

Einblick

DISKUSSION UND FORSCHUNG ZUR HOMÖOPATHIE

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HOMÖOPATHIE

Wissenschaft und aktuelle Diskussion

Diese Zusammenstellung bietet einen Überblick zu wichtigen Forschungsarbeiten aus

- ▶ der Humanmedizin
- ▶ der Tiermedizin
- ▶ der Versorgungsforschung
- ▶ der Grundlagenforschung

Die Grundlagenforschung zeigt, dass spezifische physiko-chemische Effekte für potenzierte Substanzen wie Globuli messbar sind. Darüber hinaus werden Heilungserfolge in einer wachsenden Zahl von klinischen Studien beobachtet und quantifiziert. Daher entspricht eine Verbreitung pauschaler Negativurteile nicht dem Standard guter Forschungspraxis. Die hier wiedergegebenen Abstracts aus den einzelnen Forschungsfeldern ermöglichen dem Leser einen eigenständigen Einblick in die aktuelle Entwicklung einer modernen, evidenzbasierten Homöopathie.

Voreilige Urteile - Eine Hauptquelle der menschlichen Irrtumsfähigkeit



So informierte der für seine Erfindungen geadelte Physiker und Elektrizitätsforscher Lord Kelvin die Bürger und das englische Parlament, das er zu Forschungsfragen beriet.

Da wir als Menschen - wie als Wissenschaftler - ebenso irrtumsfähig wie erkenntnisbegabt sind, gründet sich die moderne evidenzbasierte Medizin bisher auf *drei Säulen*:

1. **Die Erfahrung und die Erkenntnis des Therapeuten**
2. **Die Werte und Wünsche sowie die Erfahrung des Erkrankten**
3. **Der aktuelle Stand der Wissenschaft und des medizinisch Wissbaren**

Die womöglich wichtigste Säule der evidenzbasierten Medizin wird in der aktuellen Debatte oft ausgelassen:

Es ist der Mensch, um den es geht.

Zur zentralen patientenorientierten, zweiten Säule der evidenzbasierten Medizin

Zu den Erfahrungen und Beobachtungen der betroffenen Bürger gibt es in der EU einen hohen Forschungsbedarf für komplementäre Methoden wie die Homöopathie.¹ Zugleich existiert interessante Evidenz durch Bürgerbefragungen: In Deutschland und Frankreich² leben fast 30 % der EU Bevölkerung. Laut aktuellen und unabhängigen Befragungen haben in diesen beiden Ländern über 85 Millionen Menschen selbst Erfahrungen mit Homöopathie gemacht. 72 % von ihnen sind mit dem Ergebnis zufrieden oder sehr zufrieden.

- 73% der dazu befragten Bürger wünschen, dass die Homöopathie im Gesundheitssystem zur Verfügung steht und von den Krankenkassen finanziert wird.
- In Deutschland wünschen sich 85 % der Bevölkerung die Erforschung der Homöopathie an Universitäten.
- Rund 3 von 4 Bürgern erwarten, dass diese Erforschung durch fachkompetente Wissenschaftler auch vom Staat finanziert wird³.

Das deutsche Grundgesetz schützt diese an der eigenen Gesundheitserfahrung orientierten und selbstbestimmten Wünsche seiner Bürger ausdrücklich:



Artikel 1

Die Würde des Menschen ist unantastbar.

Artikel 2, 1)

Jeder hat das Recht auf die freie Entfaltung seiner Persönlichkeit, soweit er nicht die Rechte anderer verletzt und nicht gegen die verfassungsmäßige Ordnung oder das Sittengesetz verstößt.

¹ What Attitudes and Needs Do Citizens in Europe Have in Relation to Complementary and Alternative Medicine? N. Nissen S. Schunder-Tatzber W. Weidenhammer H. Johannessen, *Forschende Komplementärmedizin*, 19/2012, 9-17

² Deutschland Bevölkerung 2019 | Bevölkerungsuhr, <https://countrymeters.info/de/Germany>: Unserer Schätzung zufolge umfasst die Bevölkerung Deutschland 81 402 348 Menschen Ende 2018. In Frankreich leben rund 65 649 091 Menschen <https://www.laenderdaten.info/Europa/Frankreich/bevoelkerungswachstum.php>; <https://countrymeters.info/de/France>

³ Forsa Umfrage zur Homöopathie im Auftrag des BPI, Bund Pharmazeutischer Industrie, 2017

Artikel 2, 2)

Jeder hat das Recht auf Leben und körperliche Unversehrtheit. Die Freiheit der Person ist unverletzlich.

Nach den Erfahrungen von schwerem Missbrauch in deutschen Diktaturen stellt das Grundgesetz die Felder **Berufswahl⁴ sowie Forschung und Lehre ausdrücklich frei:**

Artikel 5,3)

Kunst und Wissenschaft, Forschung und Lehre sind frei⁵.

Die entsprechenden Artikel in der EU-Charta der Grundrechte sind nahezu gleichlautend.

Zur ersten Säule der evidenzbasierten Medizin

Auf nationalen wie auf internationalen Fachtagungen berichten die homöopathischen Therapeuten übereinstimmend, dass überwiegend Patienten bei ihnen Hilfe suchen, bei deren Erkrankung andere, meist konventionelle Therapieverfahren nicht oder nicht ausreichend gewirkt haben oder wenn Antibiotika bei ihnen bakterielle Resistenzen erzeugt hatten. Wenn dann die Patienten, wie die zitierten Umfragen zeigen, häufig positive Erfahrungen mit der homöopathischen Therapie machen, kommen auch weitere Familienmitglieder mit ungelösten medizinischen Fragen zur homöopathischen Therapie. Die vielfache Erfahrung umfassend ausgebildeter Therapeuten bestätigt positive Erfahrungen der meisten betroffenen Patienten.

Ärztliche Kollegen aus anderen Fachbereichen negieren diese Beobachtungen und Erfahrungen mitunter. Allerdings kennen sie selbst oft weder die therapeutischen Beobachtungen, noch die Eigenerfahrung der betroffenen Patienten, noch den Stand der Forschung. Dennoch entscheiden überwiegend fachfremd besetzte Ärztegremien in mehreren deutschen Bundesländern aktuell über den Fortbestand der ärztlichen Homöopathieausbildung. Hier zeichnet sich ein wichtiges, neues Forschungsfeld ab: Die Bedeutung und Auswirkung von Vorurteilen innerhalb jeder Säule der Evidenz.

Zur dritten wissenschaftlichen Säule der evidenzbasierten Medizin

Die bisherige Forschung weist anhand einer Reihe von gut durchgeführten Studien darauf hin, dass homöopathische Arzneimittel in klinischen Untersuchungen sowie in Grundlagenexperimenten

- wirksamer sind als Placebo und/oder
- bei bestimmten Indikationen ähnlich wirksam sind oder mitunter sogar wirksamer als eine alleinige konventionelle Standardtherapie.

⁴ DGG, Artikel 12,1

⁵ Diese Freiheit wird ausdrücklich im Kontext der anderen relevanten Artikel formuliert: Die Freiheit der Lehre entbindet nicht von der Treue zur Verfassung.

Auf den folgenden Seiten können Sie selbst Einblick in die Literatur zur Forschung über Homöopathie nehmen: Sie finden die zusammenfassenden Abstracts

- von klinischen Studien aus der Humanmedizin und Versorgungsforschung,
- von Veterinärmedizinischen Studien,
- von Metastudien sowie aus der
- Grundlagenforschung.

Ein Click im Inhaltsverzeichnis genügt, um an die entsprechende Textstelle zu gelangen.

Wenn Sie einen Artikel ganz lesen möchten, finden Sie ihn unter dem Titel, der über dem Abstract steht, über eine einfache Internetsuche.

Wichtige Artikel, die frei zugänglich sind (open Access), sind in ihrer Ganzheit im Reader abgedruckt.

Vor die verschiedenen Forschungsgebiete haben wir jeweils eine Einleitung gesetzt. Seiten mit diesen einleitenden Gedanken haben zur besseren Erkennbarkeit einen blauen Randstreifen.

Am Ende des Readers finden Sie Informationen über die Akademie.

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Wichtige klinische Studien

Die folgenden Studien zur Homöopathie zeigen entlang anerkannter Kriterien guter Forschungspraxis klare Hinweise für eine nebenwirkungsarme und gleichzeitig signifikante Wirksamkeit der homöopathischen Therapie. Sie erfüllen zentrale Kriterien für gut angelegte Studien und zeigen jede einzeln eine eindeutige Wirkung der homöopathischen Therapie im Vergleich zu Placebo oder zu einer anderen konventionellen Standardtherapie.

Das erklärt womöglich, wie sich die Homöopathie über 200 Jahre, trotz starker theoretischer Hinterfragungen zu einer der weltweit meist genutzten Einzeltherapien entwickeln konnte. Die Studien zeigen deutlich, wie wichtig es ist, die kompetente Forschung im Sinne der betroffenen Bürger zu fördern, um mehr über ihre Signifikanz, ihre sinnvolle Anwendung und über ihr Wirkprinzip zu erfahren.

Hintergrund: Die Homöopathie ist eine der am häufigsten eingesetzten Einzeltherapien der Welt:

- Alleine in Indien gibt es über 100 Universitäten, die rein homöopathisch approbierte Ärzte ausbilden, die einen großen Teil der Bevölkerung ärztlich versorgen.
- Für Europa lässt sich abschätzen, dass mehr als 100 000 000 Menschen homöopathische Arzneien eingenommen haben.⁶
- Auf dem gesamten amerikanischen Kontinent und in Afrika wird die Homöopathie ebenfalls zunehmend angewandt.

Wie einleitend dargestellt, wünschen sich 85% der von Forsa befragten Bürger eine Erforschung der Homöopathie an Universitäten und fast $\frac{3}{4}$ der Bürger fordern eine staatliche Finanzierung. Gute Forschung muss heute sehr hohe Standards erfüllen. Das macht sie kostspielig und enorm zeitaufwendig: Für eine konventionelle medizinische Studie in der Medikamentenentwicklung rechnen Universitäten und Forschungsteams heute 1-250 Millionen Euro ein.

Entgegen dem klar entwickelten Bürgerwillen sind die Bedingungen für homöopathische Forschung bislang ungewöhnlich ungünstig:

Es gibt - ganz anders als in der konventionellen Medizin und entgegen den Wahlversprechen fast aller Parteien – in Deutschland, wie in anderen EU Ländern - nahezu keinerlei staatliche Förderung. Unter diesen in der Medizin ungewöhnlich harten, förderungsarmen Bedingungen entwickelt sich die Studienlage⁷ zwar langsam, doch dafür

⁶ Allein in Frankreich und Deutschland haben laut aktuellen Befragungen über 80 000 000 Bürger homöopathische Arzneien ausprobiert. Von ihnen sind in beiden Ländern 72 % zufrieden oder sehr zufrieden (Forsa Umfrage zur Homöopathie im Auftrag des bpi 2017 und Umfrage des Ypsos Instituts, publiziert am 9.11.2018), <https://www.ipsos.com/fr-fr/lhomeopathie-plebiscitee-par-les-francais>

⁷ Frühe Studien erfüllten oft die heutigen Rahmenbedingungen für Studien noch nicht umfassend. Das gilt für ältere Studien in der konventionellen Medizin ähnlich.

erstaunlich positiv fort. In den Jahren seit der Jahrtausendwende ist das Niveau der homöopathischen Forschung kontinuierlich gestiegen und eine zunehmende Zahl von Studien erfüllt aktuell für wichtig gehaltenen Kriterien einer evidenzbasierten Medizin. Das gilt für die klinische ebenso wie für die Grundlagenforschung.⁸

Qualitätskriterien für Studien

Zu den wichtigen aktuellen Qualitätsstandards für neue Studien gehören die Cochrane Kriterien: Zum essentiellen Goldstandard zählt hier eine Studie, die als **RCT**, also „randomised controlled“ durchgeführt wurde, oder/und gegen den **SOC**, also den „Standard of Care“ gemessen wurde. RCT heißt, dass es mindestens zwei Studienarme gibt, denen die Patienten zufällig zugewiesen werden. Je nach Zuweisung erhalten sie dann - wenn möglich doppelt verblindet - entweder die zu prüfende Therapie oder Placebo oder eine Standard-Therapie.

Für alle medizinischen Studien gilt:

Naturgemäß zeigt nicht jede Studie ein positives Ergebnis. Das kann an der Fragestellung ebenso liegen, wie an den Rahmenbedingungen oder an der konkreten Durchführung. Dies gilt in der Homöopathie genauso wie in der konventionellen Medizin. Ein aktueller Review zeigt, dass bei konventionellen Studien zu neuen Wirkstoffen in der Onkologie nur 5% der Studien signifikant positive Ergebnisse zeigen und in der Psychiatrie sogar nur 2,6%⁹. Auch diese falsifizierenden Studien zu Einzelthesen ermöglichen oft wichtige Erkenntnisse, um sodann die nachfolgende Forschung im jeweiligen Fachgebiet besser auszurichten

Wichtige Studien zu ADHS, Angststörungen, Depressionen und adjuvanter Krebstherapie finden Sie auf den folgenden Seiten.

⁸ Siehe dazu den Survey zur Grundlagenforschung Seite 70, sowie Seite 71

⁹ Siehe Clinical Development Success Rates 2006-2015, <https://www.bio.org/sites/default/files/Clinical%20Development%20Success%20Rates%202006-2015%20-%20BIO,%20Biomedtracker,%20Amplion%202016.pdf>

Humanmedizin und Homöopathie

ADHS | Attention Deficit Hyperactivity Disorder

Frei H¹, Everts R, von Ammon K, Kaufmann F, Walther D, Hsu-Schmitz SF, Collenberg M, Fuhrer K, Has-sink R, Steinlin M, Thurneysen A.

Eur J Pediatr. 2005 Dec;164(12):758-67. Epub 2005 Jul 27.

Homeopathic treatment of children with attention deficit hyperactivity disorder: a randomised, double blind, placebo controlled crossover trial.

AUTHOR INFORMATION

An increasing number of parents turn to homeopathy for treatment of their hyperactive child. Two publications, a randomised, partially blinded trial and a clinical observation study, conclude that homeopathy has positive effects in patients with attention deficit hyperactivity disorder (ADHD).

The aim of this study was to obtain scientific evidence of the effectiveness of homeopathy in ADHD. A total of 83 children aged 6-16 years, with ADHD diagnosed using the Diagnostic and Statistical Manual of Mental Disorders-IV criteria, were recruited. Prior to the randomised, double blind, placebo controlled crossover study, they were treated with individually prescribed homeopathic medications.

62 patients, who achieved an improvement of 50% in the Conners' Global Index (CGI), participated in the trial. Thirteen patients did not fulfill this eligibility criterion (CGI). The responders were split into two groups and received either verum for 6 weeks followed by placebo for 6 weeks (arm A), or vice-versa (arm B).

At the beginning of the trial and after each crossover period, parents reported the CGI and patients underwent neuropsychological testing. The CGI rating was evaluated again at the end of each crossover period and twice in long-term follow-up.

At entry to the crossover trial, cognitive performance such as visual global perception, impulsivity and divided attention, had improved significantly under open label treatment ($P < 0.0001$). During the crossover trial, CGI parent-ratings were significantly lower under verum (average 1.67 points) than under placebo ($P = 0.0479$). Long-term CGI improvement reached 12 points (63%, $P < 0.0001$).

CONCLUSION

The trial suggests scientific evidence of the effectiveness of homeopathy in the treatment of attention deficit hyperactivity disorder, particularly in the areas of behavioural and cognitive functions.

Comment in

- Homeopathic treatment of children with attention deficit disorder: a randomized, double blind, placebo-controlled crossover trial. H. Frei R. Everts, K.v. Ammon et al. Eur J Pediatr. 2005; 164: 758-767. [Eur J Pediatr. 2007

Angststörungen und Depressionen | Anxiety and Depression

Grimaldi-Bensouda L^{1,2}, Abenhaim L^{3,4}, Massol J⁵, Guillemot D^{6,7}, Avouac B⁸, Duru G⁹, Lert F¹⁰, Magnier AM¹¹, Rossignol M¹², Rouillon F¹³, Begaud B¹⁴; EPI3-LA-SER group.
BMC Complement Altern Med. 2016 May 4;16:125. doi: 10.1186/s12906-016-1104-2.

Homeopathic medical practice for anxiety and depression in primary care: the EPI3 cohort study.

BACKGROUND

The purpose of the study was to compare utilization of conventional psychotropic drugs among patients seeking care for anxiety and depression disorders (ADDs) from general practitioners (GPs) who strictly prescribe conventional medicines (GP-CM), regularly prescribe homeopathy in a mixed practice (GP-Mx), or are certified homeopathic GPs (GP-Ho).

METHODS

This was one of three epidemiological cohort studies (EPI3) on general practice in France, which included GPs and their patients consulting for ADDs (scoring 9 or more in the Hospital Anxiety and Depression Scale, HADS). Information on all medication utilization was obtained by a standardised telephone interview at inclusion, 1, 3 and 12 months.

RESULTS

Of 1562 eligible patients consulting for ADDs, 710 (45.5 %) agreed to participate. Adjusted multivariate analyses showed that GP-Ho and GP-Mx patients were less likely to use psychotropic drugs over 12 months, with Odds ratio (OR) = 0.29; 95 % confidence interval (CI): 0.19 to 0.44, and OR = 0.62; 95 % CI: 0.41 to 0.94 respectively, compared to GP-CM patients. The rate of clinical improvement (HADS <9) was marginally superior for the GP-Ho group as compared to the GP-CM group (OR = 1.70; 95 % CI: 1.00 to 2.87), but not for the GP-Mx group (OR = 1.49; 95 % CI: 0.89 to 2.50).

CONCLUSION

Patients with ADD, who chose to consult GPs prescribing homeopathy reported less use of psychotropic drugs, and were marginally more likely to experience clinical improvement, than patients managed with conventional care. Results may reflect differences in physicians' management and patients' preferences as well as statistical regression to the mean.

KEYWORDS

Anxiety; Depression; Homeopathy; Primary care

Additive Homöopathie bei Krebspatienten | Additive homeopathy in cancer patients

Frass M¹, Friehs H², Thallinger C³, Sohal NK⁴, Marosi C⁵, Muchitsch I⁶, Gaertner K⁷, Gleiss A⁸, Schuster E⁹, Oberbaum M¹⁰.

Complement Ther Med. 2015 Jun;23(3):309-17. doi: 10.1016/j.ctim.2015.03.004. Epub 2015 Mar 23.

PMID: 26051564

Influence of adjunctive classical homeopathy on global health status and subjective wellbeing in cancer patients - A pragmatic randomized controlled trial.

OBJECTIVES

The use of complementary and alternative medicine has increased over the past decade. The aim of this study was to evaluate whether homeopathy influenced global health status and subjective wellbeing when used as an adjunct to conventional cancer therapy.

DESIGN

In this pragmatic randomized controlled trial, 410 patients, who were treated by standard anti-neoplastic therapy, were randomized to receive or not receive classical homeopathic adjunctive therapy in addition to standard therapy. The study took place at the Medical University Vienna, Department of Medicine I, Clinical Division of Oncology.

MAIN OUTCOME MEASURES

The main outcome measures were global health status and subjective wellbeing as assessed by the patients. At each of three visits (one baseline, two follow-up visits), patients filled in two different questionnaires.

RESULTS

373 patients yielded at least one of three measurements. The improvement of global health status between visits 1 and 3 was significantly stronger in the homeopathy group by 7.7 (95% CI 2.3-13.0, $p=0.005$) when compared with the control group. A significant group difference was also observed with respect to subjective wellbeing by 14.7 (95% CI 8.5-21.0, $p<0.001$) in favor of the homeopathic as compared with the control group. Control patients showed a significant improvement only in subjective wellbeing between their first and third visits.

CONCLUSION

Results suggest that the global health status and subjective wellbeing of cancer patients improve significantly when adjunct classical homeopathic treatment is administered in addition to conventional therapy.

Add-on Therapien bei Carcinomen | Add-on Therapies in the Treatment of Cancer Patients

Naumann J, Guethlin C, Guenther L, Bartsch HH, Walach H.
BMC Cancer. 2011 Jan 17;11:19. doi: 10.1186/1471-2407-11-19.
Rostock M1,

Classical homeopathy in the treatment of cancer patients--a prospective observational study of two independent cohorts.

BACKGROUND

Many cancer patients seek homeopathy as a complementary therapy. It has rarely been studied systematically, whether homeopathic care is of benefit for cancer patients.

METHODS

We conducted a prospective observational study with cancer patients in two differently treated cohorts: one cohort with patients under complementary homeopathic treatment (HG; n = 259), and one cohort with conventionally treated cancer patients (CG; n = 380). For a direct comparison, matched pairs with patients of the same tumour entity and comparable prognosis were to be formed. Main outcome parameter: change of quality of life (FACT-G, FACIT-Sp) after 3 months. Secondary outcome parameters: change of quality of life (FACT-G, FACIT-Sp) after a year, as well as impairment by fatigue (MFI) and by anxiety and depression (HADS).

RESULTS

HG: FACT-G, or FACIT-Sp, respectively improved statistically significantly in the first three months, from 75.6 (SD 14.6) to 81.1 (SD 16.9), or from 32.1 (SD 8.2) to 34.9 (SD 8.32), respectively. After 12 months, a further increase to 84.1 (SD 15.5) or 35.2 (SD 8.6) was found. Fatigue (MFI) decreased; anxiety and depression (HADS) did not change. CG: FACT-G remained constant in the first three months: 75.3 (SD 17.3) at t0, and 76.6 (SD 16.6) at t1. After 12 months, there was a slight increase to 78.9 (SD 18.1). FACIT-Sp scores improved significantly from t0 (31.0 - SD 8.9) to t1 (32.1 - SD 8.9) and declined again after a year (31.6 - SD 9.4). For fatigue, anxiety, and depression, no relevant changes were found. 120 patients of HG and 206 patients of CG met our criteria for matched-pairs selection. Due to large differences between the two patient populations, however, only 11 matched pairs could be formed. This is not sufficient for a comparative study.

CONCLUSION

In our prospective study, we observed an improvement of quality of life as well as a tendency of fatigue symptoms to decrease in cancer patients under complementary homeopathic treatment. It would take considerably larger samples to find matched pairs suitable for comparison in order to establish a definite causal relation between these effects and homeopathic treatment.

Add-on Therapie bei beatmeten Intensivpatienten | Add-on Therapy on COPD

Frass M¹, Dielacher C, Linkesch M, Endler C, Muchitsch I, Schuster E, Kaye A.
Chest. 2005 Mar;127(3):936-41.

Influence of potassium dichromate on tracheal secretions in critically ill patients.

BACKGROUND

Stringy, tenacious tracheal secretions may prevent extubation in patients weaned from the respirator. This prospective, randomized, double-blind, placebo-controlled study with parallel assignment was performed to assess the influence of sublingually administered potassium dichromate C30 on the amount of tenacious, stringy tracheal secretions in critically ill patients with a history of tobacco use and COPD.

METHODS

In this study, 50 patients breathing spontaneously with continuous positive airway pressure were receiving either potassium dichromate C30 globules (group 1) [Deutsche Homöopathie-Union, Pharmaceutical Company; Karlsruhe, Germany] or placebo (group 2). Five globules were administered twice daily at intervals of 12 h. The amount of tracheal secretions on day 2 after the start of the study as well as the time for successful extubation and length of stay in the ICU were recorded.

RESULTS

The amount of tracheal secretions was reduced significantly in group 1 ($p < 0.0001$). Extubation could be performed significantly earlier in group 1 ($p < 0.0001$). Similarly, length of stay was significantly shorter in group 1 (4.20 +/- 1.61 days vs 7.68 +/- 3.60 days, $p < 0.0001$ [mean +/- SD]).

CONCLUSION

These data suggest that potentized (diluted and vigorously shaken) potassium dichromate may help to decrease the amount of stringy tracheal secretions in COPD patients.

Sepsis

Frass M¹, Linkesch M, Banyai S, Resch G, Dielacher C, Löbl T, Endler C, Haidvogel M, Muchitsch I, Schuster E.

<https://doi.org/10.1016/j.homp.2005.01.002> Get rights and content

Adjunctive homeopathic treatment in patients with severe sepsis: a randomized, double-blind, placebo-controlled trial in an intensive care unit.

BACKGROUND

Mortality in patients with severe sepsis remains high despite the development of several therapeutic strategies. The aim of this randomized, double-blind, placebo-controlled trial was to evaluate whether homeopathy is able to influence long-term outcome in critically ill patients suffering from severe sepsis.

METHODS

Seventy patients with severe sepsis received homeopathic treatment (n = 35) or placebo (n = 35). Five globules in a potency of 200c were given at 12h interval during the stay at the intensive care unit. Survival after a 30 and 180 days was recorded.

RESULTS

Three patients (2 homeopathy, 1 placebo) were excluded from the analyses because of incomplete data. All these patients survived. Baseline characteristics including age, sex, BMI, prior conditions, APACHE II score, signs of sepsis, number of organ failures, need for mechanical ventilation, need for vasopressors or veno-venous hemofiltration, and laboratory parameters were not significantly different between groups. On day 30, there was non-statistically significantly trend of survival in favour of homeopathy (verum 81.8%, placebo 67.7%, P = 0.19). On day 180, survival was statistically significantly higher with verum homeopathy (75.8% vs 50.0%, P = 0.043). No adverse effects were observed.

CONCLUSIONS

Our data suggest that homeopathic treatment may be a useful additional therapeutic measure with a long-term benefit for severely septic patients admitted to the intensive care unit. A constraint to wider application of this method is the limited number of trained homeopaths.

Fibromyalgie | Fibromyalgia

Bell IR, Lewis DA 2nd, Brooks AJ, Schwartz GE, Lewis SE, Walsh BT, Baldwin CM. Rheumatology (Oxford). 2004 May;43(5):577-82. Epub 2004 Jan 20.

Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo

OBJECTIVE:

To assess the efficacy of individualized classical homeopathy in the treatment of fibromyalgia.

METHODS:

This study was a double-blind, randomized, parallel-group, placebo-controlled trial of homeopathy. Community-recruited persons (N = 62) with physician-confirmed fibromyalgia (mean age 49 yr, s.d. 10 yr, 94% women) were treated in a homeopathic private practice setting. Participants were randomized to receive oral daily liquid LM (1/50,000) potencies with an individually chosen homeopathic remedy or an indistinguishable placebo. Homeopathic visits involved joint interviews and concurrence on remedy selection by two experienced homeopaths, at baseline, 2 months and 4 months (prior to a subsequent optional crossover phase of the study which is reported elsewhere). Tender point count and tender point pain on examination by a medical assessor uninvolved in providing care, self-rating scales on fibromyalgia-related quality of life, pain, mood and global health at baseline and 3 months, were the primary clinical outcome measures for this report.

RESULTS:

Fifty-three people completed the treatment protocol. Participants on active treatment showed significantly greater improvements in tender point count and tender point pain, quality of life, global health and a trend toward less depression compared with those on placebo.

CONCLUSIONS:

This study replicates and extends a previous 1-month placebo-controlled crossover study in fibromyalgia that pre-screened for only one homeopathic remedy. Using a broad selection of remedies and the flexible LM dose (1/50,000 dilution factor) series, the present study demonstrated that individualized homeopathy is significantly better than placebo in lessening tender point pain and improving the quality of life and global health of persons with fibromyalgia.

Menopausales Syndrom | Menopausal Syndrom

Jean-Claude Colau Stéphane Vincent Philippe Marijnen François-André Allaer
August 2012, DOI: 10.2165/11640240-000000000-00000 · Source: PubMed
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial
First Online: 18 December 2012

Efficacy of a Non-Hormonal Treatment, BRN-01, on Menopausal Hot Flashes

BACKGROUND

Homeopathic medicines have a place among the non-hormonal therapies for the treatment of hot flashes during the menopause.

OBJECTIVE

The objective of this study was to evaluate the efficacy of the non-hormonal treatment BRN-01 in reducing hot flashes in menopausal women.

STUDY DESIGN

This was a multicenter, randomized, double-blind, placebo-controlled study carried out between June 2010 and July 2011.

SETTING

The study was conducted in 35 active centers in France (gynecologists in private practice). Patients: One hundred and eight menopausal women, ≥ 50 years of age, were enrolled in the study. The eligibility criteria included menopause for < 24 months and ≥ 5 hot flashes per day with a significant negative effect on the women's professional and/or personal life.

INTERVENTION

Treatment was either BRN-01 tablets, a registered homeopathic medicine containing *Actaea racemosa* (4 centesimal dilutions [4CH]), *Arnica montana* (4CH), *Glonoinum* (4CH), *Lachesis mutus* (5CH), and *Sanguinaria canadensis* (4CH), or identical placebo tablets, prepared by Laboratoires Boiron according to European Pharmacopoeia standards. Oral treatment (2 to 4 tablets per day) was started on day 3 after study enrollment and was continued for 12 weeks.

MAIN OUTCOME MEASURE

The main outcome measure was the hot flash score (HFS) compared before, during, and after treatment. Secondary outcome criteria were the quality of life (QoL) [measured using the Hot Flash Related Daily Interference Scale (HFRDIS)], severity of symptoms (measured using the Menopause Rating Scale), evolution of the mean dosage, and compliance. All adverse events (AEs) were recorded.

RESULTS

One hundred and one women were included in the final analysis (intent-to-treat population: BRN-01, n = 50; placebo, n = 51). The global HFS over the 12 weeks, assessed as the area under the curve (AUC) adjusted for baseline values, was significantly lower in the BRN-01 group than in the placebo group (mean \pm SD 88.2 \pm 6.5 versus 107.2 \pm 6.4; p = 0.0411). BRN-01 was well tolerated; the frequency of AEs was similar in the two treatment groups, and no serious AEs were attributable to BRN-01.

CONCLUSION

BRN-01 seemed to have a significant effect on the HFS, compared with placebo. According to the results of this clinical trial, BRN-01 may be considered a new therapeutic option with a safe profile for hot flashes in menopausal women who do not want or are not able to take hormone replacement therapy or other recognized treatments for this indication.

Trial registration number (EudraCT): 2009-016959-21.

Keywords: Hormone Replacement Therapy Vasomotor Symptom Homeopathic Treatment Homeopathic Medicine Menopause Rate Scale

Multimorbide Patienten | Multimorbid Patients

Heiner Frei

<https://doi.org/10.1016/j.homp.2014.09.001> Get rights and content

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Homeopathic treatment of multimorbid patients: a prospective outcome study with polarity analysis

HIGHLIGHTS

We examined the treatment outcome with polarity analysis in 50 multimorbid patients. 43 patients were successfully treated and reached an average improvement of 91%. The cost of homeopathic treatment is estimated to be 41% of a conventional therapy. Thus, homeopathy can play a substantial role in treating multimorbid patients.

BACKGROUND

The treatment of multimorbid patients who have a combination of three or more concurrent complaints is one of the core competencies of homeopathy. In this article we introduce the application of polarity analysis (PA) in multimorbidity. PA came to prominence through the Swiss homeopathic ADHD double-blind study, which successfully demonstrated a significant difference between highly dilute homeopathic remedies and placebo. PA enables homeopaths to calculate a relative healing probability, based on Boenninghausen's grading of polar symptoms. After its evaluation in the treatment of a variety of acute and chronic disease, which showed improved results compared to a conventional homeopathic approach, it was a challenge to test PA with multimorbid patients. Since such patients almost invariably have a multiple symptoms, the question was whether we can nevertheless successfully use Polarity Analysis or whether the method is rendered ineffective by the multitude of symptoms.

METHODS

We treated 50 multimorbid patients with PA and prospectively followed them over one year.

RESULTS

43 patients (86%) completed the observation period, achieving an average improvement of 91% in their initial symptoms. Six patients dropped out, and one did not achieve an improvement of 80%, and was therefore also counted as a treatment failure. The cost of homeopathic treatment was 41% of projected equivalent conventional treatment.

CONCLUSION

Polarity Analysis is an effective method for treating multimorbidity. The multitude of symptoms does not prevent the method from achieving good results. Homeopathy may be capable of taking over a considerable proportion of the treatment of multimorbid patients, at lower costs than conventional medicine.

KEYWORDS

Homeopathy Multimorbid patients Polarity analysis Prospective outcome study, Treatment costs

Diarrhoe bei Kindern | Diarrhea in Children

Jennifer Jacobs, Stephen S. Gloyd, James L. Gale, L. Margarita Jiménez, Dean Crothers
Pediatrics May 1994, VOLUME 93 / ISSUE 5

Treatment of Acute Childhood Diarrhea With Homeopathic Medicine: A Randomized Clinical Trial in Nicaragua;

OBJECTIVE

Acute diarrhea is the leading cause of pediatric morbidity and mortality worldwide. Oral rehydration treatment can prevent death from dehydration, but does not reduce the duration of individual episodes. Homeopathic treatment for acute diarrhea is used in many parts of the world. This study was performed to determine whether homeopathy is useful in the treatment of acute childhood diarrhea.

METHODS

A randomized double-blind clinical trial comparing homeopathic medicine with placebo in the treatment of acute childhood diarrhea was conducted in León, Nicaragua, in July 1991. Eighty-one children aged 6 months to 5 years of age were included in the study. An individualized homeopathic medicine was prescribed for each child and daily follow-up was performed for 5 days. Standard treatment with oral rehydration treatment was also given.

RESULTS

The treatment group had a statistically significant ($P < .05$) decrease in duration of diarrhea, defined as the number of days until there were less than three unformed stools daily for 2 consecutive days. There was also a significant difference ($P < .05$) in the number of stools per day between the two groups after 72 hours of treatment.

CONCLUSION

The statistically significant decrease in the duration of diarrhea in the treatment group suggests that homeopathic treatment might be useful in acute childhood diarrhea. Further study of this treatment deserves consideration.

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Metaanalyse: Diarrhoe bei Kindern | Diarrhea in Children

Jacobs J¹, Jonas WB, Jiménez-Pérez M, Crothers D.
Pediatr Infect Dis J. 2003 Mar;22(3):229-34.
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Homeopathy for childhood diarrhea: combined results and metaanalysis from three randomized, controlled clinical trials.

BACKGROUND

Previous studies have shown a positive treatment effect of individualized homeopathic treatment for acute childhood diarrhea, but sample sizes were small and results were just at or near the level of statistical significance. Because all three studies followed the same basic study design, the combined data from these three studies were analyzed to obtain greater statistical power.

METHODS

Three double blind clinical trials of diarrhea in 242 children ages 6 months to 5 years were analyzed as 1 group. Children were randomized to receive either an individualized homeopathic medicine or placebo to be taken as a single dose after each unformed stool for 5 days. Parents recorded daily stools on diary cards, and health workers made home visits daily to monitor children. The duration of diarrhea was defined as the time until there were less than 3 unformed stools per day for 2 consecutive days. A metaanalysis of the effect-size difference of the three studies was also conducted.

RESULTS

Combined analysis shows a duration of diarrhea of 3.3 days in the homeopathy group compared with 4.1 in the placebo group ($P = 0.008$). The metaanalysis shows a consistent effect-size difference of approximately 0.66 day ($P = 0.008$).

CONCLUSIONS

The results from these studies confirm that individualized homeopathic treatment decreases the duration of acute childhood diarrhea and suggest that larger sample sizes be used in future homeopathic research to ensure adequate statistical power.

Homeopathy should be considered for use as an adjunct to oral rehydration for this illness.

Neurodermitis | Atopic Dermatitis

Rossi E¹, Picchi M², Bartoli P², Panozzo M², Cervino C², Nurra L².

Homeopathy. 2016 Aug;105(3):217-224. doi: 10.1016/j.homp.2016.03.001. Epub 2016 Apr 13.

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Homeopathic therapy in pediatric atopic diseases: short- and long-term results.

AIM

To study the outcomes of atopic diseases in children treated with homeopathy at the Homeopathic Clinic of Lucca (Italy) and related long-term results after approximately an 8-year period.

MATERIALS AND METHODS

Our data derive from an observational longitudinal study carried out on 857 pediatric patients who consecutive visited from 1998 to 2014. Children with atopic diseases were 325 (37.9%), 126 (39%) suffered from atopic dermatitis, 72 (22%) from allergic rhinitis, and 127 (39%) from asthma.

Moreover, a long-term study was conducted on a subset of 107/165 patients, consecutively visited from 1998 to 2006, and with ≥ 5 years follow-up. The study also investigated the evolution of overall symptoms in those patients with a complex atopic symptomatology.

RESULTS

75.8% of atopic children had moderate or major improvement (67.1% with asthma as the primary disease; 84.2% rhinitis; 84.2% dermatitis). At re-evaluation after 5-10 years, complete remission of atopic symptoms was obtained in 70.1% of the children: 84.2% in dermatitis; 48.1% in allergic rhinitis; 71.4% in asthma. Children with two or three atopic diseases at the first visit were completely cured in 40% of cases.

CONCLUSION

The results seem to confirm that homeopathic medicine produces positive therapeutic response in atopic children.

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KEYWORDS:

Allergic rhinitis; Asthma; Atopic diseases; Dermatitis; Homeopathy; Short and long term results

Infektionen der oberen Atemwege | Upper Respiratory Tract Infection

Grimaldi-Bensouda L¹, Bégau B², Rossignol M³, Avouac B⁴, Lert F⁵, Rouillon F⁶, Bénichou J⁷, Massol J⁸, Duru G⁹, Magnier AM¹⁰, Abenhaim L¹¹, Guillemot D¹²
PLoS One. 2014 Mar 19;9(3):e89990. doi: 10.1371/journal.pone.0089990. eCollection 2014.

Management of upper respiratory tract infections by different medical practices, including homeopathy, and consumption of antibiotics in primary care: the EPI3 cohort study in France 2007-2008.

BACKGROUND

Prescribing of antibiotics for upper respiratory tract infections (URTI) varies substantially in primary care.

OBJECTIVES

To describe and compare antibiotic and antipyretic/anti-inflammatory drugs use, URTI symptoms' resolution and occurrence of potentially-associated infections in patients seeking care from general practitioners (GPs) who exclusively prescribe conventional medications (GP-CM), regularly prescribe homeopathy within a mixed practice (GP-Mx), or are certified homeopathic GPs (GP-Ho).

METHOD

The EPI3 survey was a nationwide population-based study of a representative sample of 825 GPs and their patients in France (2007-2008). GP recruitment was stratified by self-declared homeopathic prescribing preferences. Adults and children with confirmed URTI were asked to participate in a standardized telephone interview at inclusion, one-, three- and twelve-month follow up. Study outcomes included medication consumption, URTI symptoms' resolution and potentially-associated infections (sinusitis or otitis media/externa) as reported by patients. Analyses included calibration to account for non-respondents and groups were compared using multivariate analyses adjusting for baseline differences with a propensity score.

RESULTS

518 adults and children with URTI (79.3% rhinopharyngitis) were included (36.9% response rate comparable between groups). As opposed to GP-CM patients, patients in the GP-Ho group showed significantly lower consumption of antibiotics (Odds ratio (OR) = 0.43, 95% confidence interval (CI): 0.27-0.68) and antipyretic/anti-inflammatory drugs (OR = 0.54, 95% CI: 0.38-0.76) with similar evolution in related symptoms (OR = 1.16, 95% CI: 0.64-2.10). An excess of potentially-associated infections (OR = 1.70, 95% CI: 0.90-3.20) was observed in the GP-Ho group (not statistically significant). No difference was found between GP-CM and GP-Mx patients.

CONCLUSION

Patients who chose to consult GPs certified in homeopathy used less antibiotics and antipyretic/anti-inflammatory drugs for URTI than those seen by GPs prescribing conventional medications. No difference was observed in patients consulting GPs within mixed-practice. A non-statistically significant excess was estimated through modelling for associated infections in the GP-Ho group and needs to be further studied

Otitis Media

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The Pediatric Infectious Disease Journal: February 2001 - Volume 20 - Issue 2 - p 177-183

From the Department of Epidemiology, School of Public Health and Community Medicine, University of Washington (JJ), and Wallingford Pediatrics (DAS), Seattle, WA; and Evergreen Center for Homeopathic Medicine, Edmonds, WA (DC).

Accepted for publication Sept. 22, 2000.

Homeopathic treatment of acute otitis media in children: a preliminary randomized placebo-controlled trial

BACKGROUND

The use of antibiotics in the initial treatment of acute otitis media is currently being questioned. Homeopathy has been used historically to treat this illness, but there have been no methodologically rigorous trials to determine whether there is a positive treatment effect.

METHODS

A randomized double blind placebo control pilot study was conducted in a private pediatric practice in Seattle, WA. Seventy-five children ages 18 months to 6 years with middle ear effusion and ear pain and/or fever for no more than 36 h were entered into the study. Children received either an individualized homeopathic medicine or a placebo administered orally three times daily for 5 days, or until symptoms subsided, whichever occurred first. Outcome measures included the number of treatment failures after 5 days, 2 weeks and 6 weeks. Diary symptom scores during the first 3 days and middle ear effusion at 2 and 6 weeks after treatment were also evaluated.

RESULTS

There were fewer treatment failures in the group receiving homeopathy after 5 days, 2 weeks and 6 weeks, with differences of 11.4, 18.4 and 19.9%, respectively, but these differences were not statistically significant. Diary scores showed a significant decrease in symptoms at 24 and 64 h after treatment in favor of homeopathy ($P < 0.05$). Sample size calculations indicate that 243 children in each of 2 groups would be needed for significant results, based on 5-day failure rates.

CONCLUSION

These results suggest that a positive treatment effect of homeopathy when compared with placebo in acute otitis media cannot be excluded and that a larger study is justified.

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Übersichtsstudie zu Muskuloskeletalen Erkrankungen

Muskuloskeletale Disorders

Rossignol M1, Begaud B, Engel P, Avouac B, Lert F, Rouillon F, Bénichou J, Massol J, Duru G, Magnier AM, Guillemot D, Grimaldi-Bensouda L, Abenhaim L; EPI3-LA-SER group.
Pharmacoepidemiol Drug Saf. 2012 Oct;21(10):1093-101. doi: 10.1002/pds.3316. Epub 2012 Jul 11.
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Impact of physician preferences for homeopathic or conventional medicines on patients with musculoskeletal disorders: results from the EPI3-MSD cohort.

OBJECTIVE

The objective of this study was to assess the effect of physician practicing preferences (PPP) in primary care for homeopathy (Ho), CAM (Complementary and alternative medicines) with conventional medicine (Mx) or exclusively conventional medicine (CM) on patients with musculoskeletal disorders (MSDs), with reference to clinical progression, drug consumption, side effects and loss of therapeutic opportunity.

METHODS

The EPI3-MSD study was a nationwide observational cohort of a representative sample of general practitioners (GP) and their patients in France. Recruitment of GP was stratified by PPP, which was self-declared. Diagnoses and comorbidities were recorded by GP at inclusion. Patients completed a standardized telephone interview at inclusion, one, three and twelve months, including MSD-functional scales and medication consumption.

RESULTS

1153 MSD patients were included in the three PPP groups. Patients did not differ between groups except for chronicity of MSDs (> 12 weeks), which was higher in the Ho group (62.1%) than in the CM (48.6%) and Mx groups (50.3%).

The twelve-month development of specific functional scores was identical across the three groups after controlling for baseline score ($p > 0.05$). After adjusting for propensity scores, NSAID use over 12 months was almost half in the Ho group (OR, 0.54; 95%CI, 0.38-0.78) as compared to the CM group; no difference was found in the Mx group (OR, 0.81; 95% CI: 0.59-1.15).

CONCLUSION

MSD patients seen by homeopathic physicians showed a similar clinical progression when less exposed to NSAID in comparison to patients seen in CM practice, with fewer NSAID-related adverse events and no loss of therapeutic opportunity.

Übersichtsstudie bei chronischen Rückenschmerzen:

Chronischer Rückenschmerz | Chronic Low Back Pain

Witt CM1, Lüdtker R, Baur R, Willich SN

Clin J Pain. 2009 May;25(4):334-9. doi: 10.1097/AJP.0b013e31819050bb.

Homeopathic treatment of patients with chronic low back pain: A prospective observational study with 2 years' follow-up.

OBJECTIVES

To evaluate the details and effects of an individualized homeopathic treatment in patients with chronic low back pain in usual care.

METHODS

Prospective multicenter observational study. Consecutive patients beginning homeopathic treatment in primary care practices were evaluated over 2 years by using standardized questionnaires. Diagnoses (ICD-9) and symptoms with severity, health-related quality of life (QoL), medical history, consultations, homeopathic and conventional treatments, and other health service use were recorded.

RESULTS

One hundred twenty-nine adults (64.3% women, mean age 43.6 +/- 12.7 y) were treated by 48 physicians. The patients mainly had chronic low back pain (average duration 9.6 +/- 9.0 y) and other chronic diseases. Nearly all the patients (91.3%) had been pretreated. The initial case-taking took 113 +/- 36, and the case analysis took 31 +/- 38 minutes. The 7.4 +/- 8.1 subsequent consultations (duration: 23.7 +/- 15.2 min) cumulated to 204.5 +/- 184.6 minutes. The patients received an average of 6.8 +/- 6.3 homeopathic prescriptions. The severity of the diagnoses and complaints showed marked and sustained improvements with large effect sizes (Cohen's d from 1.67 to 2.55) and QoL improved accordingly (SF-36 physical component scale d = 0.33; mental component scale d = 0.54). The use of conventional treatment and health services decreased markedly: the number of patients using low back pain-related drugs was half of the baseline.

DISCUSSION

Classic homeopathic treatment represents an effective treatment for low back pain and other diagnoses. It improves health-related QoL and reduces the use of other healthcare services

Klinische Versorgungsforschung

Claudia M Witt,¹ Rainer Lüdtkke,² Roland Baur,¹ and Stefan N Willich¹

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Homeopathic medical practice: Long-term results of a cohort study with 3981 patients

Abstract

BACKGROUND

On the range of diagnoses, course of treatment, and long-term outcome in patients who chose to receive homeopathic medical treatment very little is known. We investigated homeopathic practice in an industrialized country under everyday conditions.

METHODS

In a prospective, multicentre cohort study with 103 primary care practices with additional specialisation in homeopathy in Germany and Switzerland, data from all patients (age >1 year) consulting the physician for the first time were observed. The main outcome measures were: Patient and physician assessments (numeric rating scales from 0 to 10) and quality of life at baseline, and after 3, 12, and 24 months.

RESULTS

A total of 3,981 patients were studied including 2,851 adults (29% men, mean age 42.5 ± 13.1 years; 71% women, 39.9 ± 12.4 years) and 1,130 children (52% boys, 6.5 ± 3.9 years; 48% girls, 7.0 ± 4.3 years). Ninety-seven percent of all diagnoses were chronic with an average duration of 8.8 ± 8 years. The most frequent diagnoses were allergic rhinitis in men, headache in women, and atopic dermatitis in children. Disease severity decreased significantly ($p < 0.001$) between baseline and 24 months (adults from 6.2 ± 1.7 to 3.0 ± 2.2 ; children from 6.1 ± 1.8 to 2.2 ± 1.9). Physicians' assessments yielded similar results. For adults and young children, major improvements were observed for quality of life, whereas no changes were seen in adolescents. Younger age and more severe disease at baseline were factors predictive of better therapeutic success.

CONCLUSION

Disease severity and quality of life demonstrated marked and sustained improvements following homeopathic treatment period. Our findings indicate that homeopathic medical therapy may play a beneficial role in the long-term care of patients with chronic diseases.

BACKGROUND

Homeopathy is one of the most frequently used and controversial systems of complementary and alternative medicine. It is based on the 'principle of similars', whereby highly diluted preparations of substances that cause symptoms in healthy individuals are used to stimulate healing in patients who have similar symptoms when ill [1]. When a single homeopathic remedy is selected based on a patient's total symptom picture, it is called 'classical' homeopathy [2]. According to a survey in the US [3], the proportion of patients obtaining homeopathic care has quadrupled in the last seven years. A survey in Britain [4] estimated that annual expenditures reached £34.04 million (out-of-pocket £30.74 million, NHS £3.3 million). For Germany, the country in which classical homeopathy originated, a recent survey demonstrated that approximately 10% of men and 20% of women in the general population used homeopathic medicines during the previous year [5]. General trends show a rise in the number of individuals utilising naturopathic and homeopathic therapeutic methods [6].

The General Medical Council in Germany grants an official certification in homeopathy to physicians upon successful completion of a three-year-long training programme. Approximately 4,500 physicians in Germany hold this additional certification [6]. However, with the exception of some randomised, controlled trials including patients with selected diagnoses [2,7] there is no data on the health care offered by classical homeopathic medical practices. Therefore, it is impossible to assess the state of homeopathic health care and its effectiveness. We designed this project with the goal of systematically collecting data in the area of homeopathic health care for the first time in Germany. The aim of the present study was to determine the spectrum of diagnoses and treatments, as well as the course of disease over time among patients who chose to receive homeopathic treatment.

METHODS

Patients were included consecutively in this prospective, multi-centre observational study upon their first consultation with a participating physician and were followed up for a total of 24 months. Evaluations were made using standardised questionnaires. In order to provide as representative a picture of homeopathic health care as possible, patients were included in the study regardless of their diagnosis. Patients were eligible for the study if they were consulting the participating physician for the first time and were at least 1 year of age. In order to participate in the study, physicians were required to have passed certified training in classical homeopathy and at least three years of experience in its practice. A total of 187 physicians belonging to four different working groups were contacted either by post or telephone and informed about the study. Of these, 103 physicians chose to participate. Each participating physician was trained in study procedures and was subject to at least one monitoring visit during the study period. All study participants provided written, informed consent, and the study protocol was approved by the appropriate ethics review boards.

OUTCOME MEASURES

For patients, we developed different questionnaires for three different age groups: 1–6 years of age, 7–16 years of age, adults (> 16 years of age). All questionnaires were designed to document sociodemographic data, as well as information on prior medical history, patient symptoms and complaints, quality of life, and the use of any treatment other than homeopathy. At baseline, patients recorded the complaints that led them to consider homeopathic treatment.

Independently of their physicians, patients rated the severity of their complaints on a numeric rating scale (0 = no complaints, 10 = maximum severity) [8]. All complaints listed by patients in their baseline questionnaire were transferred to their follow-up questionnaires by the study office personnel. This ensured that each baseline complaint was assessed at each subsequent follow-up. For children between 1 and 6 years of age, the KITA questionnaire [9] was used to assess general health-related quality of life. It was completed by the children's parents. Patients between 7 and 16 years of age completed the KINDL questionnaire [10,11]. In addition, parents were asked to provide the required medical information. For the adults, general health-related quality of life was assessed using the MOS SF-36 questionnaire [12]. The results of the SF-36 are presented in normalised scores, the results being scaled in such a way that the normal German population has a mean score of 0 and a standard deviation of 1. The first questionnaire was distributed to the patients by the study physician and completed prior to the start of therapy (baseline). Patients sent their completed questionnaires to the study office in sealed envelopes. Follow-up questionnaires were sent to all patients by the study office at 3, 12, and 24 months.

For physicians, we developed a standardised questionnaire that allowed for continuous documentation during the treatment/follow-up period (24 months), as well as standardised points of assessment at 0, 3, 12 and 24 months. At each of these time points, the severity of a maximum of 4 diagnoses and maximum of 8 symptoms was rated by participating physicians using a numerical rating scale [8]. This information was then forwarded to the study office. The type of homeopathic treatment, the use of any conventional therapy, as well as any referrals to other physicians were recorded on a continuous basis.

