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# The consequences of different definitions for recurrence of Dupuytren's disease

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## KEYWORDS

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Definitions

**Summary** *Background:* Recurrence rates are important in the evaluation of the effectiveness of treatment for Dupuytren's disease (DD). In the literature, recurrence rates vary between 0% and 100%. The definition of recurrence of DD after treatment is inconsistently used. The aim of this study is to review all definitions of recurrence after treatment of DD and to evaluate the impact of using these definitions on a single cohort of patients treated for DD.

*Methods:* A literature search was performed in PubMed and Embase to identify studies. Titles and abstracts were analysed to collect all articles that described recurrence rates or definitions of recurrence. Two independent reviewers selected relevant studies and extracted data. The different definitions of recurrence were applied on our data set of 66 patients.

*Results:* Of the 113 articles reporting recurrent rates of DD, 56 (49%) presented a definition of recurrence. We could categorise the definitions into three groups. By applying the different definition on our data set of a randomised controlled trial, the recurrence rates ranged from 2% to 86%.

*Conclusions:* In the literature, different definitions of recurrence of DD are used and many authors failed to define recurrence. This study shows that the wide range of reported recurrence rates may largely be contributed by inconsistency in recurrence definitions. As a result, it is difficult or even impossible to compare recurrence rates between different treatments reported in the literature. The study indicates that consensus on a recurrence definition is needed.

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Although the evidence for effectiveness of treatments for Dupuytren's disease (DD) is still scarce, different treatment options are available in clinical practice, such as fasciectomy, aponeurotomy and, more recently, collagenase injections.<sup>1–3</sup> However, since current treatments only remove or alter the symptoms of the disease rather than treat the underlying pathology, recurrences occur. In the literature, reported recurrence rates vary between 0% and 100%.<sup>4–10</sup> Several studies have identified factors that influence these rates, such as follow-up time and diathesis.<sup>11,12</sup> Since treatment type may also influence recurrence rates, it is an important aspect for assessing the effectiveness of treatment.

In a recent review, Becker and Davis<sup>13</sup> concluded that the outcome of surgery is inconsistent and that this inconsistency may be related to the different definitions of recurrence used. Therefore, the first aim of this study was to identify all definitions of recurrence after treatment of DD reported in the literature. Subsequently, we performed an analysis by applying the different definitions to a cohort of patients treated for primary DD, evaluating the effect of different definitions on the recurrence rate of these patients.

## Methods

### Literature search

To identify relevant articles on the recurrence of DD, we searched for studies published from January 1985 up to April 2011 using PubMed and Embase. Keywords related to recurrent DD were included, such as 'Dupuytren', 'reappear', 'recurrence', 'return', 'predict', 'prognosis', 'residual', 'remain' and 'outcome'. The complete search strategy can be found in [Appendix 1](#).

### Inclusion criteria and study selection

The search strategy results from Embase and PubMed were combined and duplicates were discarded. Titles, abstracts and subsequently full text of the articles were analysed individually by two independent reviewers to determine whether they met the following inclusion criteria: (1) the main subject of the article was DD; (2) the study used an original data set of cases; (3) the study population consisted of at least five patients; and (4) patients were 18 years or older. Only articles written in English, German, French or Dutch were included. If disagreement on inclusion of a publication arose, a consensus between the two reviewers was met. If this disagreement persisted, a third reviewer was consulted.

### Data extraction

Two reviewers independently extracted the data. Reported recurrence rates, definitions of recurrence and definitions that could be extracted from the text were identified. For example, in some studies, authors defined recurrence as the presence of new nodules or cords, without giving an explicit definition. Furthermore, characteristics such

as authors, publication year or type of surgery were extracted.

