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Homeopathic clinical case reports: Development of a supplement (HOM-CASE) to the CARE clinical case reporting guideline

R.A. van Haselen

International Institute for Integrated Medicine, 22 Eden Street, Suite 467, Kingston KT1 1DN, United Kingdom

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ABSTRACT

Objective: Develop a criteria catalog serving as a guideline for authors to improve the quality of reporting clinical case reports in homeopathy.

Method: An online Delphi process was initiated with a panel of 19 homeopathic experts from Europe, the USA and India. Homeopathy specific item selection took place in three rounds of adjusting. The selected items can be used as an extension of the CARE clinical case reporting guideline.

Results: Eight homeopathy specific 'core' items were selected from a list of 31 suggested items; (1) the clinical history from a homeopathic perspective; (2) the type of homeopathy; detailed description of the medication—(3) nomenclature, (4) manufacture, (5) galenic form + dosage; outcomes—(6) objective evidence if available, (7) occurrence homeopathic aggravation, (8) assessment possible causal attribution of changes to the homeopathic treatment.

A further 4 items were recommended for consideration as optional items when case reports are used for specific, in particular educational, purposes.

The 8 core items can be used, merged into 6 items, as a homeopathy specific (HOM-CASE) extension to the CARE clinical case reporting guideline items 6, 9 and 10.

Conclusion: Use of the HOM-CASE guideline extension will contribute to transparent and accurate reporting and can significantly improve the quality and reliability of clinical case reports in homeopathy.

1. Introduction

There is a need to promote transparent and accurate reporting of clinical case reports in CAM, including homeopathy. Despite clinical case reports being as old as medicine itself, the first official clinical case reporting guideline was only published in 2013 under the name 'CARE' guideline.[1]

In an earlier article[2] the author explained and developed a conceptual framework for improving the quality of clinical case reports in CAM. Homeopathy was chosen as a practical illustration for implementation of the proposed approach because case taking in homeopathy tends to be quite detailed. The homeopathic knowledge base is supported by data from healthy subjects obtained in so-called homeopathic pathogenetic trials (also called 'provings') that need to be further verified and validated in clinical practice.[3] Clinical cases and case series are important components of the latter process. A solid foundation in the form of high quality case reports is therefore an essential cornerstone of the further validation of homeopathic knowledge.[4] Due to the relatively high level of complexity and individualization of homeopathic case-taking, lessons learnt are likely to be easily transferable to a wide range of CAM modalities. We therefore set out to develop an agreed checklist with criteria important for improving the quality of clinical case reports in homeopathy.

2. Methods

From the existing methods for achieving maximum consensus, we chose a Delphi approach. A Delphi process is a method for structuring a group communication process, which allows a group of individuals to deal with a complex problem.[9] The modified Delphi technique generally diverges from the classical Delphi method in the use of alternative means to derive the content of the initial quantitative questionnaire round while still allowing the collection of rich data based on multiple questionnaire iterations.[5] Modified Delphi studies are particularly appropriate where relevant knowledge exists. Given the very wide geographical spread of the experts, we decided to conduct an online modified Delphi process.

Before starting the Delphi process, an initial selection of potentially relevant clinical case reporting items was identified as follows: searching of the homeopathic literature; consultation of

E-mail address: vanhaselen@intmedi.com

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colleagues during conferences and meetings; a survey of the attendants of a lecture the author gave on clinical case reporting at a conference.

Homeopathic experts were selected to ensure that an appropriate mix of the following competencies was obtained:

- Experienced homeopathic clinicians, including classical homeopathy practitioners.
- Homeopaths with research and/or methodological expertise.
- Homeopaths involved in clinical case related projects.

The modified Delphi process involved three online rounds. SurveyMonkey® was used as software for conducting the surveys.

In round 1, each expert was asked separately to comment on the importance of the homeopathy specific clinical case reporting items and asked to suggest any other items they considered important. As background information they were informed about the CARE (general) set of case reporting items, and told to focus only on homeopathy specific case reporting items. The importance of the items was rated on an 11-point scale ranging from zero ('irrelevant') to ten ('extremely important').

In round 2, each respondent received an 'individualized' document that contained their individual importance rating of an item, as well as the group average rating of that item, plus all the comments made. Participants were asked individually if they would like to change their assessment in the light of the information they had received, and if so, to provide an explanation for this. This enabled the experts to (re)consider their own answers, also based on considering the answers given by the other experts. At the end of the questionnaire, respondents were asked to rate the importance (on a scale from zero to ten) of the additional items suggested by the respondents during round 1.