STATISTICS

Data was double entered manually into an ACCESS[®] database and subsequently compared using the SAS[®] system followed by plausibility data checks if necessary. The diagnoses, documented by study physicians, were encoded in ICD-9 format and recorded by two specially trained study staff members using DIACOS.[®] Statistical analysis was performed using SAS/STAT[®] software (Version 8.2).

Data for adults (> 16 years) and for children/adolescents were analysed separately. In order to calculate the average severity of the physicians' diagnoses, we took the four diagnoses named first for each patient during the baseline examination. For each of the follow-up assessment points (i.e. at 3, 12, and 24 months) we ascertained the respective severity ratings made by study physicians.

All results reported here are based on the intention-to-treat approach, i.e. each included patient entered the final analyses. If patients dropped out or withdrew from the study we replaced the respective missing values: baseline complaints that had been cured were given a severity rating of 0 in all following examinations. For patients who died during the study, we inserted the maximum severity rating of 10. Other missing values were multiply imputed following the suggestions of Rubin [13]. Instead of filling in a *single* value as a substitute for a missing value, multiple imputation is a strategy by which each missing value is replaced simultaneously by a *set* of plausible values that represents the uncertainty about the right value to impute. Thus, the missing values are filled in several times generating several distinct data

tables, each with a complete set of data without any missing value. These complete data tables are analyzed separately using appropriate statistical models. Afterwards, the results from all statistical analyses are pooled to generate treatment effects and p-values. In our study we used the MCMC (Markov chain Monte Carlo) replacement method and created 5 multiple imputed data tables.

For each imputed data set, treatment effects were estimated on the basis of generalized linear regression models. Generalized linear regression models are flexible and powerful tools to describe data from cohort studies [14]. They are generalizations of the well known and often applied multiple regression models which often appear to be too simple to describe longitudinal data adequately. A generalized linear model is best described by two components. First, the mean course of the outcome, and second, the correlation structure for measurements taken at the same individual at different times. In our study we divided the 2-year follow-up period into two parts. During the first part (months 0–3) we assumed that mean outcome increases (or decreases) linearly. For the second part (months 3–21) we assumed that the mean outcome increases (or decreases) according to a quadratic term. Moreover, we assumed that the correlation between two measurements can be described by a simple exponential function. This essentially means, that the correlation only depends from the time span between the two measurements, and it decreases the bigger this time span is. This approach is completely analogous to the recommendations given by Diggle, Liang, and Zeeger in their standard text book on the analysis of longitudinal data [14].

Subgroup analyses are based on essentially the same statistical approach adding the respective factors as a fixed covariate into the models. For subgroup analyses adults' and children's data were pooled.

Usually, patients for clinical studies are not selected randomly from a target population but according to some selection criteria that sample patients according to extreme measurements (high blood pressure, severe pain, low quality of life, ...). This inevitably leads to regression-to-the-mean, a statistical phenomenon that makes natural variation look like real changes [15]. Separating regression-to-the-mean effects from true treatment effects can be difficult but is at least feasible when the mean and the standard deviation of the target population are known. In this situation it is possible to calculate the expected outcome for each patient when regression-to-the-mean occurs [16]. In our study we made a rather conservative assumption on the target population (chronically ill patients seeking homeopathic care): to have the same quality of life as the general German population (i.e. a mean SF-36 score of 0 and a standard deviation of 1). From this we calculated the expected regression-to-the mean effect and compared it to the actually observed change of the SF-36 scores.

RESULTS

A total of 103 physicians participated in the study (51 male, 45 ± 7 years of age; 52 female, 45 ± 7 years of age). Twenty-six percent of the participating physicians were specialists (10% internists, 9% paediatricians, 7% other) and 74% were general practitioners. The average duration of overall medical practice was 17.4 ± 8.4 years with 9.0 ± 4.4 years of practice in homeopathy (range 3–20 years). Forty percent of the physicians were certified to work in the public health care system, and 60% were in private practice.

Patients were recruited for the study between September 1997 and December 1999. Of the patients who met the inclusion criteria, 3981 (68%) chose to participate and were included in the study (for patient selection see Figure Figure1).¹). Of these, 2851 were adults (71% women) and 1130 were children (48% girls). The baseline characteristics are listed in Table Table1¹.

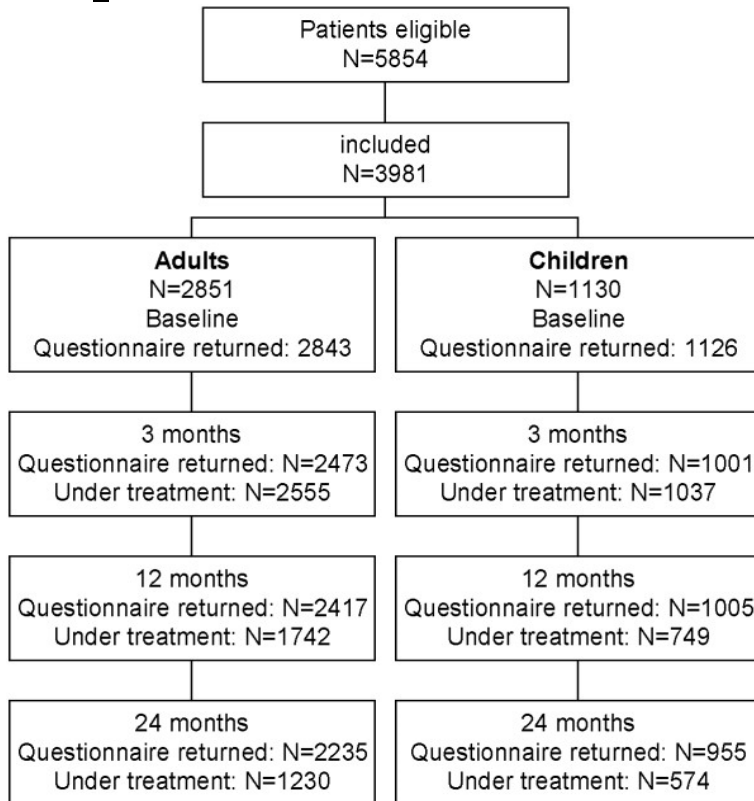


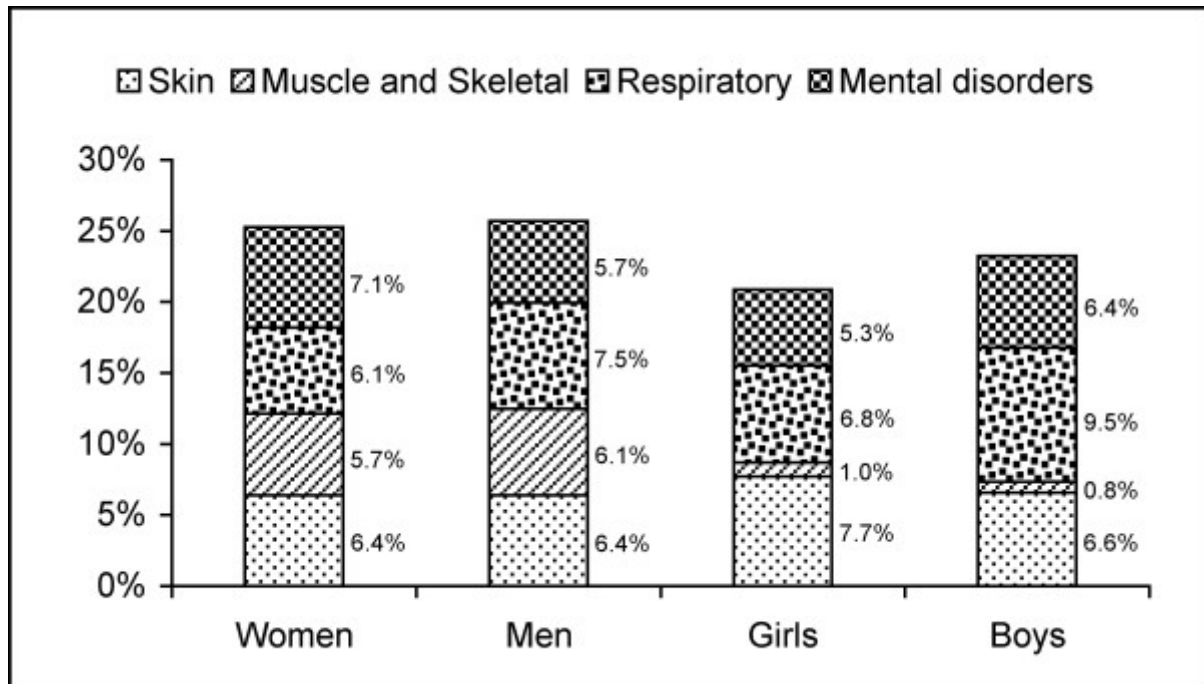
Table 1
Baseline characteristics of study population

	Adults	Children
Gender (% female)	70.8	48.3
Age (years, mean \pm std)	40.7 \pm 12.7	6.7 \pm 4.1
Marital status (% living in partnership)	84.0	/
Education (% attending school >10 years)	85.0	/
Belief in homeopathy (%)	65.7	68.6 [†]
Duration of disease (years, mean \pm std)	10.3 \pm 9.8	4.3 \pm 3.7
Intake of conventional drugs (%)	50.2	31.7

[†] Parents' perspective

On average, the homeopathic physicians made 2.6 ± 1.2 diagnoses per patient (2.8 ± 1.1 in adults, 2.3 ± 1.1 in children). Ninety-seven percent of all diagnoses were classified by these physicians as chronic with a median duration of 4.3 ± 2.7 years in children and 10.3 ± 9.8 years in adults. Almost all patients had received conventional treatment (95%) or had already contacted another physician (95%) prior to the start of this study. The most common diagnosis in women was migraine (9.7%), in men allergic rhinitis (10.3%), and in children of both

genders atopic dermatitis (20%), for details see [17]. For the most common disease groups see Figure Figure22.



Most common medical complaints as reported by the homeopathy physicians (in % of documented complaints).

All patients underwent an initial homeopathic anamnesis, lasting an average of 2.0 ± 0.7 hours. Following enrolment in the study, patients had to wait an average of 57 ± 84 days before undergoing the initial anamnesis. During the 24-month observation period, patients consulted their physicians an average of 7.8 ± 8.4 times. During the study period, half of the patients (50.3%, adults: 50.8%, children 48.9%) noted additional visits to non-study physicians (gynaecologists and dentists excluded). The intake of conventional medication decreased from 45.0% at baseline (adults: 50.2%, children 31.7%) to 26.8% after 24 months (adults: 31.8%, children 14.2%).

According to patient assessments, disease severity decreased significantly between baseline and 12 months, as well as between 12 months and 24 months (see Table Table2).2). According to physician assessments, 25.7% (adults: 21.9%, children: 37.6%) of the diagnoses were no longer present at 24 months, whereas patients judged 23.0% (adults 19.7%, children 32.8%) of the medical complaints to have resolved by this point. Thirteen percent of the patients documented that they had no complaints whatsoever at 24 months.

Table 2

Course of outcome parameters and estimated mean changes of outcome parameters

	Base- line	3 mon- ths	12 months	24 month	Estimated changes compared to baseline [†]		
					Δ 3 mon- ths	Δ 12 mon- ths	Δ 24 mon- ths
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean (95%CI)	mean (95%CI)	mean (95%CI)
Adults							
Patients assess- ments (NRS) ‡	6.2 ± 1.7	3.8 ± 2.2*	3.3 ± 2.1*	2.9 ± 2.2*	-2.4 (-2.5 to -2.3)	-2.8 (-2.9 to -2.7)	-3.1 (-3.2 to -3.0)
Physicians assess- ments (NRS) ‡	6.0 ± 1.6	3.9 ± 2.1*	2.8 ± 2.1*	2.1 ± 2.0*	-2.1 (-2.2 to -2.0)	-3.1 (-3.2 to -3.0)	-3.7 (-3.8 to -3.6)
SF-36 QoL physi- cal scale	46.5 ± 10.1	49.1 ± 9.5*	50.1 ± 9.6*	50.7 ± 9.5*	2.6 (2.3 to 2.9)	3.5 (3.0 to 3.9)	4.1 (3.5 to 4.6)
SF-36 QoL mental scale	39.3 ± 11.8	44.6 ± 10.8*	45.5 ± 10.8*	46.4 ± 10.6*	5.6 (5.2 to 6.0)	6.2 (5.7 to 6.7)	6.9 (6.3 to 7.6)
Children							
Patients assess- ments (NRS) ‡	6.1 ± 1.8	3.2 ± 2.3*	2.5 ± 2.1*	2.2 ± 2.0*	-3.1 (-3.3 to -2.9)	-3.5 (-3.7 to -3.4)	-3.9 (-4.0 to -3.7)
Physicians assess- ments (NRS) ‡	5.9 ± 1.7	3.2 ± 2.2*	2.0 ± 1.5*	1.5 ± 1.8*	-2.7 (-2.8 to -2.6)	-3.8 (-4.0 to -3.7)	-4.4 (-4.6 to -4.3)
KINDL QoL	69.3 ± 13.3	72.1 ± 12.6	68.0 ± 9.2	67.3 ± 9.9*	2.7 (1.7 to 3.7)	-0.4 (-1.5 to 0.8)	-2.2 (-3.6 to -0.8)
KITA QoL men- tal/physical dimen- sion	67.6 ± 16.9	75.4 ± 14.6*	77.0 ± 14.1*	77.5 ± 14.3*	8.3 (6.6 to 10.0)	9.3 (7.7 to 10.8)	10.0 (8.3 to 11.6)
KITA QoL aspects of daily living	58.6 ± 18.3	66.9 ± 15.9*	69.1 ± 16.7*	70.6 ± 16.0*	8.5 (7.2 to 9.8)	10.4 (8.8 to 12.0)	11.6 (9.7 to 13.5)

[Open in a separate window](#)
[†] estimations are based on generalised linear models, see text; ‡ = lower values indicate better status and negative Δ indicates improvement

QoL = quality of life; NRS = numeric rating scale, * p < 0.001 versus baseline

In adults, large improvements in quality of life were observed on both component scales (mental and physical) during the first three months of treatment, and continued to improve during the course of the study (see Table Table2).2). Even with the pessimistic assumption that the test-retest correlation of the SF-36 is only 0.7 and that the study population is no more ill than a random sample of the general population, one could expect an improvement of only 3.8 (1.2) score points on the mental (physical) component scale, attributable to regression-to-the-mean [16], markedly lower than the 5.6 (2.6) score points observed in our study (Table (Table2).2).

Statistically, the baseline quality of life of non-completers was not significantly lower than in other patients (p-values: MCS: $p = 0.37$; PCS: $p = 0.48$, Wilcoxon-tests).

Quality of life in young children (age 1–6 years) also improved markedly during the observation period (Table (Table2).2), having already risen during the first three months of study therapy as measured on both scales of the KITA questionnaire (mental-physical dimension and aspects of daily living, each $p < 0.001$, see Table Table2).2). These improvements continued over the course of treatment ($p < 0.001$, see Table Table2).2). In school children and adolescents, however, an improvement in quality of life was only visible during the first three months of study therapy ($p < 0.001$, see Table Table2).2).

The diagnosis had no relevant influence on the changes in patient complaints or quality of life as measured in this investigation.

In patient and physician assessments, younger patients showed greater improvements than did older patients and more severe disease at baseline was followed by greater improvements compared to less severe disease (see Table Table3).3). Gender, duration of disease and belief in homeopathy had only a minor influence on improvements.

Table 3

 Subgroup analyses for patients and physicians assessments (mean changes of outcome parameters after 24 months compared to baseline, negative Δ indicates improvement)

	Patients assessments (NRS)			Physicians assessments (NRS)		
	Mean [†]	95%-CI	p value*	Mean [†]	95%-CI	p value*
Total (n = 3981)	-3.3	-3.4 to -3.2		-3.9	-4.0 to -3.8	0,060
Gender						
Female (n = 2560)	-3.4	-3.5 to -3.2		-3.9	-4.0 to -3.8	
Male (n = 1412)	-3.3	-3.4 to -3.1	0.387	-3.9	-4.0 to -3.8	0,060
Age groups (years)						
<10 (n = 839)	-4.0	-4.2 to -3.8		-4.4	-4.6 to -4.2	
10–19 (n = 355)	-3.5	-3.7 to -3.2	<0.001	-4.3	-4.5 to -4.0	0.149
20–39 (n = 1456)	-3.4	-3.6 to -3.3	<0.001	-3.7	-3.8 to -3.6	<0.001
40–59 (n = 1041)	-2.8	-3.8 to -2.0	<0.001	-3.6	-3.8 to -3.5	<0.001
≥ 60 (n = 281)	-2.6	-2.9 to -2.2	<0.001	-3.5	-3.8 to -3.2	<0.001
Baseline severity of disease						
NRS < 6.0 (n = 1660)	-2.1	-2.3 to -2.0		-3.1	-3.2 to -3.0	
NRS ≥ 6.0 (n = 2310)	-4.1	-4.2 to -4.0	<0.001	-4.6	-4.7 to -4.5	<0.001
Duration of disease in adults (years)						
< 10 (n = 1878)	-3.2	-3.4 to -3.1		-3.7	-3.8 to -3.6	
≥ 10 (n = 927)	-2.9	-3.1 to -2.7	<0.001	-3.6	-3.7 to -3.4	0.043
Intake of conventional drugs at baseline						
Yes (n = 1788)	-3.3	-3.5 to -3.2		-3.8	-3.9 to -3.7	
No (n = 2188)	-3.3	-3.5 to -3.2	0.157	-3.9	-4.0 to -3.9	0.029
Belief in homeopathy						
Strong (n = 2656)	-3.4	-3.5 to -3.1		-3.9	-4.0 to -3.8	
Weak (n = 1316)	-3.1	-3.3 to -3.0	<0.001	-3.8	-3.9 to -3.7	0.563

[Open in a separate window](#)
[†] estimations are based on generalised linear models, NRS = numeric rating scale; * per item each subgroup compared to the first listed subgroup

DISCUSSION

Patient and physician assessments of disease severity and quality of life consistently demonstrated substantial improvements following homeopathic treatment, which were maintained through 24 months' follow up. Improvements were more pronounced in younger patients and in those with greater disease severity compared to older patients and those with less severe disease at baseline.

To our knowledge, the present study is the first to evaluate systematically the range of diagnoses and therapies in classical homeopathic medical practices in Germany and Switzerland. In addition, the study provided information on the course of illness in patients receiving homeopathic treatment, as assessed by patients and physicians.

The methodological strengths of our study include consecutive enrolment of a large sample size, the participation of approximately 2% of all physicians certified to practice homeopathy in Germany and 28% of all members of the Hahnemann Association (an organisation for physicians practicing only 'classical' homeopathy) and the use of standardised outcome instruments also used in studies on conventional therapy.

One limitation of our study is that the observed effects cannot be categorized with respect to specificity, i.e. we cannot draw conclusions as to the beneficial mechanisms. Furthermore patients were allowed to use conventional therapies during the study period in addition to homeopathic treatment. Thus, the observed improvement cannot be attributed to homeopathic treatment alone. The aim of the investigation, however, was not to test the effectiveness of homeopathic treatment alone, but rather provide systematic and detailed information about the current status of homeopathic medical care in routine practice and its effectiveness.

These data may also be helpful in the planning of further research projects on homeopathy. The effects observed by patient and the physician assessment, as well as those seen with regard to quality of life, deserve additional comments. The average severity of the chronic diseases was reduced by approximately 50% after only 3 months of homeopathic treatment, and remained around this level during the follow-up period. Physician assessments tended to be more positive than patient assessments.

The improvements we observed in our patients cannot be attributed solely to regression-to-the-mean, because the improvements were greater than could be expected even under conservative model assumptions. This is supported by the fact that patients did not visit the study physicians when they were feeling the worst, but rather after a long waiting period. A strength of this study is that patients with all diagnoses were included. Therefore, no disease-specific measurement instruments could be used. To assess the severity of different medical complaints, there is no other generally accepted measuring instrument available. Instead numerical rating scales [8] were applied, which would allow for the determination of illness severity in a diagnosis-independent manner.

Compared to the other quality of life questionnaires used in our study, the KINDL questionnaire for the age group 7 to 16 years was not sensitive to change, as has been shown in other studies [18,19]. Other explanations might be that children adapt easier to perceived quality of life and that the dimensions of Quality of life used for adults are not transferable to children. However, there is no other generally accepted measuring instrument available in German-speaking countries.

In the range of baseline diagnoses, chronic illnesses clearly predominated (>95% of diagnoses). Among these, headache and atopic disease (allergic rhinitis, asthma and atopic dermatitis) were the most common diagnoses. As the clinical histories of our patients showed, most

of our patients decided to consult a homeopathic physician only after having received conventional treatment. This, together with the extensive initial case taking and the reputation of homeopathy as a "medicine designed to treat the individual as a whole" causes a selection for chronic illnesses.

We were unable to confirm the common notion that homeopathy is frequently used for trivial complaints or diseases. The duration of disease in study patients was very long and their symptoms were, on average, of moderate severity.

In this study we were not able to evaluate different types of homeopathic strategies. For quality assurance purposes, we avoided selecting a random sample of homeopathic physicians for the study, choosing instead to recruit physicians schooled and certified in 'classical' homeopathy. The results of our study are, therefore, representative only for the classical type of homeopathy that was practised by participating physicians. Compared to conventional medical practices, headache and atopic disease (allergic rhinitis, asthma and atopic dermatitis) were the most common diagnoses in homeopathic practices (as opposed to hypertension, hyperlipidemia and low back pain in 70,000 patients treated conventionally) [9]. An American study [20] found asthma, depression, otitis media, and allergic rhinitis to be the most common diagnoses treated in homeopathic practices, compared to hypertension, upper respiratory tract infection, otitis media and diabetes mellitus, which were treated most commonly in conventional practices.

A health insurance company project that included about 900 patients treated with homeopathy in routine care [21] showed an improvement in quality of life and in physician assessment. In Gütthlin's study [21], however, only physicians certified to work in the public health care system were able to participate. Homeopaths working in private practices (i.e. the great majority in Germany) were excluded. The advantage of the present study is that doctors in private practice were also included, thus providing a more detailed and broader basis for describing the current status of homeopathic health care. Another controlled study in cooperation with a German health insurance company [22], indicated similar overall effectiveness of homeopathically versus conventionally treated patients for selected diagnoses and in some groups, superiority of homeopathic treatment.

CONCLUSION

We evaluated for the first time the range of diagnoses and therapies at medical practices offering classical homeopathic treatment in Germany and Switzerland. The findings of our study demonstrate that patients who seek homeopathic treatment are primarily those suffering from long-standing, chronic disease. Both according to physician and patient assessments, the severity of complaints decreased markedly over the 24-month observation period. Younger patients and those with more severe disease appear to benefit most from homeopathic treatment. Among adults and children, we observed an increase in quality of life. Our findings indicate that homeopathic medical therapy may play a beneficial role in the long-term care of patients with chronic diseases.

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

CW participated in the design of the study, coordination and statistical analysis. RL participated in its design and performed the statistical analysis. RB participated in the design of the study and data acquisition. SNW conceived of the study, and participated in its design and statistical analysis and had the overall scientific responsibility. All authors helped to draft the manuscript, read and approved the final manuscript.

Pre-publication history

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<http://www.biomedcentral.com/1471-2458/5/115/prepub>

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J Altern Complement Med. 2005 Oct;11(5):793-8.[^]
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PMID: 16296912 DOI: 10.1089/acm.2005.11.793

Homeopathic treatment for chronic disease: a 6-year, university-hospital outpatient observational study.

Abstract

OBJECTIVE

The aim of this study was to assess health changes seen in routine homeopathic care for patients with a wide range of chronic conditions who were referred to a hospital outpatient department.

DESIGN

This was an observational study of 6544 consecutive follow-up patients during a 6-year period.

SETTING

Hospital outpatient unit within an acute National Health Service (NHS) Teaching Trust in the United Kingdom.

PARTICIPANTS

Every patient attending the hospital outpatient unit for a follow-up appointment over the study period was included, commencing with their first follow-up attendance.

MAIN OUTCOME MEASURE

Outcomes were based on scores on a 7-point Likert-type scale at the end of the consultation and were assessed as overall outcomes compared to the initial baseline assessments.

RESULTS

A total of 6544 consecutive follow-up patients were given outcome scores. Of the patients 70.7% (n = 4627) reported positive health changes, with 50.7% (n = 3318) recording their improvement as better (+2) or much better (+3).

CONCLUSIONS

Homeopathic intervention offered positive health changes to a substantial proportion of a large cohort of patients with a wide range of chronic diseases. Additional observational research, including studies using different designs, is necessary for further research development in homeopathy.

COMMENT IN

- Observational study on homeopathic treatment. [J Altern Complement Med. 2006]

Keil T¹, Witt CM, Roll S, Vance W, Weber K, Wegscheider K, Willich SN.
Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center
Berlin, D-10098 Berlin, Germany. thomas.keil@charite.de, Complement Ther Med. 2008 Feb;16(1):15-
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Oct;21(10):1093-101. doi: 10.1002/pds.3316. Epub 2012 Jul 11.

Homoeopathic versus conventional treatment of children with eczema: a comparative cohort study.

Abstract

OBJECTIVES

To assess, over a period of 12 months, whether homoeopathic treatment could influence eczema signs/symptoms and quality of life (QoL) compared with conventional treatment.

DESIGN

PROSPECTIVE MULTI-CENTRE COHORT STUDY.

SETTING

Children with eczema aged 1-16 years were recruited from primary care practices.

INTERVENTIONS

Conventional versus homoeopathic treatment.

OUTCOME MEASURES

Patients (or parents) assessed eczema symptoms by numerical rating scales as well as disease-specific Atopie Lebensqualitaets-Fragebogen (ALF) and general quality of life (KINDL, KITA) at 0, 6 and 12 months.

