



Original Article

Defining adverse events in manual therapies: A modified Delphi consensus study

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ABSTRACT

A pragmatic agreed definition of adverse events in manual therapy is required to explore incidence and prevalence. We aimed to identify and describe such adverse events and seek a consensus definition.

A focus group identified issues surrounding the definition of adverse events and generated the content for a questionnaire. This questionnaire was used to conduct a modified Delphi consensus survey with an expert panel ($n = 50$). Consensus was defined as $>74\%$ agreement. Three consensus rounds were executed.

There was a 50% response rate for round one, 62% for round two and 55% for round three. A layered pragmatic definition was agreed:

- **'Major' adverse events** are medium to long term, moderate to severe and unacceptable, they normally require further treatment and are serious and distressing;
- **'Moderate' adverse events** are as 'major' adverse events but only moderate in severity; and
- **'Mild' and 'not adverse' adverse events** are short term and mild, non-serious, the patient's function remains intact, and they are transient/reversible; no treatment alterations are required because the consequences are short term and contained.

We concluded that classifying adverse events was difficult without context or detail. Classification may be improved by using the taxonomy and descriptions suggested in this study.

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1. Introduction

The incidence of adverse events from manual therapy is of considerable interest to manual therapists and to the general public. Good quality data are sparse, with scientific debate about incidence of adverse events foundering on differences in opinion as to what constitutes a therapy-related adverse event rather than the incidence itself. Defining therapy-related adverse events in manual therapy is difficult as they occur in many guises, contexts and settings. They can range in severity and impact; also, patient and practitioner views and expectations about what constitutes an important adverse event may differ. The literature about manual therapy-related adverse events is dominated by studies concerning manipulation (Stevenson and Ernst, 2002; Kerry et al., 2008); specifically, high velocity thrust techniques used on the cervical

spine and consequential cervical artery dissections – vertebral and internal carotid arteries, vertebrobasilar accidents and strokes (Haneline et al., 2003, 2005; Kawchuk et al., 2008; Dittrich et al., 2007). There is, however, a large spectrum of adverse events that can occur with varying degrees of severity and duration, from transient muscle aches to bruising to fracture.

The World Health Organisation Adverse Reaction Team (WHO-ART) and the pharmaceutical industry have each been considering the definition of adverse events for decades and have clearer definitions than many other organisations (Leape and Abbokire, 2003). In addition, adverse events, reactions, harm, safety and side effects are defined and used in the revised and extended 2003 CONSORT statement (Ioannidis et al., 2004) for reporting clinical trial data. Whilst these definitions and guidelines are useful to the manual therapy professions, they are not entirely applicable as it is often difficult to assign causality, or to measure the 'dose' of a manual therapy.

Malone et al. (2002) defined an adverse 'effect' as any detrimental result of a treatment; a 'reaction' as a slight or clinically insignificant short lived symptom and an 'incident' as an

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unexpected event resulting in serious impairment, injury or fatality or an irreversible complication. Thiel et al. (2007) used a pharmaceutical definition (Edwards and Aronson, 2000) and applied it pragmatically to a prospective cohort study about adverse events in chiropractic. Serious adverse events were defined as: 'referred to hospital accident and emergency and/or severe onset or worsening of symptoms immediately after treatment and/or resulted in persistent or significant disability/incapacity'. Other graded definitions have been used such as: 'certain neurological deficits'; 'severe neurological deficits'; and 'serious complications' (Dvorak and Orelli, 1985). The problem with these definitions is that they do not cover the range of adverse events that may exist in manual therapies.

Manual therapy professions such as chiropractic, osteopathy and physiotherapy are obliged under their codes of conduct to seek consent before administering treatment. Gaining *informed* consent, however, is difficult as we know little about risks involved with different treatments. As a first step towards quantifying risk, and

health researchers with a research interest in this field; secondary care clinicians; pharmacists, general practitioners and researchers internationally. These were drawn from those who had published in this field, our own peer networks and practitioners attending the UK General Osteopathic Council 2008 conference. We then asked that any other interested parties (colleagues of those approached) be included, by free circulation of the questionnaire. We contacted all the identified experts in our panel via email and all subsequent participation in the study took place via email.