### Comparing definitions using our data set

To evaluate the effect of different definitions of recurrence found in the literature, we applied the different definitions of recurrence on a single data set of the Dupuytren Rotterdam Trial (Du Ro Trial) (NTR1692). This data set consisted of preliminary data from patients who participated in the randomised controlled trial and were treated by limited fasciectomy or extensive percutaneous aponeurotomy and lipografting. This extensive percutaneous aponeurotomy and lipografting technique consists of extensive percutaneous aponeurotomy that completely disintegrates the cord and separates it from the dermis. Autologous fat from the abdomen is injected in the operated area. In a recent study, we described this technique in detail and published data from an initial cohort study.<sup>14</sup> For the present study, we analysed data from patients that were included in the Du Ro trial between May 2009 and October 2010. Medical ethical approval was obtained for this study and all subjects signed informed consent (MEC-2008-264).

We used the passive range of motion (ROM) data of the most affected digit, measured at 2 weeks and 6 months postoperatively. Extension goniometry was measured with all joints (metacarpophalangeal (MP), proximal interphalangeal (PIP), and distal interphalangeal (DIP)) maximally extended. Further, preoperatively, the surgeon visually estimated the passive ROM. Since all joints of the treated digits were measured with goniometry, the total passive extension deficit (TPED) could be calculated, representing the sum of joint angles of the MP-joint, PIP-joint and DIP-joint.

