs: 100 mg of indomethacin, 600 mg of tiaprofenic acid, 3,000 mg of acetyl salicylic acid, 150 mg of diclofenac, 900 mg of fenbufen, 300 mg of flurbiprofen, 1,600 mg of ibuprofen, 200 mg of ketoprofen, 1,000 mg of naproxen, 1,100 mg of sodic naproxen, 400 mg of phenylbutazone, 20 mg of piroxicam, 400 mg of sulindac, and 20 mg of tenoxicam. This score enabled us to determine the equivalent dosage of NSAIDs, which was necessary to obtain an equivalent comfort level in patients. Drug consumption was thus quantified in a NSAID equivalence score on a weekly basis.

Application to a controlled clinical trial

The four measurement methods of drug consumption described above were applied to the data of a randomized clinical trial to address our research question. We examined whether the drug consumption reduction was concomitant with functional disability level so that we could appreciate the consistency of these changes across methods over time.

Controlled clinical trial as a basis for analysis. This controlled clinical trial was aimed at the assessment of the overall effectiveness of spa therapy versus usual routine drug therapy in patients with chronic low back pain (13). A total of 121 patients who had chronic low back pain and lived around Saint-Nectaire, France, participated from April to November 1993 and were randomly allocated to two groups. The treatment group underwent routine drug therapy and spa therapy;

the control group received routine drug therapy. Both groups were compared on different judgment criteria, with functional disability as the primary effectiveness criterion. Drug consumption (analgesics and NSAIDs) was one of the secondary criteria used.

Collection of information concerning drug consumption. Drug consumption was recorded in a diary (self-questionnaire) that contained analgesic and NSAID drug names, dosage in milligrams, and dose for the period of a week. The diary was completed during the week preceding each primary outcome (functional disability) assessment at three different times before and after spa therapy (i.e., at baseline, at 3 weeks, and at 2 months), a schedule selected for the purpose of illustrating the present work.

Statistical analysis. The baseline characteristics in both groups were compared by Student's t test. An analysis of variance with repeated measures (14, 15) was performed to compare the magnitude of drug consumption change from baseline in each group. For the purpose of this analysis, baseline, 3 weeks', and 2 months' data are reported because they correspond to a balanced time period of measurement and because data reveal a linear trend of change in each group. This analysis of variance with repeated measures is suitable for taking into account the measures of drug consumption repeated (thus correlated) in time on each subject in the trial, with baseline consumption as the covariate. This analysis was applied separately to the data of drug consumption for two secondary judgment criteria (analgesic and NSAID consumption) with each of the four measurement methods. To take into account non-independent evolution of the two secondary judgment criteria, the level of significance was set at $\alpha' = 0.025$ to obtain an overall type I error $\alpha = 0.05$ (16). The Pearson correlation coefficients between the score changes obtained from the four measurement methods were computed to assess whether the methods detect drug consumption changes similarly and in the same direction.

The measurement methods were compared directly in terms of sensitivity to change. The standardized response mean (SRM), i.e., the ratio of the difference of means of differences in the treatment and control groups to the pooled standard deviation of differences, indicating the magnitude of change detected by a measurement method, were calculated for each main therapeutic class of drugs (analgesics and NSAIDs) and for each method (17). The SRMs of different methods were compared in each class by computing their relative efficiency, i.e., the squared ratio of SRM by one method to SRM by another method. Z tests were used to draw inferences about statistical significance of differences in SRM estimates among measurement methods (18). All analyses were performed using BMDP software (14).

RESULTS

The original study underlined the positive effects of spa therapy at 3-week and 6-month intervals. There was a statistically significant improvement of patients' health status in the treatment group compared with the control group. The functional disability, the pain duration, the pain intensity, and the finger to floor distance decreased in the treatment group. In the treatment group, overall health status of the back improved and drug consumption decreased significantly.

