

Research Bulletin No.3 November 2016

Excellence in homeopathic practice, using science, large-scale evidence and state-of-the-art technology.

Statistical confirmation of the Repertory: A historic step towards evidence-based practice.



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A new age of evidence-based homeopathy

Introduction

Dear fellow members of the homeopathy community,

It is with great pleasure that we are introducing our third Research Bulletin, representing our collaborative scientific work in classical homeopathy during the past 16 months. During that period Vithoulkas Compass, as a platform for homeopathic practice, was being used daily by a growing community of enthusiastic users with great results, at the same time helping us to continuously improve all its aspects. Further on VC also clearly represents the logical step towards the collective participation of practitioners in the development of an evidence-based intelligent expert system, a reliable and truly coherent repertory, and an accurate, 'low-noise' Materia Medica. In fact, given the possibilities brought by during its first 5 years of operation, we are increasingly confident that VC is signalling the future in homeopathic software and homeopathic practice.

This bulletin includes an important new development: In 2016 the vision of an evidence-based repertory started to materialise. The mathematics and statistics team carefully analysed the contents of the user cases database using the concept of likelihood ratios, and, for the first time in homeopathic history, tens of thousands of statistically confirmed symptom-remedy relationships emerged, providing a new level of visibility of the repertory along with several other valuable outcomes. Already the VC expert system engine has gained from these results, achieving greater accuracy by incorporating new parameters in the algorithms and adjustments in the repertory. In fact, the success of this experimental exercise was such that we are concentrating our work into making repertory confirmation a standard continuous process.

An important aspect of our current analysis work is the validation of statistical results of previous years with new cases. We were extremely pleased to observe consistency and a welcome narrowing of confidence intervals in likelihood ratios (LRs), which demonstrates the soundness of the approach. Along with the pure research activities, all the content in VC has been improving with studies and constant consultations with experienced homeopaths and Professor Vithoulkas. We are happy to report these combined efforts resulted in positive feedback from our user community.

The analysis of repertory utilization is giving a clear message. A good repertory has to be precise and as "noise-free" as possible. The high accuracy and coherence of the first 10-15 thousand core key rubrics is the most crucial factor for effective repertorisation, which guides homeopaths in prescribing correctly and at the same time extends their skills. The remaining rubrics are mainly useful for the confirmation of candidate remedies in a case. Additionally, the analysis shows that in many cases the Materia Medica is necessary for the final decision, especially when psychological symptoms and the essence of the remedy has to be taken into account. In order to assist homeopaths in their final decision, the VC team has developed "Repertory Metadata", which is a unique combination of the Repertory with the Materia Medica. "Repertory Metadata" tool presents valuable case-related information regarding candidate remedies.

Today, despite its very positive health and social impact, homeopathy is being increasingly challenged by different movements in the scientific community. We believe the answer to these challenges can come from high quality collaborative research, and also from the application of evidence-based methodologies. The Vithoulkas Compass team is fully committed to serve this purpose. The consultation database, now crossing the 350,000 mark, is an invaluable asset for studies and analyses, and we hope that the homeopathic community takes full advantage of this unique growing resource.

We hope that you enjoy reading this third Research Bulletin. We would like to thank all our friends and supporters for their help and encouragement. We are committed to continue R&D with the same enthusiasm and energy into 2017 working on very interesting projects. In the meantime, we hope that all together we can overcome external pressures against homeopathy and that homeopathic practice advances as positively as it deserves to.

Kyriakos Xagoraris (Managing Director of CHOES Ltd)
October 2016

1. VC is evolving in key directions addressing important requirements of the homeopathic community.

Since its inception, Vithoulkas Compass has been a project with a long term vision concerning development of a powerful and efficient toolbox for homeopaths. We are working to meet the requirements of the homeopathic community in the best way. Continuous improvement of the content and an approach centered on developing more efficient ways to help practitioners, have been the greatest part of our work. Key areas where improvements and good results have been achieved are the following:

- Leading Expert System accuracy
- Coherent, 'low-noise' Repertory
- Accurate Materia Medica
- Unique Repertory Metadata information
- Alternative Synapse Workflow for increased efficiency
- Advanced System Infrastructure

1. VC is evolving in key directions addressing important requirements of the homeopathic community.

Significant work has been performed analysing the effectiveness of prescriptions in numerous cases. Valuable results have been produced, that include quality criteria derived for repertorisation like distribution of symptoms in different chapters, underlining distribution, use of key rubrics together with common symptoms. The scope and methods utilised have been presented in the previous editions of the Research Bulletin (June 2014, June 2015).

The latest important breakthrough in VC development was to create an evidence-based repertory accompanied by evidence-based differential and specific remedy analysis modules. These were based on the application of statistical outcomes on the repertory and expert system parameters resulting in a significant positive effect in performance. In this way we are closing the feedback loop in an evidence-based online system, a historical step for homeopathic practice.

At this stage, the main projects for the VC evolution are:

- Intensive work on the repertory, utilizing new field data and likelihood ratios which
 are continuously generated and assessed, both on symptom-remedy pairs and on
 symptom combinations for each remedy
- Addition of repertory metadata information for more symptom differentiations between remedies, performed in cooperation with experienced homeopaths and using new sources
- Reliability analysis of information passed through casetaking in order to overcome noise and bias problems and provide quality checks
- Synapse workflow validation and improvements in the usability and content of the materia medica
- Preparation of the next VC version, which will embed case management intelligence
- Development of a comprehensive statistical analysis tool for easier extraction of preliminary outcomes from data on file

According to our experience, gained in developing VC, homeopathic treatment, despite its long history, has important unrealised potential and there is still a lot to be revealed. We consider that systematic studies can lead to significant findings. For this reason, the VC platform supports collaborative studies in order to go beyond the limits of our team. We carry out research studies because we appreciate evidence and measurable outcomes, which are core components in our mission. In general, we are progressing step by step by addressing problems and issues that can be solved or improved. Using this approach in analysing cases, new findings are revealed, which are useful in supporting homeopaths of all levels of experience in their practice.