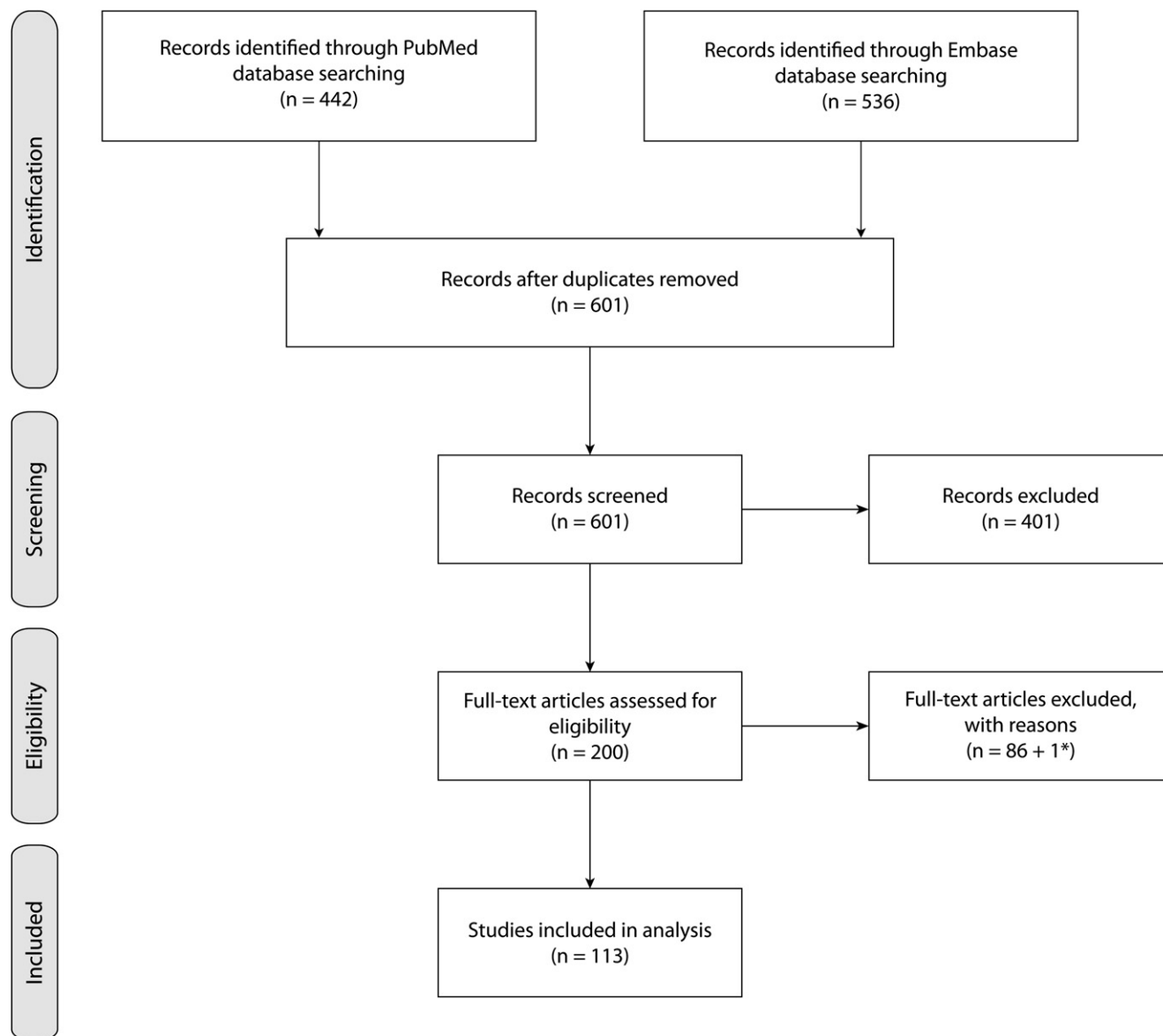
## Results

### Literature search

The initial search resulted in the identification of 606 studies from PubMed and Embase. After analysing the titles, abstracts and full text, 113 articles were included ([Figure 1](#)). One article could not be found online or requested at the medical library of the Netherlands and medical library of England. Therefore this article was excluded from analysis.<sup>15</sup>

### Recurrence definitions

Of all 113 included articles describing a recurrence rate, only 56 articles described a definition of recurrence. Definitions found in the articles could be categorised into three groups. [Table 1](#) describes these definition categories, the corresponding studies and the exact definition used in the individual studies. The first category (type I) defines recurrent DD based on the return of disease (nodules or cords) in the operated area or in the operated hand (63% of all studies used this definition). The second category (type II) defines recurrent DD based on the return of contractures, with the minimal degree of contracture required for defining recurrence varying from 1° ('any increase in contracture') to 50° (27%). The third category (type III) is



**Figure 1** Flow chart of literature search PubMed and Embase were used to find articles about recurrence of Dupuytren’s disease. From the total 606 articles 113 articles were included for this study.<sup>15</sup>

based on the patient’s self-report of a recurrence or whether a recurrent surgery was performed (10%).

Figure 2 summarises the recurrence rates for the different treatment types and recurrence definition categories. The recurrence rates reported in the studies ranged from 0% to 100%. We found that all types of definition categories (I–III) were used for all types of treatments. However, articles on collagenase injections were the most consistent in the type of definition that was used (type II) (Figure 2 and Table 1).

**Applying the definitions on our data set**

We used data from 66 patients (56 males and 10 females) affected by primary DD from the Du Ro trial. Since the extensive percutaneous aponeurotomy and lipografting

technique does not remove any tissue and since therefore a palpable nodule is always present in the operated hand, we could not apply the first definition category to our data.

Figure 3 shows the different recurrence rates when using different angular thresholds for the category-2 definitions. The lower dark line represents the difference in joint angle between 2 weeks postoperatively and 6 months postoperatively, analysed in the most affected joint only. This recurrence rate strongly decreases from 49% when applying a change of 5° in angle as the threshold for recurrence, to 2% when applying a 50° threshold. The upper light-grey line, indicating the threshold in angle of the most affected joint when comparing peroperative data with the 6 month follow-up, shows the same pattern. Since more extension is measured peroperatively than at 2 weeks’ follow-up, higher recurrence rates are found. Because some authors used TPED, we added two extra lines for the TPED, showing

**Table 1** *Recurrence definitions.* This table shows all articles that report a definition of recurrence. We categorized the definitions into 3 categories, based on 1. the presence of nodules or cords the operated hand, 2. joint contracture in degrees, 3. patient's self-report or recurrent surgeries. When the author explicitly defined recurrence, this was stated as 'yes' in the fourth column; if the definition was extracted from the context it was stated as 'no'.

