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ORIGINAL PAPER

Reporting experiments in homeopathic basic research (REHBaR) – A detailed guideline for authors

B Stock-Schröer[1,*], H Albrecht[1], L Betti[2], PC Endler[3], K Linde[4], R Lüdtke[1], F Musial[5], R van Wijk[6], C Witt[7] and S Baumgartner[8]

[1]*Karl and Veronica Carstens-Foundation, D-Essen, Germany*
[2]*Department of Agro-Environmental Science and Technology, Faculty of Agriculture, Bologna University, I-Bologna, Italy*
[3]*Interuniversity College for Health and Development, A-Graz, Austria*
[4]*Institute of General Practice, Technical University, D-Munich, Germany*
[5]*Department of Complementary and Integrative Medicine, University of Duisburg-Essen, D-Essen, Germany*
[6]*International Institute of Biophysics, D-Neuss, Germany*
[7]*Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, D-Berlin, Germany*
[8]*Institute of Complementary Medicine KIKOM, University of Bern, CH-Bern, Switzerland*

Background: **Reporting experiments in basic research in homeopathy is an important issue as comprehensive description of what exactly was done is required. So far, there is no guideline for authors available, unlike criteria catalogues common in clinical research.**
Methods: **A Delphi Process was conducted, including a total of five rounds, three rounds of adjusting and phrasing plus two consensus conferences. European researchers who published experimental work within the last five years were involved.**
Results: **A checklist of 23 items was obtained and supplemented with detailed examples emphasizing what each item implies. Background, objectives and possible hypotheses should be given in the part 'introduction'. Special emphasis is put on the 'materials and methods' section, where a detailed description of chosen controls, object of investigation, experimental setup, replication, parameters, intervention, allocation, blinding, and statistical methods is required. The section 'results' should present sufficient details on analysed data, descriptive as well as inferential. Authors should discuss their results and give an interpretation in the context of current evidence.**
Conclusion: **A guideline for Reporting Experiments in Homeopathic Basic Research (REHBaR) was compiled to be applied by authors when preparing their manuscripts, and to be used by scientific journals in the reviewing process. Furthermore the guideline is a commitment to a certain minimum quality level needed in basic research, e.g. blinding and randomisation. Feedback is encouraged on applicability, strength and limitations of the list to enable future revisions.** *Homeopathy* (2009) **98**, 287–298.

Keywords: Fundamental research; Delphi; Guideline; Publication; Criteria catalogue

*Correspondence: Beate Stock-Schröer, Karl and Veronica Carstens-Foundation, Am Deimelsberg 36, 45276 Essen, Germany.
E-mail: b.stock-schroeer@carstens-stiftung.de
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Introduction

Several catalogues emerged within the last years to improve the quality of reporting clinical research. The Consolidated Standards of Reporting Trials CONSORT[1] was the first well-known initiative of experts that created a criteria catalogue for necessary items to be given in reports on randomized controlled trials. The CONSORT recommendations were revised in 2001[2] and 2005[3] and extension documents were published for improving the quality of abstracts,[4] pragmatic trials[5] and non-pharmacological trials[6] (see also http://www.consort-statement.org/). The latest initiative to provide an overview of available reporting guidelines is EQUATOR (Enhancing the QUAlity an Transparency of health Research), a new international initiative based on a network concept.[7]

Further checklists were proposed for meta-analyses (Quality of Reporting of Meta-analyses (QUORUM))[8,9] and recently a new checklist called PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[10] For observational studies, including cohort, case-control and cross-sectional studies STROBE was published,[11] extended with STREGA (STRengthening the Reporting of Genetic Association studies).[12] In addition, there is a list available for improving the quality of reports on acupuncture trials: STRICTA,[13] and SQUIRE) was published to enhance reporting on quality improvement studies in health care.[14] STARD was compiled as catalogue of criteria for a complete and accurate reporting of studies of diagnostic accuracy.[15] Concerning reports on clinical trials dealing with homeopathic topics Red-Hot, an unofficial extension for CONSORT, is available.[16]

Reporting experiments in basic research concerned with homeopathic topics requires a complete and detailed explanation of what exactly the experiment was about, which materials were used and how it was conducted and evaluated. Authors should provide transparency in techniques, methods and data evaluation to enable readers to understand and scientists to replicate the experiments. There are about 1300 experiments published in about 900 publications in different fields of basic research collected in the HomBrex Database.[17] As far as we know there are no reporting guidelines comparable to those for clinical research in this area outside of homeopathy. As for homeopathy, three papers concentrate on questions of quality enhancement.[18–20] Two catalogues have been compiled and designed as evaluation scores usable for recipients to assess the quality of reported experiments.[21,22] At least there is one paper which recommends items to be described in papers dealing with ultra low dose effects.[23]

The intention of our paper is to point out how to report basic research in homeopathy, not how research should be done. Each item we consider as important to be stated and explained is listed and defined shortly in Table 1. As this short form is not sufficient or convenient for authors we offer in this publication a section of detailed explanations and examples to illustrate what each item implies. The criteria catalogue with 23 items shall serve as a checklist for scientists to tick off point by point while preparing their report.