In round 3, the principal results were presented to the respondents, as well as how the included items would supplement the CARE clinical case reporting guidelines. The respondents were also asked some questions about any item that was close to the 'borderline' of the predefined cut-off point, At the end of the third round, participants were asked if there was any remaining concept that they felt should be retained from the deleted items.

An average 'importance' score of greater than 8 was used as criterion for the selection of the 'core' homeopathy specific items, referred to by the acronym 'HOM-CASE'. Items with a score greater than 8 that were already covered by one of the items in the CARE guideline were excluded from the list of homeopathy specific (HOM-CASE) items.

Some items with an average score less that 8 were recommend as items that could still be considered for optional inclusion, if it was felt that these items were important in the context of specific objectives.

3. Results

A preliminary collection of 20 potentially relevant case reporting items was identified. Five of these items were taken from the 'RedHot' supplement to the CONSORT guideline for the reporting of clinical trials of homeopathy.[6] In the first round, the respondents suggested an additional 11 items.

28 homeopathic experts with clinical and/or research experience were identified, of these 19 responded to the online survey and provided usable data. 15 experts completed all three Delphi rounds.

An overview of the included and excluded items is given in Table 1.

Eight of the 31 items was selected for the 'core' list. This included all 5 RedHot guideline items. For instance the homeopathic symptoms used for the decision, as part of the clinical history. This would also include transparency regarding the homeopathic school and/or practitioner(s) system adhered to. All three clinical case reporting specific 'core' items were in the category 'Follow up and outcomes'.

The item 'occurrence of homeopathic aggravation', was rated just below the borderline for inclusion as a core item. This was mainly due to two experts rating it as of 'low' importance. This topic was therefore addressed further in the third Delphi round. The main reasons given for the low importance rating by the two experts was the perceived difficulty of defining homeopathic aggravations in a clear and consistent way. Since the definition of homeopathic aggravations is something that can be refined and improved further (see Discussion section), it was decided to include this item in the 'core' list.

Five excluded items (indicated as 'Excluded/Optional' in the table) were rated as important by some, but not consistently so by all. This was related to the item being very important in the context of the use of clinical case reports, e.g., for educational/teaching purposes, but not important and/or too specialized in the context of most other purposes. It is therefore recommended to consider the addition of any of these five items for optional inclusion on a 'purpose matched' basis.

One item (attribution of observed changes to particular remedy) was considered to be important but judged to be a part of the assessment of the possible causal attribution of changes, and therefore excluded as a separate item. Something similar applied to the item on the assessment of disease evolution in according with homeopathic principles (e.g., 'Hering's law'). Despite a low importance rating, which was mainly due to reservations associated with the term 'Hering's law', the aspect of 'disease evolution' is actually an important criterion for the possible causal attribution of changes, and this aspect has been integrated as two criteria on the 'direction of cure' in the Modified Naranjo causality criteria referred to below.

The relationship of the selected HOM-CASE items to the CARE clinical case reporting guideline items is given in Table 2.

Table 2 illustrates how and where the 8 core items can be added to the CARE checklist as 6 supplementary items the CARE items 6, 9 and 10. The reduction from 8 to 6 items was due to merging of the three 'medication' items into a single item as an extension of CARE item 9 'Therapeutic intervention'.

4. Discussion

In this study 8 'core' items were identified that are important to be included in homeopathic clinical case reports, and these items can be integrated with the CARE clinical case reporting items as 6 supplementary items. A further 5 'optional' items were identified that can be considered when case reports are written up for specific, for instance educational, purposes.

The selected criteria were identified based on consensus between a broad international panel of experts, making use of the well-established and validated Delphi method.

A possible limitation was the absence of a face-to-face meeting between the participating experts. Such a meeting could have been helpful to further deepen the understanding of the various items, including the identification of items that will need further explanation in an 'explanation and elaboration' document. Despite the absence of such a face-to-face a meeting, three items/topics clearly emerged as being in need of further explanation and elaboration.

A key issue is how to assess the likelihood that the observed changes are attributable to the homeopathic treatment(s). In a separate context, further work on this topic has been conducted by the Clinical Data Working Group (of which the author is the lead) of the Homeopathic Pharmacopoea of the United States (HPUS). This Working Group has been given a mandate to develop a guideline

Table 1
Overview of the included and excluded items following the Delphi rounds.