Definition category		Year	Author	Explicitly defined	Definition
1. Recurrence based on nodules or cords	Irrespective of the operated area	2010	Betz et al.	No	Return of nodules or cords in the operated field, or both in and out the operative field.
		2007	Abe et al.	No	Nodules or cords under the skin graft or outside of the skin graft.
		2000	Armstrong et al.	No	Return of nodules or cords.
		1997	Hall et al.	No	Return of nodules or cords under the graft or on the edge of the graft.
		1997	Moermans	Yes	The presence of a nodule or of an identifiable cord without taking the loss of extension into account. The reappearance of a nodule anywhere in an operated ray was considered as a recurrence even if that precise location was not directly in the original surgical field.
		1996	Moermans	Yes	
		1996	De Maglio et al.	Yes	The simple occurrence of a nodule without contracture.
		1992	Searle et al.	No	Clinically recurrent disease, observed as nodules at the graft inset.
		1992	Kelly et al.	No	Recurrence of the disease within the same ray as the skin graft, under the graft or outside of the graft.
		1991	Andrew et al.	Yes	The presence of any detectable disease in the operated ray.
	1987	Langenberg	No	Return of nodules, in or out of the operated ray.	
	1985	Herbst et al.	No	Recurrence only observed at the edge of the irradiated field.	
	In operated area	2009	Balaguer et al.	Yes	The reappearance of DD in a zone previously operated on.
		2008	Juriscic et al.	Yes	The development of new Dupuytren's disease lesions including the smallest palpable nodule irrespective of a presenting contracture in the same area where fasciectomy had been performed.
		2006	Hindochoa et al.	Yes	
		2007	Anwar et al.	Yes	Disease within previously operated sites.
		2005	Del Frari et al.	Yes	Reappearance of contracture cords in the operated area, including the reappearance of isolated nodules or cords.
		2005	Citron et al.	Yes	Any new nodule of disease in the operative field under the flaps (Leclerq, 2000).
		2004	Abe et al.	Yes	
2004		Abe et al.	Yes		
2004		Abe et al.	Yes		
2003	Citron et al.	Yes	The reappearance of Dupuytren's tissue in the operative field. This included isolated nodules, without contracture, but did not include extension beyond the operative field.		

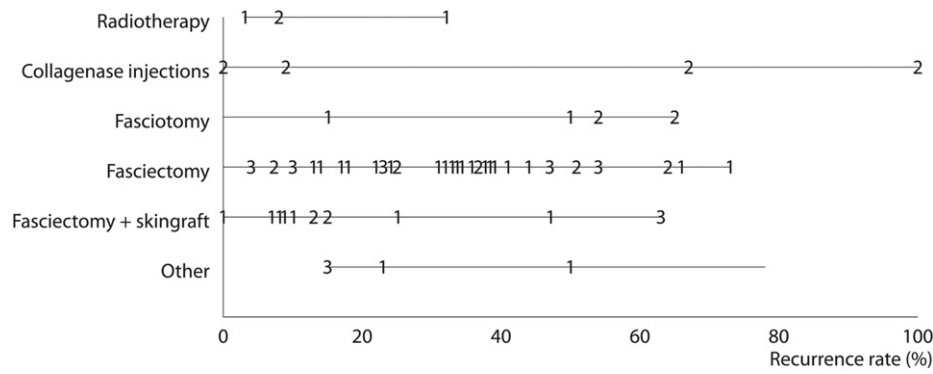
**Table 1** (continued)