Methods

A Delphi Process is a widely used consensus method to structure a group communication process.[24] A group dealing with a complex research question undergoes several steps of adjusting and wording to achieve a compromise and a common course of action. A Delphi process can be initiated for a wide range of questions: From developing a criteria list for the quality assessment of randomized clinical trials[25] up to an implementation of guidelines, as, for example the treatment of endometriosis with Chinese herbal medicine.[26]

In our case we elaborated an agreed checklist with criteria important for improving the quality of reports in basic research in homeopathy. We initiated a Delphi Process including a total of five rounds, three rounds of adjusting and phrasing plus two consensus conferences. A detailed description of the Delphi process (**preparatory phase, Delphi I–IV**) is given elsewhere.[27]

This paper focuses on the last Delphi round (**Delphi V**) where detailed explanations were developed and a prime example for each item was selected.

Results

As result of the first four steps (**Delphi I–IV**) the criteria catalogue of Reporting Experiments in Homeopathic Basic Research (REHBaR) is given in Table 1. We had the impression that such a catalogue is only applicable for authors when each item is explained thoroughly and illustrated by citing an appropriate example, collected from different publications. The selection of examples does not imply that beside the cited part the whole study was reported well. Examples are given in the boxes tinged with grey.

Title

Explanation: An accurate title is important to indicate what the publication is about and to catch the interest of the reader who is concerned with this research. Make sure that the title includes either the exact name or a description of the used test system as well as the type of intervention. If indicated, terms for identifying the experiments as 'in vivo' or 'in vitro' should be given.

> Activation of mononuclear bone marrow cells treated in vitro with a complex homeopathic medication.[28]

Abstract

The abstract provides more information on what was done in the experiment(s). Give enough details to enable the reader to decide, whether the publication is worth reading or not. To provide a sufficient overview we recommend – as a lot of journals demand already – a short text structured by the following headings: Background, Objective, Materials and Methods, Results and Conclusions. The investigated test system should be clearly defined by a commonly used term or a brief description. Abstracts should inform the reader of the main intention of the experiments, the methods and the intervention. Give the

name of the applied substance or other interventions (e.g. heat, radiation) as well as the method of application (e.g. oral, intravenously), the dose (e.g. ml, μmol) and the potencies of homeopathic remedies used (potency level and ratio, e.g. 6c, 30×). The abstract accentuates the main results supported by numbers and estimates of associations, variability and uncertainty.

> BACKGROUND: Efficacy of higher homeopathic potencies is controversial. Universally accepted specific detection assays for homeopathic dilutions do not exist. Basic research has to develop a spectrum of standardized tools to investigate the mode of action and nature of homeopathic potencies. OBJECTIVE: Can the shoot growth reaction of dwarf peas (gibberellin- deficient mutants) be regarded as evidence of treatment with homeopathic potencies of plant growth substances? MATERIALS AND METHODS: Pea seed (Pisum sativum L. cv. Fruher Zwerg) is immersed for 24 h in homeopathic potency or control solutions for soaking. Plants germinate and grow in a standard cultivation substrate under controlled environmental conditions. Shoot length is measured 14 days after planting. RESULTS: A screening of homeopathic potencies (12×–30×) of four different plant growth substances revealed biological activity of certain potency levels of gibberellin and kinetin ($p < 0.05$). Growth stimulation through gibberellin 17× ($5 \times 10(-18$ M)) was assessed in six independent replications; results confirmed those of the screening ($p < 0.05$). The effect of gibberellin 17× seemed to weaken during the course of the experiments. CONCLUSION: The results back the hypothesis that homeopathic potencies of plant growth substances affect pea shoot growth. Dwarf peas might thus be an interesting system model for studying the action of homeopathic potencies. Further work is required to identify all boundary conditions modulating the reactivity of this system.[29]

Introduction

Background

The background section should give readers a general idea of the specific topic the publication deals with. Cite pertinent scientific literature or previous work on the subject to document the relevance of the examined topic. You should provide sufficient information on what was going on before this particular research question came up, why the experimental model and the main parameters were chosen and also why they are adequate for answering the research question. Concerning homeopathy, refer to the homeopathic principle which forms the basis of the investigation: e.g. the similia principle, potentisation, proving. The type of homeopathy investigated should be defined e.g. isopathy, classical vs. complex homeopathy.

> …Published results of homeopathic studies in poultry are rare. Vizzani and Novelli (1992) examined the ability of homeopathic remedies as growth promotor in broilers and found an effect similar or slightly better than that of the standard antimicrobial growth promotor. However, homeopathic preparations and antimicrobial food additives were not specified, nor was statistical analysis performed… The present study was intended to determine the efficacy of several combinations of isopathic and pluralist homeopathic medicines on experimentally induced colibacillosis in broilers.[30]

Objectives/hypotheses

Beside the general scientific background, we recommend an illustration of the objectives of the present study. Be aware of what kind of experiments is being presented. For confirmatory experiments, specific hypotheses and clearly defined primary outcome measures are essential. For exploratory experiments, it is often not possible to define primary outcome measures or parameters. In this case you should emphasize the hypotheses inducing the investigations.