2.4. Questionnaires

The first consensus questionnaire sought opinion about constructs used to define 'major', 'moderate' and 'minor' adverse events. We made each construct into a bipolar statement and used a six point numerical rating scale to rank importance of each statement for 'minor', 'moderate' and 'major' adverse events. Example:

Distressing 1.....2.....3.....4.....5.....6 Not distressing

providing patients with realistic estimates of the incidence of important therapy-related adverse effects, there is a need for a pragmatic definition of adverse events applicable to manual therapy. The aim of this study was, therefore, to seek an expert consensus definition of adverse events in relation to manual therapy by exploring understanding and meaning using a modified Delphi technique (Dalkey and Helmer, 1963).

2. Method

2.1. Modified Delphi consensus study

A Delphi consensus study is a questionnaire survey of expert opinion conducted in 'rounds'; responses to each round of questionnaires are fed anonymously back to participants until an agreement or consensus is evolved or established. We selected this approach both to avoid key individuals' views dominating any open discussion and to ensure we could achieve international representation on our panel. In all three rounds of this Delphi study, consensus was defined as >74% agreement. We reviewed a number of published Delphi studies to determine an acceptable level of consensus; consensus levels ranged from two thirds majority (Behrens et al., 2006) to 83% agreement (Armon et al., 2001). We, therefore, deemed 75% agreement as a reasonable consensus level.

2.2. Developing the questionnaire

A focus group comprising a chiropractor, an osteopath, a GP, and a physiotherapist, all with specific and extensive interest and/or experience in the area of adverse events was convened. This group generated a taxonomy of adverse events and the initial content for the first round Delphi questionnaire. In addition, the results of the focus group were forwarded to a pharmaceutical industry specialist and an anaesthetist working in both primary and secondary care for their comments before the questionnaire was finalised.

2.3. Participants for Delphi study

To obtain a sample of experts we contacted: practitioners representing each statutory regulated manual therapy profession;

Participants were asked, systematically, to indicate on the numerical rating scale where a 'major', 'moderate' or 'minor' adverse event would lie using this continuum. We also sought comment on the hierarchical taxonomy decided by the focus group i.e. 'major', 'moderate' and 'minor'.

For the second round of the Delphi study we presented the results back to the group (the numerical rating scale rankings) and asked members to further define those areas where there had been insufficient consensus in round one. We also asked the group to classify a list of 36 potential adverse events (signs or symptoms) into 'major', 'moderate', 'minor' and 'not adverse'. This list was developed by reviewing the adverse event literature and extracting adverse events recorded in articles. We used the constructs that had achieved consensus in the previous round, to provide a description/definition for 'major', 'moderate' and 'minor' adverse events.

The questionnaire used in round three was designed to seek further consensus and opinion about adverse events; it depended on the outcomes from rounds one and two. Additionally, each of the questionnaires provided participants the opportunity for free text feedback about issues surrounding adverse events and the questionnaire.

2.5. Analysis

We used percentage agreement to determine the level of consensus in each round. Any responses to the free questions were coded into themes and summarised.

3. Results

3.1. Focus group

The focus group discussed the issues surrounding adverse events in manual therapy and highlighted the need for a hierarchy that could: a) classify adverse events in order of importance and b) take into account 'non-adverse' adverse events. The group decided on a hierarchical taxonomy using the terms 'minor', 'moderate', 'major' and 'not adverse'. The definitions of these terms were to be decided by the Delphi process. The focus group

Table 1

Round one: % agreement for each scale, 'major', 'moderate' and 'minor' adverse events.