Definition catry	Year	Author	Explicitly defined	Definition	
2. Recurrence based on degrees of contracture	Contracture only	2000	Ketchum et al.	No	A reactivation of disease in the nodules 1–3 years after the last injection, necessitating one or more injections.
		1995	Foucher et al.	Yes	Disease reappearing in a site which had been operated on, in contrast to an extension of the disease process when it appeared at a distance from the previous operative site.
		1992	Foucher et al.	Yes	
		1994	Cools et al.	Yes	New DD within the operated field. The appearance of Dupuytren's disease in an area already cleared by operation.
		1992	Adam et al.	Yes	
		1991	Moermans	Yes	The reappearance of Dupuytren's tissue in an area already cleared by operation, recurrent nodules without any sign of contraction have been interpreted as true recurrences.
		1991	Ebelin et al.	No	Recurrences under the graft.
		1989	Rombouts et al.	Yes	The appearance of new lesions (bands or nodules) determined by appearance and palpation in an already operated area.
		1987	Merlo et al.	Yes	The appearance of new fascial nodules or bands, determined by appearance and palpation where fasciectomy had been previously performed.
		1987	Ketchum et al.	No	Recurrence of Dupuytren's disease to the grafted area of the palm.
		1986	Schneider et al.	No	Definite recurrence in the operative field.
		1986	Leclercq et al.	Yes	Return of clinical disease, including isolated nodules, in the operative field.
		1985	Logan et al.	No	Return of disease beneath the graft.
		2010	Watt et al.	Yes	Any increase in the degree of contracture of the injected joint compared with maximal extension achieved after injection.
		2010	Gilpin et al.	Yes	An increase in joint contracture to 20° or greater in the presence of a palpable cord at any time during the study in joints that attained a reduction in contracture to 0°–5° of normal.
2009	Hurst et al.	Yes	An increase in joint contracture to 20 degrees or more in the presence of a palpable cord at any time during the study, was evaluated in primary joints that reached the primary end point (a reduction in primary-joint contracture to 0–5 degrees of full extension).		

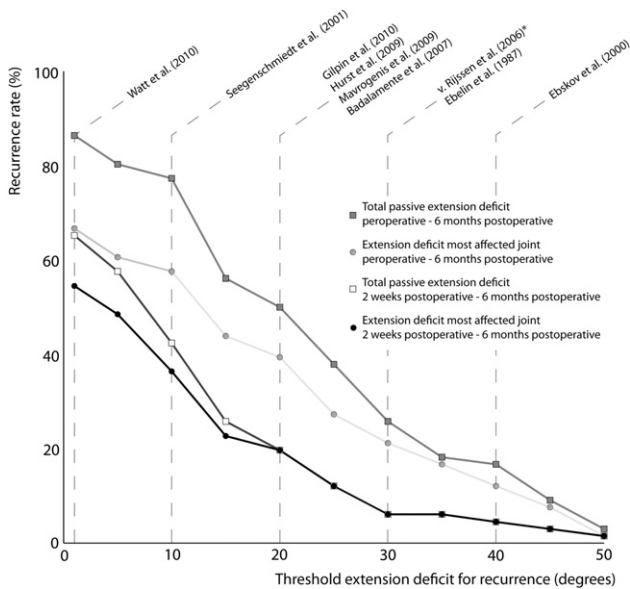
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Table 1 (continued)

Definition category	Year	Author	Explicitly defined	Definition	
Contracture or nodules	2009	Walton et al.	Yes	Residual contracture present at six months post-operation.	
	2009	Mavrogenis et al.	No	Recurrent proximal interphalangeal joint contracture of $>20^\circ$ .	
	2007	Badalamente et al.	Yes	Return of contracture ( $20^\circ$ ) in successfully treated joints (reduction in deformity to within $0^\circ$ (normal) to $5^\circ$ (flexion) of normal ( $0^\circ$ )).	
	2006	van Rijssen et al.	Yes	A Total Passive Extension Deficit increase during follow-up of $30^\circ$ or more compared to the immediate postoperative measurements.	
	2000	Ebskov et al.	No	Changes in extension: Same = change of $10^\circ$ or less during the stated period; increase of $10^\circ$ – $40^\circ$ in the contracture; increase of more than $40^\circ$ in the contracture.	
	1998	Foucher et al.	No	Increased contracture ( $29^\circ$ mean in the presented recurrent cases).	
	1985	Gonzales	No	Recurring contracture in fully released joints.	
	2009	Villani et al.	Yes	The presence of nodules, plaques, cords or extension deficit in the operative field.	
	2001	Seegenschmiedt et al.	No	New nodules, new cords, or increased flexion deformity of palm or any finger in the range of $10$ – $50^\circ$ .	
	1991	Zemel	Yes	Nodules and contractures reappearing in the area of the previous operation.	
	1987	Ebelin et al.	Yes/No	Dupuytren's disease under the graft/Extension deficit above 30 degrees.	
	1986	Mayer et al.	Yes	Return of skin contractions, nodules or flexion contracture.	
	3. Recurrence stated otherwise	Self-reported by patients	2009	Degreef et al.	Yes
2003			Wilbrand et al.	Yes	The patient's response to "the fingers operated on are beginning to bend again" in one of the questions, or reports of medical examinations in the patient records.
Repeated operation		2006	Dias et al.	Yes	The reappearance of a contracture sufficient to require surgery, according to Hueston's table-top test (Hueston, 1982). This correlates with any deformity greater than a mild metacarpophalangeal joint contracture in the images of our questionnaire.
		1999	Wilbrand et al.	No	Patients had more than two operations, indicating a definite recurrence or extension of disease.
		1996 1992	Shaw et al. Foucher et al.	No No	Recurrence requiring repeat surgery. Recurrence severe enough to necessitate another operation.