RESULTS

A total of 118 children were included: 54 from homoeopathic (mean age \pm S.D. was 5.1 \pm 3.3 years; 56% boys) and 64 from conventional practices (6.2 \pm 3.8 years; 61% boys). Eczema symptoms (assessed by patients or their parents) improved from 0 to 12 months for both treatment options, but did not differ between the two groups: 3.5-2.5 versus 3.4-2.1; $p=0.447$ (adjusted). Disease-related quality of life improved in both groups similarly. In the subgroup of children aged 8-16 years the general quality of life showed a better trend for conventional treatment compared with homoeopathic treatment ($p=0.030$).

CONCLUSIONS

This observational study is the first long-term prospective investigation to compare homoeopathic and conventional treatment of eczema in children. Over a period of 12 months, both therapy groups improved similarly regarding perception of eczema symptoms (assessed by patients or parents) and disease-related quality of life.

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PMID: 15022657, Complement Ther Med. 2003 Dec;11(4):243-8.

NHS patients' perspective on complementary medicine: a survey.

Abstract

OBJECTIVES

To examine patients' reasons for seeking complementary and alternative medicine (cam) in the national health service, including the nature and duration of the patient's main health problem, the impact of cam on this, satisfaction with clinical care, and usage of conventional prescription medication.

DESIGN

survey (n=499).

SETTING

Out-patient department, the royal London homeopathic hospital, a national health service facility dedicated to cam.

RESULTS

Five hundred and six questionnaires were returned, 499 were analysed. patients' most frequent reasons for seeking cam were that other treatment had not helped, and concerns about or experience of adverse treatment reactions. two hundred and ninety-seven patients (63%) had had their main problem for more than 5 years. musculoskeletal system problems were the most frequent diagnostic group (n=151, 32%). satisfaction with clinical care was high (443/490: 90%). three hundred and eighty patients (81%) indicated their main problem had improved very much, moderately or slightly. Of the 262 patients who had been taking prescription medicines when they first attended, 76 (29%) had stopped, and 84 (32%) had reduced their intake.

CONCLUSIONS

The results suggest that orthodox medicine is not meeting the needs of some patients and that cam may wholly or partly substitute for conventional medicines. Most patients indicated their problem had improved with cam. Implications for future research are discussed.

Zusammenfassung HRI

Eine Erhebung unter 500 Patienten am Royal London Homeopathic Hospital (RLHH) zeigte, dass viele Patienten die Einnahme schulmedizinischer Medikamente nach einer homöopathischen Behandlung verringern oder diese sogar absetzen konnten. Der Grad der Besserung variierte in Abhängigkeit von der Diagnose. Beispielsweise berichteten 72 % der Patienten mit Hautbeschwerden, sie hätten ihre schulmedizinische Medikation absetzen oder senken können; bei Krebspatienten konnte die schulmedizinische Medikation nicht reduziert werden. Die Studie zeigte zudem, dass viele Patienten sich homöopathischen Therapien zuwenden, da sie Bedenken hinsichtlich der Sicherheit einer schulmedizinischen Behandlung haben.

Thompson EA¹, Mathie RT, Baitson ES, Barron SJ, Berkovitz SR, Brands M, Fisher P, Kirby TM, Leckridge RW, Mercer SW, Nielsen HJ, Ratsey DH, Reilly D, Roniger H, Whitmarsh TE.

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Towards standard setting for patient-reported outcomes in the NHS homeopathic hospitals.

Abstract

INTRODUCTION

We report findings from a pilot data collection study within a programme of quality assurance, improvement and development across all five homeopathic hospitals in the UK National Health Service (NHS).

AIMS

(1) To pilot the collection of clinical data in the homeopathic hospital outpatient setting, recording patient-reported outcome since first appointment; (2) to sample the range of medical complaints that secondary-care doctors treat using homeopathy, and thus identify the nature and complexity of complaints most frequently treated nationally; (3) to present a cross section of outcome scores by appointment number, including that for the most frequently treated medical complaints; (4) to explore approaches to standard setting for homeopathic practice outcome in patients treated at the homeopathic hospitals.

METHODS

A total of 51 medical practitioners took part in data collection over a 4-week period. Consecutive patient appointments were recorded under the headings: (1) date of first appointment in the current series; (2) appointment number; (3) age of patient; (4) sex of patient; (5) main medical complaint being treated; (6) whether other main medical complaint(s); (7) patient-reported change in health, using Outcome Related to Impact on Daily Living (ORIDL) and its derivative, the ORIDL Profile Score (ORIDL-PS; range, -4 to +4, where a score ≤ -2 or $\geq +2$ indicates an effect on the quality of a patient's daily life); (8) receipt of other complementary medicine for their main medical complaint.

RESULTS

The distribution of patient age was bimodal: main peak, 49 years; secondary peak, 6 years. Male:female ratio was 1:3.5. Data were recorded on a total of 1797 individual patients: 195 first appointments, 1602 follow-ups (FUs). Size of clinical service and proportion of patients who attended more than six visits varied between hospitals. A total of 235 different medical complaints were reported. The 30 most commonly treated complaints were (in decreasing order of frequency): eczema; chronic fatigue syndrome (CFS); menopausal disorder; osteoarthritis; depression; breast cancer; rheumatoid arthritis; asthma; anxiety; irritable bowel syndrome; multiple sclerosis; psoriasis; allergy (unspecified); fibromyalgia; migraine; premenstrual syndrome; chronic rhinitis; headache; vitiligo; seasonal allergic rhinitis; chronic intractable pain; insomnia; ulcerative colitis; acne; psoriatic arthropathy; urticaria; ovarian cancer; attention-

deficit hyperactivity disorder (ADHD); epilepsy; sinusitis. The proportion of patients with important co-morbidity was higher in those seen after visit 6 (56.9%) compared with those seen up to and including that point (40.7%; $P < 0.001$). The proportion of FU patients reporting ORIDL-PS $\geq +2$ (improvement affecting daily living) increased overall with appointment number: 34.5% of patients at visit 2 and 59.3% of patients at visit 6, for example. Amongst the four most frequently treated complaints, the proportion of patients that reported ORIDL-PS $\geq +2$ at visit numbers greater than 6 varied between 59.3% (CFS) and 73.3% (menopausal disorder).

CONCLUSIONS

We have successfully piloted a process of national clinical data collection using patient-reported outcome in homeopathic hospital outpatients, identifying a wide range and complexity of medical complaints treated in that setting. After a series of homeopathy appointments, a high proportion of patients, often representing "effectiveness gaps" for conventional medical treatment, reported improvement in health affecting their daily living. These pilot findings are informing our developing programme of standard setting for homeopathic care in the hospital outpatient context.

Zusammenfassung HRI

Eine Beobachtungsstudie am Bristol Homeopathic Hospital umfasste mehr als 6.500 konsekutive Patienten mit über 23.000 Patientenbesuchen in einem Zeitraum von sechs Jahren. 70 % der nachuntersuchten Patienten berichteten, dass sich ihr Gesundheitszustand gebessert hätte; 50 % stuften die Besserung sogar als „deutlich“ ein. Am ausgeprägtesten war dies bei kindlichem Ekzem oder Asthma sowie bei entzündlichen Darmerkrankungen, Reizdarm, Wechseljahresbeschwerden und Migräne.

Witt C, Keil T, Selim D, Roll S, Vance W, Wegscheider K, Willich SN.
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10098 Berlin, Germany. claudia.witt@charite.de,
Complement Ther Med. 2005 Jun;13(2):79-86.
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Outcome and costs of homoeopathic and conventional treatment strategies: a comparative cohort study in patients with chronic disorders.

OBJECTIVES

To evaluate the effectiveness of homoeopathy versus conventional treatment in routine care.

DESIGN

Comparative cohort study.

SETTING

Patients with selected chronic diagnoses were enrolled in medical practice.

INTERVENTIONS

Conventional treatment or homeopathy.

OUTCOME MEASURES

Severity of symptoms assessed by patients and physicians (visual rating scale, 0-10) at baseline, 6 and 12 months and costs.

RESULTS

The analyses of 493 patients (315 adults, 178 children) indicated greater improvement in patients' assessments after homoeopathic versus conventional treatment (adults: homeopathy from 5.7 to 3.2; conventional, 5.9-4.4; $p=0.002$; children from 5.1 to 2.6 and from 4.5 to 3.2). Physician assessments were also more favorable for children who had received homoeopathic treatment (4.6-2.0 and 3.9-2.7; $p<0.001$). Overall costs showed no significant differences between both treatment groups (adults, 2155 versus 2013, $p=0.856$; children, 1471 versus 786, $p=0.137$).

CONCLUSION

Patients seeking homoeopathic treatment had a better outcome overall compared with patients on conventional treatment, whereas total costs in both groups were similar.

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Homeopathy. 2005 Jan;94(1):10-6.
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Patients' assessments of the effectiveness of homeopathic care in Norway: a prospective observational multicentre outcome study.

OBJECTIVE

To evaluate the patient reported effects of homeopathic care 6 months after first consultations.

METHODS

Prospective uncontrolled observational multicentre outcome study. All patients visiting 80 homeopaths all over Norway for the first time in eight different time periods from 1996 to 1998 were approached. Patients wrote down their main complaint and scored its impact on daily living on a 100 mm Visual Analogue Scale (VAS) at the first consultation. Six months later they were asked to score again. The homeopaths recorded treatments given for up to two follow-up consultations.

MAIN OUTCOME MEASURE

Predefined as a reduction of at least 10 mm in the VAS score between the first consultation and follow-up.

RESULT

Patients 1097 were recruited, 654 completed the follow-up questionnaire. The main complaint improved by at least 10mm on the VAS for 71% (95% confidence interval 67-74%) of patients. The average reduction was 32mm (95% CI 30-35 mm). Fifty-one per cent (95% CI 48-55%) of the patients had an improvement in their general well being of more than 10 mm. The mean reduction in the whole group was 14mm (95% CI 12-16 mm). The proportion of patients using conventional medication reduced from 39% to 16%. Regression analysis showed that lower age and higher baseline score were predictors of better outcome.

CONCLUSION

In this study, seven out of ten patients visiting a Norwegian homeopath reported a meaningful improvement in their main complaint 6 months after the initial consultation.

Veterinärmedizin und Homöopathie

Auch in der Veterinärmedizin sind in den letzten Jahren einige sehr gute Studien und Reviews und eine Metaanalyse erschienen:

- In einer randomisierten, Placebo-kontrollierten, doppelblinden Studie zur Anwendung der Homöopathie bei durch das Bakterium *Escherichia coli* hervorgerufenem Durchfall bei Ferkeln konnte bereits 2010 gezeigt werden, dass in der homöopathischen Gruppe signifikant weniger Ferkel an durch *E. coli* bedingtem Durchfall erkrankten ($p < 0,0001$; linear model)
Zudem war der Schweregrad der Erkrankung geringer und der Durchfall, sofern er auftrat, von kürzerer Dauer (CAMERLINK et al., 2010)
 - ▶ CAMERLINK, I., ELLINGER, L., BAKKER, E.J., LANTINGA, E.A. Homeopathy as replacement to antibiotics in the case of *Escherichia coli* diarrhea in neonatal piglets. *Homeopathy* 2010;99:57-62

- Eine randomisierte kontrollierte Studie verglich die Wirksamkeit homöopathischer Behandlung mit antibiotischer Therapie und Placebo bei milder bis moderater klinischer Mastitis bei Kühen
Bei pathogen-positiven Mastitiden war die Heilungsrate nach vier und acht Wochen ähnlich zwischen den beiden Behandlungsstrategien (21% vs 18% bzw. 24% vs 31%), die Differenz zwischen homöopathischer Therapie und Placebo war am Tag 56 signifikant (31% vs 4%; $p < 0,05$; Kruskal-Wallis Test)
Die Ergebnisse indizieren einen therapeutischen Effekt der homöopathischen Behandlung bei milder und moderater Mastitis bei Kühen (WERNER et al., 2010)
 - ▶ WERNER, C., SOBIRAJ, A., SUNDRUM, A. (2010): Efficacy of homeopathic and antibiotic treatment strategies in cases of mild and moderate bovine clinical mastitis. *J Dairy Res* 77(4): 460-467.

- ZEISE und FRITZ (2019) untersuchten 32 Studien zu Mastitis von Kühen von 1982 bis 2016 unter Anwendung eines Qualitätsscores und schlussfolgerten aus den 8 qualitativ hochwertigsten Studien Wirksamkeit der Homöopathie
In einer Studie bei durch euterpathogene Bakterien bedingter Mastitis bei Kühen wurde im Vergleich zu Placebo die Wirksamkeit der homöopathischen Therapie ($p < 0,05$; Chi-Quadrat-Test, t-Test, logistische Regression) sowie gesamt eine Reduktion des Antibiotikaeinsatzes um bis zu 75% gezeigt (MERCK 2004)
 - ▶ ZEISE, J., FRITZ, J. (2019): Use and efficacy of homeopathy in prevention and treatment of bovine mastitis. *Open Agricult* 4: 203-212.

- ▶ MERCK, C. C. (2004): Etablierung der homöopathischen Mastitistherapie in einem biologisch-dynamischen wirtschaftlichen Milcherzeugerbetrieb unter Berücksichtigung ökologischer, epidemiologischer und ökonomischer Gesichtspunkte, Abschlussbericht zum Forschungsvorhaben 99UM032, Tierklinik für Fortpflanzung, Fachbereich Veterinärmedizin, Freie Universität Berlin.
- MAESCHLI et al. (2019) konnten zeigen, dass im Rahmen des Kometian Projekts in der Schweiz bei komplementärmedizinischer, vorwiegend homöopathischer Betreuung die betriebliche antibiotische Behandlungsinzidenz signifikant ($p < 0,001$; Wilcoxon-signed-rank Test) von 27 auf 18 Behandlungen pro 100 Tiere im ersten Jahr sank
- ▶ MAESCHLI, A., SCHMIDT, A., AMMANN, W., SCHURTENBERGER, P., MAURER, E., WALKENHORST, M. (2019): Einfluss eines komplementärmedizinische telefonischen Beratungssystems auf den Antibiotikaeinsatz bei Nutztieren in der Schweiz. *Complement Med Res* 9: 1-8.
- KELLER et al. (2019) untersuchten Milchviehbetriebe in Deutschland, Frankreich und Spanien und stellten fest, dass lege artis durchgeführte homöopathische Behandlungen inklusive Nachkontrollen sowie adäquater Dokumentation genau wie für andere komplementärmedizinische Verfahren und die konventionelle Medizin entscheidend sind.
Ein adäquates Monitoringsystem würde zur weiteren Prüfung der Wirksamkeit der Homöopathie beitragen. Entsprechend ausgebildete Tierärzte sind Grundvoraussetzung, dass Landwirte diese in die homöopathische Therapie involvieren.

Zur Erfüllung dieser Forderungen braucht es weitere hochqualitative Studien und entsprechend in Homöopathie ausgebildete Tierärzte

- ▶ KELLER, D., BLANCO-PENEDO, I., DE JOYBERT, M., SUNDRUM, A. (2019) How target-orientated is the use of homeopathy in dairy farming= A survey in France, Germany and Spain. *Acta Vet Scand* 61(1):30.
- Auch die Metaanalyse zu Veterinärhomöopathie von MATHIE und CLAUSEN (2015) zeigt eine limitierte Evidenz für die Wirksamkeit der veterinärmedizinischen Homöopathie gegenüber Placebo.
18 RCTs – Placebo-kontrolliert, 3 ausgeschlossen, da Daten nicht auslesbar, N = 15
p=0,01 für n=15, pooled OR=1,69 (CI=1,12–2,56)
p=0,02 für n=2, pooled OR=2,62 (CI=1,13–6,05)
- ▶ MATHIE, R. T., CLAUSEN, J. Veterinary homeopathy: meta-analysis of randomised placebo-controlled trials. *Homeopathy* 2015;104: 3-8

Camerlink I¹, Ellinger L, Bakker EJ, Lantinga EA.

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Homeopathy (2010) 99, 57–62 _ 2009 The Faculty of Homeopathy

doi:[10.1016/j.homp.2009.10.003](https://doi.org/10.1016/j.homp.2009.10.003), available online at <http://www.sciencedirect.com>

PMID: 20129177 DOI: [10.1016/j.homp.2009.10.003](https://doi.org/10.1016/j.homp.2009.10.003)

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Diarrhoe (E.coli) bei Ferkeln

In einer randomisierten, Placebo-kontrollierten, doppelblinden Studie zur Anwendung der Homöopathie bei durch das Bakterium Escherichia coli hervorgerufenem Durchfall bei Ferkeln konnte bereits 2010 gezeigt werden, dass in der homöopathischen Gruppe signifikant weniger Ferkel an durch E. coli bedingtem Durchfall erkrankten ($p < 0,0024$; linear model) Zudem war der Schweregrad der Erkrankung geringer und der Durchfall, sofern er auftrat, von kürzerer Dauer (CAMERLINK et al., 2010); CAMERLINK, I., ELLINGER, L., BAKKER, E.J., LANTINGA, E.A. Homeopathy as replacement to antibiotics in the case of Escherichia coli diarrhea in neonatal piglets. Homeopathy 2010;99:57-62, Homeopathy. 2010 Jan;99(1):57-62. doi: 10.1016/j.homp.2009.10.003.

Homeopathy as replacement to antibiotics in the case of Escherichia coli diarrhoea in neonatal piglets.

BACKGROUND

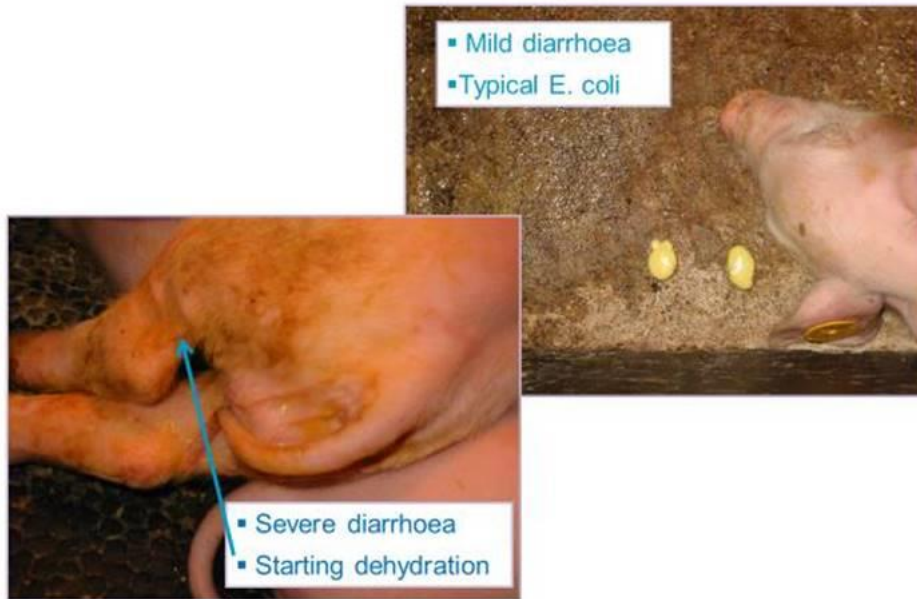
The use of antibiotics in the livestock sector is increasing to such an extent that it threatens negative consequences for human health, animal health and the environment. Homeopathy might be an alternative to antibiotics. It has therefore been tested in a randomised placebo-controlled trial to prevent Escherichia coli diarrhoea in neonatal piglets.

METHOD

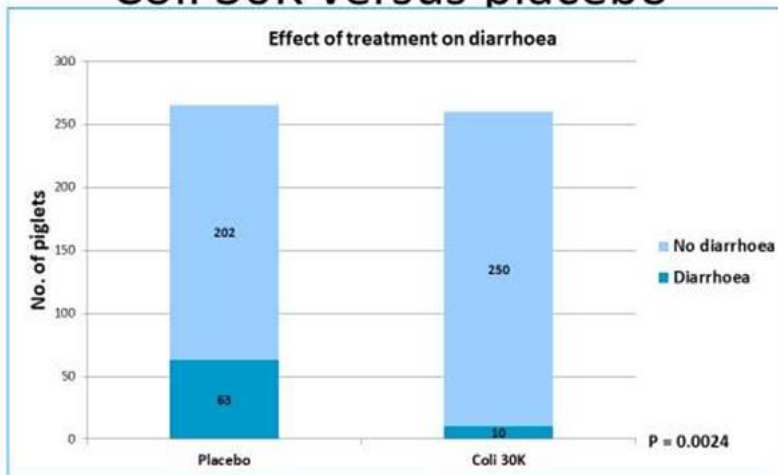
On a commercial pig farm 52 sows of different parities, in their last month of gestation, were treated twice a week with either the homeopathic agent Coli 30K or placebo. The 525 piglets born from these sows were scored for occurrence and duration of diarrhoea.

RESULTS

Piglets of the homeopathic treated group had significantly less E. coli diarrhoea than piglets in the placebo group ($P < 0.0024$). Especially piglets from first parity sows gave a good response to treatment with Coli 30K. The diarrhoea seemed to be less severe in the homeopathically treated litters, there was less transmission and duration appeared shorter.



Coli 30K versus placebo



Complement Med Res. DOI: 10.1159/000496031

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Einfluss eines komplementärmedizinischen telefonischen Beratungssystems auf den Antibiotikaeinsatz bei Nutztieren in der Schweiz

HINTERGRUND

Der Antibiotikaeinsatz bei Nutztieren fördert die Entwicklung antibiotikaresistenter Bakterien. Die Komplementärmedizin könnte einen Beitrag zur Reduktion von Antibiotika leisten, wird bisher jedoch nicht flächendeckend angeboten. Das Beratungsprogramm "Kometian" unterstützt teilnehmende Landwirte darin, ihre Tiere komplementärmedizinisch zu behandeln.

METHODEN UND RESULTATE

128 von 223 teilnehmenden Betrieben nutzten in den ersten 3 Projektjahren die telefonische Beratung von Kometian. Die Mehrheit der Landwirte hielt Milchkühe. Frühestens 1 Woche nach der Kometianberatung wurde eine telefonische Nachfrage beim Tierbesitzer hinsichtlich des Gesundheitszustandes des Tieres durchgeführt. Es konnten so 661 Beratungsfälle recherchiert werden. In 486 Fällen erfolgte keine weitere schulmedizinische Behandlung, in 373 Fällen gab der Landwirt einen Behandlungserfolg an. Von 188 angefragten und seit mindestens einem Jahr an Kometian teilnehmenden Betrieben stellten 46 ihre Behandlungsjournale zur Verfügung. Die betriebliche antibiotische Behandlungsinzidenz sank signifikant ($p < 0,001$) von 27 vor Beitritt auf 18 Behandlungen pro 100 Tiere im ersten Jahr.

SCHLUSSFOLGERUNG

Es scheint, dass Kometian einen Beitrag dazu leisten konnte, den Antibiotikaeinsatz auf Betriebsebene zu reduzieren.

Johanna Zeise*, Jürgen Fritz

<https://doi.org/10.1515/opag-2019-0019> received September 28, 2018; accepted February 10, 2019

Use and efficacy of homeopathy in prevention and treatment of bovine mastitis

Abstract

Bovine mastitis is an important disease in dairy farming. As alternative therapy to antibiotics, whose use is seen as increasingly critical, farmer try to treat mastitis with homeopathy, for example. The present study examined whether homeopathic treatments for bovine mastitis can have positive treatment outcomes, ii) which treatments have been successful and under which conditions, iii) indications for future studies and applications for homeopathy to treat mastitis. 32 studies published to date have been evaluated. Assessment criteria and a rating score of 0 to 5 points were fixed for the appraisal. Healing and prophylaxis of mastitis were the primary focus to highlight the medication success and its framework for suitable mastitis therapy. The top eight studies of this quality ranking were subjected to differentiated evaluation. The selected studies showed a positive treatment outcome of homeopathy. Due to the homeopathic effect and the most used remedies in the selected studies, the medication should be chosen according to the homeopathic drug picture. With homeopathic drugs it was possible to reduce the antibiotic use by up to 75%. Some studies indicated that homeopathy might have a positive long-term effect. Furthermore, the results suggested a high self-healing ability in bovine mastitis.

Keywords:

homeopathy, dairy cow, complementary; veterinary medicine, antibiotics, clinical trials

Reviews und Metastudien

Zum Thema der Meta-Analysen sei verwiesen auf das aktuelle Gutachten von Helmut Kiene und Harald J. Hamre vom Institut für angewandte Erkenntnistheorie und medizinische Methodologie an der Universität Witten/Herdecke **„Wissenschaftliches Gutachten zum Antrag V-0 „Echter Patient*innenschutz: Bevorteilung der Homöopathie beenden!“ zur Bundesdelegiertenkonferenz von Bündnis90/DieGrünen am 15.-17. November 2019 in Bielefeld.**

Dieses Gutachten ist gewissermaßen wie das Exzerpt einer Meta-Meta-Analyse. Wir empfehlen dringend die Lektüre dieses Gutachtens, auch über das Thema der Meta-Analysen hinaus. Hinsichtlich der Meta-Analysen sind die zentralen Aussagen: Seit 1996 wurden sechs Meta-Analysen von randomisierten, Placebo-kontrollierten klinischen Homöopathiestudien veröffentlicht; sie umfassten alle Behandlungsindikationen der Humanmedizin: Drei der Meta-Analysen betrafen jegliche Art von Homöopathie:

- Boissel 1996 und Cucherat 2000
- Linde 1997 und 1999
- Shang et al 2005/Lüdtke 2008

Zwei Meta-Analysen betrafen nur individualisierte Homöopathie:

- Linde 1998
- Mathie et al 2014

Eine Meta-Analyse betraf nur nicht-individualisierte Homöopathie:

- Mathie et al 2017

Alle sechs Meta-Analysen zeigen positive Therapieeffekte der Homöopathie über Placebo hinaus (6 von 6 Meta-Analysen), die statistisch signifikant sind (explizit 5 von 6 Meta-Analysen). Sofern in diesen Meta-Analysen zusätzliche Sensitivitätsanalysen durchgeführt wurden, blieben die positiven Therapieeffekte weiterhin überwiegend signifikant, auch unter Berücksichtigung einer hohen Zahl von Qualitätsindikatoren und neuen verbesserten Analysestandards.