Item	Average score	Decision regarding item[a]	Reason/comment
TYPE OF HOMEOPATHY: individualized/formula: single- or multi-constituents/isopathy	8.5	INCLUDED	Average ≥ 8/RedHot item
MEDICATION(S): nomenclature (list individual prescriptions, or constituents (including trade names)	8.8	INCLUDED	Average ≥ 8/RedHot item
MEDICATION(S): manufacture: potency and scale	9.1	INCLUDED	Average ≥ 8/RedHot item
MEDICATION(S): dosage, dosage repetition, galenic form	8.9	INCLUDED	Average ≥ 8/RedHot item
CONSULTATION: clinical history detail (homeopathic symptoms used for decision, etc.)	9.4	INCLUDED	Average ≥ 8/RedHot item
FOLLOW UP AND OUTCOMES: possible causal attribution of changes explicitly assessed/discussed	8.6	INCLUDED	Average ≥ 8/likelihood of causal attribution of changes to homeopathic treatment(s) is clearly a key prerequisite
FOLLOW UP AND OUTCOMES: objective evidence (if applicable/available)	8.0	INCLUDED	Average ≥ 8/is in principle a 'generic' aspects, but considered to be particularly relevant with regard to further recognition of effectiveness of homeopathy. Clear definition what is meant with 'objective' is needed. Definitions proposed in reduced Modified Naranjo Criteria developed in HPUS context can be used
FOLLOW UP AND OUTCOMES: occurrence homeopathic aggravation	7.8	INCLUDED	Considered important or very important by most except for 2 respondents. Main concerns around difficulty to define aggravations. This will be clarified further as much as possible based on the latest literature
CONSULTATION: individualizing symptoms reported	6.2	EXCLUDED/OPTIONAL	Average ≤ 8/can be considered for educational/teaching purposes
HOMEOPATHIC PRESCRIPTION: provision of repertorization data	5.9	EXCLUDED/OPTIONAL	Average ≤ 8/can be important, for instance if case report used for educational/teaching purposes
FOLLOW UP AND OUTCOMES: assessment disease evolution in accordance with homeopathic principles (e.g., Hering's law)	5.9	EXCLUDED/OPTIONAL	Average ≤ 8/reference to "Hering's law" led to a number of 'negative' reactions. However, disease evolution according to homeopathic principles is important as part of assessing possible causal attribution and has been integrated in the Modified Naranjo Criteria (Appendix 1)
HOMEOPATHIC PRESCRIPTION: prescription strategy: totality of symptoms, keynotes, essence, etiological, etc.	7.6	EXCLUDED/OPTIONAL	Average ≤ 8/can be important, for instance if case report used for educational/teaching purposes
FOLLOW UP AND OUTCOMES: individual remedy related symptoms are identified and analyzed	7.2	EXCLUDED/OPTIONAL	Average ≤ 8/can be important for research purposes, addition to repertory/materia medica, etc.
FOLLOW UP AND OUTCOMES: attribution of observed changes to particular remedy, including when more than one medicine is given at the same time, or when a sequence of different remedies is given	7.8	EXCLUDED	Excluded as a separate item, but can be incorporated in the assessment of the 'possible causal attribution of changes' (core item)
FOLLOW UP AND OUTCOMES: concomitant therapies	9.1	EXCLUDED	Important, but already covered by CARE item 9a ('Types of intervention')
FOLLOW UP AND OUTCOMES: treatment adherence	8.0	EXCLUDED	Important, but already covered by CARE item 10 c ('Intervention adherence and tolerability')
FOLLOW UP AND OUTCOMES: duration follow up, including assessment is sufficient	8.5	EXCLUDED	Important, but to be covered as part of CARE item 7 ('Timeline')
FOLLOW UP AND OUTCOMES: outcome verified by appropriate conventional measures	7.2	EXCLUDED	Average ≤ 8
CONSULTATION: duration, frequency, dates of consultations	7.1	EXCLUDED	Average ≤ 8/dates of consultation should be integrated as part of CARE guideline item 7 ('Timeline')
QUALITY ASSURANCE: quality scoring system utilized	6.7	EXCLUDED	Average ≤ 8
MEDICATION(S): manufacture: dilution method (e.g., Korsakovian, Hahnemannian)	6.7	EXCLUDED	Average ≤ 8
MEDICATION(S): manufacture: manufacturer, pharmacopoeia reference	6.3	EXCLUDED	Average ≤ 8
FOLLOW UP AND OUTCOMES: Patient Reported Outcome Measure (e.g., MYMOP)	6.3	EXCLUDED	Average ≤ 8/can be important, already covered by CARE item 12 ('Patient perspective')