> On the basis of the experimental evidences in wheat and tobacco models, our hypothesis is that a systematic reduction of variability might be one of the peculiar actions of UHD (Ultra High Dilutions). Therefore we propose to consider variability as a central theoretical issue worthy of study in its own right.[31]

Materials and methods

This part of the publication is a detailed list of instructions and information that should enable any interested scientist to replicate the work. If a journal cannot provide enough space to publish all details, we recommend making additional information available by using an online appendix or by giving a link to the website of the authors' institute.

Materials

A detailed description of the biological or physical or biochemical model in the experiment is essential. State the name of the used model explicitly: e.g. growth model, toxicological model. Transparency of the different laboratory procedures is necessary to attest reliability and validity of results. Remember to describe all devices, dilutions and materials as well as all instruments, that were used and to give the proper names, device and lot numbers as well as serial numbers. If the measurement procedure is not commonly used or known, it needs to be specified. To provide an exact description on how many units per experiment were investigated and absolute number of experiments, we recommend a clear outline.

…Luminescence readings were made with a luminometer (Lumistox 300, Dr. B. Lange, Düsseldorf, Germany) at 15.0 ± 0.2 °C. Sterile filter tips with a polyethylene filter (800 μl, Brand) were used to pipette the samples. Samples were kept in cylindrical glass vials (diameter 12 mm, Dr. Bruno Lange GmbH, Düsseldorf, Germany) while the measurements were made… Luminescent bacteria were freeze-dried (V. fischeri, strain NRRL-B-11177, supplier Dr. B. Lange). All were from one batch and certified according to DIN EN ISO 11348-3.[32]

Materials (homeopathy specific)

All manufacturers and manufacturing processes should be given in detail. If possible refer to a Pharmacopeia or other guidelines as a reference (e.g., Korsakovian single-vial-method, Hahnemannian multi-vial-method or continuous fluxion). If an individual method of preparation was chosen, give explanations as to why the preparation steps differ from the commonly used methods and give enough information on how they were done: Number of strokes, time period of shaking, frequency of shaking, horizontal or vertical shaking, shaking against a soft pad or in the air, using a special machine or manual shaking. State which starting point was chosen and which substance (e.g. mother tincture, D1, nosode) Commercially available preparations should be correspondingly named. If substances were stored, report where and for how long.

…Dilutions were made up in 15 ml sterile polystyrene conical tubes provided with caps; the serial dilutions were prepared with an actual histamine concentration four times greater than the intended final concentration, because the protocol subsequently called for a further fourfold dilution in the cell incubation mixture (see below). A 4.4×10^{-2} mol/l histamine solution (designated 1C) was made by diluting 500 μl of histamine stock in 4500 μl of ultrapure water. From that preparation, a series of incremental 1/100 dilutions were prepared by diluting 50 μl of the preceding solution in 4,950 μl of ultrapure water and shaking by vigorous mechanical shaking (7.5 s at 20 strokes/s, vertical amplitude 7 ± 2 mm) using an instrument from MGA Technologies, Lyon, France. The chosen working dilutions/succussions were 2C (10^{-4} mol/l histamine in the final sample assay) as a positive control, and seven ultra high dilutions from 10C (10^{-20} mol/l histamine in the final sample assay) to 16C (10^{-32} mol/l histamine in the final sample assay). …. The histamine and water control dilutions/successions were prepared fresh each day just before the experiments, and stored at room temperature and protected from light until use.[33]

Homeopathic controls

Precise description of the manufacturing and the Pharmacopoeias of the test and control substances is indispensable. Make it obvious to the reader why the particular control substance or situation was chosen. Is the control adequate to the objective? Some examples:

1. if the expected effect is caused by the succussion process only, unpotentised solvent is the adequate control
2. if the effect expected is to be specifically caused by a potentised substance, a potentised solvent or another potentised substance (at the same potency level) are adequate
3. if experiment investigates the importance of the succussion step of potentised substances, a combination of potentised solvent and diluted mother tincture is adequate
4. if experiment investigates the simile-principle the adequate control is a variety of substances which represent different degrees of similarity with the diseased state.

Example 1:…As a control, a pool of homeopathic potencies of water 15–20c was prepared according to the procedure described above, except for the starting dilution in which cadmium chloride was omitted. The… effect was calculated with respect to potentised water in order to account for the physicochemical effects of the potentization procedure.…[34]

Example 2:…Experiments with highwater dilutions were performed using control test samples made up by an identical procedure, with the only difference that the stock starting solution was pure water rather than histamine…..[33]

System perfomance controls

In basic research it is good practice to include positive and negative controls. If done so, state it; if not, give reasons why such a control was not conducted.