2. Statistical analysis projects

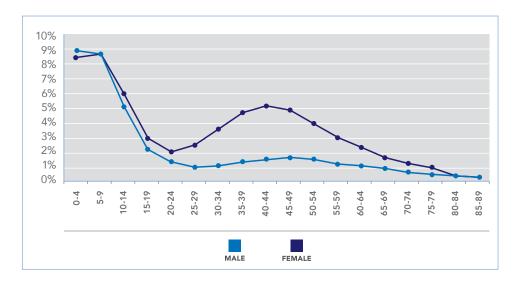
- Analysis of Acute Cases and initial Statistical results
- Updated statistical results from new cases with depression treated with classical homeopathy
- The relationships between remedies and symptoms under the prism of Likelihood ratios

a. Analysis of Acute Cases and initial Statistical results

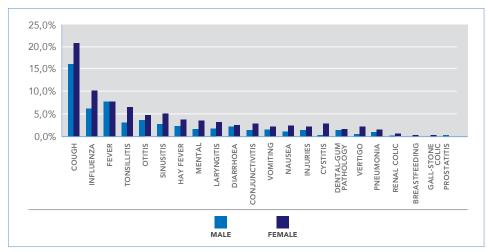
The VCAcute module supports acute cases with a specially structured Acute repertory and a dedicated expert system with the same standards and targets as VC. Symptoms from the complete repertory can also be included. However, they are treated accordingly to the acute case, for example the importance of physical symptoms is adjusted. Further on, a com-

prehensive Acute Materia Medica provides clear information for the selected remedy. In the following graphs, statistical results from acute cases showing age distribution, common pathologies, symptoms and remedies are presented. (Analyses of remedy effectiveness, acute prescriptions, likelihood ratios and relevant outcomes are under development.)

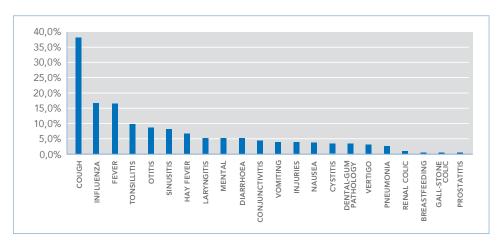
1. Age Distribution of Patients in Acute Pathology Cases



2. Distribution of Acute Pathologies per Gender

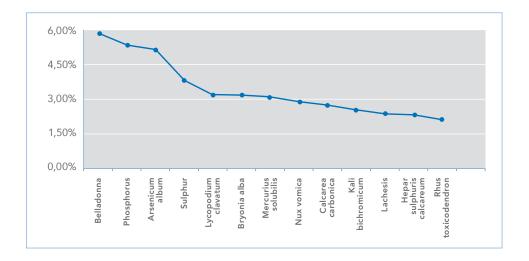


3. Common Acute Pathologies



2. Statistical analysis projects

4. Most Commonly Prescribed Remedies in Acute Cases



b. Updated statistical results from new cases with depression treated with classical homeopathy

This presentation is a follow up to the results presented in previous bulletin no.2 (June 2015) and provides new evidence, since the number of selected cases has increased considerably.

Depression is a disease with high prevalence worldwide and a great number of patients seek homeopathic treatment for this problem. This update also confirms previous studies of depression cases, which have been treated from homeopathic practitioners worldwide and shows that results become more accurate and consistent with the processing of more cases. The statistical analysis for remedy

effectiveness includes the main following parameters:
(a) Gender, (b) Age, (c) Geographical Distribution, (d)
Prescribed Remedies, (e) Reported Treatment Effectiveness.
The treatment effect was derived from the evaluation
by the homeopath in the following categories "Large
improvement", "Moderate improvement", "Small
improvement" and "No effect", and "remedy did not act
as expected", during the follow-up session

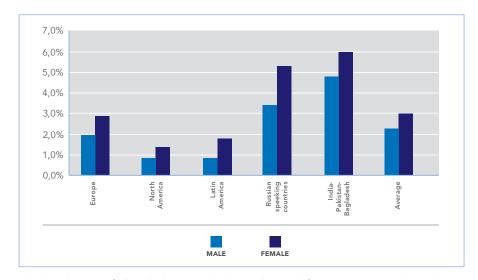
In the following the most common mind symptoms found in depression cases are given.

5. Common Mind Symptoms in Depression Cases

MIND - SADNESS, mental depression	293
MIND - CONFIDENCE - want of self-confidence (low)	273
MIND - ANXIETY - health, about	249
MIND - GRIEF - ailments from	200
MIND - SYMPATHETIC	190
MIND - WEEPING, tearful mood, etc.	188
MIND - SIGHING	180
MIND - IRRITABILITY	179
MIND - FEAR - high places, of	167
MIND - OFFENDED, easily	148
MIND - FORSAKEN feeling	144
MIND - RESERVED	141
MIND - CONSOLATION - amel.	135
MIND - DWELLS - on past disagreeable occurences	128
MIND - MOOD - changeable, variable, etc.	124

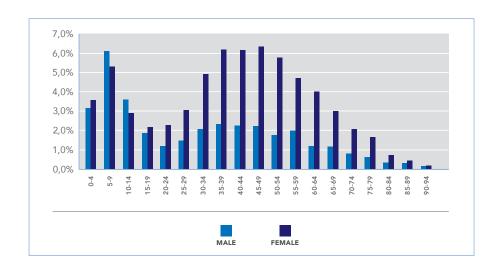


6. Percentage of Depression Cases in Different Regions



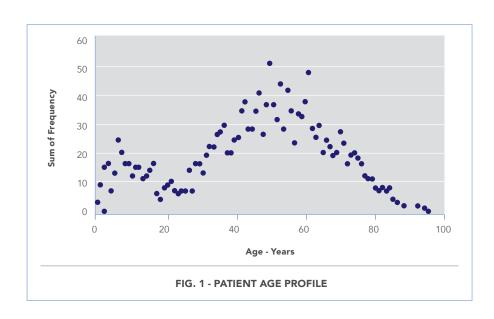
The distribution of all pathologies in both genders and for age groups is shown below.

7. Age Distribution of Patients in all Pathologies



8. "Towards standard setting for patientreported outcomes in the NHS homeopathic hospitals", Elizabeth A. Thompson et. Al., Homeopathy (2008) Vol. 97, p. 114–121

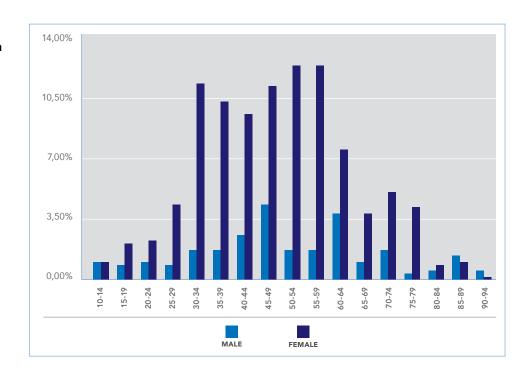
In chart 8 we see a similar distribution curve on 1797 patients in the NHS homeopathic hospital study comparable with the distribution curve from cases of VC users.