Noch eine kurze Bemerkung zu der Meta-Analyse von Shang et al (2005): In dieser Meta-Analyse waren Auswertungstechniken verwendet worden, die nicht empfohlen sind und kritisch diskutiert werden¹⁰ - siehe dazu auch die Analyse auf S.57. Unter

¹⁰ *Cochrane Handbook for Systematic Reviews of Interventions* (<https://training.cochrane.org/handbook/current>)

diesen Vorzeichen ist auch das damals als negativ interpretierte Ergebnis dieser Meta-Analyse zu sehen. Durch Re-Analyse von Lüttke (2008) entstand schließlich ein differenzierteres und für die Homöopathie positives Ergebnis.

Die methodisch mit Abstand beste Meta-Analyse ist die von Mathie (2014) zur individualisierten Homöopathie. Sie zeigt ein statistisch signifikantes positives Ergebnis, das robust ist gegenüber Sensitivitätsanalysen.

Metaanalyse von Linde

Linde K¹, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, Jonas WB.

Lancet. 1997 Sep 20;350(9081):834-43. Erratum: Lancet 1998 Jan 17;351(9097):220.

Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials.

Die Evidenz der analysierten 89 Studien ist in dieser Metaanalyse von 1997 statistisch signifikant positiv zu Gunsten der Homöopathie (OR: 2.45; 95% CI 2.05 – 2.93). Dies schließt auch die Subgruppenanalyse der 26 Studien ein, diese mit bester Qualität, fällt deutlich positiv aus (OR: 1.66; 95% CI 1.33 – 2.08). Die Autoren kommentieren zurückhaltend kritisch und fordern, wie in der Wissenschaft üblich, weitere Studien:

“The results of our meta-analysis are not compatible with the hypothesis that the clinical effects of homeopathy are completely due to placebo. However, we found insufficient evidence from these studies that homeopathy is clearly efficacious for any single clinical condition. Further research on homeopathy is warranted provided it is rigorous and systematic.”

BACKGROUND

Homeopathy seems scientifically implausible, but has widespread use. We aimed to assess whether the clinical effect reported in randomised controlled trials of homeopathic remedies is equivalent to that reported for placebo.

METHODS

We sought studies from computerised bibliographies and contracts with researchers, institutions, manufacturers, individual collectors, homeopathic conference proceedings, and books. We included all languages. Double-blind and/or randomised placebo-controlled trials of clinical conditions were considered. Our review of 185 trials identified 119 that met the inclusion criteria. 89 had adequate data for meta-analysis, and two sets of trial were used to assess reproducibility. Two reviewers assessed study quality with two scales and extracted data for information on clinical condition, homeopathy type, dilution, "remedy", population, and outcomes.

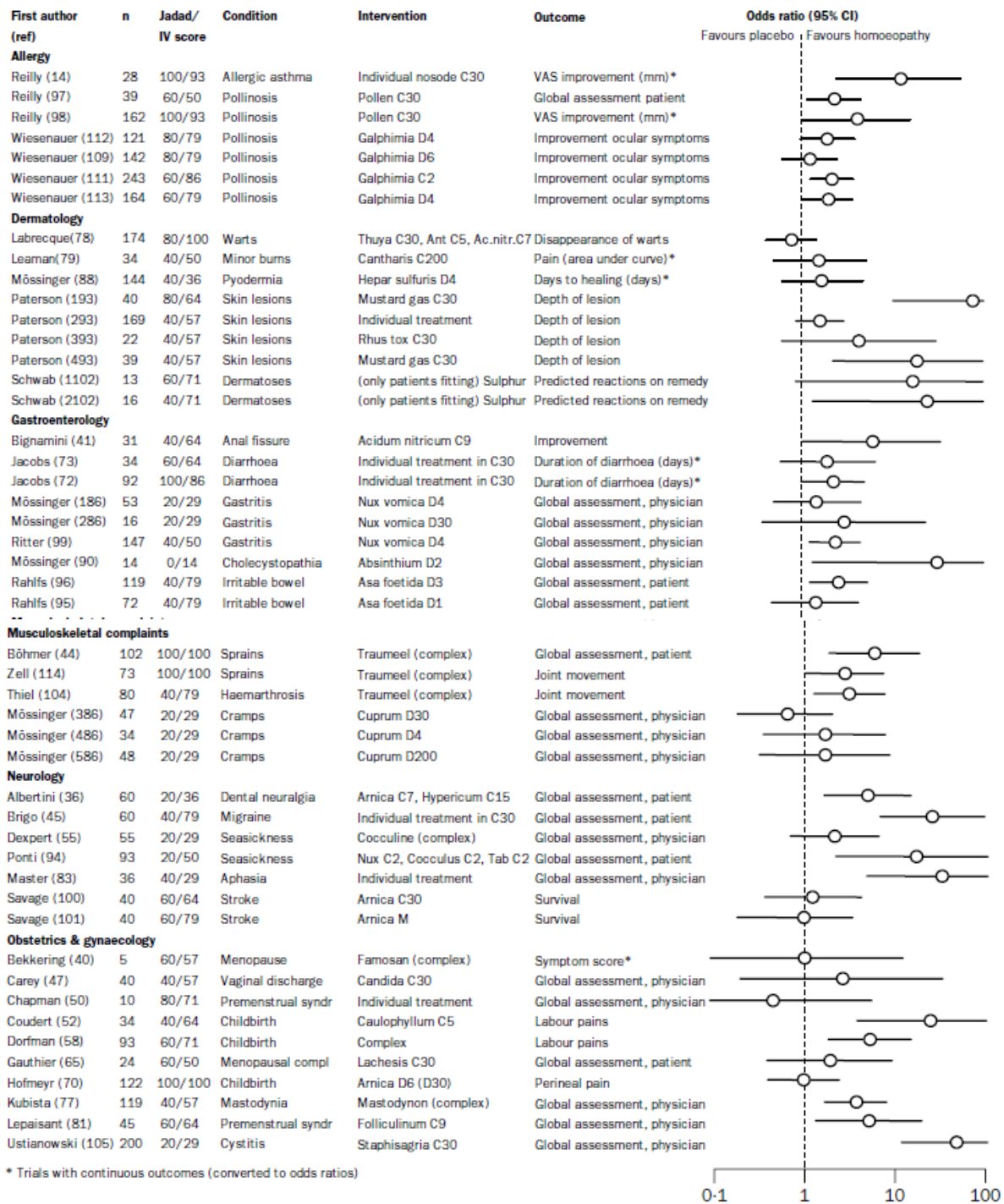
FINDINGS

The combined odds ratio for the 89 studies entered into the main meta-analysis was 2.45 (95% CI 2.05, 2.93) in favour of homeopathy. The odds ratio for the 26 good-quality studies was 1.66 (1.33, 2.08), and that corrected for publication bias was 1.78 (1.03, 3.10). Four studies on the effects of a single remedy on seasonal allergies had a pooled odds ratio for ocular symptoms at 4 weeks of 2.03 (1.51, 2.74). Five studies on postoperative ileus had a pooled mean effect-size-difference of -0.22 standard deviations (95% CI -0.36, -0.09) for flatus, and -0.18 SDs (-0.33, -0.03) for stool (both $p < 0.05$).

INTERPRETATION

The results of our meta-analysis are not compatible with the hypothesis that the clinical effects of homeopathy are completely due to placebo. However, we found insufficient evidence from these studies that homeopathy is clearly efficacious for any single clinical condition. Further research on homeopathy is warranted provided it is rigorous and systematic.

THE LANCET



* Trials with continuous outcomes (converted to odds ratios)

Table 2: Trials in meta-analysis

**For prevention trials, presented odds ratio=1÷actual odds ratio. Jadad/IV score: actual number of quality criteria met×100÷maximum possible score. URI=upper respiratory tract infection, ENT=ear, nose, and throat, VAS=visual analogue score.

Übersicht der Effektstärken oberhalb der Signifikanz-Linie (>1)

Tab. 2: Forest-Plot zur grafischen Veranschaulichung der Ergebnisse einer Metaanalyse. Die senkrechte Linie bezeichnet jenes Chancenverhältnis oder Risikoverhältnis, welches keinem Zusammenhang zwischen untersuchtem Einflussfaktor und der abhängigen Variable entspricht. Die Kreise stellen das Risiko-Maß der Einzelstudien dar, die waagerechten Linien die jeweiligen Konfidenzintervalle. (aus Wikipedia)

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Randomised placebo-controlled trials of individualised homeopathic treatment: systematic review and meta-analysis

Robert T. Mathie, Suzanne M. Lloyd, Lynn A. Legg, Jürgen Clausen, Sian Moss, Jonathan RT Davidson and Ian Ford

Mathie et al. Systematic Reviews 2014, 3:142

<http://www.systematicreviewsjournal.com/content/3/1/142>

Abstract

BACKGROUND

A rigorous and focused systematic review and meta-analysis of randomised controlled trials (RCTs) of individualised homeopathic treatment has not previously been undertaken. We tested the hypothesis that the outcome of an individualised homeopathic treatment approach using homeopathic medicines is distinguishable from that of placebos.

METHODS

The review's methods, including literature search strategy, data extraction, assessment of risk of bias and statistical analysis, were strictly protocol-based. Judgment in seven assessment domains enabled a trial's risk of bias to be designated as low, unclear or high. A trial was judged to comprise 'reliable evidence' if its risk of bias was low or was unclear in one specified domain. 'Effect size' was reported as odds ratio (OR), with arithmetic transformation for continuous data carried out as required; OR > 1 signified an effect favouring homeopathy. Results: Thirty-two eligible RCTs studied 24 different medical conditions in total. Twelve trials were classed 'uncertain risk of bias', three of which displayed relatively minor uncertainty and were designated reliable evidence; 20 trials were classed 'high risk of bias'. Twenty-two trials had extractable data and were subjected to meta-analysis; OR = 1.53 (95% confidence interval (CI) 1.22 to 1.91). For the three trials with reliable evidence, sensitivity analysis revealed OR = 1.98 (95% CI 1.16 to 3.38).

CONCLUSIONS

Medicines prescribed in individualised homeopathy may have small, specific treatment effects. Findings are consistent with sub-group data available in a previous 'global' systematic review. The low or unclear overall quality of the evidence prompts caution in interpreting the findings. New high-quality RCT research is necessary to enable more decisive interpretation.

KEYWORDS

Individualised homeopathy, Meta-analysis, Randomised controlled trials, Systematic review

In an empirical evaluation of the funnel plot, researchers could not visually identify publication bias.

J Clin Epidemiol. 2005 Sep;58(9):894-901.

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Abstract

BACKGROUND AND OBJECTIVE

Publication bias and related biases can lead to overly optimistic conclusions in systematic reviews. The funnel plot, which is frequently used to detect such biases, has not yet been subjected to empirical evaluation as a visual tool. We sought to determine whether researchers can correctly identify publication bias from visual inspection of funnel plots in typical-size systematic reviews.

METHODS

A questionnaire with funnel plots containing 10 studies each (the median number in medical meta-analyses) was completed by 41 medical researchers, including clinical research fellows in a meta-analysis class, faculty in clinical care research, and experienced systematic reviewers.

RESULTS

On average, participants correctly identified 52.5% (95% CI 50.6-54.4%) of the plots as being affected or unaffected by publication bias. The weighted mean percent correct, which adjusted for the fact that asymmetric plots are more likely to occur in the presence of publication bias, was also low (48.3 to 62.8%, depending on the presence or absence of publication bias and heterogeneous study effects).

CONCLUSION

Researchers who assess for publication bias using the funnel plot may be misled by its shape. Authors and readers of systematic reviews need to be aware of the limitations of the funnel plot.

Diese empirisch hergeleitete Kritik bedeutender Statistiker an der funnel plot Methode als bias-fördernd setzt ein wichtiges wissenschaftliches Fragezeichen vor die nachfolgende Shang-Studie, deren Ergebnisse sich aus dieser Methode herleiten. Dennoch ist die Shang Studie in der Regel die einzige Studie, die von grundsätzlichen Gegnern der Homöopathie zitiert wird.

Metanalyse von Shang

Shang A1, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, Pewsner D, Egger M.
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Lancet. 2005 Aug 27-Sep 2;366(9487):726-32.

Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy.

BACKGROUND

Homoeopathy is widely used, but specific effects of homoeopathic remedies seem implausible. Bias in the conduct and reporting of trials is a possible explanation for positive findings of trials of both homoeopathy and conventional medicine. We analysed trials of homoeopathy and conventional medicine and estimated treatment effects in trials least likely to be affected by bias.

METHODS

Placebo-controlled trials of homoeopathy were identified by a comprehensive literature search, which covered 19 electronic databases, reference lists of relevant papers, and contacts with experts. Trials in conventional medicine matched to homoeopathy trials for disorder and type of outcome were randomly selected from the Cochrane Controlled Trials Register (issue 1, 2003). Data were extracted in duplicate and outcomes coded so that odds ratios below 1 indicated benefit. Trials described as double-blind, with adequate randomisation, were assumed to be of higher methodological quality. Bias effects were examined in funnel plots and meta-regression models.

FINDINGS

110 homoeopathy trials and 110 matched conventional-medicine trials were analysed. The median study size was 65 participants (range ten to 1573). 21 homoeopathy trials (19%) and nine (8%) conventional-medicine trials were of higher quality. In both groups, smaller trials and those of lower quality showed more beneficial treatment effects than larger and higher-quality trials. When the analysis was restricted to large trials of higher quality, the odds ratio was 0.88 (95% CI 0.65-1.19) for homoeopathy (eight trials) and 0.58 (0.39-0.85) for conventional medicine (six trials).

Review von Robert G. Hahn

Homeopathy: Meta-Analyses of Pooled Clinical Data, Robert G. Hahn^{a,b}
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Pooled Clinical Data on Homeopathy

SUMMARY

In the first decade of the evidence-based era, which began in the mid-1990s, meta-analyses were used to scrutinize homeopathy for evidence of beneficial effects in medical conditions. In this review, meta-analyses including pooled data from placebo-controlled clinical trials of homeopathy and the aftermath in the form of debate articles were analyzed. In 1997 Klaus Linde and co-workers identified 89 clinical trials that showed an overall odds ratio of 2.45 in favor of homeopathy over placebo. There was a trend toward smaller benefit from studies of the highest quality, but the 10 trials with the highest Jadad score still showed homeopathy had a statistically significant effect. These results challenged academics to perform alternative analyses that, to demonstrate the lack of effect, relied on extensive exclusion of studies, often to the degree that conclusions were based on only 5–10% of the material, or on virtual data. The ultimate argument against homeopathy is the 'funnel plot' published by Aijing Shang's research group in 2005.

However, the funnel plot is flawed when applied to a mixture of diseases, because studies with expected strong treatments effects are, for ethical reasons, powered lower than studies with expected weak or unclear treatment effects. To conclude that homeopathy lacks clinical effect, more than 90% of the available clinical trials had to be disregarded. Alternatively, flawed statistical methods had to be applied. Future meta-analyses should focus on the use of homeopathy in specific diseases or groups of diseases instead of pooling data from all clinical trials.

INTRODUCTION

Homeopathy has a long tradition in European medicine but remains controversial due the unknown mechanism of action. Although the lack of such knowledge is not unique for treatments used in the clinic, the skepticism expressed by academic scientists in this case is fueled by the difficulty perceiving a biologically reasonable explanation for why homeopathy would be effective [1].

A new era in the dispute between believers and non-believers began in the mid-1990s when evidence-based medicine was first popularized. A mechanism of action no longer needed to be proved as long as it could be demonstrated statistically that the therapy was effective. What 'worked' could be shown with large randomized double-blind trials but, more commonly, by systematic reviews and meta-analyses.

METHODOLOGY

Evidence-based medicine initiated a decade of struggle

between believers and non-believers in which meta-analyses were used as the tool of analysis. All of them were based on virtually the same material, but authors arrived at different conclusions. The aim of the present re-appraisal of this period was to scrutinize the arguments used and to illustrate what non-believers rely on to advocate abandoning homeopathy in the evidence-based era.

RESULTS

Linde and Colleagues' Meta-Analysis In 1997 Klaus Linde and co-workers in Munich received much attention after publishing a meta-analysis of homeopathy clinical trials in *The Lancet* [2]. The researchers had searched for homeopathy studies in a wide selection of databases. Out of 186 trials, the group identified 119 that were randomized placebo-controlled studies of clinical conditions. Of these studies, 89 provided data that were adequate for a meta-analysis.

When all data were pooled, the odds ratio and 95% confidence interval (CI) were 2.45 (2.05–2.93) in favor of homeopathy. After correction for publication bias, the odds ratio decreased to 1.78 (1.03–3.10). When only the 26 studies of highest quality were included, the benefit was somewhat weaker but still statistically significant, 1.66 (1.33–2.08).

The study by Linde and co-workers [2] demonstrated, with a likelihood of more than 95% CI, that homeopathy is overall a more effective remedy than placebo. The path was then opened for the unusual approach of pooling all published studies of one type of treatment regardless of disease and specific remedy used for the cure.

STUDY QUALITY

The earliest criticism of Linde et al.'s meta-analysis [2] focused on the fact that high-quality studies seemed to show weaker effects than studies of lower quality. In 1999, Linde's group re-assessed this issue [3]. They divided the studies into subgroups instead of using a weighting system to consider differences in quality. Naturally, the use of subgroups reduced the capacity of the available clinical trials to demonstrate differences between treatment and placebo.

The 89 clinical trials were grouped according to the Jadad score, which describes the quality of clinical trials on a scale ranging from 0 to 5. Linde et al. [3] found that the strength of a meta-analysis became gradually poorer when dealing with studies of higher quality, but the relationship was not linear; the 10 studies with the highest quality score (Jadad 5) had greater strength in favor of homeopathy than those with Jadad 3 (19 studies) and Jadad 4 (11 studies). For all 6 Jadad score levels, homeopathy was still statistically superior compared to placebo.

Linde et al. [3] also divided the studies into 12 subgroups according to the group's own Internal Validity Scale, in which the capacity to disclose statistically significant differences at each step was further reduced. Here, homeopathy was statistically superior to placebo at all quality levels except the highest, where 5 clinical trials yielded an odds ratio of 1.55 (0.77– 3.10). However, the best estimate of the odds ratio did not differ from previous evaluations, and the lack of statistical significance is explained by the fact that the calculation is based on only a few studies. In a subanalysis of 32 trials of individualized homeopathic treatment, Linde and Melchart [4] found an overall odds ratio of 1.62 (1.17–2.23) in favor of homeopathy. Based on the study with the best quality, the odds ratio was 1.12 (0.87–1.44), which is not statistically significant.

EDZARD ERNST

Since 1997, attempts to invalidate Linde et al.'s [2–4] results have followed the path of excluding most of the clinical trials or, for various reasons, focused on smaller subgroups of studies. The first claim was made by the German-British physician Edzard Ernst, a former professor of complementary medicine in UK. In 1998, he selected 5 studies using highly diluted remedies from the original 89 and concluded that homeopathy has no effect [5].

In 2000, Ernst and Pittler [6] sought to invalidate the statistically significant superiority of homeopathy over placebo in the 10 studies with the highest Jadad score. The odds ratio, as presented by Linde et al. in 1999 [3], was 2.00 (1.37–2.91). The new argument was that the Jadad score and odds ratio in favor of homeopathy seemed to follow a straight line (in fact, it is asymptotic at both ends). Hence, Ernst and Pittler [6] claimed that the highest Jadad scores should theoretically show zero effect. This reasoning argued that the assumed data are more correct than the real data.

Two years later, Ernst [7] summarized the systematic reviews of homeopathy published in the wake of Linde's first metaanalysis [2]. To support the view that homeopathy lacks effect, Ernst cited his own publications from 1998 and 2000 [5, 6]. He also presented Linde's 2 follow-up reports [3, 4] as being further evidence that homeopathy equals placebo. Moreover, Ernst cited a book chapter [8] that will be commented upon later.

CUCHERAT AND COLLEAGUES

Another meta-analysis of pooled clinical data on homeopathy was authored by Cucherat et al. [9]. The group identified 118 randomized controlled clinical trials as being potentially evaluable, but excluded all except 17 (hence, 86% were disregarded). The most common reason for exclusion was that the primary end point was judged to be unclear. Prevention trials and those evaluating only biological effects were also excluded.

The patient outcomes were not pooled which is an uncommon approach in meta-analyses. Instead, the significance values (p) from the different studies were combined to arrive at an overall grand p . Out of 7 ways to combine such significance values the authors chose the one that was least prone to show a favorable outcome for homeopathy. The overall treatment effect in the 17 studies was still highly statistically significant in favor of homeopathy, $p < 0.000036$ (risk is less than 3.6 out of 100,000 that the difference can be explained by chance). The clarity of this result was diluted by the subsequent removal of studies according to quality. Not much strength was lost when studies were removed that were open instead of blinded. When the 9 studies included that were randomized and double-blinded but had lost less than 10% of patients on follow-up, the p value was still 0.0084 (risk is less than 8.4 out of 1,000 that the effect is due to chance). Finally, when only the significance values for the 5 studies with less than 5% loss during follow-up were pooled, the difference between homeopathy and placebo was only close enough to be statistically significant ($p = 0.082$, risk of 8.2 in 100 that the superiority of homeopathy over placebo is explained by chance). Cucherat et al. [9] remained skeptical about homeopathy although their data, even after most of the statistical power was removed by excluding 86% of the clinical trials, showed that the therapy is superior to placebo. Their impression was that the studies were of poor quality, a view not shared by others [2, 10]. Cucherat et al. [9] provided odds ratios along with the exclusion exercise, which is honest. However, the reasons for exclusion and the subsequent loss of analyzing power are unbalanced. For example,

there is little reason to exclude half of the material (from 9 to 5 studies) just because the dropout incidence is reduced from <10 to <5%. In fact, a dropout incidence much higher than 10% would normally be acceptable in a clinical trial and can be handled by statistical methods.

SHANG AND COLLEAGUES

The meta-analysis published by Shang et al. in 2005 [10] identified essentially the same set of clinical trials as Linde et al., although some recently published material was added. The purpose was to compare homeopathic remedies with conventional medical therapy, although the aftermath focused entirely on the clinical efficacy of homeopathy. The group identified 165 publications and excluded 60 for various reasons, one being that an appropriate match with a conventional medical treatment study could not be found. The authors also excluded crossover studies. The final material consisted of 110 homeopathic trials and 110 using conventional medications.

No odds ratio was presented for the effect of homeopathy versus placebo in these 110 studies, although the authors mentioned that it was in favor of homeopathy. Instead, all except 21 studies were excluded, based on quality measures. Again, no statistics were provided. The authors then created a second set of exclusions, down to 8 studies, without clearly explaining why. Their final claim, after having disregarded 95% of the available clinical trials, was that the inverse odds ratio for homeopathy was 0.88 (0.65–1.19), which is not statistically significant. This means that the best estimate of the treatment effect is $1/0.88$, i.e. homeopathy is 13% more effective than placebo.

Shang et al. [10] used the 'funnel plot' in the same way as the senior author (M. Egger) applied to Linde's work in a book chapter 4 years earlier [8]. This is a scatter plot of the odds ratios versus the standard errors for a group of studies. Small studies are more likely to be published when they show a positive result, while such publication bias is more unlikely to occur when a study sample is large. As larger studies usually have smaller standard errors, the overall 'true' odds ratio is the one indicated when the regression line in the funnel plot approaches a standard error of zero. This means that the positive results of smaller studies are disregarded as they are assumed to be balanced by negative outcomes in studies that never came to press. By relying on a funnel plot for interpretation, conclusions are based on the existence of data we believe exist, although we do not know for sure.

The funnel plot is a hopeless research tool when making conclusions about treatment effects in a mixed set of medical conditions, because studies are powered according to expected treatment effects. For example, new studies of homeopathy in allergic and rheumatic diseases cannot, for ethical reasons, include a large sample due to the positive effects reported in previous publications [7, 11, 12]. In contrast, studies of conditions where the treatment effect is expected to be low or uncertain have to have a larger sample to reach adequate 'power.' Therefore, when applied to a mixture of diseases, it is impossible to alter the shape of the funnel plot shown by Shang et al., regardless of how effective homeopathy might be in allergic and rheumatic diseases. Treatment effects will always be poorer in the largest studies if we power them according to previous works in the field.

These calculations made by Shang et al. [10] have been widely used by academics and skeptics as well as by the Editor of *The Lancet* to claim that homeopathy lacks clinical effect. A critical discussion about this conclusion followed in a later issue of the journal [13–15].

DISCUSSION

Meta-Analysis as a Research Tool Many researchers are skeptical to the placebo-controlled randomized clinical trial (RCT) as the optimal tool to evaluate methods in complementary medicine. The RCT provides highly valid information about the efficacy of clearly defined treatments but is poorly suited to evaluate the efficiency of more complex interventions [16]. However, one cannot disregard the fact that the placebo-controlled RCT and the subsequent pooling of data in the form of meta-analyses are highly ranked scientific methods in school medicine. Their results will continue to have a strong impact in society's opinion about the usefulness of complementary medicine. However, meta-analyses can arrive at different conclusions despite being based on virtually the same material. They are not performed according to strict methodology and are, to a variable extent, guided by creativity, interpretation, and personal bias. This is why everyone can find arguments for and against homeopathy in the meta-analyses of the pooled clinical data. The heterogeneity encourages critical reading including personal reflections about why the various authors have chosen to present their analysis in the way they do.