1. Positive controls are performed to demonstrate the reactivity of the system. Describe how the units were treated in a way or with a substance, which causes a certain reaction, and give the results.
2. Negative controls serve to demonstrate the non-existence of carry-over-effects, and in some experimental designs they are necessary to characterize the state of the undisturbed experimental system (e.g. human basophils without activation). Give details on the procedure or state performance of this control.
3. Systematic negative control experiments (also called blind runs or non toxicant tests) are conducted to demonstrate the stability of the test system and to exclude false-positive results (artefacts), e.g. due to differences in spatial position (e.g. of plants in a growth chamber, or of cells in a microtiter plate, due to inhomogeneous temperature or light exposition) or in time order (e.g. treating

or measuring objects one after the other). Give details on how they were performed.

> …Three blind runs were performed in order to assess the stability of the experimental set-up, i.e. the experiment was performed with the same number of plants (525 = 25 plants × 21 trays) as in an experiment with homeopathic potencies; however, instead of 21 different parameters (19 potency levels and 2 controls) we used 21 times the same parameter (distilled water). None of these yielded statistically significant differences between the 21 pseudo-parameters (Table 4)…[29]

Quality control

The conductor of the experiment has to guarantee the quality of the study. Therefore we recommend a description of all efforts, which were undertaken to enhance the quality of the study. The report ideally gives information on: training of the experimenter, calibration of devices, supervision of co-workers, information about how the experimenters avoided contaminations of the substances and test systems.

> …The experiments were carried out independently by Scherer, Suanjak and the Weber/Welles team in the laboratory of the Interuniversity College…
>
> …An external observer who came to the laboratory, the veterinarian M. Wurn, was responsible for the blinding…
>
> For reasons of laboratory convenience (danger of cross-contamination) we did not use more than one vial per substance. The project was organized by Endler.[35]

Object of investigation

A detailed description of the researched system is necessary. Define the object precisely: animal, gender, organ, organism, cell compartments (e.g. mitochondria, nuclei), part of cell line, origin of cells, plants, parts of plants, fungi, bacteria, viruses, physical system (e.g. spectroscopy), biochemical (e.g. enzymes), chemical system. The authors should give reasons why the particular system was chosen.

> The rat hepatoma cell line Reuber H35 was routinely grown at 37 °C in subconfluent monolayers in plastic flasks (Greiner, Frickenhausen, ermany). Standard growth medium consisted of Leibovitz (L15) medium, pH 7.4 (Flow/ICN Laboratories, CA, USA) supplemented with 10% fetal calf serum (Gibco Life Technologies, Alphen a/d Rijn, The Netherlands), and the antibiotics streptomycin sulfate (100 μg/ml) and potassium penicillin G (100 U/ml).[36]

Experimental setup

In experiments with plants, specify all important biological conditions like soil, time of cultivation, time of the year when experiments took place, harvest time, charge number of seeds. In experiments concerning animals, gender, age, weight, feeding, holding conditions and intake of fluids should be described. When reporting experiments done *in vitro* (e.g. enzymes, physical parameters) take into account any parameters that could have influenced experimental conditions. Report on preparation procedure and origin of material, incubation time and cleaning methods.

Every detail for a standardisation of the physical conditions be stated (e.g. humidity, temperature, light). Information about any particular equipment for running the experiments is needed. If any procedure was described in an earlier publication refer to that report.

A precise schedule of when what was done as well as a step by step description of the experiment should be given, e.g. in a flow chart. Provide an exact description on how many units per experiment were investigated and on the absolute number of experiments.

> …one ml of each solution was placed in aluminium test cups of 20-mm diameter and 2-mm depth and frozen to 253 K (−20 °C). Each test cup had a number and the numbers corresponding with each of the four solutions were noted. The frozen samples were kept l day at 253 K to achieve stability of the crystalization pattern… Irradiation of the two holders with cups was performed with the Co-60 source Gammacell 220 Excell (GC220E) from MDS Nordion (Fleurus, Belgium). A special Dewar vessel in a size to fit in the radiation chamber was used. The dose selected was l kGy. The average dose rate was approximately 30 cGy/second; irradiation time was 58 min… Thermoluminescence equipment (IMD electronique, Monpelier, France) was equipped with a Statop 4849 temperature Controller (Chauvin Arnoux. Vaulx en Velin, France). For each measurement, the Dewar of the thermoluminescence equipment was filled with liquid nitrogen. When the aluminium temperature block had reached 78 K, a cup was transferred rapidly to the block and heating was started. The average time to increase the temperature of the block was approximately 20 min before the sensors registered a linear increase of temperature in time. Temperature increase was 6 °C per minute from 85 K to 235 K.[37]

Replication

State explicitly if experiments were internally or externally repeated and give number of independent experiments (an internal repetition means that the same experiment is replicated with new material and new samples within the same laboratory). Mention if some of the substances or materials were reused.