9 —

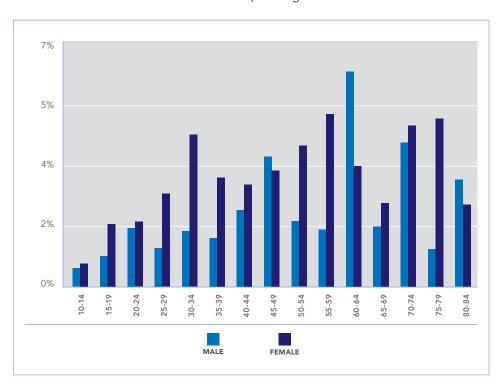
2. Statistical analysis projects

9. Age Distribution of Patients in Depression Cases



In chart 10 the percent of depression towards the remaining pathologies is given. For example, in the age group "60-64" for male gender, depression cases are about 6% and the cases with other pathologies are 94%.

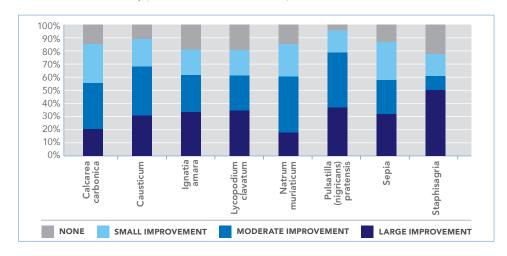
10. Percentage of Depression Cases per Age Group Relative to All Cases of Similar Age





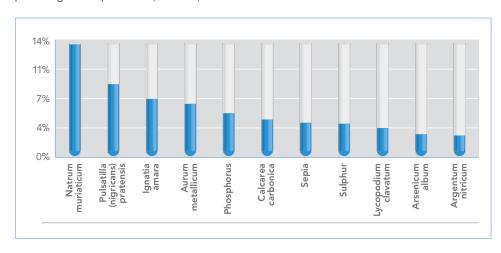
The effect of commonly prescribed remedies in depression cases is shown below.

11. Common RemediesRemedy Effectin Depression cases

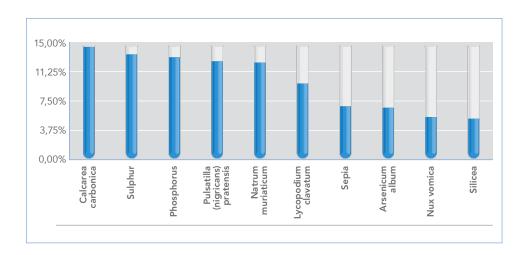


In chart 12 the commonly prescribed remedies in depression cases and then for all pathologies are provided (chart 13).

12. Commonly
Prescribed Remedies
in Depression Cases



13. Most Commonly Prescribed Remedies in all cases



2. Statistical analysis projects

c. The relationships between remedies and symptoms under the prism of Likelihood ratios

During the past year many more symptom-remedy relations have been studied and the corresponding likelihood ratios and confidence intervals were calculated. Results show that previous computations are compatible and now confidence intervals are reduced, a significant finding pointing to the validity of the analysis. Further on, we have studied common symptoms alone and in combinations that were present in successful prescriptions and symptoms present in unsuccessful prescriptions.

Table 1.Likelihood Ratio for combined symptoms appearing in the same consultation case for eleven common remedies.

Remedy - Symptoms Combination	Sensitivity (true positive)	Specificity (true negative)	LR+	LR+ min	LR+ max
Argentum nitricum					
GENERALITIES - FOOD and DRINKS - sweets – desire in in	combination wi	th:			
GENERALITIES - FOOD and DRINKS - salt - desire	6%	96%	1.6	0.9	2.8
GENERALITIES - WARM - agg.	14%	96%	4.0	2.7	5.8
MIND - ANXIETY - health, about in combination with:					
MIND - FEAR - high places, of	17%	98%	8.8	6.3	12.4
Arsenicum album					
GENERALITIES - COLD - agg. in combination with:					
MIND - FASTIDIOUS	20%	98%	12.4	9.3	16.4
STOMACH - THIRST - small quantities, for (in sips) - often	10%	100%	19.9	12.8	30.8
MIND - FASTIDIOUS in combination with:					
STOMACH - THIRST - small quantities, for (in sips) - often	10%	100%	25.5	16.4	39.4
Calcarea carbonica					
GENERALITIES - FOOD and DRINKS - sweets - desire <i>in cor</i>	mbination with:				
GENERALITIES - FOOD and DRINKS - eggs - desire	18%	97%	5.7	4.7	7.0
MIND - FEAR - high places, of	11%	96%	2.9	2.3	3.7
MIND - FEAR - high places, of in combination with:					
EXTREMITIES - COLDNESS - Foot	7%	99%	5.2	3.7	7.4
Causticum					
MIND - SYMPATHETIC in combination with:					
MIND - INJUSTICE, cannot support	30%	98%	15.1	11.6	19.5
Ignatia amara					
MIND - CONSOLATION - agg. in combination with:					
MIND - SIGHING	15%	99%	26.3	18.6	37.2
MIND - SIGHING in combination with:					
MIND - GRIEF - silent	12%	100%	32.5	21.9	48.3
MIND - MOOD - changeable, variable, etc.	15%	99%	27.6	19.6	38.9
Lycopodium clavatum					
GENERALITIES - FOOD and DRINKS - sweets - desire <i>in cor</i>	mbination with:				
SLEEP - UNREFRESHING	5%	98%	2.6	1.6	4.4