A description of the initial drug consumption in each group is reported in table 1. The treatment group had a greater consumption of analgesic and NSAID

TABLE 1. Initial drug consumption (analgesic and NSAID*) as measured by four methods in low back pain sufferers in treatment and control groups, Saint-Nectaire, France, April to November 1993

Initial measurement time of drug consumption	Control group (n = 62)		Treatment group (n = 59)		p†
	Mean	(SD)*	Mean	(SD)	
Method 1: no. of tablets/week					
Analgesics	3.8	(6.7)	6.6	(10.4)	0.07
NSAIDs	1.4	(3.8)	2.8	(6.0)	0.12
Method 2: no. of DDD* units/week					
Analgesics	0.5	(0.8)	0.8	(1.1)	0.09
NSAIDs	0.5	(1.8)	1.5	(2.8)	0.03
Method 3: active principle/week (mg)					
Analgesics	1,899.3	(3,185.2)	2,720.9	(3,692.0)	0.10
NSAIDs	11.1	(53.7)	111.2	(486.0)	0.05
Method 4: NSAID equivalence score/week	6.4	(17.6)	14.0	(23.6)	0.04

* NSAID, nonsteroidal antiinflammatory drug; SD, standard deviation; DDD, defined daily dose.
† p values from Student's t test for between-groups baseline comparisons.

drugs compared with the control group depending on the measurement method.

Changes over time of analgesic and NSAID drug consumption

At 3 weeks and at 2 months, the analgesic drug consumption decreased significantly in the treatment group compared with the control group by methods 1, 2, and 3 (p = 0.002, 0.007, and 0.009, respectively) (table 2). The NSAID consumption decreased significantly over time in the treatment group compared with the control group by methods 1, 2, and 4 (p = 0.001, 0.007, and 0.011, respectively) (table 3).

Concomitant changes of functional disability and drug consumption

The difference of functional disability score change between both groups was 3.3 and 5.1 at 3 weeks and at 2 months, respectively. These differences indicated a higher decrease of functional disability in the treatment group compared with the control group.

The difference of analgesic drug consumption change between groups at 3 weeks and at 2 months, respectively, was a reduction of the following: three and four tablets taken per week by the first method; 0.38 and 0.58 unit of DDD taken per week by the second method; 1,068 and 1,881 mg of active principle taken per week by the third method. All of these differences in change reflected a greater reduction of analgesic drug consumption in the treatment group compared with the control group.

The difference of NSAID consumption change between groups at 3 weeks and at 2 months, respectively, was a reduction of the following: 0.9 and 3.6 tablets taken per week by the first method; 0.38 and 1.13 units of DDD taken per week by the second method; 36 and 106 mg of active principle taken per week by the third method; 4.5 and 11.1 in NSAID equivalence scores per week by the fourth method. Again, all of these differences in change indicated a greater reduction of NSAID drug consumption in the treatment group compared with the control group.

Correlation between changes by the measurement methods

For the analgesic drug consumption (table 4), the score changes obtained from the three measurement methods were positively correlated (p values $<$ 0.001). For the NSAID consumption (table 4), the score changes at 3 weeks were positively correlated (p values $<$ 0.001) except between methods 1 and 3 (p = 0.08); the score changes of methods 1, 2, and 4 at 2 months were positively correlated (p values $<$ 0.001).

Comparison of the sensitivity to change of measurement methods

For the analgesic drug consumption (table 5), relative efficiency indicates that method 1 is significantly more sensitive to change than method 3 at 3 weeks (p = 0.016) and than method 2 at 2 months (p = 0.038). For NSAID consumption (table 5), method 1 is significantly more sensitive to change than method 3 at 3 weeks (p = 0.01) and more than method 2 (p = 0.0001) and method 3 (p = 0.028) at 2 months. Method 4 did not show consistent or significantly different sensitivity to change compared with method 1.