Example 1: Growth stimulation of through gibberelin 17× (5×10^{-18} M) was assessed in six independent replications…[29]

Example 2: The aim of the present study was to reproduce the original experiment in order to verify whether the same significant results could be obtained working in a different place and with a different experimental team.[38]

Parameters

All measurement parameters should be clearly defined. Explain why these particular parameters were chosen and why the selected parameters are adequate to answer the research question. In confirmative experiments, declare the principal outcome measure.

Systematic measurements of the specific conductivity were performed on the SDA, using a conductometer, YSI mod. 3200, employing a conductivity cell with constant equal to 1.0 cm^{-1}. Before measuring the conductivity of the sample, the cell had to be calibrated by determining the cell constant K (cm^{-1}). The specific conductivity, χ ($\mu S\ cm^{-1}$), was then given by the product of the cell constant and the conductivity of the solution. For a chosen conductivity measuring cell, the cell constant was determined by measuring the conductivity of a KCl solution with a specific conductivity that was known with great accuracy for several concentrations and temperatures. All the values of conductivity were temperature corrected to 25 °C, using a prestored temperature compensation for pure water.[39]

Intervention

We recommend the specification of all drug interventions (homeopathic and/or substantial) as follows:

1. Dose: which volume in which concentration was administered?
2. Time and intervals: when was it applied for the first time and for how long and how often were test and control substances administered?
3. Application mode: how were test and control substances applied? Globules? Tablets? Liquid?
4. Method of application: which way was chosen for test and control substance? Oral? By injection?

Batches of 30 young male Wistar rats, each weighing approximately 70 g, were given, *via* oesophageal tube, a single dose of 10 mg/kg arsenious anhydride and a tracer dose of 100 μ Ci/kg ^{73}As in the form of arsenious acid (Amersham). These were suspended in 5% gum Arabic syrup, and administered in a volume of 0.5 ml per 20 g body weight. Twelve hours later oral dosing ($T_0 + 12$ h) the animals were given a single intraperitoneal injection of 1 ml of the Hahnemannian dilution of arsenicum album or the same volume of control (succussed distilled water). Following this the rats were isolated in metabolism cages and allowed water and normal feed ad libitum.[40]

Allocation

Describe exactly how it was decided which unit received the test or the control treatment. If allocation was done randomly, describe exactly who generated the randomisation list and which random procedures were used (drawing lots, software etc.).

…Therefore, it was decided to perform a further series of experiments in which $HgCl_2$ potencies and controls were tested blind after randomisation by a statistician (RL) and coding by the team supervisor (SH) (experiment 2: see Table 2)…[41]

Blinding

Give details if and how it was ensured that the conductor was unaware which unit received which treatment (concealment of the randomisation list).

…The experiments were carried out independently by Scherer, Suanjak and the Weber/Welles team in the laboratory of the Interuniversity College. All experiments including application of test and control substances 10^{-30} as well as scoring of the stage of the animals, were performed blind. An external observer who came to the laboratory, the veterinarian M. Wurm, was responsible for the blinding procedures. The same blinding method was used in each case. Substances used for treatment (see below) were prepared in sets each consisting of the test solutions and the control solution. The plaintext labels were the removed by the person responsible for blinding and replaced with labels bearing encoded designations. The code was not made known until after the presentation of the results…[35]

Statistical methods

It is essential to give an exact description which statistical methods and tests were applied. Provide an explanation as to why these methods were used and considered appropriate. If appropriate, describe whether or not the statistical tests were adjusted for multiplicity. Furthermore, describe any

statistical methods used to control for confounding, and how drop-outs and missing data were handled.

> Statistical Analysis: All data analysis was performed with the statistics software 'Statistica 4.1 for Mac' (Statsoft, Inc., Tulsa, OK 74104, USA). If not otherwise stated, *p*-values refer to analysis of variance *F* tests. Planned comparisons were evaluated with the LSD (Least Significant Difference) test only if the preceding *F* test was significant ($p < 0.05$). This procedure (protected Fisher's LSD) gives a good safeguard against type I error without being too conservative, i.e. it also gives good security against type II errors… As a complementary statistical analysis, non-parametrical Wilcoxon tests were calculated whenever applicable.[29]

Results

Numbers analysed

Report every step of calculating and including or excluding results. How were results calculated, how much data contributed to this analysis, and how were missing samples, failures of devices and/or drop-outs taken into account?

Depending on the model system it may be imperative to exclude samples (e.g. because of errors in treatment, handling or measurement). On the other hand, it may be important to include drop-outs in the statistical analysis or to otherwise discuss drop-outs (e.g. animals died in an experimental study where survival is not an explicit endpoint).