Table 1 (*Continued*)

Item	Average score	Decision regarding item[a]	Reason/comment
DISCUSSION: reflection on implications for practice	6.3	EXCLUDED	Average ≤ 8, already covered by CARE items 11 ('Discussion')
INTRO: explicit patient authorization	6.1	EXCLUDED	Average ≤ 8/already covered by CARE item 13 ('Did the patient give informed consent?')
CONSULTATION: setting (primary/secondary care, public/private provision, etc.)	5.7	EXCLUDED	Average ≤ 8
PRACTITIONER: qualifications, clinical practice experience in years/hours per week, etc.	5.6	EXCLUDED	Average ≤ 8
QUALITY ASSURANCE: case report reviewed by, or discussed with, colleagues	5.2	EXCLUDED	Average ≤ 8/considered important by some, but impractical in most situations
INTRODUCTION: aims stated	4.9	EXCLUDED	Average ≤ 8/but there is of course nothing wrong with explicitly stating the aims in the introduction. No specific reference is made to this in the CARE item checklist
FOLLOW UP AND OUTCOMES: confirmation by external observer	4.6	EXCLUDED	Average ≤ 8/considered important by some, but not feasible in most cases. If available, it could possibly contribute to 'objective evidence' and the assessment of causal attribution
HOMEOPATHIC PRESCRIPTION: confidence in prescription(s)	4.5	EXCLUDED	Average ≤ 8/generally considered to be subjective and unreliable

[a] INCLUDED: included as one of the core items, EXCLUDED/OPTIONAL: excluded from core items, but can be considered optionally depending on the objective of the case report, EXCLUDED: excluded.

for the assessment of submitted clinical case material as part of monograph submissions; a key eligibility criterion is that it is considered probable that the observed changes are attributable to the homeopathic treatment(s). In another project, Rutten proposed criteria[4] based on the criteria developed by Naranjo et al.[7] for causality assessment in the context of identifying possible adverse drug reactions. These 'Modified Naranjo Criteria' were reviewed and further modified by the Clinical Data Working Group and piloted in the USA and India. These Modified Naranjo Criteria as currently proposed, including the 'weights' or 'scores' given to the various items, are given in Appendix 1. It should be noted these criteria are still in the process of further validation and therefore subject to change. Despite this, the incorporation of the current criteria in assessing and making transparent the possible causal attribution of changes in homeopathic clinical case reports is already a major step forward.

The second issue is the necessity for a clear definition of a homeopathic aggravation that can be consistently applied. This definition should include a clear demarcation between a homeopathic aggravation and an adverse drug reaction. Despite good intentions, the current definition as formulated in the Dictionary of Homeopathy[8] is lacking the necessary detail and clarity: "A homeopathic or therapeutic aggravation (also sometimes referred to as 'healing crisis') is a temporary worsening of existing symptoms following the administration of a correctly chosen homeopathic prescription, which indicates a favorable response to treatment". Fortunately, significant advances have been made by Stub et al.[9,10] who are conducting a research program on this topic. Unlike the findings of a review by Grabia and Ernst[11] on the occurrence of aggravations in clinical trials of homeopathy, Stub et al. argue that homeopathic aggravations are often 'subtle' (rather than dramatic) events that require homeopathic experience to identify. They propose the identification of a homeopathic aggravation according to the following criteria: (i) increase of patients' existing symptoms (ii) and/or a feeling of well-being that emerges 1–3 days after taking the remedy (iii) and/or headache and/or fatigue may accompany these symptoms.[12] The Homeopathic Pharmacopoeia of the United States (HPUS) is also looking into this issue and currently proposing the following definition: "A temporary worsening of pre-existing symptom(s) within a plausible time frame after the administration a homeopathic medicine, followed by an improvement in the patient's condition". So whilst there is no consensus and further work is still needed, further attempts are made to better define homeopathic aggravations as part of a desirable 'healing response' and delineating this from 'undesirable' adverse drug reactions. Assessing the occurrence of homeopathic aggravations is also one of the 'Modified Naranjo Criteria' referred to above. There are likely to be further synergies/overlap with the 'Modified Naranjo Criteria'; for instance, 'improved overall wellbeing' is one of the criteria, and this could be similar to the criterion 'a feeling of well-being emerges 1–3 days after taking the remedy' used by Stub et al. for identifying homeopathic aggravations. A further exploration of this conceptual overlap is clearly indicated and could lead to further improvements in the Modified Naranjo Criteria as well as promote a more consistent assessment of homeopathic aggravations. Despite these promising advances, it should be mentioned that it has not been assessed yet how well the Stub criteria will be accepted by the homeopathic community in other countries, or from different schools. Following further discussion in the homeopathic community, it is likely that criteria for identifying homeopathic aggravations are likely to develop further. From the point of view of reporting aggravations in clinical case reports, the most important aspect is that the criteria used should be made explicit. In this way, high quality case reports will also be able to contribute to the further elaboration and clarification of this item.