DISCUSSION

We have examined and compared four measurement methods and have consistently detected a difference of

TABLE 2. Comparison of analgesic drug consumption change as measured by three methods between treatment and control groups at 3 weeks and 2 months, Saint-Nectaire, France, April to November 1993

Measurement time of analgesic drug consumption	Control group (n = 62) Mean ± SE*	Treatment group (n = 59) Mean ± SE	p†
Method 1: no. of tablets/week			
3 weeks	−0.8 ± 0.5	−3.8 ± 1.0	0.002
2 months	−0.1 ± 0.6	−4.1 ± 0.9	
Method 2: no. of DDD* units/week			
3 weeks	−0.06 ± 0.0	−0.44 ± 0.1	0.007
2 months	+0.06 ± 0.1	−0.52 ± 0.1	
Method 3: active principle/week (mg)			
3 weeks	−384.7 ± 297.1	−1,453.1 ± 497.4	0.009
2 months	+94.5 ± 444.3	−1,786.6 ± 441.2	

* SE, standard error; DDD, defined daily dose.
† p values for between-groups change over time at 3 weeks and 2 months from analysis of variance with repeated measures (significance level α = 0.025).

TABLE 3. Comparison of NSAID* consumption change as measured by four methods between treatment and control groups at 3 weeks and 2 months, Saint-Nectaire, France, April to November 1993

Measurement time of NSAID consumption	Control group ($n = 62$) Mean ± SE*	Treatment group ($n = 59$) Mean ± SE	p†
Method 1: no. of tablets/week			
3 weeks	+0.2 ± 0.6	−0.7 ± 0.6	0.001
2 months	+2.0 ± 0.7	−1.6 ± 0.7	
Method 2: no. of DDD* units/week			
3 weeks	−0.18 ± 0.1	−0.56 ± 0.3	0.007
2 months	+0.32 ± 0.2	−0.81 ± 0.3	
Method 3: active principle/week (mg)			
3 weeks	+3.1 ± 8.4	+39.9 ± 63.8	0.11
2 months	+35.7 ± 22.7	−70.4 ± 54.3	
Method 4: NSAID equivalence score/week			
3 weeks	−1.2 ± 1.4	−5.7 ± 2.9	0.011
2 months	+3.8 ± 2.7	−7.3 ± 2.8	

* NSAID, nonsteroidal antiinflammatory drug; SE, standard error; DDD, defined daily dose.
† p values for between-groups change over time at 3 weeks and 2 months from analysis of variance with repeated measures (significance level $\alpha = 0.025$).

TABLE 4. Correlation coefficients between score changes obtained from drug consumption measurement methods, Saint-Nectaire, France, April to November 1993

Main therapeutic class of drugs	Correlation coefficients			
	Method 1	Method 2	Method 3	Method 4
Analgesics				
3 weeks				
Method 1	1.00			
Method 2	0.79*	1.00		
Method 3	0.84*	0.96*	1.00	
2 months				
Method 1	1.00			
Method 2	0.85*	1.00		
Method 3	0.86*	0.98*	1.00	
NSAIDs†				
3 weeks				
Method 1	1.00			
Method 2	0.50*	1.00		
Method 3	0.15	0.57*	1.00	
Method 4	0.45*	0.96*	0.45*	1.00
2 months				
Method 1	1.00			
Method 2	0.36*	1.00		
Method 3	0.17*	0.06	1.00	
Method 4	0.31*	0.93*	−0.10	1.00

* $p < 0.05$.
† NSAID, nonsteroidal antiinflammatory drug.

drug consumption change over time between groups. Thus, in terms of relative efficiency, method 1 is more sensitive to change of drug consumption than methods 2 and 3.

Pros and cons of each measurement method

First method. Measuring the number of tablets taken per week simplifies the calculation of the consumed weekly dose. This quantification system is known and used in therapeutic trials and other studies (19–22). For those authors, the method allows the transmission of information to physicians in the same unit as that used in their prescriptions. Thus in pragmatic therapeutic trials, this unit of measure has a clinical meaning for the practitioners. Furthermore, economic assessments are feasible from the price associated with the tablet unit. However, it is difficult to establish a comparison between the delayed form or drop form with the tablet form, as stated by Taboulet (9). This method is therefore inadequate for measuring the drug consumption for a pharmacology study because different dosages of different drugs are mixed. Nevertheless, in a public health approach, this quantification is useful for studying the behavior of patients and their drug consumption after a therapeutic intervention.