	Responses to 6 point numerical rating scale for:									Construct (5 or 6)
	Major adverse events			Moderate adverse events			Minor adverse events			
Construct (1 or 2)	1–2	3–4	5–6	1–2	3–4	5–6	1–2	3–4	5–6	
Mild	0	0	76	5	91	24	95	9	0	Severe
Acceptable	0	0	73	9	62	23	91	38	4	Unacceptable
Expected	0	5	43	5	50	48	95	45	9	Unexpected
Requires no further intervention	0	0	70	14	62	30	86	38	0	Requires further intervention
Non-serious	0	15	95	5	65	5	95	20	0	Serious
Function remains intact	0	19	85	32	66	15	68	14	0	Function impaired
Transient/reversible	5	41	100	36	55	0	59	5	0	Permanent
Not distressing	0	0	68	5	57	32	95	43	0	Distressing
Short term	5	25	95	36	70	5	59	5	0	Long term
No treatment alterations required	5	24	81	32	48	14	64	29	5	Treatment alterations required
Short term consequences	5	38	100	36	62	0	59	0	0	Long term consequences
Contained	10	37	90	55	63	10	35	0	0	Uncontained
Occurs after consultation	11	22	52	74	78	48	16	0	0	Occurs during consultation

Numbers in **Bold** = consensus >74%.

generated constructs that they believed to be important descriptors providing meaning for adverse events. These constructs were made into bipolar statements; the focus group proposed that the Delphi participants rank their beliefs about the importance, or not, of each level of adverse event according to each statement. The bipolar statements are shown in the first (least) and last columns (most) of [Table 1](#).

3.2. Participants

The professions of the people chosen to be in our expert panel are shown in [Table 2](#); response rates are given by profession as the percent of those participating at each stage of the consensus process. There were no responses from secondary care physicians (an orthopaedic surgeon, a vascular surgeon, a rheumatologist and an anaesthetist had been invited to participate) despite numerous follow-up emails.

3.3. Round one

We contacted 50 experts and practitioners: 25 (50%) of these responded. More than 74% of responders in round one agreed that the following were descriptors of 'minor' adverse events (ranked 1 or 2): mild, non-serious, function remains intact, transient/reversible, short term, no treatment alterations required, short term consequences and contained. More than 74% agreed that constructs/descriptors for 'major' adverse events (ranked 5 or 6) were: severe, unacceptable, requiring further treatment, serious and distressing. Overall there was little consensus achieved for descriptors of 'moderate' adverse events. 'Moderate' adverse events, ranked as 3 or 4, that achieved consensus, were described as

being between mild and serious and could occur either during or after treatment ([Table 1](#)).

3.4. Round two

In round two we asked the Delphi panel to classify a list of 36 potential adverse events (signs and symptoms) as either 'major', 'moderate', 'minor' or 'not adverse' adverse events. The consensus-agreed constructs from round one were used as definitions for 'major' and 'minor' adverse events to guide responders about their choice ([Table 3](#)).

The panel agreed (i.e. >74% of them) that 'major' adverse events were: coma, dislocation, fracture and loss of bladder and bowel control. For the rest of the signs and symptoms there was poor consensus (i.e. <75%) agreement about whether the sign or symptom was either 'major', 'moderate', 'minor' or 'not adverse'.

When we reviewed the data, the responses for 'major' and 'moderate' classifications were closely allied in distribution, as were 'minor' and 'not adverse' adverse events. For this reason we collapsed the classification of specific adverse events into 'major/moderate' and 'minor/not adverse' ([Table 3](#)).

The free response feedback question in round two indicated that the experts found the task of classifying specific potential adverse events very difficult without having any context or history about the event itself. The details requested/required by the experts concerned severity and duration.

3.5. Round three

In round three we explored severity and duration as these were seen as important when classifying signs and symptoms as adverse

Table 2

Delphi survey rounds: response rates by profession.