The third item/topic concerns the reporting of the presence of objective outcome data, which if available, are perceived to be adding significant value to a case report. This should not be interpreted that the absence of objective data is something 'negative', merely that the availability of objective follow up and outcomes is something 'positive'. However, there is no clearly agreed definition on what is meant with 'objective'. Within the HPUS Clinical Data Working Group this topic was discussed extensively because confirmation of the health improvement by objective evidence was deemed to be a positive contributor to the assessment of causal attribution (one of the items of the Modified Naranjo Criteria). An 'inclusive' definition of 'objective evidence' was formulated as follows: "Findings that reflect expert external observation of any measurement of the patient: Objective evidence includes 'lab tests, X-ray reports, health care provider examination or observation, or other similar data'.

Table 2
The HOM-CASE guideline items (in bold type font), and their proposed position in conjunction with the CARE guideline items (plain type font).

Topic	HOM-CASE guideline extension items (circled by dotted lines)
Title	The words "case report" should be in the title along with what is of greatest interest in this case
Keywords	The key elements of this case in 2–5 keywords
Abstract	Introduction—what is unique about this case? What does it add to the medical literature? The main symptoms of the patient and the important clinical findings The main diagnoses, therapeutics interventions, and outcomes Conclusion—what are the main "take-away" lessons from this case?
Introduction	Brief background summary of this case referencing the relevant medical literature
Patient information	Demographic information (such as age, gender, ethnicity, occupation) Main symptoms of the patient (his or her chief complaints) Medical, family, and psychosocial history including co-morbidities, and relevant genetic information Relevant past interventions and their outcomes
Clinical findings	Describe the relevant physical examination (PE) findings **Clinical history detail (homeopathic symptoms used for decision, etc.)**
Timeline	Depict important milestones related to your diagnoses and interventions (table or figure)
Diagnostic assessment	Diagnostic methods (such as PE, laboratory testing, imaging, questionnaires Diagnostic challenges (such as financial, language, or cultural) Diagnostic reasoning including other diagnoses considered Prognostic characteristics (such as staging in oncology) where applicable
Therapeutic intervention	Types of intervention (such as pharmacologic, surgical, preventive, self-care) **Type of homeopathy: individualized/formula: single- or multi-constituents/isopathy** **Medication(s): nomenclature (list individual prescriptions or constituents+trade names), manufacture, potency, scale and galenic form** Administration of intervention (such as dosage, strength, duration) Changes in intervention (with rationale)
Follow-up and outcomes	Clinician- and patient-assessed outcomes Important follow-up test results Intervention adherence and tolerability (How was this assessed?) Adverse and unanticipated events **Objective evidence[a] (if applicable)** **Occurrence homeopathic aggravation[b]** **Possible causal attribution of changes explicitly assessed/discussed[c]**
Discussion	Discussion of the strengths and limitations in the management of this case Discussion of the relevant medical literature The rationale for conclusions (including assessment of possible causes) The main "take-away" lessons of this case report
Patient perspective	Did the patient share his or her perspective or experience? (include whenever possible)
Informed consent	Did the patient give informed consent? Please provide if requested

[a] Objective evidence: findings that reflect expert external observation of any measurement of the patient. Objective evidence includes lab tests, X-ray reports, health care provider examination or observation, or other similar data (proposed by the HPUS Clinical Data Working Group).
[b] Homeopathic aggravation: criteria should be specified, e.g., definition in accordance with Stub et al.[9,10]
[c] Causal attribution of changes: for assessment, consider using the 'Modified Naranjo Criteria' (Appendix 1).