Remedy - Symptoms Combination	Sensitivity (true positive)	Specificity (true negative)	LR+	LR+ min	LR+ max		
Natrum muriaticum							
GENERALITIES - FOOD and DRINKS - fat - aversion in com	bination with:						
MIND - CONSOLATION - agg.	8%	98%	5.6	4.0	7.8		
MIND - RESERVED	11%	98%	6.4	4.8	8.6		
GENERALITIES - FOOD and DRINKS - salt - desire in comb	ination with:						
GENERALITIES - FOOD and DRINKS - fat - aversion	12%	97%	4.4	3.3	5.7		
MIND - CONSOLATION - agg.	11%	99%	8.8	6.6	11.8		
Nux vomica							
MIND- IRRITABILITY in combination with:							
MIND - IMPATIENCE	15%	98%	8.6	5.9	12.6		
Phosphorus							
GENERALITIES - FOOD and DRINKS - sweets – desire in co	ombination with:						
MIND - SYMPATHETIC	11%	96%	3.0	2.2	4.0		
MIND – SYMPATHETIC in combination with:							
MIND - ANXIETY - health, about	12%	97%	4.5	3.5	5.9		
Pulsatilla (nigricans) pratensis							
GENERALITIES - FOOD and DRINKS - fat – aversion in con	nbination with:						
MIND - CONSOLATION - amel.	17%	98%	9.6	7.7	12.0		
MIND - CONSOLATION - amel. in combination with:							
EXTREMITIES - UNCOVER, inclination to - Feet	7%	99%	7.2	5.2	10.4		
GENERALITIES - AIR - open - amel.	10%	99%	9.5	7.1	12.6		
MIND - WEEPING, tearful mood, etc.	15%	99%	10.8	8.5	13.7		
Sepia							
GENERALITIES - COLD - agg. in combination with:							
GENITALIA-FEMALE - SEXUAL desire - diminished	8%	99%	8.5	5.5	13.2		

The calculation of Likelihood Ratio (LR) has been further improved as the number of cases increased and the 95% confidence interval of each mean value has been reduced. We have also computed LR-(minus) for key symptoms. If LR-(minus) is small, then the practitioner should ask if the key symptom is present before prescribing a remedy. This information is also utilised in the differential analysis functions of the system.

2. Statistical analysis projects

Table 2.The corresponding relationship of remedies with each symptom separately, from table 1.

e corresponding relationship of remedies with eac	, ,							I
emedy - Symptoms Combination	Sensitivity (true positive)	Specificity (true negative)	LR+	LR+ min	LR+ max	LR-	LR- min	LR ma
gentum nitricum								
GENERALITIES - FOOD and DRINKS - salt - desire	15%	87.0%	1.2	0.8	1.7	1.0	0.9	1.0
GENERALITIES - FOOD and DRINKS - sweets - desire	42%	77.3%	1.8	1.5	2.2	0.8	0.7	0.9
GENERALITIES - WARM - agg.	25%	89.5%	2.4	1.8	3.1	0.8	0.8	0.9
MIND - ANXIETY - health, about	33%	89.6%	3.2	2.6	4.0	0.7	0.7	0.
MIND - FEAR - high places, of	37%	90.7%	3.9	3.2	4.8	0.7	0.6	0.8
senicum album								
GENERALITIES - COLD - agg.	32%	89.2%	2.9	2.4	3.6	0.8	0.7	0.
MIND - FASTIDIOUS	39%	94.9%	7.7	6.5	9.2	0.6	0.6	0.
STOMACH - THIRST - small quantities, for (in sips) - often	14%	98.8%	12.1	8.6	17.1	0.9	0.8	0.
alcarea carbonica								
EXTREMITIES - COLDNESS – Foot	13%	95.6%	3.0	2.4	3.8	0.9	0.9	0.
GENERALITIES - FOOD and DRINKS - eggs - desire	37%	93.2%	5.4	4.8	6.1	0.7	0.6	0.
GENERALITIES - FOOD and DRINKS - sweets - desire	37%	77.4%	1.6	1.4	1.8	0.8	0.8	0.
MIND - FEAR - high places, of	24%	90.7%	2.6	2.2	3.1	0.8	0.8	0
nusticum								
MIND - INJUSTICE, cannot support	56%	96.1%	14.3	12.3	16.7	0.5	0.4	0
MIND – SYMPATHETIC	41%	90.1%	4.1	3.4	5.0	0.7	0.6	0
natia amara								
MIND - CONSOLATION - agg.	23%	95.8%	5.4	4.3	7.0	0.8	0.7	0
MIND - GRIEF – silent	21%	98.4%	13.3	10.2	17.4	0.8	0.7	0
MIND - MOOD - changeable, variable, etc.	21%	96.2%	5.5	4.2	7.1	0.8	0.8	0
MIND - SIGHING	48%	96.2%	12.6	10.9	14.6	0.5	0.5	0
copodium clavatum								
GENERALITIES - FOOD and DRINKS - sweets - desire	36%	77.3%	1.6	1.4	1.9	0.8	0.8	0
SLEEP - UNREFRESHING	13%	94.8%	2.5	1.8	3.4	0.9	0.9	1
atrum muriaticum								
GENERALITIES - FOOD and DRINKS - fat - aversion	26%	88.8%	2.4	2.0	2.8	0.8	0.8	0
GENERALITIES - FOOD and DRINKS - salt - desire	40%	87.4%	3.1	2.8	3.6	0.7	0.6	0
MIND - CONSOLATION - agg.	20%	95.9%	4.9	4.0	5.9	0.8	0.8	0
MIND - RESERVED	24%	94.8%	4.6	3.8	5.5	0.8	0.8	0
ux vomica								
MIND - IMPATIENCE	25%	95.9%	6.1	4.7	8.0	0.8	0.7	0
MIND - IRRITABILITY	30%	92.2%	3.9	3.1	5.0	0.8	0.7	0
osphorus								
GENERALITIES - FOOD and DRINKS - sweets - desire	19%	77.1%	0.8	0.7	1.0	1.0	1.0	1
MIND - ANXIETY - health, about	21%	89.6%	2.0	1.6	2.4	0.9	0.8	0
MIND - SYMPATHETIC	41%	90.4%	4.3	3.8	4.8	0.7	0.6	0
ılsatilla (nigricans) pratensis								
EXTREMITIES - UNCOVER, inclination to - Feet	15%	94.9%	2.9	2.3	3.7	0.9	0.9	0
GENERALITIES - AIR - open - amel.	21%	95.8%	5.0	4.1	6.0	0.8	0.8	0
GENERALITIES - FOOD and DRINKS - fat - aversion	33%	89.0%	3.0	2.6	3.4	0.8	0.7	0
MIND - CONSOLATION - amel.	38%	95.0%	7.7	6.8	8.7	0.6	0.6	0
	26%	94.5%	4.7	4.0	5.5	0.8	0.7	0
MIND - WEEPING, tearful mood, etc					, 5.5	1 3.3	1 5.7	
MIND - WEEPING, tearful mood, etc.	2070							
MIND - WEEPING, tearful mood, etc. Ppia GENERALITIES - COLD - agg.	19%	89.1%	1.7	1.3	2.2	0.9	0.9	1.