Expert panel (n = 50) ^a	Round one (n/50)	Round two (n/50)	Round three (n/31)
Chiropractors (n = 3, 6%)	2 (4%)	3 (6%)	2 (6%)
General practitioners (n = 7, 14%)	4 (8%)	6 (12%)	3 (10%)
Osteopaths (n = 12, 24%)	9 (18%)	11 (22%)	8 (26%)
Pharmacists (n = 4, 8%)	1 (2%)	1 (2%)	1 (3%)
Physiotherapists (n = 7, 14%)	2 (4%)	2 (4%)	0 (0%)
Psychologists (n = 5, 10%)	1 (2%)	2 (4%)	1 (3%)
Researchers (n = 8, 16%)	6 (12%)	6 (12%)	2 (6%)
Secondary care consultants (n = 4, 8%)	0 (0%)	0 (0%)	0 (0%)
Totals (50)	25 (50%)	31 (62%)	17 (55%)
International representation	5 (10%)	5 (10%)	4 (13%)

^a Some people had dual roles, overseas representation = 7 (14%).

Table 3

Round two: classification of signs and symptoms.

Consensus 75–100% ^a	
'Major or moderate' adverse events	'Minor or not adverse' adverse events
Black out	Headache
Breathing difficulties	Muscle tenderness
Coma	Short term stiffness
Dislocation	Short term soreness
Fracture	Short term increase in pain
Loss or reduced bladder/bowel control	
Medium/long term loss of movement	
Medium/long term increased pain	
Stroke	
Transient ischaemic attack	
Visual disturbance	

^a Signs and symptoms not achieving consensus: reduced range of movement, short term loss of movement, pins and needles, numbness, fainting, psychological distress, anxiety, panic attack, dizziness, muscle ache, increased pain on movement, palpitations, skin rash, depression, migraine, altered sensation, joint pain, radiating pain.

events. We asked our panel to choose where each type of adverse event would lie in a matrix using severity and duration; their responses are shown in Table 4.

3.6. Definition of an adverse event

Our original intention of obtaining a short, succinct definition of an adverse event was not achieved. Instead, we have a layered pragmatic definition which is summarised in tabular form (Table 5). It shows:

- 'Major' adverse events are seen as medium to long term, moderate to severe and unacceptable; they normally require further treatment and are serious and distressing.
- 'Moderate' adverse events are described as the same as 'major' adverse events but only moderate in severity.
- 'Mild' and 'not adverse' adverse events are short term and mild, they are non-serious, the patient's function remains intact, they are transient/reversible and no treatment alterations are required because the consequences are short term and contained.

4. Discussion

We believe that this Delphi study is the first of its type to address the issue of defining an adverse event in the context of manual therapy in a systematic, non individual and interdisciplinary way. We developed a layered approach for defining adverse events. The first layer identifies duration and severity and the second layer provides context and description about the nature of the adverse event; this enables us to classify any adverse event into a hierarchy of minor, moderate, or major.

This layered, pragmatic definition does not incorporate any underlying assumptions about causality, and therefore this is not an aspect of our definition. Whilst we recognise that causality is a huge

Table 4

Round three: severity and duration of 'minor', 'moderate', 'major' and 'not adverse' adverse events.

>74% consensus	Mild severity	Moderate severity	Major severity
Short term duration (hours)	Minor not adverse		
Medium term (days)		Moderate	Major
Long term (weeks)	Moderate	Major	Major

Table 5

Summary table of results: final definition of adverse events in manual therapy.

Adverse Event	Duration	Severity	Descriptor
Major	Medium/long term	Moderate/severe	Unacceptable
Moderate	Medium/long term	Moderate	Requires further treatment
			Serious
			Distressing
Minor	Short term	Mild	Non-serious
Not adverse	Short term	Mild	Function remains intact,
			Transient/reversible
			No treatment alterations required
			Short term consequences
			Contained

area of concern it would detract from the usefulness of the definition in manual therapy as causality is often very hard to prove: by incorporating an element of causality into the definition it is unlikely to encourage practitioners to study, recognise and record adverse events. At present, the manual therapy professions are still trying to understand, quantify and identify risk associated with treatment and practitioners (Kerry et al., 2008); a definition independent of causality may be more relevant for this purpose. No doubt as the manual therapy professions progress with research on this topic it will be possible to make a clear distinction between an adverse event (as discussed here) and an adverse treatment effect (any unfavourable or unintended response to treatment) as has been achieved in other fields of healthcare research (BSI British Standards, 2003).