The other HOM-CASE 'core' items concerned the therapeutic intervention, and the description of the clinical history, including the homeopathic symptoms used for treatment decisions. In general, these items seem to be more 'straightforward' in their application, so the principal explanation and elaboration is needed with regard to the three core items discussed above.

As a next step, the further and broader dissemination in the homeopathic community of the reporting guideline and its importance for fostering high quality clinical case reporting is essential. This should also take place via lectures, seminars and clinical case reporting workshops. Selectively targeting teachers, opinion leaders and very experienced homeopaths, could be an efficient strategy to increase the awareness and acceptation of the clinical case reporting guideline in the homeopathic community. Ultimately, learning to apply clinical case reporting guidelines should be an important dimension of the education of all homeopathic practitioners.

The development of this reporting guideline is principally focused on using clinical cases as 'observational' data, with an emphasis on 'improving', rather than 'proving', homeopathy. For the latter purpose, clinical trials, including single case experimental studies,[13] are more likely to be appropriate. The chosen research design should be always be optimally tailored to the objective.

In homeopathy, there are currently a number of initiatives linked to the topic of clinical case reports. One is the Journal of Case Studies in Homeopathy (http://www.jcshom.com/index.php/jcsh/index), which was founded in 2013. Further initiatives worth mentioning are; the 'Archive for Homeopathy' (http://www.archiveforhomeopathy.com/); 'Homeopathy Case Reports' (http://homeopathycasereports.com/); 'Empirical homeopathy via the documentation of cases' as fostered by 'WissHom', the (German) Scientific Society for Homeopathy (http://www.wisshom.de/index.php?menuid=15); the 'Making Cases Count initiative by Relton et al.[14]; and various projects by the (Dutch) Committee for Methods and Validation led by Rutten.[4]

More generally, in the CAM domain, there are a number of 'best case series programs', pioneered particularly in the area of oncology, where it is difficult or not possible to conduct RCTs on CAM modalities for ethical and/or practical reasons. There are a variety of programs in a variety of countries including Canada,[15] the USA,[16,17] Denmark,[18] Norway,[19–21] and Germany[22] that aim to collect 'best' or 'exceptional' cases. Launsø et al.[21] distinguish four different approaches to the collection of cases: three collect case histories from the treatment provider and one collects case histories mainly from patients themselves. There is however no agreement on the definition of what is a 'best' case. Adams et al.[15] criticize various 'best case' models[17,21,22] as focused too much on researcher/clinician defined objective criteria, and propose a 'hybrid model' which incorporates patient selected outcome criteria. Integration of a more 'patient centred' approach, fits well with the CARE guideline, which recommends to include reporting on whether the patient shared his or her perspective whenever possible. The CARE guideline could however emphasize this aspect more, by including this as a compulsory item in the 'Discussion' section items, rather than as an optional item as currently listed after the 'Discussion' section items. This seems particularly appropriate for homeopathic – as well as many other CAM modalities – where treatment is highly individualized and 'patient centred' as a central tenet of the therapeutic system. It is clear that all the above-mentioned approaches will benefit from having high(er) quality clinical case reports available.

A general limitation is that clinical case reports, even if perfectly managed and written up, are rarely sufficient as proof of causality. The latter may be possible exceptionally, e.g., in the case of clear-cut and intense adverse drug reactions to conventional medicines, but when adverse or therapeutic effects are less dramatic, such as is usually the case in CAM and homeopathy, clinical case material on its own is insufficient as proof of causality. Nonetheless, the methodological framework associated with clinical case research has significantly advanced further in recent years. These developments have been driven both by advances in the domains of medicine and epidemiology,[23–26] as well as via 'cross-fertilization' from the domains of the social sciences[27,28] and psychology,[29] and by developments and initiatives in the CAM field, including in particular anthroposophic[30–32] and homeopathic[4,33,34] medicine.

Clinical case report based data play an important role as a basic 'building block' of the evidence framework proposed for traditionally used CAM modalities,[35] the flow of which can be summarized as 'from bedside to bench'. This is in contrast with the evidence framework for conventional medicines, the flow of which is often referred to as 'from bench to bedside'.