**Figure 2** Distribution of definition categories and recurrence rates within treatment options Graphical representation of all recurrence rates in literature, sorted by their corresponding treatment category. The numbers (1–3) represent the definition categories described in Table 1. The location of placement of the numbers indicates the percentage of the recurrence rate reported in the individual article. The grey lines indicate the range of recurrence rates reported for that specific treatment category. Since not all articles reporting a recurrence rate also report a definition of recurrence, the grey lines sometimes exceed the location of the numbers.



**Figure 3** Recurrence rates based on our trial data set Relation between the acquired extension deficit and the recurrence rate in the single data set. The extension deficit was based on the most affected joint per hand ( $n = 66$ ). The lower dark line represents the difference in joint angle between 2 weeks postoperative and 6 months postoperatively. For example, when one degree extension deficit is applied as a threshold for recurrence, we found that 55% of our patients had a change in angle that exceeded this threshold and that would therefore have a recurrence. With a 30 degrees threshold, however, only 6% of our cohort has a recurrence. The upper light-grey line indicates the same threshold in angle, however using peroperative data as the initial baseline data instead of data 2 weeks postoperative. Furthermore the TPED was used instead of the most affected joint. The vertical lines are the specific angular thresholds used in different articles; they indicate how these different thresholds lead to incomparable recurrence rates when applied to the same data. \* Used TPED for the definition.

a similar pattern compared to using the most affected joint only (Figure 3).

Since the Du Ro trial was not designed for this study purpose, patient-reported recurrence was not measured. Furthermore, this is an ongoing study and recurrent surgeries were not performed within 6 months of the initial operation. Therefore, the third definition category could not be evaluated using the Du Ro data set.

### Discussion

Reporting recurrence rates is an essential part of evaluating the effectiveness of treatment for DD.<sup>13</sup> In this literature study, we found a wide range of different definitions for recurrence after treatment of DD. This resulted in recurrence rates within one data set ranging from 2% to 86% when using different types of definitions. This study shows that the wide range of reported recurrence rates may largely be contributed by inconsistency in recurrence definitions. As a result, it is presently difficult or even impossible to compare recurrence rates between different treatments reported in the literature.

In this study, we found that 51% of the publications reporting recurrence rates did not present a definition of recurrence, while the remaining articles could be grouped into three main categories. In general, these categories are based on 1) the return of nodules and cords, 2) the return of joint contractures, or 3) the patient's self-report of a recurrence or whether a recurrent surgery was performed. When visualising all reported recurrence rates, we still found wide ranges even for the same treatment and definition categories (Figure 2). We found that recurrence rates at 6 months' follow-up can range from 2% to 86% in the same data set, based on applying different angular thresholds, different baseline measurement and different selected joints.