This study has shown that using the term 'adverse event' tells us very little about the event that has occurred. Accounts of randomised controlled trials often state 'no adverse events were reported' or 'n' number of adverse events were recorded' (Gross et al., 2002) but this information is relatively meaningless unless the term 'adverse event' is elaborated upon. Our results show we can distinguish between 'minor' and 'major' adverse events. If outcome data for both trials and cohort studies included details about adverse events such as severity, duration and nature, we could start to understand and measure the prevalence and incidence of the different types of adverse events and whether they are 'major', 'moderate' or 'minor'. Applying our definitions to such data may provide some useful distinctions as the repercussions that may occur for 'minor' as opposed to 'major' adverse events are different.

Most manual therapy trials and cohort studies report worsening or improvement of pain, function or mobility as outcome measures. Clinical changes can reflect improvement and/or efficacy, or worsening and/or harm. Worsening or deterioration after treatment may or may not necessarily constitute an adverse event; without detail about duration and severity we cannot say if a negative or worsening reaction is a normal 'within treatment' variation or indeed an adverse event. Using our definition of adverse events and providing more information about 'quality' and 'nature' of any worsening of symptoms could enable researchers to achieve better classification and understanding of changes occurring in patients and the impact of any interventions being tested. Defining and recording adverse events in trials and cohort studies would enable researchers to study the incidence and prevalence of adverse events that occur in controlled study environments, as proposed by the CONSORT guidelines for reporting trial data (Ioannidis et al., 2004).

There are a number of limitations to this study and indeed to the Delphi approach (Jones and Hunter, 2000). Participants in Delphi studies are selected because they are experts in the field being researched but they may not necessarily be representative of the

population to which findings are being targeted. Our expert panel included a range of professional disciplines, with both practising and non-practising clinicians, so we hoped to reduce this potential conflict. Our results did not show any major differences in classification between professions. We had more osteopaths complete the surveys than any other professional discipline and this may have affected our findings. We had no responses from the secondary care consultants approached, which might affect the generalisability of our conclusions. Whilst this group comprises those who are likely to treat people who have sustained major adverse events, there is no *a priori* reason to expect their definition of severity to differ from other clinicians. Since nearly all manual therapy is delivered in primary care it is the primary care perspective of the severity of adverse events that is important when seeking informed consent. We have not, in this study, been able to include a patient/public view on defining adverse events.

Our proposed definitions and taxonomy will require further discussion and research. Our definitions should be tested for reliability (inter, intra and test/re-test reliability) and validity to ensure appropriate application of the definition and taxonomy in both research and clinical environments. Our approach to classifying adverse events necessitates the requirement for added detail when signs and symptoms are reported, in either research studies or case notes. Additional detail will enable users to apply the taxonomy and definition appropriately. The practical application of our taxonomy, however, and definitions will inevitably expose anomalies, for example, the occurrence of multiple different minor adverse events in one person. The combined effect of a number of minor adverse events may indeed render them moderate or major. We see this taxonomy as a useful standard in research but it may also assist clinicians to record in case notes, logically and systematically, adverse responses to treatment.

5. Conclusions

The definitions obtained following this Delphi study can be used to categorise or classify adverse events in the context of manual therapy. Not only is a logical hierarchy presented, but also this definition allows for classifying those events that occur that may be regarded as 'not adverse'. The application of this definition may be useful in both research and clinical settings for recording and documenting the nature and type, prevalence and incidence of adverse events to increase understanding and contribute to knowledge in this area.

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