The evidence framework for CAM also contrasts with the evidence framework in conventional medicine: the latter is centred around a 'hierarchy of evidence', with systematic reviews and meta-analyses at the top, and clinical case reports at the bottom. In the above-mentioned 'CAM appropriate' framework, the perspective on different types of evidence tends to be non-hierarchical and is referred to as an 'evidence mosaic',[36] an 'evidence house',[37] or a 'circular'[38] – rather than hierarchical – perspective on evidence. Rather than being at the bottom of an 'evidence hierarchy', high quality clinical case reports clearly play an important role in this 'circular' framework.

Using the above-mentioned metaphors 'building block' and 'evidence house', it is clear that high quality 'building blocks' are an essential foundation for the construction of a solid 'evidence house'. High quality case reports, are the basis for high quality 'case series' as a further aspect of such a broader framework. The description of two cases with the same exposure (e.g., treatment) and/or disease outcome (e.g., an adverse event) effectively constitutes a small 'case series', albeit most likely an incomplete one. A larger case series is likely to be more complete, and therefore more reliable. It should be noted that a large case series is distinct from a cohort study in terms of its design. These terms are not always fully understood, and used inconsistently in the medical literature.[39] The main difference is that a cohort study also assesses the 'non-exposed' individuals both with, and without, the outcome(s) of interest. This enables the calculation of the probability of the desirable, or non-desirable, outcomes in relation to an exposure (e.g., treatment) of interest. The latter is not possible in a case series.

In the course of the work on this project the author has increasingly come to realize that the ability to 'think critically' is an important additional prerequisite to fully 'harvest' the potential benefits of reporting guidelines.[40] Clinicians tend to associate the domain of critical thinking more with science and research than with clinical practice. I am of the opinion that critical thinking is as important for clinicians as for researchers and the topic of clinical case reports aptly illustrates this: if properly and 'critically applied', high quality clinical case reports can make valuable contributions to the homeopathic knowledge base. On the other hand, clinical case reports as observational (rather than experimental) data can be affected by a number of biases,[41] ranging from decision making and behavioral biases to biases in probability and belief, to social biases and memory errors. E.g., an important potential bias could be due to observed changes being wrongly, or too generously, attributed to the homeopathic treatment. If 'uncritically applied', even well reported clinical cases will only add more 'confusion' and inaccuracies to the homeopathic knowledge base. Education about, and awareness of, the different types of biases that can affect clinical case reports is therefore essential for improving decision making in both research and practice.

Use of the HOM-CASE guideline extension contributes to transparent and accurate reporting and can greatly improve the quality and reliability of clinical case reports in homeopathy. Other CAM modalities are likely to benefit as well from the addition of 'therapy specific' clinical case reporting guideline items.

Conflict of interest

The author previously worked for Heel.

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Appendix 1. : Modified Naranjo Criteria as proposed by the HPUS Clinical Data Working Group (status December 2015)

Maximum score = 13
Minimum score = −3

	Yes	No	Not Sure or N/A
1. Was there an improvement in the main symptom or condition for which the homeopathic medicine was prescribed?	+2	−1	0
2. Did the clinical improvement occur within a plausible time frame relative to the drug intake?	+1	−2	0
3. Was there an initial aggravation of symptoms? (need to define in glossary)	+1	0	0
4. Did the effect encompass more than the main symptom or condition, i.e., were other symptoms ultimately improved or changed?	+1	0	0
5. Did overall wellbeing improve? (suggest using validated scale)	+1	0	0
6 (A) *Direction of cure*: did some symptoms improve in the opposite order of the development of symptoms of the disease?	+1	0	0
6 (B) *Direction of cure*: did *at least two* of the following aspects apply to the order of improvement of symptoms: - from organs of more importance to those of less importance - from deeper to more superficial aspects of the individual - from the top downwards	+1	0	0
7. Did "old symptoms" (defined as non-seasonal and non-cyclical symptoms that were previously thought to have resolved) reappear temporarily during the course of improvement?	+1	0	0
8. Are there alternate causes (other than the medicine) that – with a high probability – could have caused the improvement? (consider known course of disease, other forms of treatment, and other clinically relevant interventions)	−3	+1	0
9. Was the health improvement confirmed by any objective evidence? (e.g., lab test, clinical observation, etc.)	+2	0	0
10. Did repeat dosing, if conducted, create similar clinical improvement?	+1	0	0

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