> …The entire presented study originally involved 2700 beakers (100 beakers × 27 experiments). Data of 17 beakers were excluded due to spilling. Furthermore, the open controls ($n = 135$, 5 beakers × 27 experiments) were removed from the data set (they had to be includes only due to requirements of the image processing software). For the remaining 2548 beakers, images of three time points (day 0, 3 and 7, corresponding to 7644 beaker images) were used for calculation of $n = 2548$ growth rates for each $r_{(area)}$ day 0–7, 0–3 and 3–7, respectively. Thus 7644 growth rates entered the statistical analysis…[42]

Data (descriptive)

We recommend providing a detailed descriptive summing up of the findings. Exact numbers are best reported in tables. Figures are particularly useful to provide an intuitive summary of the main results. Usually means and standard deviations, or medians and ranges are appropriate if parameters are scaled continuously. If scaled discretely, it is helpful not only to report absolute frequencies but also percentages.

Data (inferential)

The final step of explaining and presenting the results should be achieved by giving the measures of effect size, i.e. the mean differences between treatment and control. This information is only reliable and valuable if numbers of uncertainty of measurement (e.g. standard error or confidence intervals) and calculation of probability (*p*-values) are stated as well. Calculation of effect sizes is recommended. Report any *p*-value calculated, regardless whether the test was significant or not. Report the *p*-values of the main outcome not only in tables or figures, but also in the text body. If applicable, report power calculations.

> …For a final analysis, data of all experiments with gibberellin 17x were pooled (Table 6, Figure 6). A two-way analysis of variance of the dependent variable pea shoot length and of the independent variables treatment (gibberellin 17× and water) and experiment number yielded significant differences for both main effects treatment ($p = 0.012$) and experiment number ($p = 0.0001$), but no significant effect for the interaction ($p = 0.337$)… Thus analysis of variance comes to the conclusion that the effect of treatment with gibberellin 17× is fairly reproducible and independent of external factors. On average, treatment with gibberellin 17× increased pea shoot length by $+(4.6 \pm 1.8)\%$ (mean ± standard error) relative to the water control plants. As an alternative statistical analysis, a Wilcoxon Matched Pairs Test was performed for the gibberellin 17× and water treatment means of all 11 experiments (Table 6). This test also yielded significant results ($p = 0.033$)…[29]

Discussion

Interpretation

The interpretation should be appropriate to the data presented in the section above. The analyses of results ought to take into account the underlying hypotheses of the study and/or the expected results. It should be linked with existing findings. Shortcomings, like potential bias, e.g. setting or handling, should be discussed. Discuss dangers associated with multiplicity of analyses and outcomes.

> …We found for all samples potentised with Aqua bidest., in almost all frequencies where potencies differed from plain solvent, that remedy values were higher than controls values, mostly with significant differences ($p < 0.01$)… Surprisingly (and not known from homeopathic literature), remedy-control differences increased with sample age and conductivity, while depending on glass as Container material and Aqua bidest. as solvent. Vessel-induced changes in

> trace elements may be a necessary co-factor in potentizing and may be responsible for the difference between potentised and plain Aqua bidest… Because of the blinded preparation we consider differences in potentizing (stroke force or frequency) an unlikely explanation. Given these, solitary remedy-control differences being adjacent to differences for more than one remedy are very unlikely to identify a remedy, therefore we did not calculate differences between experiments.[44]

Evidence

The author should give an overview of the relevant literature. How are the results to be seen in context with previous research done in the field? Is there an overall validity of data universal for other experiments? Are the limitations of the experiment presented? A general interpretation should demonstrate that all relevant problems and limitations are considered.

> …In this paper we show that various chemical stressors at concentrations that do not exert any effect on tolerance development or hsp synthesis in control cells are able to stimulate these parameters when applied to heat-treated cells. In previous work we showed that under specific circumstances a low dose of a stressor is able to exert a stimulatory action in cells that had been previously treated with a high dose of the same agent… As an extension of this work, the present paper aimed at identifying the specificity of this paradoxical stimulatory effect exerted by minute amounts of various chemical Stressors. We determined whether the pattern of hsps which is observed upon low dose application in heat shock sensitised cells resembles the pattern of hsps of the first Stressor (heat shock) or of the second chemical Stressor. Interestingly, a significant correlation was observed with the pattern of hsps induced by the second Stressor ($r = 0.621$; $P < 0.001$) and not with the pattern induced by the first Stressor. In this respect, Cabin and Buchman suggested… The data presented in this paper are partly in agreement with the phenomenon indicated as 'hormesis'; the paradoxical stimulatory action of low doses of conditions that are toxic in higher concentrations. However, there are also differences. Hormetic effects are usually… In this respect, our data are more in agreement with the so-called 'principle of similarity', which suggests that recovery processes in a disordered condition can be stimulated specifically by low doses of compounds that in high doses are able to induce a similar disorder. With respect to the underlying mechanism of the observed stimulation by low dose conditions, further research is required…[45]

Experimental model

One of the limiting factors could be an inadequate model or insufficient parameters chosen for proving the hypotheses. When concerned with the specialities of basic research, it is important to demonstrate the eligibility of the experimental model. In experiments investigating homeopathic aspects it is important to focus on the underlying homeopathic theory. Is the expected effect due to the ''similia principle'' or does it belong to the field of isopathy? We recommend giving all reasons as to why this cell line or plant was chosen and which parameters within this study object are true for the investigation.