Second method. This method allows a comparison of weekly drug consumption both nationally and internationally (23–26) and uses DDD as the unit of measure. The number of drugs prescribed in daily doses is calculated in each diagnoses-related group to compare them between countries or within the same country at the population level according to the number of patients treated. This method establishes a link between observed drug consumption and morbidity, in addition to focusing on levels and structures of consumption. Because the DDD is a technical unit of measure, it can easily be used for an economic assessment. However, many authors believe that a major disadvantage of DDD is that it is calculated with all ages confounded (9). In addition, because drug consumption differs for each drug according to age, standardized estimates adjusted to age differences should

TABLE 5. Comparison of sensitivity to change of different measurement methods based on drug consumption data from Saint-Nectaire, France, April to November 1993

	Δ_t†	Δ_c†	$\Delta_t - \Delta_c$†	Pooled SD†	SRM†	RE†	*z*
Analgesics							
Method 1							
3 weeks	−3.84	−0.87	−2.97	6.51	−0.45	1	
2 months	−4.15	−0.17	−3.98	6.39	−0.62	1	
Method 2							
3 weeks	−0.44	−0.05	−0.39	0.94	−0.41	0.82	0.70
2 months	−0.52	+0.06	−0.58	1.10	−0.52	0.69	2.08*
Method 3							
3 weeks	−1,453.20	−384.78	−1,068.42	3,153.25	−0.33	0.53	2.40*
2 months	−1,786.70	+94.50	−1,881.20	3,514.70	−0.53	0.72	1.91
NSAIDs†							
Method 1							
3 weeks	−0.77	+0.28	−1.05	5.78	−0.18	1	
2 months	−1.68	+2.01	−3.69	5.97	−0.61	1	
Method 2							
3 weeks	−0.56	−0.18	−0.38	1.96	−0.19	1.10	0.11
2 months	−0.81	+0.32	−0.49	2.22	−0.22	0.12	3.90*
Method 3							
3 weeks	+39.92	+3.17	+36.75	286.86	+0.12	0.44	2.58*
2 months	−70.47	+35.71	−106.18	306.17	−0.34	0.30	2.28*
Method 4							
3 weeks	−5.73	−1.26	−4.47	17.30	−0.25	1.91	0.75
2 months	−7.36	+3.88	−11.24	22.06	−0.50	0.66	1.05

* $p < 0.05$.

† Δ_t, mean of differences in the treatment group; Δ_c, mean of differences in the control group; SD, standard deviation of differences; SRM, $\Delta_t - \Delta_c$/SD; RE, relative efficiency; NSAID, nonsteroidal antiinflammatory drug.

be obtained. Furthermore, DDD changes over time with the appearance of new molecules and different dosages. And finally, calculating drug consumption is more difficult when several active principles are mixed in the same drug.

Other measurement methods that have been derived from DDD are sometimes used. The defined daily dose per 1,000 inhabitants per day ("DHD") provides an estimate of the daily proportion of the population that receives drug treatment in ambulatory care at national, regional, local, and institutional levels (23). The defined daily dose per 100 consumers per day ("DCD") allows the determination of daily drug utilization from community provider allocation in cities (23). The prescribed daily dose ("PDD") is the average dose prescribed per day from a representative sample of prescriptions (24). The consumed daily dose ("CDD") is defined as the average quantity of a drug actually used per day from a representative sample of patients (24). These methods were not applied because they did not serve our purpose.

Third method. This method allows the specification of qualitative drug consumption and uses milligrams of active principle taken per week as the unit of measure. Although this method is useful for pharmacology studies, the calculations of weekly consumed doses are burdensome. In addition, changes in NSAID consumption over time are not detected consistently.

Fourth method. This method produces a NSAID equivalence score, and its main advantage is that it allows the calculation of equivalent doses of NSAIDs for the different and numerous molecules existing on the market. In pragmatic studies, this score has been proposed as a standard for following the course of rheumatic diseases. Nevertheless, as emphasized by Dougados and colleagues (12), this score is of little use in daily practice for an individual. The major disadvantage of this method is that because the modes of prescription change over time with the appearance of new molecules and different dosages, equivalent doses of NSAIDs must be updated regularly to integrate new molecules on the market.