Most studies base definitions of recurrence on the reappearance of nodules or cords in the operated hand (category 1). While this may be suitable to define recurrences when performing a fasciectomy, it is less suitable



when performing a needle aponeurotomy or injecting collagenase since these techniques leave nodules and cords in place.<sup>16</sup> This may explain why most of the recent trials on needle aponeurotomy and on collagenase injection use contracture-based definitions (category 2).<sup>1,2</sup> In addition, it can be argued that the return of nodules alone should not be the main aspect of a recurrence definition, since the indication for operation generally is not based on nodules or cords alone, but on the severity of the joint contracture.<sup>17</sup>

Within category 2, angular threshold for defining recurrence varied from 1°<sup>10</sup> to 50°.<sup>18</sup> Our analysis shows that this threshold should be chosen carefully because of its great influence on the recurrence rate. Furthermore, while some authors describe recurrence as relapse of contracture of the treated finger in degrees relative to 'normal', they did not define 'normal'.<sup>7,19</sup> Since the maximum degree of extension is different in each person, this 'normal' should be carefully defined. Other authors compared the relapse of contracture at follow-up with the peroperative measurement or with the first measurement after surgery.<sup>1,10</sup> Within our data set, this difference alters the recurrence rate up to 20% (Figure 3). In contrast, our data showed little difference between using data of the most affected joint and using the TPED. A reason for this may be that the change in TPED is largely based on the change in the most affected joint (Figure 3).

The third category of definitions was based on the patient's self-report of a recurrence or whether a recurrent surgery was performed. While the patients' perception is an important indicator for operation and important to measure after intervention, it may be influenced by many factors, such as the patient's overall satisfaction with the treatment process and the patient's profession. Therefore, we suggest that the patient's perspective may be more suited as an addition to more objective definitions of recurrence. While the performance of recurrent surgery is also an important variable, the operation indication may be influenced by many patient-related factors as well as the surgeons' indication criteria.

Our study has a number of limitations. First, we excluded all articles to use for this review that were written in a language other than English, French, German or Dutch. We also excluded publications before 1985. However, overall, we believe that this will not have affected the main message of this study that definitions for recurrence are inconsistently used, leading to widely varying recurrence rates. Another limitation was that the data set used for the analysis was not constructed specifically for this study. Therefore, the definitions based on nodules and cords and those based on patients' perception or operation indication could not be applied to our data. Despite this, we feel that we were able to demonstrate the importance of a clear definition of recurrence and the effect of applying different angular thresholds for recurrence.

From the present study, it is clear that an international consensus on the definition of recurrence is needed to allow comparison of recurrence rates of treatments. The present review highlights a number of important points to consider for such an international consensus. First, since a number of recent treatments do not remove cords or nodules, we suggest using a contracture-based definition in degrees. In

such a definition, it is important to establish a consensus on which joints are evaluated. From this study, we suggest to evaluate the most contracted joint (MP or PIP) of the most contracted finger only. Including multiple joints or digits from a similar patient has well-described statistical problems.<sup>20</sup> When using a contracture-based definition, postoperative long-term measurements should be related to early postoperative measurements (for instance after 2 weeks) since not all joints are completely corrected. In addition, peroperative measurements lead to higher recurrence rates than postoperative measurement at 2 weeks. The angular threshold for recurrence is more or less arbitrary. However, it is important to have a threshold that is larger than the inherent measurement errors of goniometry of approximately 5–10°.<sup>21</sup> As the angular threshold, the duration for the follow-up measurement may be more or less arbitrary but should be standardised. From a clinical point of view, a longer follow-up measurement may express more precisely the amount or recurrent surgeries that are needed. However, from a research perspective, a 1-year follow-up measurement may already show differences between techniques. In addition, it should be noted that dichotomising recurrence as a "yes" or "no" per patient reduces the amount of information compared to reporting exact angular changes in degrees per patient. A more sensitive measure could therefore be to compare the change in joint contracture between groups over time, leading to a higher statistical power.

## Conflict of interest/Funding

None.

## Appendix 1

Literature database	Search query
Pubmed	(Dupuytren*[tw]) AND (reappear*[tw] OR recurr*[tw] OR return*[tw] OR predict*[tw] OR prognos*[tw] OR residu*[tw] OR remain*[tw] OR outcome*[tw]) AND (English[lang] OR dutch[lang] OR german[lang] OR french[lang])
Embase	(Dupuytren*): de, ab, ti AND (reappear* OR recurr* OR return* OR predict* OR prognos* OR residu* OR remain* OR outcome*): de, ab, ti AND ([English]/lim OR [dutch]/lim OR [german]/lim OR [French]/lim)

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