> Example 1: …We did not observe any effect of water succussion on pea shoot growth. Thus the present pea model does not seem to sensitive to the unspecific effects associated with succussion, such as air suspension and dissolution, pH alterations radical formation, and enhanced ion release from potentization vessel walls. This further validates the stability of the system, and the reliability and specificity of the effects of gibberellic acid 17×….[43]
>
> Example 2: …The authors hypothesize that the stimulatory effect observed is the result of a real homeopathic effect according to the *similia* principle…[34]

Discussion

An international team of researchers with extensive experience in basic and clinical research in homeopathy, experimental physiology, general research methodology and statistics developed in a Delphi process a comprehensive catalogue of items necessary to be reported in publications of homeopathic basic research. It was primarily designed as a guideline for authors and therefore named REHBaR = Reporting Experiments in Homeopathic Basic Research.

A publication is the operative instrument for scientists to present their observations, experiments, underlying hypotheses and findings. Without accurate reporting it is impossible to understand what was done in a scientific study, and what resulted from it, since the publication is the first and main source of information for readers. Adequate reporting is especially important since any publication of research in homeopathy is under scrutiny, particularly if reporting positive results. REHBaR was designed to use as a checklist. We adapted phrasing to the style of catalogues already common in clinical and epidemiological research, mainly CONSORT[1,2] and STROBE.[11]

Despite the fact that in clinical research guidelines for nearly every kind of trial and study exist, adherence is still poor and inconsistent.[46,47] This applies to entire disciplines like the field of endocrinology,[48] but also quite generally to abstracts published in main general medical journals.[49] In some reports important details like randomisation and blinding procedures are still missing.[50] Although quality of reporting acupuncture trials improved significantly after the

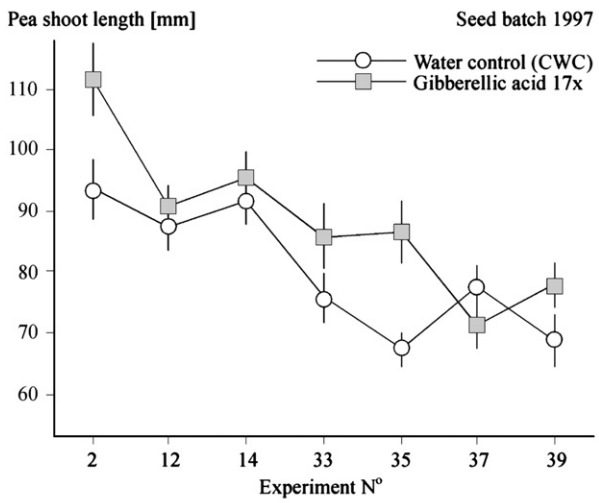

Figure 1 Pea shoot length (mean ± standard error [mm]) of all experiments involving seed batch 1997, treated with either water or gibberellic acid 17x. Data of the water control group (combined water control, CWC) were pooled from the plants treated with either unsuccussed or succussed water. Data of the experiments No. 2, 12, and 14 have been published earlier.

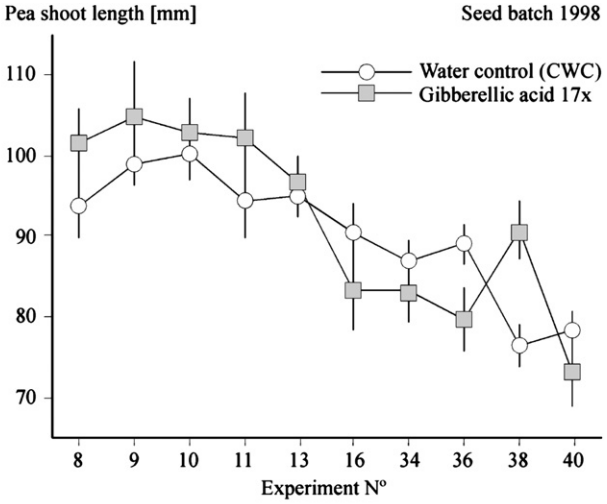

Figure 2 Pea shoot length (mean ± standard error [mm]) of all experiments with seed batch 1998, treated with either water or gibberellic acid 17x. Data of the water control group (combined water control, CWC) were pooled from the plants treated with either unsuccussed or succussed water. Data of the experiments No. 8–11, 13, and 16 have already been published earlier.