3. Successful first attempt towards a highly confirmed repertory, a historical breakthrough

3. Successful first attempt towards a highly confirmed repertory, a historical breakthrough

A successful first attempt towards a highly confirmed repertory has been done through statistical analysis of many real cases. The following table from SCIENTIFIC FRAMEWORK OF HOMEOPATHY, revised edition after LMHI Congress by Dr Raj K. Manchanda, 2015 summarizes studies for clinical verification of homeopathic symptoms.

SCIENTIFIC FRAMEWORK OF HOMEOPATHY, Evidence Based Homeopathy, Revised edition after 69th LMHI Congress, July 2014 (Paris, France), Dr Raj K. Manchanda, 2015.

Condition/Study	N	Design	N Sympt	N Rem	Results
Van Wassenhoven ³⁴⁷ (2005)	2148	LR retrospective	>230	100	Symptoms – Similarity – Globality
CCRH ³⁴⁸ Damiana (2007)	3032	Trad. Method	?	1	Symptoms
Rutten & all ³⁴⁹ (2008)	4094	LR Prospective	6	75	Similarity
Araujo (*). Anacardium orientale (2008)	5	Trad. Method	?	1	16 groups of symptoms – Similarity (constitution)
Gnaiger & all (*) ³⁵⁰ Petroleum (2008)	25	Trad. Method	?	1	6 groups of symptoms – Similarity (constitution)
Dominici (*) Hydrogenium peroxidatum (2008)	18	Trad. Method	10	1	Symptoms of proving – Similarity
AFADH (*) Latrodectus Tredicim Guttatus (2008)	4	Trad. Method	?	1	24 groups of symptoms – Similarity (constitution)
AFADH (*) Tarentula Lycosa (2008)	5	Trad. Method	?	1	36 groups of symptoms – Similarity (constitution)
Louis (*) Borax (2008)	12	Trad. Method	?	1	6 groups of symptoms – Similarity (constitution)

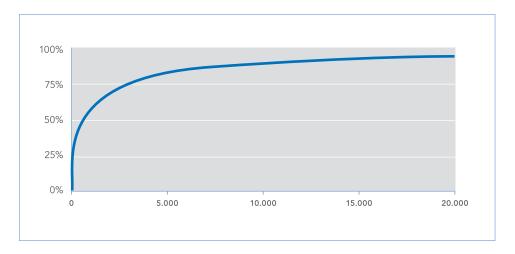
The main criteria for case filtering were: the time period from prescription to follow up, distribution of symptoms in different chapters and underlining. In this way 29097 cases with follow-up were selected. The repertory used in the cases has approximately 75000 symptoms, is based on Kent and classical authors and is continuously improved with input by the VC team, associated collaborators and the VC community. Through statistics 9071 remedy-symptom likelihood ratios have been derived with the corresponding confidence intervals, regarding 194 different remedies and 2288 different symptoms.

This analysis has been utilised:

- (a) for the evaluation and improvement of the repertory data,
- (b) for enhancing differential analysis module,
- (c) for improving remedy selection algorithms, (where initial estimations show there is potential for improvement in at least 10% of the cases).

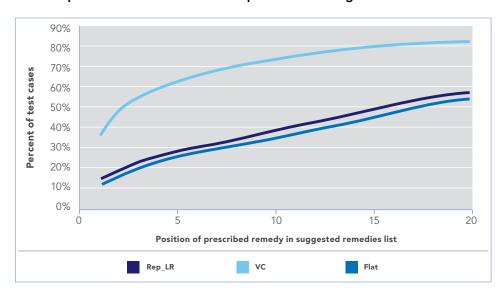


14. Cumulative Occurrence of Most Used Rubrics



Although the number of symptoms and remedies that have been statistically confirmed might be considered small, these 2288 different symptoms represent a significant percentage 73% of repertory usage in all cases. In the following evaluation test using a thousand real test cases, the value of the above computations is evident. A very small confirmed repertory based only on LR computations with 2288 different symptoms, 194 different remedies and 9071 remedy-symptom pairs can provide results similar to a flat remedy selection algorithm utilizing the whole repertory (Chart 15). This approach is also validated in another software system, which uses different algorithms. There we see the value of repertory confirmation and coherence between different authors in the following way. We examine the performance on test cases first utilizing a small number of authors and second when using the whole repertory (Chart 16). The improvement in performance and effective selection of the appropriate remedy is obvious when a small number of selected authors are included in the repertory.

15. Comparison between different repertories and algorithms



3. Successful first attempt towards a highly confirmed repertory, a historical breakthrough

16. Importance of rubrics confirmation in the repertory

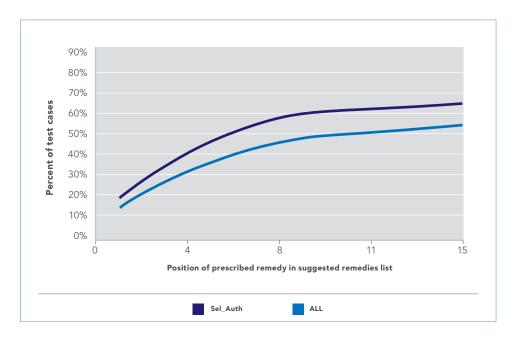


Chart 16 shows considerable results improvement in another software system when only selected authors are utilized compared to the whole repertory. Obviously the merge of many authors reduces the coherence of the repertory and the results of the algorithms are inferior despite the fact that additional information is included. The main conclusion from the study of the relationships between remedies and symptoms through the effectiveness of the treatment, is that it provides useful information, which can lead to an accurate and confirmed repertory. A confirmed and coherent repertory can lead to improved homeopathic practice, which is consistent with evidence based models.

4. Pilot project evaluating the predictive capacity of homeopathic provings with regard to clinical effectiveness

A pilot study together with Todd Hoover, MD and Dr. Robbert van Haselen has been designed to perform an evaluation of the predictive capacity of homeopathic provings with regard to clinical effectiveness for a single remedy.

The study will progressively answer the question of whether symptoms derived from provings represent valid indicators for the successful clinical use of that remedy.

The Data Analysis steps include:

- **a.** Comparing rubrics that were associated with positive clinical outcomes for a particular remedy to rubrics that were identified in provings of the remedy, and
- **b.** Comparing rubrics assessed to have higher likelihood associated with clinical improvement to rubrics from provings that were assessed to be more important in the clinical picture of the remedy.