EXTENSIVE EXCLUSION OF DATA

Our considerations should include the fact that some studies rely on extensively excluding data. There must always be a sound balance between the scientific gain made by excluding studies and the limitations imposed by the associated loss of statistical power. Some of the works reviewed here, and in particular works by authors who are negative about homeopathy, reach their conclusions after having excluded 90–95% of the available trials. This is done with reference to quite small differences in quality, such as whether the dropout frequency is <10 or <5%, or with no reference at all. Little attention is given to the fact that the statistics then become based on much smaller groups of patients, which rapidly hampers the possibility of disclosing true differences between homeopathic and placebo treatments. Extensive exclusion exercises are normally excused by academic rigor but also constitute a tempting way for the non-believer to ruin any evidence there might be. The challenge for the researcher is to evaluate the available data and not to exclude virtually all of them. Studies of very poor quality and those that do not contain necessary data must always be excluded, but the remainder should be allowed to contribute to the conclusion, possibly after having been given graded importance depending on how well the studies have been conducted.

Another drawback of excluding a large number of studies is that the composition of the finally analyzed mix of conditions becomes very important to the conclusion. Here, one must remember that the overall conclusion made in these meta-analyses relates to the overall efficacy of a heterogeneous group of treatments for a heterogeneous group of diseases. One example of this problem is that the nonsignificant odds ratio for the effectiveness of homeopathy versus placebo presented by Shang et al. [10] seems to be due to a single study of muscle soreness in 400 long-distance runners [17]. Without this study, the result would have shown the statistically significant superiority of homeopathy over placebo. Moreover, Shang et al. [10] excluded all except 21 studies based on quality, and providing the results from all of them would have demonstrated the statistically significant benefit of homeopathy over placebo [13]. Why the number was further reduced from 21 to 8 was not explained beyond that the latter were 'large'. Critical readers suspect that the authors played around with the study selection until eventually they found the desired result. Strong conclusions made about the usefulness of homeopathy made in a previous report [7] and in public [14] could fuel such behavior.

In the following debate Shang's study was criticized for lack of transparency and the highly selected nature of the finally evaluated studies [13–15, 17].

EVIDENCE VERSUS RECOMMENDATION

Therapies should be evaluated in 2 steps. The first one is objective and summarizes the evidence for the efficacy of the therapy. The second step is to make recommendations for use. The clinical value of a treatment is then judged more subjectively with reference not only to evidence but also to scientific, ethical, economic, and practical perspectives.

Authorities often ask different persons to do these parts when formulating clinical recommendations or guidelines. The reason is that an objective evaluation of existing evidence should be carried out regardless of what the consequences might be. If the same individual performs both evaluations it is tempting to distort the evidence when other considerations disagree with the evidence. This author believes that overlap between these 2 roles has been common in the meta-analyses of the pooled clinical data about homeopathy. That is also why the conclusions are vastly different and the debate about the evidence contains a certain degree of emotion. Distortion of the evidence is also common in society.

The present review is based on a series of blog articles published in 2011 as a reaction to a summer campaign against homeopathy organized by skeptics in Sweden. One claim was that homeopathy is poorly studied. This is not true as the number of RCTs in this area is quite large. Many therapies used in clinical medicine are based on much less data. Another widespread argument, which was even adopted by politicians, is that not a single study on homeopathy shows a positive treatment effect. In reality, the majority of RCTs on homeopathy shows positive effects. A third claim was that the studies are of low quality, which does not receive support from researchers who have specifically evaluated this issue [2, 10]. A fourth point spread to newspapers by a professional academic was that the analyses by Ernst [7] and Shang et al. [10] demonstrate beyond a doubt that homeopathy is fraud and humbug. As we have seen, these publications represent a biased selection of the literature.

IDEOLOGY PLAYS A PART

The reader of this literature must be aware that ideology plays a part in these meta-analyses. For example, Ernst [7] makes conclusions based on assumed data [6] when the true data are at hand [3]. Ernst [7] invalidates a study by Jonas et al. [18] that shows an odds ratio of 2.19 (1.55–3.11) in favor of homeopathy for rheumatic conditions, using the notion that there are not sufficient data for the treatment of any specific condition [6]. However, his review deals with the overall efficacy of homeopathy and not with specific conditions. Ernst [7] still adds this statistically significant result in favor of homeopathy over placebo to his list of arguments of why homeopathy does not work. Such argumentation must be reviewed carefully before being accepted by the reader.

The most believable of the meta-analyses is still Linde et al.'s work from 1997 [2] along with the associated consideration of study quality [3] as the authors appear to maintain a reasonable balance between exclusion and statistical power. The follow-up analyses by Cucherat et al. [9] and Shang et al. [10] rest on such extensive exclusion of data that the conclusions are based on only a tiny fraction of the published studies. These meta-analyses are good examples of

how the same data can yield results that are statistically in favor and not in favor of homeopathy, and having a negative result is most likely when making conclusions based on as little material as possible. Applying funnel plots to a heterogeneous mix of remedies and diseases is another example of playing around with data. If this approach is statistically correct, all further clinical trials would have to include the same number of patients regardless of the expected clinical effect. Alternatively, all treatments must exert the same effect. If not, the funnel plot is flawed.

THE WAY FORWARD

Meta-analyses of pooled data from the treatment of many conditions are difficult to interpret. From a clinical point of view, such analyses are warranted only if the same effect is measured [14]. They also provide many opportunities for those who strive to reach a predetermined conclusion to choose selectively. Further meta-analyses should focus on areas where homeopathy tends to be effective instead of diluting the results with data from diseases in which an effect is unlikely. Socioscientific issues are also relevant to discuss [19]. In the meantime, the issue continues to be a struggle between believers and non-believers, guided by plausibility bias [20].

Homeopathy is not a very strong remedy but seems to show better effects than placebo particularly in conditions that either are known or can be assumed to arise from the immunologic system. A guide was given in Linde et al.'s study [2] in which good clinical effects were to be found in allergic rhinitis, rheumatology, dermatology (except warts), and certain neurological disorders, such as seasickness and migraine. Benefit was more uncertain or absent in asthma, surgery, gastrointestinal disorders, anesthesiology, and gynecology [2].

As already stated, it can be argued that evidence-based approaches including the RCT are not the best forms of evaluating the efficacy of homeopathic remedies, as well as the efficiency of more complex interventions in complementary medicine. Traditional therapy might be a better comparator than placebo due to the fact that complementary therapies often show a large nonspecific effect ('efficacy paradox') [13, 16]. Recently, Mathie et al. [21] collected all current 263 highstandard RCTs of homeopathy in humans to enable future systematic reviews based on specific traits, such as the type of condition and whether placebo or other treatments serve as controls. Until alternative methods of evaluation have gained widespread acceptance, homeopaths have a lot to gain by aligning their therapeutic ambitions to the areas and treatments in which placebo-controlled studies have shown a better outcome than placebo. In reality, homeopathic treatments are usually individualized while most of the performed clinical trials are nonindividualized [13, 22]. Therefore, the practice is not evidence-based, regardless of the results of all the trials.

CONCLUSION

Clinical trials of homeopathic remedies show that they are most often superior to placebo. Researchers claiming the opposite rely on extensive invalidation of studies, adoption of virtual data, or on inappropriate statistical methods. Further work with meta-analyses should abandon the concept of summarizing all available clinical trials and focus on the effects of homeopathy versus placebo or other treatments in specific diseases or groups of diseases. One way to reduce future emotional-driven distortion of evidence by investigators and skeptics would be to separate the evidence-seeking process from the formulation of clinical guidelines more clearly.

NOTE

The author has never practiced, received, or studied homeopathy, but has worked in clinical medicine and performed traditional medical research in anesthesiology and surgery for the past 30 years.

DISCLOSURE STATEMENT

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The best studies show individualised homeopathic treatment has beneficial effects beyond placebo

Several systematic reviews and meta-analyses of homeopathy have been performed. However, none had looked solely at placebo-controlled trials of individualised homeopathic treatment as delivered by homeopaths in practice. The research team of Mathie et al. ¹ have now performed such an analysis and found that homeopathic medicines, when prescribed during individualized treatment, are 1,5 – 2-times more likely to have a beneficial effect than placebo. Use of a rigorous and transparent methodology, including a sensitivity analysis, gives credibility to these findings, which fundamentally challenge claims that homeopathy is purely a placebo effect.

INTRODUCTION

To date, many of the systematic reviews of clinical studies on homeopathy have analysed studies on all forms of homeopathic treatment together, in an attempt to answer the general question, "Is homeopathy better than placebo?". However, homeopathy takes several forms. 'Individualised homeopathic treatment', consisting of a consultation plus personalised prescription, is considered to be usual care as provided by homeopaths in real world clinics. In contrast, 'non-individualised homeopathy' involves the same remedy being used by all patients, based on a clinical diagnosis only (e.g. over-the-counter homeopathic preparations containing multiple remedies for conditions such as hay fever or travel sickness). There is no reason to assume that different homeopathic treatment approaches are equally effective or ineffective. It is therefore not surprising that studies combining the results of all homeopathy trials, with little or no attempt to disentangle the different types of treatment involved, have led to some negative studies and reports^{2,3} and ensuing heated debate. In Mathie et al.'s study, placebo-controlled trials of individualised homeopathy have been analysed in isolation¹, allowing us to explore the key question - do homeopathic medicines, when prescribed during individualised homeopathic treatment (IHT) have an effect beyond placebo?

META-ANALYSIS OF INDIVIDUALISED HOMEOPATHIC TREATMENT (IHT)

Mathie et al. identified 22 eligible clinical trials comparing Individualised Homeopathic Treatment (IHT) to placebo for a range of clinical conditions. To ensure that the results would be recognised by the wider academic world, Mathie's team used state-of-the-art methods for analysing a large body of clinical trial data, namely a systematic review and meta-analysis (see Definition box).

All 22 trials were assessed for quality using the well recognised Cochrane collaboration's assessment tool⁴ and given an overall "reliability" rating of A, B or C. Three of the 22 trials met the strict criteria set by Mathie et al. to be designated as the most "reliable" evidence (i.e. rated B1 and above); a meta-analysis of these three top trials found that IHT is more beneficial than placebo. It is important to note that this definition of "reliable" is more stringent than that used in previous meta-analyses of homeopathy performed by other groups (e.g. Shang et al ²). Also,

this method of classifying study quality and "reliability" should not be misinterpreted as suggesting that the remaining 19 trials are not meaningful: rather, they are simply lower down the scale of relative reliability

KEY FINDINGS

Overall, IHT had a positive effect that was statistically different from placebo. Specifically, individually prescribed homeopathic medicines were found to be 1.5- to 2- times more likely to have a beneficial effect than placebo. The size of the treatment effect was measured by the 'Odds Ratio' (OR); if an OR is greater than 1.0, the effect of the intervention is positive, and the greater the OR, the greater the size of that positive effect.

The treatment effect seen in the 3 trials designated as most "reliable" was calculated to be OR= 1.98 (95% CI [1.16 - 3.38]; $p = 0.013$.) As these results were based on only 3 studies, Mathie et al. performed a 'sensitivity analysis' to check that they were robust i.e. the choice of trials analysed was changed in multiple ways according to their quality rating to see whether this caused the final result to alter (see Figure 1).

When analysing the 12 trials rated as B6 and above, the OR did not change significantly: OR= 1.63 (95% CI [1.24 - 2.14]; $p < 0.001$) (Fig. 1. Remove C1.0 studies); and when all 22 trials were analysed together, regardless of quality, the result was again not significantly different: OR= 1.53 (CI [1.22 - 1.91]; $p < 0.001$) (Fig. 1. All studies). This sensitivity analysis demonstrates that Mathie et al.'s findings are robust. It is also important to note that there is no evidence of larger treatment effects being found in lower-quality trials, contradicting the notion that only poor quality studies on homeopathy show positive results.

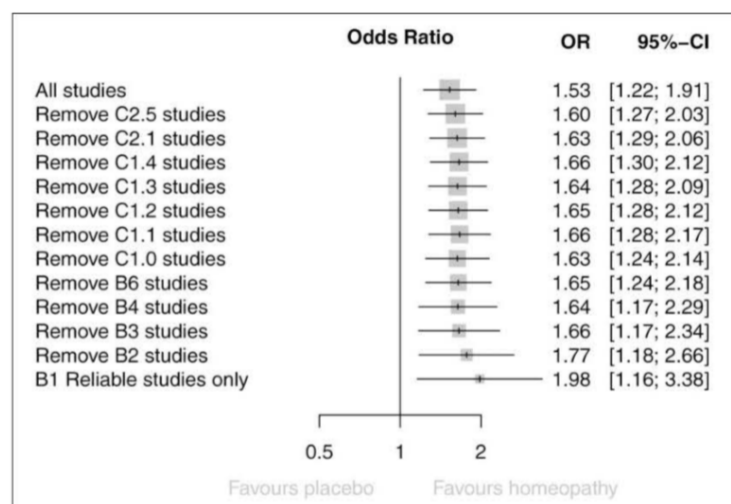


Figure 1: Sensitivity analysis. Meta-analysis results for various sub-groups of the 22 eligible trials. Each line represents a different sub-group of trials according to their quality/reliability rating (C2.5 being the lowest and B1 the highest). The top line ("All studies") represents the odds ratio (OR) results from all 22 studies pooled together. Successive lines from top to bottom represent the results after step-wise removal of trials with the next reliability rating. The bottom line ("B1 Reliable studies only") represents the results when analysing the three 'best' trials only. (Figure reproduced with permission from Mathie et al.1).

When testing the efficacy of IHT for several different clinical conditions, one might expect the results to vary depending on the condition being treated, making it more difficult to detect a specific effect when all conditions are pooled: interestingly this was not the case. Additionally, two of the three most "reliable" trials used homeopathic remedies that were diluted beyond the Avogadro limit, yet a significant specific effect was still detected. This is a striking finding considering that many detractors of homeopathy argue that this is either scientifically implausible or simply impossible.

While the effect of individually prescribed homeopathic medicines was greater than placebo, the clinical 'effect size' detected was "small". To put this into context, conventional drugs with a similar effect size include sumatripan for migraine, fluoxetine for major depressive disorder and cholinesterase inhibitors for dementia.

COMPARISON WITH OTHER STUDIES

Two previous systematic reviews of IHT have been performed. Ernst et al. (published in 1999) located 3 randomised controlled trials comparing IHT to conventional medicine and the low trial quality prevented any conclusions from being drawn⁷. In 1998 Linde et al's study looked at 32 trials of IHT versus placebo and found a positive, but unconvincing, trend. Mathie et al. added an extra level of significance to these previous systematic reviews performing a state-of-the-art meta-analysis.

When the meta-analysis of Mathie et al. is directly compared with perhaps the most often cited meta-analysis of "global" homeopathy performed by Shang et al.¹², which reached negative conclusions, key differences between the two studies become clear:

- the criteria for reliability of the clinical trials used by Mathie et al. were more stringent
- the trials used by Mathie et al. were more up-to-date (14 of the 22 trials identified were not included in Shang et al., published in 2005)
- the positive results of this study are based on trials which test individualised homeopathic care; Shang et al. final conclusion that homeopathy does not have an effect beyond placebo was based only on trials of non-individualised homeopathy
- Mathie et al. performed a rigorous sensitivity analysis to confirm that despite basing their main conclusion on only 3 of 22 available studies, the findings are reliable. Shang et al. did not perform such an analysis on their data, but other authors have shown that their results (based on only 8 of 110 available studies) fail a rigorous sensitivity analysis and are therefore unreliable.

IMPACT OF THE STUDY

In summary, Mathie et al. have taken the three most reliable, high quality studies of individualised homeopathic treatment available and found that when the results are analysed together, the result is positive, showing a beneficial effect of homeopathic medicines beyond placebo. The input from two highly respected, independent biostatisticians from the University of Glasgow as co-authors gives further credibility to the findings.

Although the authors remain only cautiously optimistic about their findings, the meta-analysis by Mathie et al, is well constructed and methodologically sound, providing a strong argument

in favour of the existence of specific effects beyond placebo in real-world homeopathic treatment. The results of this meta-analysis challenge the commonly repeated argument, 'the best studies show homeopathy doesn't work', and provide strong evidence that the opposite is actually correct, i.e. the best studies show homeopathy works.

Definition box

A **systematic review** is a highly structured scientific method used to locate, collate, critically assess and evaluate all research studies available that address a particular question. The highest quality evidence is then used to synthesise a final position and draw conclusions.

A **meta-analysis** is a statistical method used to assess overall trends in the combined data extracted from multiple individual studies identified through systematic review. A meta-analysis assigns a level of statistical significance to the combined results (i.e. how likely it is that the result is 'real' and not simply due to chance).

Grundlagenforschung

Die Grundlagenforschung zeigt einen klaren Trend:

Die Qualität der Grundlagenstudien nimmt seit der Jahrtausendwende deutlich zu - siehe den Review von Klein, Würtenberger, Wolf, Baumgartner und Tournier Seite 67. Ergebnis dieser Forschung sind klare Hinweise auf eine biologische oder physikalische Wirkung potenziertes, also sukzessive verdünnter und dabei verschüttelter Substanzen. Diese beiden Schritte - verschütteln und verdünnen - müssen offenbar kombiniert werden, da dann eine signifikante Wirkung in doppelblinden, placebokontrollierten Versuchen an Pflanzen, Tieren oder in Kristallisationsprozessen messbar wird.

Besonders interessante Ergebnisse zeigen die rein physikalischen Untersuchungen von potenzierten Substanzen durch Spektroskopie, in Kristallisationsprozessen, sowie in den NMR-Messungen potenziertes homöopathischer Substanzen von Demangeat.

Fazit

Die Qualität der klinischen Forschung und der Grundlagenforschung in der Homöopathie nimmt eindeutig zu. Sie zeigt in ganz verschiedenen hochwertigen Studien beim Menschen, aber auch bei Pflanzen und Tieren und in Kristallisationsprozessen eine signifikant erhöhte Wirkung gegenüber Placebo. Diese Forschung im Sinne der Bürger auszubauen, bedarf der ausreichenden Forschungs-Finanzierung. Nur so lassen sich schrittweise auch die Wirkmechanismen selbst erforschen.

Wichtig wird der wissenschaftliche Austausch mit anderen Forschungsfeldern

Alle medizinischen Wirkstoffe leisten einen Informationstransfer, sobald sie in Körpern wirken. Aber können nur Atome physikalisch-chemisch wirken? Dann müssten wir ab sofort GPS-Navigation und Smartphone abschalten, weil die Geräte mit der Information, die sie für uns abrufen und senden, kein Atom mit den zugehörigen Satelliten austauschen, sondern physikalische Felder generieren und nutzen. Gerade weil sie keine trägen Atome, sondern Feldwirkungen im Datentransfer einsetzen, sind sie so schnell und weitreichend.

In der Biologischen Forschung liefert die neu entstehende Quantenbiologie interessante Hinweise, dass in lebenden Organismen ebenfalls nicht atomare Prozesse¹¹ zum schnellen und weitreichenden Informationstransfer genutzt werden.

¹¹ - Klinman JP, Kohen A. 2013 Hydrogen tunneling links protein dynamics to enzyme catalysis. *Annu. Rev. Biochem.* 82, 471–496.

- Narth C, Gillet N, Cailliez F, Lévy B, de la Lande A. 2015 Electron transfer, decoherence, and protein dynamics: Insights from atomistic simulations. *Acc. Chem. Res.* 48, 1090–1097.

-Brookes JC, Hartoutsiou F, Horsfield AP, Stoneham AM. 2007 Could humans recognize odor by phonon assisted tunneling? *Phys. Rev. Lett.* 98, 38101.

Physicochemical Investigations of Homeopathic Preparations:

A Systematic Review and Bibliometric Analysis—Part 1

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Stephan Baumgartner, PhD,^{1,3,4} and Alexander Tournier, PhD^{1,5}

Abstract

OBJECTIVES

The last systematic review of physicochemical research performed on homeopathic preparations was published in 2003. The aim of the study is to update and expand the current state of knowledge in the area of physicochemical properties of homeopathic preparations.

In part 1 of the study, we aim to present an overview of the literature with respect to publication quality and methods used. **In part 2**, we aim to identify the most interesting experimental techniques. With this, we aim to be in a position to generate meaningful hypotheses regarding a possible mode of action of homeopathic preparations.

METHODS

A two-step procedure was adopted: (1) an extensive literature search, followed by a bibliometric and quality analysis on the level of publications and (2) a thorough qualitative analysis of the individual physicochemical investigations found. In this publication, we report on step (1). We searched major scientific databases to find publications reporting physicochemical investigations of homeopathy from its origin to the end of 2015. Publications were assessed using a scoring scheme, the Manuscript Information Score (MIS). Information regarding country of origin of the research and experimental techniques used was extracted.

RESULTS

We identified 183 publications (compared to 44 in the last review), 122 of which had an MIS ≥ 5 . The rate of publication in the field was ≈ 2 per year from the 1970s until 2000. Afterward, it increased to over 5.5 publications per year. The quality of publications was seen to increase sharply from 2000 onward, whereas before 2000, only 12 (13%) publications were rated as "high quality" (MIS ≥ 7.5); 44 (48%) publications were rated as "high quality" from 2000 onward. Countries with most publications were Germany ($n = 42$, 23%), France ($n = 29$, 16%), India ($n = 27$, 15%), and Italy ($n = 26$, 14%). Techniques most frequently used were electrical impedance (26%), analytical methods (20%), spectroscopy (20%), and nuclear magnetic resonance (19%).

CONCLUSIONS

Physicochemical research into homeopathic preparations is increasing both in terms of quantity and quality of the publications.

KEYWORDS

systematic review, homeopathy, physics, very high dilutions, serially diluted and agitated solutions, ultrahigh aqueous dilutions

A Systematic Review and Bibliometric Analysis—Part 2

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Abstract

OBJECTIVES

In Part 1 of the review of physicochemical research performed on homeopathic preparations the authors identified relevant publications of sufficient reporting quality for further in-depth analysis. In this article, the authors analyze these publications to identify any empirical evidence for specific physicochemical properties of homeopathic preparations and to identify most promising experimental techniques for future studies.

METHODS

After an update of the literature search up to 2018, the authors analyzed all publications in terms of individual experiments. They extracted information regarding methodological criteria such as blinding, randomization, statistics, controls, sample preparation, and replications, as well as regarding experimental design and measurement methods applied. Scores were developed to identify experimental techniques with most reliable outcomes.

RESULTS

The publications analyzed described 203 experiments. Less than 25% used blinding and/or randomization, and about one third used adequate controls to identify specific effects of homeopathic preparations. The most promising techniques used so far are nuclear magnetic resonance (NMR) relaxation, optical spectroscopy, and electrical impedance measurements. In these three areas, several sets of replicated high-quality experiments provide evidence for specific physicochemical properties of homeopathic preparations.

CONCLUSION

The authors uncovered a number of promising experimental techniques that warrant replication to assess the reported physicochemical properties of homeopathic preparations compared with controls. They further discuss a range of experimental aspects that highlight the many factors that need to be taken into consideration when performing basic research into homeopathic potentization. For future experiments, the authors generally recommend using succussed (vigorously shaken) controls, or comparing different homeopathic preparations with each other to reliably identify any specific physicochemical properties.

Introduction

Homeopathy is a very popular complementary medicine worldwide.¹ Scientific interest into therapeutic efficacy of homeopathic remedies is reflected in the growing number of studies and meta-analyses in clinical research.² However, specific efficacy and the mode of action of homeopathic remedies—especially in high dilution—is still the subject of scientific debate. A major challenge of homeopathic basic research is to decode any physicochemical mode of action. The aim of this review project was to contribute to this effort through a systematic literature search and a thorough evaluation of the state of research in this field.

In Part 1 of this review the authors presented the methodology of the literature search and a bibliometric classification of the publications that were found.³ In the present, second article, the authors report on a methodological analysis of the investigations in the different physicochemical research areas. The authors focus on criteria such as blinding, randomization, use of statistics, controls, independent sample preparation, and replicated experiments. The aim was to identify any empirical evidence for specific physicochemical properties of homeopathic preparations, and to identify most promising experimental techniques for future studies. In the forthcoming Part 3 of this review, a qualitative in-depth analysis of the research field will be performed to get clues about possible hypotheses for the physicochemical mode of action.

Materials and Methods

In Part 1 of this review the authors described how they performed the literature search and the procedure by which they assigned to each publication a Manuscript Information Score (MIS) as a proxy for the reporting quality of the article.³ A total of 183 publications on physicochemical experiments in homeopathy were retrieved; 122 of these had an MIS ≥ 5 and were thus considered to be of sufficient quality to be included in this part of the review. On closer inspection seven of these publications were found not to be relevant to this review and were excluded (six because of duplications⁴⁻⁹ and one because it was not standard homeopathy¹⁰).

The authors performed an update of the literature search to cover all publications up to December 2018. The same search criteria and methods as previously were used.³ The update uncovered 19 publications, reporting on 32 experiments. In this part of the review the authors analyzed these 134 publications in terms of the 203 experiments they describe.^{9,11-143} The definition of an experiment was taken as an intellectually conceivable unit with uniform measurement methods and a homogenous set of samples. Thus, the authors split publications into multiple experiments when different measurements procedures and/or differing sample preparation methods had been applied. An experiment could be described in several publications and quite often a publication would contain several relevant experiments.

Detailed information for each experiment was extracted from the publications (see [Box 1](#)). All data were independently extracted by two authors and compared. Conflicts were resolved through discussion. The detailed data extraction sheet is available as [Supplementary Data](#). Two authors worked on each of the 11 research areas. Because of the search criteria excluding nonhomeopathy-specific articles, some work potentially relevant to the mode of action of homeopathic dilutions were not included (see [Limitations](#) section).

To quantitatively compare any empirical evidence for specific effects of homeopathic preparations for the 11 research areas, we constructed a methodological score—the Methodological and Frequency of Investigation (MFI) score—by taking the average of 5 quality criteria (randomization, blinding, statistics, use of succussed controls, and use of multiple independent production lots) and weighing it by the number of studies in that research area.

BOX 1

GENERAL INFORMATION

Authors, year of publication, title of publication, research area (one of 11 predefined categories), and type of Publication (journal, book, etc.) were the general information.

HOMEOPATHIC PREPARATIONS

Homeopathic preparations included potentized substances (Latin or chemical names), method of potentization (multiple tube vs. single tube, hand vs. machine, succussion vs. vortex vs. sonication), potency levels and dilution ratio, Substance of potency vessel, composition of potentization medium, production of potencies (self-made, off the shelf, and specific external production), and physical modifications.