Table 4 Assessment of variability *within* experiments

Seed batch	Combined water control (CWC)		GA_3 17x	
	S.D.† [%]	*n**	S.D.† [%]	*n**
1997	35.34	360	32.43	221
1998	25.92	608	28.57	326
1999	20.65	894	20.28	469
2000	22.17	780	23.30	391

Calculation: see 'Data evaluation and statistical analysis.'
Included experiments: see Table 3 (analysis 2).
† S.D. = standard deviation [%].
* *n* = number of plants measured.

Table and figure out of [43]

introduction of CONSORT in 1996, the impact of the STRICTA guidelines referring specifically to acupuncture interventions is still low.[51] The main criticism in the field of guidelines for reporting clinical trials is due to the fact that many journals refer to e.g. CONSORT but do not strictly enforce realisation.[52] Vandenbroucke complains about too many guidelines, leading to confusion about how and when to use them.[53]

Nevertheless, guidelines gained in a decision process by consensus are very useful as scientists have to follow a scheme to understand each others research: to speak the same language. Naturally, any guideline should be a kind of baseline and not too specific in order to be applicable to a variety of topics. Once a catalogue is evaluated by scientists it is important for journals to advertise the guideline.

The intention of our catalogue was to develop a first version of something like a gold standard of perfect reporting. We are well aware of the difficulties due to space limitations in some scientific journals. REHBaR is a comprehensive and detailed guideline, and we know that instructions about reporting are very precise and maybe sometimes difficult to realize. In the case of space limitations, we recommend authors to refer to a website address to make further information available. If certain methods or the procedure of positive and negative controls are already published, it may be sufficient to refer to that publication. REHBaR is also addressed to editors of scientific journals, however. We think that the peculiarities of homeopathic basic research make it necessary to enhance reporting especially of methodological details to facilitate inter-laboratory reproductions. This is important since there are still considerable difficulties developing experimental models in homeopathic basic research that are easy to reproduce in other laboratories.[54]

REHBaR is the first itemized guideline to improve reporting basic research on homeopathic issues. We tried to end up with a basic inventory of items applicable for

Table 1 Items to be included when Reporting Experiments in Homeopathic Basic Research (REHBaR)

Item	*Nr.*	*Descriptor*
Title	1	Title indicates the experimental model and intervention
Abstract	2	Abstract provides an informative and balanced summary of what was done and found
Introduction		
Background	3	Scientific background, presentation of experimental model(s), explanation of rationale, including homeopathic principles (e.g. similia principle, potentisation, proving) and type of homeopathy (isopathy, classical vs complex homeopathy)
Objectives/Hypotheses	4	Objectives and hypotheses with outcome measures. For confirmatory experiments: specific hypotheses and clearly defined primary outcome measure. For exploratory experiments: hypotheses inducing the investigations
Materials and methods		
Materials	5	Detailed description of all used materials (e.g. biological system, devices, substances, instruments)
Materials (homeopathy specific)	6	Manufacturer, Pharmacopoeia (or process) of medications, potency and steps of dilution, dilution method, substance starting point of dilution (e.g. mother tincture, D1, nosode)
Homeopathic controls	7	Precise details on the preparation of the control substance
System performance controls	8	Report on negative and positive controls
Quality control	9	Procedures and efforts used to enhance the quality and reliability of the experimental procedure
Object of investigation	10	Selection criteria for the particular system used: in vivo, in vitro, biological, physical, biochemical
Experimental Setup	11	Detailed description of experimental conditions and procedure
Replication	12	If experiment has internal replications, detailed description is given of which materials were reused and which have been changed
Parameters	13	All measured parameters described in detail
Intervention	14	Precise details of the interventions intended for each group and how and when they were actually administered
Allocation	15	Method used to generate the group allocation including details (e.g. randomisation, blocking, stratification)
Blinding	16	Description if any procedures or interventions were concealed (if yes, details given)
Statistical methods	17	Statistical tests and procedure of calculation are described: Methods for additional analyses like adjusted analyses
Results		
Numbers analysed	18	Number of experiments with exact number of treated units per setting which were included in each analysis and reporting missing samples, drop-outs
Data (descriptive)	19	Results are given in tables or figures showing mean or median together with variability (e.g. SD and/or range) for absolute data (and differences)
Data (inferential)	20	Gives appropriate measures of effect size, uncertainty and probability
Discussion		
Interpretation	21	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision
Evidence	22	General interpretation of results in the context of current evidence. Discuss the generalisability/external validity of the study results
Experimental model	23	Explanation why this model, these parameters were chosen and its adequacy for answering the questions including homeopathic aspects

an ample variety of experiments. REHBaR was not compiled to give instructions on good laboratory practice (GLP) or to assess the quality of scientific work. However the selection of items and explanations reflect at least our opinion of how basic research in this field should be accomplished. Moreover it is the first attempt to bring together the knowledge from diverse disciplines to incorporate all relevant aspects in one list. Obviously, the team was a relatively small and convenient sample of individuals, and other researchers might have introduced other items. We hope that many researchers and authors take notice of our catalogue and may find it useful. We encourage the use of the list and hope for critical feedback, so an improved version could be published in a few years.

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