5. Highlights of VC improvement projects

- Analysis of the case taking process through information theory science
- Continuous improvement iterations of VC brain
- Evolution of the VC Synapse Workflow
- Dynamic Repertory Metadata: supplementing the repertory with comparative Materia Medica entries
- User Generated Content in VC, a vital addition

a. Analysis of the case taking process through information theory science

An important guide in our work has been the full mapping of the case-taking process, in order to display in an organized manner, the multitude of parameters, which come into play and can influence remedy selection. Information reliability analysis of case-taking process includes the characterization of every parameter in terms of its importance for remedy scoring, its usefulness, its potential to add noise to the results, the bias potential, the practicality factor, the objectivity and others. This systematic approach is emerging step by step in the supporting software system and provides a blueprint for

future development of the method. This evolving analysis attempts to include all parameters related to the process, from the symptomatology to the final remedy decisions, including patient and practitioner communication factors, experience of the method, prior knowledge of remedies, different kinds of bias and many more aspects. These parameters are generally handled efficiently by most experienced practitioners and their classification and characterization proved very helpful as the resulting, still growing, tree is a valuable tool collecting best practices. An example:

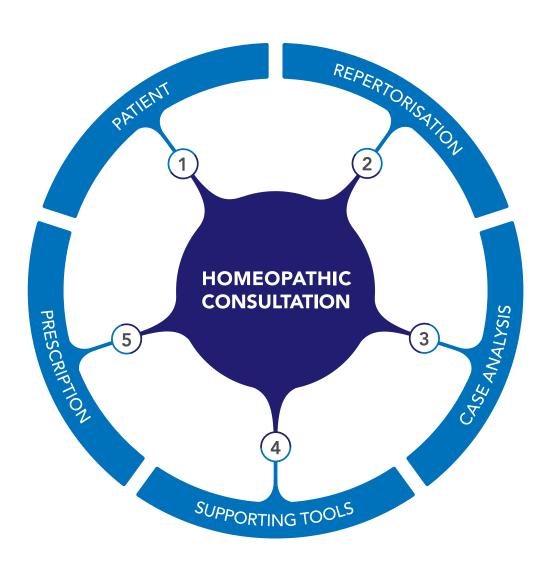


Figure 1a: Homeopathic consultation, first level

5. Highlights of VC improvement projects

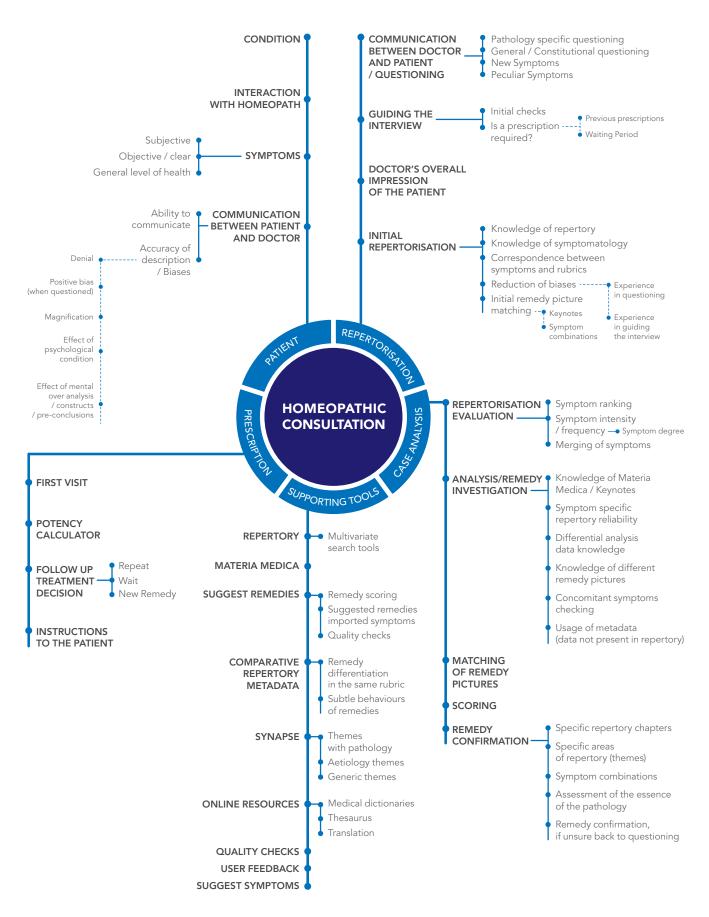


Figure 1b: Homeopathic consultation, four levels



b. Continuous improvement iterations of VC brain

During the last year the core of the VC scoring module, the complex algorithmic brain of the system has been benefiting from the statistical analysis of cases and computations of likelihood ratio which together with user feedback leads to continuous improvement of remedy selection algorithms. The target is to provide high quality and high accuracy, robust and useful software. The methodology is based on 'Quality improvement paradigm', a goal-driven feedback-oriented improvement paradigm for software engineering based on total quality principles, and on the plan/do/check/act management cycle. Users and statistical analysis provide useful feedback for improving both algorithms and the repertory. For example, if a remedy heals a symptom many times this is either confirmation for an existing rubric or a case study for a new relation between the remedy and the symptom.

PRACTICE DATA COLLECTION INITIAL Data Set Reference Cases INITIAL Rules Parametres Statistics

Figure 2a: VC Evidence Based Methodology

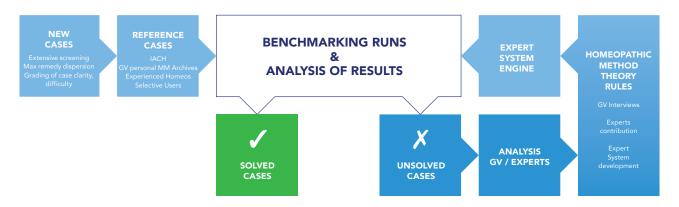


Figure 2b: VC Expert System Development

5. Highlights of VC improvement projects

c. Evolution of the VC Synapse Workflow

The Synapse Workflow has been a successful new addition to the VC toolbox. It has already gathered a following within the VC community, as a new way of working with symptoms, circumventing limitations in the traditional structure of the repertory and using a much more functional approach. It is a unique repertory wizard, based on real-world practice, which has been developed to assist in selecting the correct rubrics for every area of questioning during repertorisation. In this way it makes repertorisation more intuitive, efficient and reliable. With just a couple of clicks the homeopath has available a custom repertorisation template and can immediately start checking the case symptoms.