CONTROLS

Types of controls (unsuccussed medium, dilution without succussion, succussed medium, potentized medium, none, and other).

BIAS PREVENTION AND STATISTICS

Number of independent homeopathic and control sample production lots; blinding, randomization, statistics (none, descriptive, inferential).

TECHNIQUES AND RESULTS

Measurement technique in more detail, summary of results, results reported by authors (evidence or no evidence for empirical differences between homeopathic preparations and controls).

FORMAL OVERVIEW

The 134 publications analyzed reported on a total of 203 experiments ([Fig. 1](#)). The majority of experiments (72%) reported findings in line with the notion that homeopathic preparations are different from the controls used ([Table 1](#)).

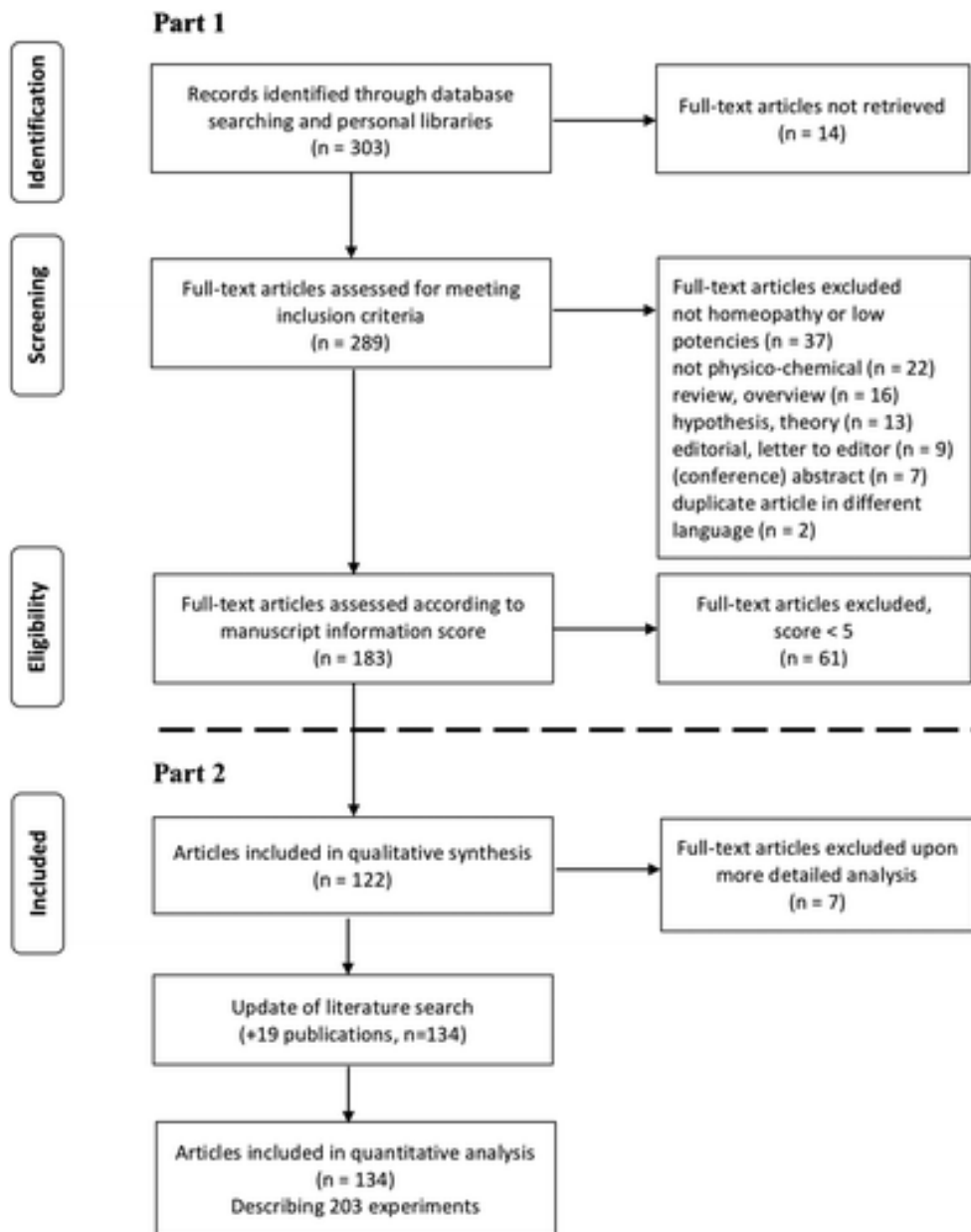


FIG. 1. PRISMA flow diagram describing the process of paper inclusion through Part 1 and Part 2 of the review to arrive at the 203 experiments being described. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1. Physicochemical Experiments Reporting Differences Between Homeopathic Preparations and Controls

<i>Findings</i>	<i>Count</i>	<i>%</i>
Differences reported	147	72
No differences reported	35	17
Mixed results	2	1
NA	19	9

Most experiments used plain (unsuccussed) potentizing medium as control, whereas less than one third used potentized medium (Table 2); 23% of experiments used more than one control. Twenty-three percent of experiments reported blinding and 21% reported randomization. Only 15% of the experiments reported measurements of multiple independent sample production lots. Most of the experiments (59%) did not report the use of statistics to analyze the data, whereas 28% reported use of inferential statistics.

Table 2. Controls, Bias Prevention and Statistics Used in Physicochemical Experiments

	Count	%
Controls^a		
Potentized medium	57	28
Succussed medium	18	9
Dilution without succussion	24	12
Unsuccussed medium	109	54
Other	50	25
Unknown	15	7
Blinding		
Yes	46	23
No	22	11
Not described	135	67
Randomization		
Yes	43	21
No	20	10
Not described	140	69
Independent production lots		
Unique production lot	43	21
Multiple production lots	31	15
Unknown	129	64
Statistics		
Inferential	56	28
Descriptive	27	13
None	120	59

Types of controls used in experiments, and information on whether sample blinding and randomization was used, whether experiments used independent production lots (i.e., how many times the homeopathic preparations were produced from the original substance) and whether statistics were used and what type.^a Experiments often used several controls.

Table 3 reports on specific aspects of the sample production. Two thirds of the experiments used the multiple-tube method for potentization. Nearly half of the experiments declared use of some form of potentizing machine. The majority of experiments used succussion as potentization method. About two thirds of the preparations investigated were prepared by the researchers in their own laboratory. Experiments most often investigated samples both above and below the theoretical limit where nothing would be left of the original substance (12c/24x, roughly corresponding to the inverse of Avogadro's number). Although the assumption is generally that the effects of homeopathy are the result of as yet unknown water characteristic, only 24% of experiments used ultrapure water as the medium for the dilution/succussion process. Most experiments (35%) used ethanol at different concentrations. Of interest, 20% of experiments used specifically prepared water-based mediums such as solutions of sodium bicarbonate, silicic acid, sodium chloride, and lithium chloride.

Table 3. Homeopathic Sample Preparation

	<i>Count %</i>	
Potentizing method		
Multiple tube (Hahnemann)	124	61
Single tube (Korsakov)	11	5
Mixed	25	12
Unknown	43	21
Succussion method		
Hand	56	28
Machine	81	40
Mixed	10	5
Unknown	56	28
Production		
Self-made	119	59
Specific external	40	20
Off the shelf	27	13
Mixed	17	8
Potencies		
<12c, 24x	17	8
≥12c, 24x	42	21
Mixed	141	69
Unknown	3	1
Composition of potentization medium		
Ethanol high concentration (>50%)	56	28

Table 3. Homeopathic Sample Preparation

	Count %	
Ethanol low concentration	15	7
Ultrapure water	49	24
Water-based inorganic solutions	40	20
Mixed	13	6
D ₂ O	3	1
Unknown	27	13

Methods that were employed in the production of the samples: potentizing method (multiple- or single-vessel method), succussion method (hand, machine), production location (in-house or outsourced), and dilution level (below or above the inverse Avogadro number, i.e., whether any of the original substance could be expected to remain in the sample).

A total of 192 different substances were investigated. The most used potentized substance was *Natrium muriaticum* (sodium chloride), followed by 2,4-dichlorophenoxyacetic acid, *Arnica montana*, sulfur, *Nux vomica*, and *Silicea* (Table 4).

Table 4. Substances Potentized Most Used in Experiments

Remedies	Usage
<i>Natrium muriaticum</i>	28
2,4-dichlorophenoxyacetic acid	24
<i>Arnica montana</i>	24
Sulfur	21
<i>Nux vomica</i>	17
<i>Silicea</i>	15
<i>Argentum nitricum</i>	12
<i>Arsenicum album</i>	12
<i>Argentum metallicum</i>	11
<i>Cuprum sulfuricum</i>	10
<i>Magnesium muriaticum</i>	10
<i>Arsenicum sulphuratum rubrum</i>	9
<i>Plumbum nitricum</i>	7
<i>Aurum muriaticum</i>	7
<i>Lycopodium clavatum</i>	6
<i>Aurum metallicum</i>	6
<i>Zincum metallicum</i>	6
<i>Histaminum</i>	5
<i>Zincum oxidatum</i>	5
<i>Alcoholus (ethanol)</i>	5

Table 4. Substances Potentized Most Used in Experiments

<i>Remedies</i>	<i>Usage</i>
<i>Bryonia</i>	5

Usage in number of experiments.

The most frequently used measurement techniques were electrical impedance, spectroscopy followed by nuclear magnetic resonance (NMR) (Table 5). From the breakdown per method we see that blinding and randomization was used most often in NMR, although still less than half of the experiments used them. Use of inferential statistics was generally low except for NMR where they were used often (77%). In terms of the use of succussed controls, these were used less than half of the time except for NMR (63%). The use of independent production lots was generally very low except for NMR (33%) and chromatography (100%). According to the methodological score applied (MFI score, see [Materials and Methods](#) section), NMR comes out as the method with the most reliable empirical evidence for specific properties of homeopathic preparations (MFI score of 15.8), followed by spectroscopy techniques (MFI score of 10.2), analytical methods (6.2), and electrical impedance (MFI score of 6.0).

Table 5. Experimental Methods Used

<i>Methods</i>	<i>Count</i>	<i>Blinding (%)</i>	<i>Randomization (%)</i>	<i>Statistics (%)</i>	<i>Succussed controls (%)</i>	<i>Independent production lots (%)</i>	<i>MFI score</i>	<i>Differences reported (%)</i>
NMR	30	40	50	77	63	33	15.8	73
Spectroscopy	39	31	21	31	38	10	10.2	79
Analytical methods ^a	22	27	32	14	45	23	6.2	18
Electrical impedance	41	12	12	12	22	15	6.0	80
Imaging methods	16	25	25	38	50	6	4.6	69
Surface tension/various physical	9	33	22	22	56	11	2.6	56
Luminescence	11	18	18	27	36	9	2.4	100
Calorimetry	16	0	0	13	13	0	0.8	94
Raman spectroscopy	7	29	0	0	29	0	0.8	86
Chromatography	3	0	0	0	0	100	0.6	100
Electrochemistry	9	0	0	0	11	0	0.2	89

Ordered by MFI score (see the [Materials and Methods](#) section). Count, number of experiments per method. Blinding, randomization, inferential statistics, succussed controls, and independent production lots, frequency of use. Differences between homeopathic preparations and controls as reported in publication: frequency.

^aThe low level of reported differences in the Analytical Methods group is because of the fact that many experiments used analytical methods to control sample purity, not as a technique to compare samples.

MFI, Methodological and Frequency of Investigation.

If we look at the best experiments, defined as those that used blinding, randomization, and inferential statistics, we find overall 24 experiments, of which 79% reported differences between homeopathic preparations and controls ([Table 6](#)). Of those, 10 fulfilled a further two methodological criteria (use of succussed controls and use of independent lot production), 80% of which reported differences between homeopathic preparations and controls.

Table 6. High-Quality Experiments

<i>Method</i>	<i>Experiments fulfilling three criteria</i>	<i>Reported differences (%)</i>	<i>Experiments fulfilling five criteria</i>	<i>Reported differences (%)</i>
NMR	10	90	6	100
Spectroscopy	7	86	1	100
Imaging methods	4	75	1	0
Analytical methods	2	0	0	—
Surface tension/various physical	2	100	2	50
Electrical impedance	2	50	0	—
Luminescence	2	100	0	—
Grand total	29	79	10	80

Number of experiments fulfilling three quality criteria (blinding, randomization, and inferential statistics) along with percentage of experiments reporting differences, number of experiments fulfilling an additional two quality criteria (succussed controls and independent series production) along with corresponding percentages of experiments reporting differences. NMR, nuclear magnetic resonance.

Replications

For the purposes of this review, we define a replication as an experiment that used the same investigative technique to measure the same physicochemical properties of homeopathic potencies made of the same substances. Note that this is different from a reproduction where the same instrument and potencies would have to be used, along with the same statistical analysis, experiment protocol, and materials.

We extracted the replication data for all research techniques. The data tables summarizing these replications for each of the 11 experimental methods are given in the [Supplementary Tables S1, S2, S3, S4, S5, S6, S7, S8, S9, S10, S11](#). A synthesis of the replication data is given in [Table 7](#). To score the different replications, we defined the Experimental Replication (ER) score as the number of replications times the average methodological score of these replica-

tions times the percentage of experiments reporting differences. This score enables to determine which replications have most reliably reported differences between homeopathic preparations and controls and should therefore be replicated further to confirm (or not) their results.

Table 7. Replicated Experiments

Technique	Replication series	No. of replications	Average MFI score	No. of reported differences (%)	ER score
NMR	T1, T2: <i>Silicea</i>	7	4.4	100	31.0
NMR	T1, T2: Histamine	5	3.4	100	17.0
Spectroscopy	UV: Sulfur	4	4.0	100	16.0
Spectroscopy	UV: <i>Cuprum sulfuricum</i>	3	4.3	100	13.0
NMR	T1, T2: Sulfur	9	2.1	44	8.4
Electrical impedance	REDEM: <i>Argentum nitricum</i>	2	4	100	8.0
Electrical impedance	REDEM: <i>Aurum</i>	2	4	100	8.0
NMR	T1, T2: <i>Nuxvomica</i>	3	2.3	100	7.0
Luminescence	Thermo: <i>Lithium muriaticum</i>	3	2.0	100	6.0
Imaging methods	GDV: <i>Natrium muriaticum</i>	2	2.5	100	5.0
Spectroscopy	UV: <i>Aconitum napellus</i>	3	1.7	100	5.0

Number of replications of a given experiment, showing average methodological (MFI) score of experiments within a replication, how often differences between homeopathic preparations and controls were reported and associated ER score. Replications with ER score ≥ 5 sorted according to ER score.

ER, Experimental replication; GDV, gas discharge visualization; MFI, Methodological and Frequency of Investigation; NMR, nuclear magnetic resonance; UV, ultraviolet.

We see that the seven replications investigating T1 and T2 NMR relaxation times of potentized silica have high methodological scores and that all seven experiments reported differences between homeopathic preparations and controls, leading to a high ER score of 31.0. Similarly, NMR relaxation time investigations of potentized histamine have a high score of 17.0 with 5/5 replications reporting differences.

In spectroscopy, we have two sets of ultraviolet (UV) measurements (*Cuprum sulfuricum*, sulfur potencies) with high ER scores. In electrical impedance, the two replications of the REDEM experiments (black box measurements) stand out as having high methodological scores, and both replication lines reported differences between homeopathic preparations and controls

leading to a decent ER. We also see the three studies of thermoluminescence using homeopathic preparations of *Lithium muriaticum*.

Discussion

Appropriate controls for potentized preparations

A major question that came up during this review is how to define the most appropriate controls for homeopathic preparations in physicochemical measurements. We can distinguish two main classes of controls: (1) plain (unsuccussed) solvent or diluted (but not succussed) homeopathic samples and (2) potentized or succussed (vigorously shaken) solvent. It is quite evident that succussion of a fluid in ambient air leads to a number of effects such as formation of air bubbles of different size with differential lifetimes, increased dissolution of air components (N_2 , O_2 , CO_2) in the fluid, increased dissolution of potentization vessel wall material (Si, B, Na, K etc.), and maybe cavitation effects.¹⁴⁴ These processes may lead to further consequences such as increased oxidative processes (because of O_2 dissolution), changes in pH (because of CO_2 dissolution and acid formation), changes in nuclear magnetic relaxation (O_2 as relaxation agent), increased silica-hydrogel formation (because of increased Si dissolution), radical formation (because of cavitation), and potentially other effects.

When investigating the hypothesis that potentization of a given material leads to remedies with specific effects, it is evident that any such specific effects have to be different from pure succussion effects that are unspecific in the sense that they are not related to the substance potentized. From this point of view, only succussed or potentized controls are valid controls for demonstrating any evidence for specific (remedy-related) properties of potentized preparations.

Considering the hypothesis that succussion leads to some information transfer of the substance potentized to the potentization medium, the question arises what happens when pure medium is potentized as control sample (e.g., potentized water). One could speculate that the potentization process is amplifying some random information. This would lead to a situation where samples with specific information (homeopathic preparations) would be compared with samples with random information (potentized water as control). In this sense potentized medium (and by extension succussed medium too) might not to be the best controls possible as they could introduce a random element.

On the contrary, one can argue that it would not be wise to compare homeopathic preparations with each other in case the measurement method used is not able to distinguish the putative homeopathic structures. Because the nature of the homeopathic structures is not known yet, it cannot be decided at present if a given measurement method is able or not to distinguish the presumed structures.

We therefore recommend in future investigations the use of two types of controls: (1) potentized solvent and (2) other homeopathic preparation(s). The use of several homeopathic samples increases the probability to identify different structures. Furthermore, if possible, we recommend the additional use of (3) unsuccussed and (4) succussed control samples that would allow determining the effect of pure succussion. A study of the effect of succussion on the observed physicochemical activities would be a welcome endeavor as it is currently lacking, in

particular investigating the effect of the number of succussions would be very interesting. Such a study would complement the work by Betti et al., which used wheat germination assays and the droplet evaporation method to explore this topic, showing a sigmoidal type behavior as a function of the number of succussions.¹⁴⁵

As mentioned previously, certain experimental methods might be more suitable to investigating the presence/absence of such structures rather than distinguishing between such structures. The issue here is in conceiving appropriate controls that would not suffer from confounding factors such as gas dissolution for example. Such an approach is being pioneered by the group of Prof. Elia in their conductivity measurement experiments; they used trace analytics methods to levels of sodium in their samples and are thereby able to calculate the theoretical conductivity of the sample (sodium being the most relevant element for conductivity in their setup) to obtain the so-called "excess conductivity" as the difference between the measured conductivity and the theoretical prediction. This technique is interesting as in principle it probes directly for the presence of structures with unexplained properties (here in terms of conductivity). However, the technique does not currently control for other elements and gases originating from the succussion process that could also play a role.

Bias prevention and statistics

Most of the studies neither used blinding nor randomization. This is not entirely unusual in physicochemical research where one usually does not expect experimenter effects. Most of conventional research does not invoke blinding on such experiments for that very reason. Giving the history and heated debate surrounding homeopathy, we recommend implementing blinding and randomization protocols in future investigations to ensure that experimenters do not have any effect on the results.

Rather worrying is the lack of use of proper statistical tools. Part of the problem here is that many of the studies are quite dated and statistical tools were often not used at that time. Another effect is that many experiments such as in spectroscopy have been rather descriptive and therefore did not use statistical tools. Now, again given the controversy in the field, there is a great need for proper statistical methods to be implemented, so as to quantify the degree of uncertainty in the results and to avoid Type I and Type II errors.

We recommend the implementation of systematic negative control (SNC) experiments on a regular basis. SNC experiments are full experiments with identical design and evaluation as experiments with homeopathic preparations, but all samples are either from the same source material (e.g., plain potentization medium) or consist of potentized medium, prepared analogously as the homeopathic samples.¹⁴⁶ Depending on the design of the experiments, systematic positive control (SPC) experiments may also be a valid approach, consisting of the same sample (either a positive control or a homeopathic preparation), independently prepared in the number of samples assessed in the "true" experiments. SNC and SPC experiments are excellent scientific tools to evaluate the stability of a given experimental system, to identify any systematic error, and to assess applicability of statistical models. In this review, only one investigation implemented SNC experiments.⁹⁷

Another aspect that needs to be addressed in the future is the inherent variability present in physicochemical studies of homeopathic remedies. It is quite clear that there is a high degree

of variability in the experimental measurements,¹³⁹ which cannot be solely attributed to instrumental error and are because of the high variability inherent in water itself.¹⁴⁷ SNC and SPC experiments are well suited to address these issues. In addition, adapted statistical models may be necessary to address variability in itself.

Most promising techniques

Looking at the results gathered in this review a number of experiments emerge as deserving further replication and exploration. First of all, NMR relaxation studies of potentized silica and histamine preparations have shown the most methodological rigor and the most promising results, demonstrating the ability to distinguish between potentized silica or histamine, and potentized controls. Of interest, potentized sulfur seems to be harder to distinguish from corresponding controls.

Based on the available data, UV spectroscopy seems to be the second most interesting technique. With this experimental approach only, a formal meta-analysis over three independent experimental series yielded statistically significant differences between potencies of copper sulfate and succussed medium.

Thermoluminescence on potentized lithium chloride seems to be the third promising technique, although it requires quite sophisticated and expensive equipment.

In contrast, both NMR relaxation and UV spectroscopy can be performed with desktop instruments, and can additionally be equipped with autosamplers to allow a high number of samples to be measured. From a pragmatic point of view, these two methods therefore seem to be most promising to be recommended for further replication studies.

Of interest, two unconventional experimental methods (so-called REDEM spectroscopy and gas discharge visualization) also seem to have a potential to distinguish between potentized preparations (silver nitrate, gold, sodium chloride) and controls. The disadvantage of these approaches is that the exact measurement process is only partially understood, and cannot be scientifically interpreted in a straightforward way.

Limitations

The search criteria defined homeopathic preparations as having undergone succussion steps, as such a number of publications from the field of water research and of high-dilutions research were not included. In particular the work of Pollack on "Exclusion Zone" (EZ) water, which is often cited as a possible line of enquiry for explaining homeopathy, did not fulfill the criteria and was not retained (for a overview of this field, the reader is referred to the book by Pollack: "The Fourth Phase of Water"¹⁴⁸). Similarly, the work of Konovalov and Ryzhkina on structures terms "Nanoassociates" at ultralow dilutions, did not meet the criteria and was not retained (for more details the reader is referred to the review of the field by Konovalov and Ryzhkina¹⁴⁹). It is quite clear that the homeopathic remedy production process with iterative dilution and succussion steps raises fundamental questions in the realm of physics and chemistry that go far beyond the field of homeopathy research. A review on water structures and water/ethanol structures and on physicochemical effects of succussion would be a very valuable complementary approach for homeopathic basic research.

Conclusions

We reviewed 134 publications describing 203 experiments in the area of physicochemical research into homeopathically potentized preparations, which we analyzed in detail with the aim of extracting relevant information about what has been learned in the field and which experiments to undertake in the future.

To conclude, the most promising techniques used so far are NMR relaxation, optical spectroscopy, and electrical impedance measurements. In these three areas, several sets of replicated high-quality experiments provide evidence for specific physicochemical properties of homeopathic preparations.

For future experiments, we recommend using succussed controls, or comparing different homeopathic preparations with each other to reliably identify any specific physicochemical properties. We also recommend the use of systematic positive and negative control experiments as a way of measuring the inherent variability in an experimental setup.

Further in-depth analysis of the experiments published is warranted to extract hypotheses regarding a possible mode of action of potentized remedies; such an analysis will be published as Part 3 of this review.

Author Disclosure Statement

S.W. was an employee of Hevert-Arzneimittel GmbH & Co. KG, Germany; however, none of the publications included in this review used Hevert products. All other authors have no competing financial interests.

Information

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Keywords

- physics
- very high dilutions
- serially diluted and agitated solutions
- ultrahigh aqueous dilutions

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Grundlagenforschung – Einzelne Abstracts wichtiger Untersuchungen:

Jean Louis Demangeat*

Towards a Rational Insight into the Paradox of Homeopathy

Department of Nuclear Medicine, General Hospital, France

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Submission: March 09, 2018; **Published:** April 10, 2018;

Bio

Review Article

ABSTRACT

Biological efficacy of infinitesimally diluted substances is still controversial. However, homeopathic remedies are manufactured through an iterative dilution/dynamization procedure which induces collateral phenomena, especially nanobubbles and release of silica from the glass container.

Our own NMR studies and a review of the literature show that dilutions could contain much more molecules than expected, moreover in nanoparticulate forms which increase with dilution.

Dilution/dynamization beyond a threshold of 10^{-6} - 10^{-8} generates superstructures associated with the solute, which grow at each step by affixing layers of nanobubbles and silica, or by self-assembly. Sizes from 1-2nm to hundreds of nanometers could be demonstrated by electron microscopy.

Dynamization appears crucial, by producing specific superstructures (distinguishable according to the dissolved substance), and inducing paradoxical biological effects. Superstructures are neither observed without dynamization nor at low dilution, where even a paradoxical chaotropic effect on the solvent is observed by NMR.

Thus, a dual structure of the homeopathic medicine is highlighted. We postulate that dynamization and nanobubbles ensure formation, stereospecificity, growth and transfer of superstructures across dilutions.

The sampling tip may play a major role by catching the superstructures and conveying the encaged remedy across the successive dilutions.

Some studies managed to show the presence of the remedy source, as a non-zero asymptote, in ultrahigh dilutions, far beyond the Avogadro's limit. Owing to this physical duality, low dilutions would act on organ receptors through ligand-receptor interactions, and high dilutions on systemic size-dependent targets, due to peculiar properties of nanoparticles, able, as a function of size,

- to cross physiological barriers,
- stimulate endocrine and immune systems or
- enter nerves to directly reach the brain.