Some authors (27, 28) tend to develop measurement methods similar to method 4 in an effort to improve application. For each individual NSAID, they have used "standard doses," which have been defined by the manufacturers as the lowest recommended daily dose for treating rheumatoid arthritis (27). Physicians have thus established a posologic equivalence between 1,800 mg of ibuprofen, 75 mg of indomethacin, 300 mg of sulindac, 500 mg of naproxen, 900 mg of fenoprofen, and 20 mg of piroxicam. These equivalent

doses of NSAIDs have been used for establishing classes of different dosages (low, mean, high) to compare the levels of patients drug consumption (28). This method was not applied in our study because these equivalent doses of NSAIDs are specific only for rheumatoid arthritis, which was not a part of this trial.

In the treatment of knee and hip osteoarthritis, some authors (10) have established a posologic equivalence between 150 mg of diclofenac, 1,100 mg of sodic naproxen, 20 mg of piroxicam, 300 mg of ketoprofen, 2,400 mg of ibuprofen, 150 mg of indomethacin, 20 mg of tenoxicam, and 300 mg of flurbiprofen. In this way, they have been able to convert NSAID consumption into a diclofenac equivalent and to quantify this in a summarized way for controlled clinical trials. Nevertheless, the authors did not indicate whether specialists agree on the use of this measurement method, and we did not apply it in our study.

Comments on drug consumption in controlled clinical trials

In this trial, the difference in change between treatment and control groups was significant for the clinical measure, for analgesic drug consumption (with methods 1, 2, and 3), and for NSAID consumption (with methods 1, 2, and 4). A decrease of functional disability was observed with a reduction of analgesic and NSAID drug consumption in the treatment group compared with the control group. This reduction of symptomatic treatments occurs simultaneously with the alleviation of symptoms. This reflects, perhaps indirectly, the effects of a therapeutic intervention.

The observed results of the four measurement methods for the analgesics and NSAID consumption are in agreement. These methods similarly detect a decrease of drug consumption over time except for method 3, which can detect the variability of change over time. Furthermore, the drug consumption change was consistent with the functional disability change even if the reduction did not have the same magnitude according to the method used for measuring the drug consumption. Nevertheless, the analysis of variance with repeated measures allows only an indirect comparison of measurement methods. The calculation of correlation coefficients between the score changes obtained from the four measurement methods shows that methods detect drug consumption change similarly and in the same direction, except for method 3, for NSAIDs.

Relative efficiency allows direct comparison of measurement methods. Therefore, in terms of sensitivity to change, method 1 detects significantly more change than methods 2 and 3 for analgesics and for NSAIDs. In addition, method 1 can detect smaller changes of drug consumption over time compared with the other methods.

The ATC classification of drugs provokes misgivings from pharmacologists because it does not take into account the pharmacologic characteristics of drugs. In our study, we have used only the main therapeutic classes because there is too much diversity in the therapeutic subclasses.

In the domain of pragmatic controlled clinical trials, we have attempted to identify the measurement method that corresponded to our purpose, i.e., an easily used and practical method for detecting a significant drug consumption change over time. Method 1 appears to correspond best to this purpose for several reasons. First, this method uses the same unit of measure that is employed daily in the prescriptions of practitioners. Second, the detected changes are meaningful both statistically and clinically. Third, this unit of measure is meaningful for the patients who note their drug consumption in a diary. Fourth, no further calculation is necessary. Nevertheless, method 2 could be useful for morbidity studies or economic assessments. In method 3, the calculations are more burdensome. Method 4 must be updated over time to obtain equivalent doses of NSAIDs.

In conclusion, the application of a unique measurement method of drug consumption adapted to controlled clinical trials would allow comparisons between different studies both in terms of effectiveness and in terms of cost. This study suggests that the four analyzed measurement methods of drug consumption similarly detect a drug consumption change over time between patient groups after treatment. However, the method that specifically records the number of tablets taken daily appears to be the most appropriate for detecting a drug consumption change in controlled clinical trials on rheumatic diseases. Furthermore, this method is simple to use and it expresses the results in a measurement unit that is clinically meaningful.

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