The Synapse Workflow is based around the concept of Themes, which represent areas of questioning the patient, and areas the homeopath concentrates on during repertorisation. Using themes, the Repertory is effectively organized in a new more meaningful way, and the selection of the rubrics becomes easier and more focused. 'Synapse' makes all relevant questions to the patient readily available, for simple or more complex cases. For every one of these questions the homeopath is presented with the most important rubrics, and with a click, all possible answers to this question. Of course, at any moment, the user can very easily add rubrics from the full Repertory utilising VC's search capabilities.

Consistent prescribing requires mastering all repertory areas in order to be able to ask the appropriate questions during the homeopathic consultation. It is not easy to learn and remember the useful and proven rubrics for every theme of case taking and therefore accurately select the

rubrics relevant to a specific pathology every time. The Synapse Workflow is a tool to help the homeopath be as thorough and effective as possible in his/her consultations. In this way young homeopaths can be more efficient than ever by quickly and effortlessly going through all the themes of homeopathic questioning.

By analysing case data and user experience, the VC team is continuously working on making Synapse more effective and complete. The rubrics included in the themes are being assessed by a number of experienced homeopaths and by studying the supplemental rubrics in Synapse cases, the rubrics possibly missing from Synapse are identified. In addition, a new structure, based on polar symptoms has been recently added (Q2 2016).

Synapse presents several challenges for development, in terms of both content and the user interface. The observed use of Synapse by homeopaths, of different levels, provides useful information to increase the potential of the tool. The goal is to provide maximum symptom coverage, minimization of biases (especially by inexperienced users), and maximum efficiency and productivity by the user.

A notable observation during the initial Synapse period was its potential as a training tool for less experienced homeopaths. As it includes the basic and most proven symptoms for casetaking, it helps an inexperienced user to quickly become comfortable with a respectable repertory of themes, including all important, reliable and useful rubrics. The mastery of such a repertory is one of the first observations when interviewing experienced homeopaths. The Synapse Workflow is being continuously refined and periodic updates will be appearing.



d. Dynamic Repertory Metadata: supplementing the repertory with comparative Materia Medica entries

A significant amount of remedy information is generally absent from the repertory. An important and valid reason for this omission is the specificity of a particular remedy characteristic, the 'fineness' of the particular symptom. Another reason is the relative nature of the symptom, when within the same rubric there is a distinctive difference between two remedies. Finally, a third reason is the intricate nature of some particularities of remedies, which, if added to the repertory, would make it huge and impractical. For all the above reasons a typical statement of many homeopathic teachers to their students is 'you will not find this in the repertory' or even the incorrect statement that 'this is why the repertory is not so important after all'.

The other pillar of homeopathic information, the Materia Medica, should, and does, normally include such specific data. The more recognised Materia Medica books contain a wealth of fine differential and other information about remedies, which can be invaluable to practitioners. The problem is that, as MM books have a large amount of 'overlap', but also each one contains particular useful information, any attempt to include all this fine data in one document would be a huge project and result in an impractically large work. There have been attempts to produce 'comparative repertories' to catalogue the differences of remedies within specific rubrics, but many of them are not accurate. The latest version of VC incor-

porates a breakthrough solution to this information handling problem. All information falling in the described categories, while previously uncategorisable, is now present within VC, connected with rubrics and remedies in the form of a database. Whenever the user requires a fine distinction between the strongest candidate remedies and there is an entry in the Metadata database, the user can instantly read it and use it to decide about the case.

The Dynamic Repertory Metadata is, in effect, a new platform in VC and most probably a unique approach in homeopathic software. During its development the team and testing homeopaths were delighted to 'recall' this fine data, and the less experienced stated categorically that the metadata produced a quantum jump in their knowledge in many remedies. The Dynamic Metadata database includes information from Prof. Vithoulkas's books and the Materia Medica Viva, but also a large additional volume of statements by other classic authors including Kent's Materia Medica, Farrington's Materia Medica and others. Users can already propose metadata additions effortlessly from within VC. Very soon a user will be able to add personal metadata and tag it with rubrics and remedies, like system metadata. In this way, every user can create a personal environment of homeopathic knowledge and useful information.

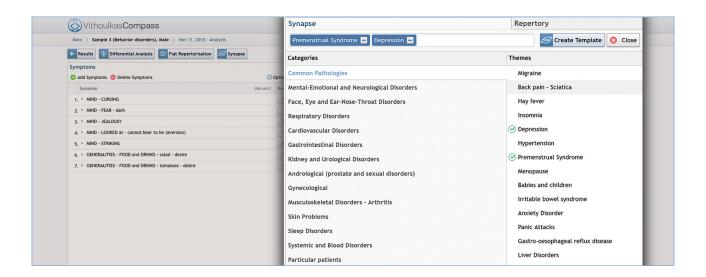


Figure 3: VC Synapse

5. Highlights of VC improvement projects

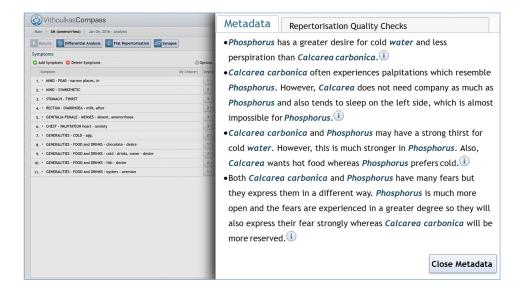


Figure 4a:

VC Metadata, Phosphorus, Calcarea Carbonica

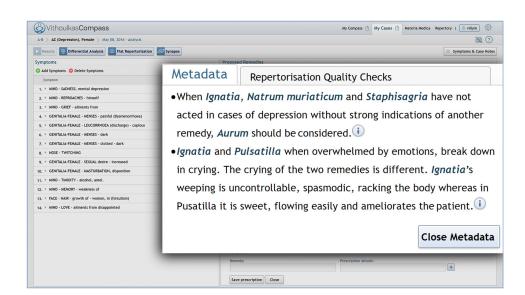


Figure 4b:

VC Metadata, Ignatia Amara, Pulsatila, Natrium Muriaticum

Such additions can contribute to the user generated content initiative to improve VC. Let us see the usefulness of Dynamic Repertory Metadata through an example. Let's assume that a repertorisation shows towards the direction of Pulsatilla and Ignatia and a symptom that is present in the repertorisation is the symptom Mind –Weeping. In the repertory both Puls. and Ign. are listed under the symptom weeping, Ignatia in third degree and Pulsatilla in forth degree. The degree in the repertory, although useful, does not help very much in differentiating between the two remedies. Dynamic Repertory Metadata offer fine information that helps very much in differentiating. When both remedies, based on the repertorisation, are candidates, the following statement from Farrington's Materia Medica will come up:

"The Pulsatilla woman is tearful, sad, and melancholy like Ignatia, but there is not that introspective mood that there is in the Ignatia patient. She makes her grief known to everyone who comes near her. She seeks sympathy. She is timid and yielding in her disposition." It is a piece of information that shows up when needed and assist us get nearer to the correct remedy.