Inverse effects, observed within the 10⁻³-10⁻⁶ range, might correspond to the onset of the nanoparticulate form.

The number of dynamizations could be the true factor for biological activity, rather than the rate of dilution.

KEYWORDS

Homeopathy; Ultrahigh dilutions; NMR relaxation; Dynamization; Nanobubbles; Nanostructures; Homeopathic remedy as nanomedicine; Hormesis; Hypotheses about biological effects

ABBREVIATIONS

NMR: Nuclear Magnetic Resonance; NS: Nanostructure; NB(s): Nanobubble(s); NP(s): Nanoparticle(s); DLS: Dynamic Light Scattering; R/B: Rayleigh/Brillouin; (T)EM: (Transmission) Electron Microscopy; AFM: Atomic Force Microscopy; BBB: Blood-Brain-Barrier; OB: Olfactory Bulb

CONCLUSION AND PROSPECTS

Homeopathic dilutions differ from conventional dilutions of physicochemistry. The specific dilution/dynamization procedure induces collateral phenomena, especially production of NBs and release of silica and ions from the glass container, which lead, at high dilution beyond C3-C4, to the formation of nanometric superstructures or NPs stabilized by internal and/or coating silica. It has been here emphasized the fundamental role of dynamization and of NBs which ensure the formation and growth of the nanostructures, their stereospecificity, their transfer across dilutions, and their enhancement and/or regeneration by a second dynamization.

It has been hypothesized, from NMR studies, a structural duality of the homeopathic remedy, likely to explain the differential and paradoxical actions recognized by the medical practice. The remedy, in the "molecular" form at low dilution would act on organ molecular targets through ligand-receptor interactions, as conventional medicines, and on systemic targets (immune, endocrine, nervous) and transcriptional function at high dilution, due to the peculiar properties of its nanoparticulate form.

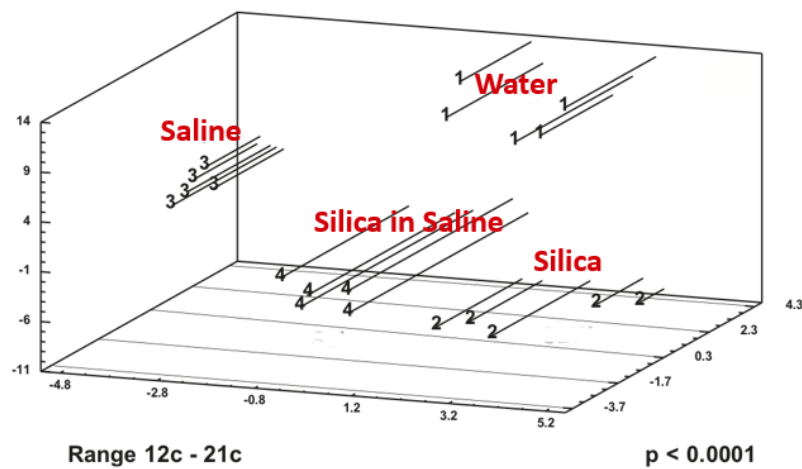
Undoubtedly, homeopathic solutions can no more be considered as pure water. Numerous studies in physics and EM attest the presence of nanoparticulate material in very high homeopathic dilutions, even far beyond Avogadro's limit.

However, although many studies do suggest it, the residual presence of the initial ingredient in the ultramolecular dilutions remains to be proved, as the question of contamination cannot be ignored [127,128]. But if this was definitely established, the notion of "Memory of water" would definitively lapse. Homeopathy would then be reduced to microdose pharmacology, exhibiting hormetic-type responses which justifies the simile therapeutic principle [129], and would be included in the present panoply of nanomedicine.

Research in this field has accelerated in recent years; efforts should focus on confirming first the hypothesis of the residual presence of the remedy in ultramolecular dilutions (this could be achieved quickly with current high-performance analytical methods), and second:

the crucial role of the dynamization process, as it will probably emerge that the true factor of the biological activity of homeopathic remedies is the number of dilution/dynamization steps applied to reach a given dilution level, or the number of succussions applied within each step. The use of decimal dilution and of various levels of dynamization could reach the same biological activities as ultra highly centesimal dilutions, while staying below the limit of Avogadro and thus conferring a more rational character to homeopathy.

Nuclear Magnetic Resonance



Demangeat Homeopathy (2013) 102, 87-105

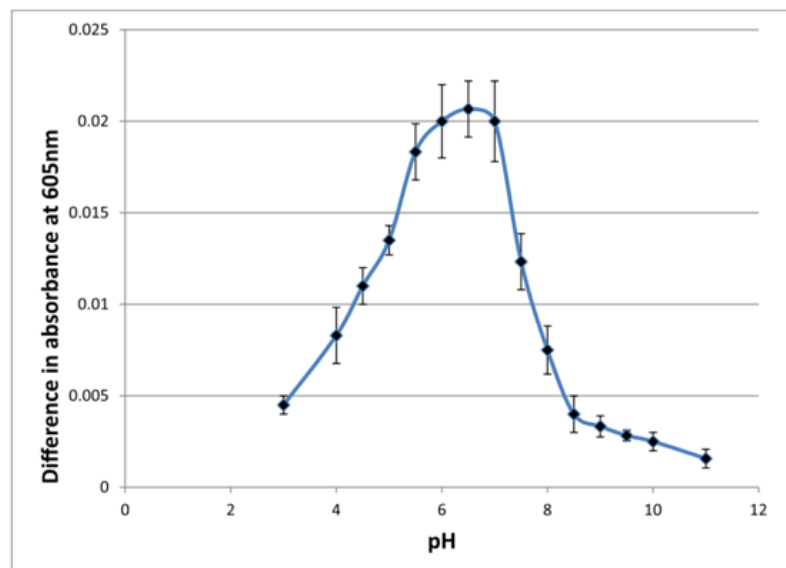


Figure 5 Difference in absorbance at 605 nm between control and *Glycerol* 50M solutions of BDF as a function of pH. BDF is at a concentration of 15 μ M. Buffers (citrate pH 3–6; phosphate pH 6–8; borate pH 8–10; CAPS pH 10–11) are at a concentration of 20 mM (see [Materials and methods](#)). Difference absorbance is shown at t = 12 h; n = 5 for each pH value.

Cartwright SJ

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Solvatochromic dyes detect the presence of homeopathic potencies

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A systematic approach to the design of simple, chemical systems for investigating the nature of homeopathic medicines has led to the development of an experimental protocol in which solvatochromic dyes are used as molecular probes of serially diluted and agitated solutions. Electronic spectroscopy has been used to follow changes in the absorbance of this class of dyes across the visible spectrum in the presence of homeopathic potencies. Evidence is presented using six different solvatochromic dyes in three different solvent systems. In all cases homeopathic potencies produce consistent and reproducible changes in the spectra of the dyes.

Results suggest that potencies influence the supramolecular chemistry of solvatochromic dyes, enhancing either dye aggregation or disaggregation, depending upon dye structure. Comparable dyes lacking the intramolecular charge transfer feature of solvatochromic dyes are unaffected by homeopathic potencies, suggesting potencies require the oscillating dipole of solvatochromic dyes for effective interaction.

The implications of the results presented, both for an eventual understanding of the nature of homeopathic medicines and their mode of action, together with future directions for research in this area, are discussed.

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KEYWORDS

Aggregachromism; Dye aggregation and disaggregation; Homeopathic potencies; Intramolecular charge transfer; Solvatochromic dyes; Solvatochromism; Supramolecular chemistry

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Homeopathic Potencies May Possess an Electric Field(-like) Component: Evidence from the Use of Encapsulated Solvatochromic Dyes

Abstract

BACKGROUND

Homeopathic potencies have been shown to interact with a range of solvatochromic dyes to produce spectroscopic changes in the visible region of the electromagnetic spectrum. Furthermore, the nature of the changes observed under different experimental conditions is beginning to limit the number of possible hypotheses that can be put forward regarding the fundamental identity of potencies.

AIMS AND METHODS

The present study uses β -cyclodextrins to encapsulate solvatochromic dyes of widely varying structures. The purpose of this approach is to de-couple the primary dye–potency interaction from any subsequent aggregation effects.

RESULTS

Despite large differences in molecular structure between dyes, results show that potencies affect all dyes according to the same fundamental principles. Specifically, positively and negatively solvatochromic dyes collectively respond in opposite and complementary ways to potencies in accordance with the differential stabilisation of their excited and ground electronic states. Under the conditions of encapsulation, positively solvatochromic dyes display a bathochromic shift of, on average, 0.4 nm with a 2% absorbance change, and negatively solvatochromic dyes display a hypsochromic shift of, on average, 0.2 nm with a 1% absorbance change. This behaviour is only ever seen in two situations—where solvent becomes more polar or where an electric field is applied to solutions of dyes.

CONCLUSIONS

The conditions used in this and previous studies to investigate the interaction of potencies with solvatochromic dyes preclude increased polarity of solvent as being responsible for the observed effects and that an explanation in which potencies carry an electric field (or electric field-like) component is by far the more likely. From the magnitude of the spectral changes induced in the dye Brooker's merocyanine by Arsenicum 10M, an estimate of the strength of the postulated electric field of 1.16×10^7 V/m can be made, which is comparable with the potential difference across cell membranes.

KEYWORDS

solvatochromic dyes, β -cyclodextrin, Arsenicum 10M, electric field, metastable state

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Characterization of Antimonium crudum Activity Using Solvatochromic Dyes

Abstract

OBJECTIVE

The objective of the current study was to compare the biological effects of Antimonium crudum (AC) previously obtained by our group and already described in the literature with now measurable physico-chemical effects on solvatochromic dyes.

METHODS

Different dilutions of AC and succussed water have been characterized with respect to their effect on the visible spectra of the solvatochromic dyes methylene violet (MV), a pyridinium phenolate (ET33), and a dimethylamino naphthalenone (BDN) compared with in-vitro action against Leishmania amazonensis-infected macrophages.

RESULTS

Dye responses varied according to the dye used and the level of AC dilution and results were found to corroborate previously published in-vivo and in-vitro effects of AC. In addition, a very significant enhancement in the absorbance increase of MV was seen using the supernatant from AC 200cH-treated cells (15%; $p < 0.0001$) over that seen with AC 200cH itself (4%; $p = 0.034$), suggesting the amplification of ultra-high dilution effects by biological systems. Furthermore, supernatants from AC-treated cells increased the range of dilutions of AC that were capable of producing effects on the spectra of MV. The effect of AC dilutions on dye ET33 was eliminated by a weak electric current passed through potency solutions.

CONCLUSION

The data confirm a correspondence between the biological effects of dilutions of AC in-vitro and physico-chemical effects on solvatochromic dyes as measured by changes in their visible spectra. Results also indicate high dilutions of AC are sensitive to exposure to electric currents and biological systems.

KEYWORDS

Antimonium crudum, Leishmania, amazonensis, solvatochromic dyes, macrophages, electric current

Bio-Crystallization

P Doesburg J.-O Anderse C Scherr S Baumgartner
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Replication of specific effects of a *Stannum metallicum* 30x preparation in a cress seedling/biocrystallization test system

One of the aims of basic homeopathic research is to reveal any specific mode of action of potentized preparations. This requires stable and reliable preclinical tests measuring either specific physicochemical properties or biological effects of homeopathic preparations.

Within a precursor project, we developed a bio-assay which yielded highly significant evidence for specific effects of an ultra-molecular *Stannum metallicum* 30x preparation relative to *Water* 30x, based on 15 independent randomized and blinded experiments performed at two independent laboratories.

The test system is based on cress seed germination, biocrystallization and subsequent computerised image analysis of the biocrystallization patterns. The biocrystallization method is based on the phenomenon that self-organizing, additive-specific crystallization patterns emerge when a $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ solution with additives is crystallized on a glass plate. The method acts as an indicator for systemic properties of the applied additive.

In the present project we investigated the reproducibility of the effects found in repeated experiments based on improved methodology towards:

- (i) optimization of the laboratory procedures to avoid any processing order effects,
- (ii) full implementation of blinded systematic negative control (SNC) experiments, and
- (iii) *Water* 30x was replaced by *Lactose* 30x to control for the trituration of *Stannum metallicum*. In total 10 + 10 independent randomized, coded experiments were performed in two independent laboratories. In addition, 10 + 10 SNCs were performed to control experimental stability.

Meta-analysis of the data revealed the same data structure in both projects, i.e. a reproduction of the significant differences between the two homeopathic preparations. The SNCs showed no significant intra-day, inter-day or inter-lab differences, indicative of a robust and reproducible test system.

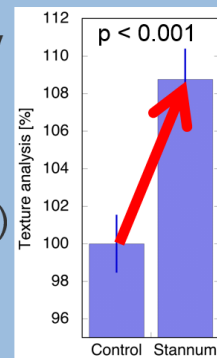
We were thus able to establish a test system yielding reproducible biological effects of an ultra-molecular homeopathic preparation. These ground-breaking results point to a promising potential of the method to contribute to basic homeopathic research.

KEYWORDS

Bio-assay - Systemic properties - *Stannum metallicum* 30x - Systematic negative control experiments - Reproducible effects

Effects of potentised *Stannum met. 30x* in a bioassay with *Lepidium sativum*

- > Treatment of *L. sativum* with *Stannum met. 30x* or Water/Lactose 30x, growth for 4 days *in vitro*
- > 35 independent randomized blinded experiments in 3 laboratories (n=15 1st series, n=20 2nd series)
- > Pre-metabolomic analysis (crystallization patterns of *L. sativum* extract with CuCl₂ added, analysis by computerized texture analysis)
- > Experimental stability verified by independent internal biological replicates (15 exp.) or full Systematic Negative Control experiments (20 exp.)
- > Texture analysis: $p < 0.001$ for *Stannum metallicum 30x* compared to Water/Lactose 30x



Doesburg et al. 2019 [Eur J Pharm Sci](#)

Maria Olga Kokornaczyk, Grazia Trebbia, Giovanni Dinellia, Iliara Marottia, Valeria Bregolaa, Daniele Nanib, Francesco Borghinic, Lucietta Bettia,
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Droplet evaporation method as a new potential approach for highlighting the effectiveness of ultra high dilutions

Summary

OBJECTIVE

This study sought to verify whether the droplet evaporation method (DEM) can be applied to assess the effectiveness of ultra-high dilutions (UHDs). We studied the shape characteristics of the polycrystalline structures formed during droplet evaporation of wheat seed leakages.

METHODS

The experimental protocol tested both unstressed seeds and seeds stressed with arsenic trioxide 5 mM, treated with either ultra-high dilutions of the same stressor substance, or with water as a control. The experimental groups were analyzed by DEM and *in vitro* growth tests. DEM patterns were evaluated for their local connected fractal dimension (measure of complexity) and fluctuating asymmetry (measure of symmetry exactness).

RESULTS

Treatment with arsenic at UHD of both stressed and non-stressed seeds increased the local connected fractal dimension levels and bilateral symmetry exactness values in the polycrystalline structures, as compared to the water treatment. The results of *in vitro* growth tests revealed a stimulating effect of arsenic at UHD *vs.* control, and a correlation between the changes in growth rate and the crystallographic values of the polycrystalline structures was observed.

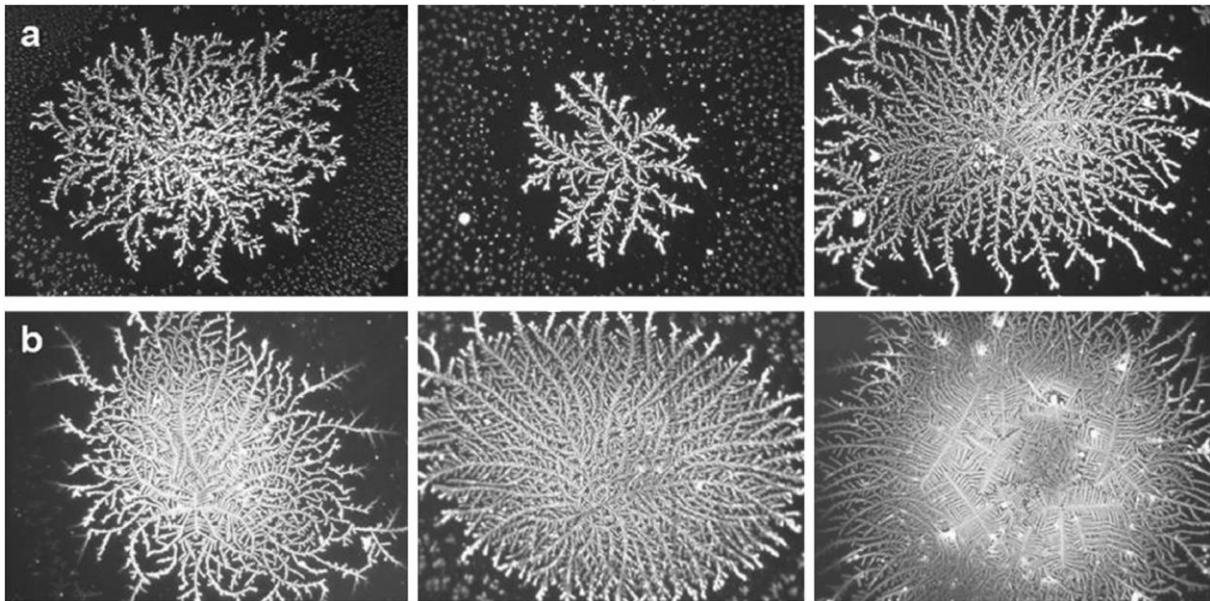
CONCLUSIONS

The results indicate that polycrystalline structures are sensitive to UHDs, and so for the first time provide grounds for the use of DEM as a new tool for testing UHD effectiveness. DEM could find application as a treatment pre-selection tool, or to monitor sample conditions during treatment. Moreover, when applied to biological liquids (such as saliva, blood, blood-serum, *etc.*), DEM might provide information about UHD effectiveness on human and animal health.

KEYWORDS

Droplet evaporation method; Fractal dimension; Fluctuating a symmetry; Wheat seedling growth; Arsenic trioxide; Ultra high dilutions; Polycrystalline structures.

Für diese Versuche wurden für jede der 4 Anordnungen 5 intakte Weizenkeime ausgesucht, möglichst uniform nach Farbe, Größe und Form.

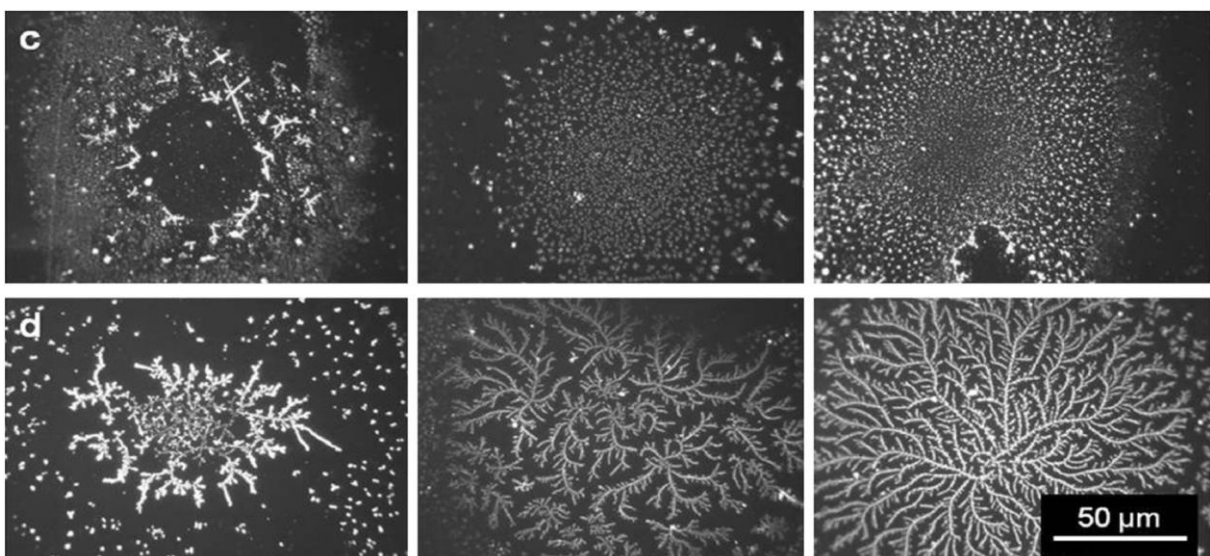


- Die beiden Chargen für Versuch a) und b) wurden für 1 Stunde in destilliertem Wasser inkubiert,
- Die beiden Chargen für Versuch c) und d) wurden zeitgleich in einer wässrigen Lösung des Zellgifts Arsen (5 millimolar) inkubiert.

Anschließend wurden aus allen Chargen Flüssigkeitsüberstände entnommen und auf einen sauberen Objektträger getropft und bei 25 Grad in einem Wärmeofen getrocknet. Während dieses Trocknungsprozesses bildet der wässrige Überstand von gesunden Weizenkeimen regelmäßige Kristallisationsmuster, die das bloße Auge ähnlich einer Pflanzenformation wahrnimmt (Abb a), die jedoch zur objektiven Messung eine computergesteuerte Strukturanalyse durchlaufen.

Der Überstand aus den mit Arsen geschädigten Keimen löst diese Strukturbildung nicht mehr aus (Abb c).

Anschließend wurden beide Weizenkeim-Chargen a) und c) mit einer homöopathisch potenzierten Verdünnung von Arsen (D 45, jenseits der Avogadro Konstante) imprägniert. Daraufhin zeigten die anschließend entnommenen Flüssigkeitschargen bei den gesunden b) wie bei den mit Arsen geschädigten Chargen d) diesmal beide eine Kristallisationsbildung. Die Versuche wurden an insgesamt 4 Tagen 3x repliziert.



Evidenz und evidenzbasierte Medizin

Evidenz bezeichnet ursprünglich das dem Auge unbezweifelbar Erkennbare oder die unmittelbare, mit einem besonderen Wahrheitsanspruch auftretende vollständige Erkenntnis.

Immanuel Kant hat für die geistige Bewegung der Aufklärung formuliert, dass wir ein „Ding an sich“ nicht erfassen können, sondern nur eine durch unsere Sinne vermittelte indirekte Anschauung der Dinge wahrnehmen können. Messgeräte können die Anschauung unserer Sinne erweitern, doch das Ding an sich erfassen sie ebenfalls nicht. Er hat sodann Evidenz als eine anschauende Gewissheit definiert. Innerhalb der Evidenz definiert er apodiktische Aussagen genau wie Aristoteles als diejenigen, deren Wahrheitswert vollkommen unstrittig ist¹². Dieses so sagt Kant, ist im strengen Sinne nur in der Mathematik gegeben.

Evidenzbasierte Medizin

Herkunft:

Der schottische Arzt George Fordyce veröffentlicht bereits 1793 eine Schrift *An Attempt to Improve the Evidence of Medicine*.

Einführung in die moderne Medizin:

Die Bezeichnung evidence-based Medicine wurde in den 90er Jahren von Gordon Guyatt eingeführt. Die beste Übersetzung wäre: **Nachweisorientierte Medizin**

Die moderne evidenzbasierte Medizin basiert bisher auf *drei Säulen*.

1. **Die Erfahrung und die Erkenntnis des Therapeuten**
2. **Die Werte und Wünsche und die Erfahrung des Erkrankten**
3. **Der aktuelle Stand der Wissenschaft und des medizinisch Wissbaren**

¹² siehe dazu Immanuel Kant, Die *Kritik der reinen Vernunft*

Fazit

- In der klinischen Forschung und in der Versorgungsforschung finden sich in zahlreichen Studien **deutliche Hinweise auf die Wirksamkeit einer homöopathischen Therapie.**
- Eine Reihe von Grundlagenuntersuchungen - wie die von Baumgartner, Cartwright und Demangeat etc. - zeigen eindeutig, dass homöopathische Zubereitungen **reproduzierbar messbare Effekte auf biologische und physikalische Systeme haben**, die signifikant über einer Placebo-Wirkung liegen.
- WIE genau und WARUM es zu diesen Effekten kommt, ist **bisher noch nicht schlüssig erklärbar.**
- Genau das ist der idealtypische Fall für ein forschungswürdiges Feld: **Es wird ein Naturphänomen wiederholt beobachtet, das man mit bisherigen Modellen nicht erklären kann.**
- Exakt hier muss Forschung ansetzen und **genau hier weist die Natur die Richtung zu neuen Erkenntnisebenen.**

Eine vierte Säule der Evidenz ist sinnvoll

Wir möchten abschließend anregen, dass die Auswirkung von Bias also von Vorurteilen innerhalb der ersten, interkollegialen“ und der zweiten patientenbasierten, sowie der dritten wissenschaftlich begründeten Säule ein ausdrücklich gefördertes, neues Forschungsfeld wird. So kann mit einer vierten, tragfähigen Säule durch die Vorurteilsforschung eine besser evidenzbasierte Medizin entstehen.

Die Akademie

Die Akademie Wissenschaftliche Homöopathie fördert die

- Integrative Kooperation von internationalen Forscherteams
 - Kooperation mit den bestehenden seriösen Verbänden und Institutionen im Bereich der Homöopathie, der Komplementärmedizin, der Psychotherapie sowie der Schulmedizin und mit Patientenverbänden
 - Internationale Vernetzung exzellenter wissenschaftlicher Teams
 - Entwicklung von traditionsorientierter zu evidenzbasierter Homöopathie
- An die Homöopathen stellt sich aus Sicht der Wissenschaft die zukunftsorientierte Anforderung, ihr Fachgebiet aus einem historisierenden Kontext zu befreien und forschend weiter zu entwickeln.

Die Akademie Wissenschaftliche Homöopathie stärkt die internationale Forschung zu

- den charakteristischen Merkmalen von Krankheit, Gesundheit und Heilung
- der Wirkweise des Simileprinzips und der Homöopathie
- der Methodenqualität in der Homöopathie
- der Optimierung einer Integrativen Versorgung.

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