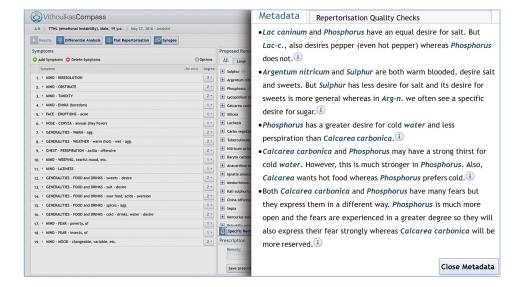
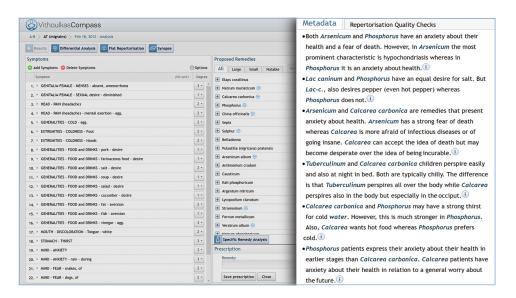


Figure 4c:

VC Metadata, Sulphur, Argentum Nitricum, Phosphorus, Calcarea Carbonica

Figure 4d:

VC Metadata, Natrum muriaticum, Calcarea Carbonica, Phosphorus, China officinalis, Sulphur, Arsenicum album, Pulsatilla, Stramonium, Veratum album



e. User Generated Content in VC, a vital addition.

The online VC platform makes it possible for users to provide input to the VC team very easily. VC now provides this possibility throughout the application. Users can directly send propositions and comments for:

- Any repertory rubric
- Any Repertory Metadata entry
- Any Materia Medica entry
- The VC application in General

by pressing the "+" contribution button.

The usage of the " \oplus " icon means that the user participates in the project to make homeopathic practice more reliable and evidence—based. Of course all gathered entries are carefully studied, discussed with expert homeopaths, and ultimately benchmarked against numerous real-world cases before their inclusion to the expert system.

6. Appendices

a. Likelihood ratio (LR) in homeopathy

The Likelihood ratio is an indication of the patient's improvement related to the pertinent combination [symptom(s)-remedy]. When LR is greater than 1, there is an increased likelihood of the event happening, i.e. the patient with the specified symptom(s) will have an improvement when treated with the specified remedy. The table below shows the interpretation of the different value ranges.

LR	Interpretation
> 10	Large and often conclusive increase in the likelihood of the event
5 - 10	Moderate increase in the likelihood of event
2 - 5	Small increase in the likelihood of event
1 - 2	Minimal increase in the likelihood of event
1	No change in the likelihood of event

Likelihood Ratio

LR+ = sensitivity / (1-specificity), is the percentage (prevalence) of a symptom in the population cured by a certain remedy divided by the percentage of the same symptom in the remainder of the treated population

LR- =(1-sensitivity) / specificity, is the percentage (prevalence) of the population without the symptom cured by a certain remedy divided by the percentage of the population without the symptom in the remainder of the treated population

$$sensitivity = rac{TP}{TP+FN}$$
, $specificity = rac{TN}{FP+TN}$
 $LR +_{min} = e^{\ln(LR+) - Z_a \times SE_{LR+}}$,
 $LR +_{max} = e^{\ln(LR+) + Z_a \times SE_{LR+}}$,

The smaller the absolute difference the better: $abs(LR+_{max}-LR+_{min})$

$$where \, SE_{LR+} = \sqrt{\frac{1}{TP} - \frac{1}{TP + FN} + \frac{1}{FP} - \frac{1}{FP + TN}}$$

 $Z_{\frac{\alpha}{2}}$: confidence coefficient = 1.96 for α = 95%, confidence level

$$LR-_{min} = e^{\ln(LR-)-Z_{a}^{\alpha}\times SE_{LR-}},$$

 $LR-_{max} = e^{\ln(LR-)+Z_{a}^{\alpha}\times SE_{LR-}},$

The smaller the absolute difference the better: $abs(LR-_{max}-LR-_{min})$

$$where \, SE_{LR-} = \sqrt{\frac{1}{TN} - \frac{1}{TN + FP} + \frac{1}{FN} - \frac{1}{FN + TP}}$$



The possible outcomes of a homeopathy case are shown when applying diagnostic test statistics:

	Remedy worked Improvement	Remainder of cases	
Symptom present	True positive (TP) (symptom present and remedy worked)	False positive (FP) (symptom present)	Positive predictive value = TP / (TP + FP)
Symptom not present	False negative (FN) (symptom not present and remedy worked)	True negative (TN) (symptom not present)	Negative predictive value = TN / (FN + TN)
	Sensitivity = TP / (TP + FN)	Specificity = TN / (FP + TN)	

- Number of Total Cases = (TP+FN+FP+TN)
- \bullet TP, FN, FP, TN are the corresponding number of cases for each respective result
- Sensitivity is the percentage that a symptom will be present when the remedy resulted in a large improvement of the homeopathy case (true positive rate)
- Specificity is the percentage that a symptom will not be present when the remedy resulted in no improvement of the homeopathy case (true negative rate)

6. Appendices

b. Follow-up Questionnaire

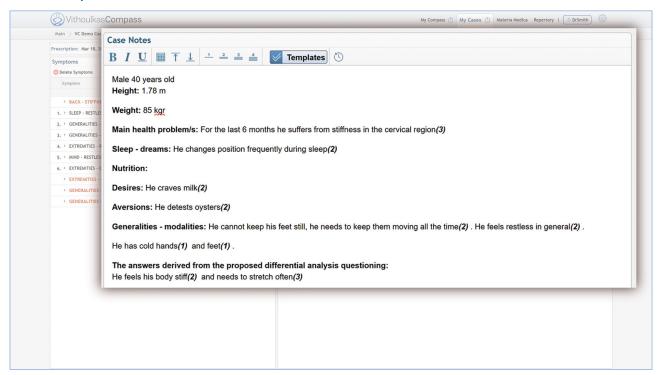


Figure 5a: Case notes

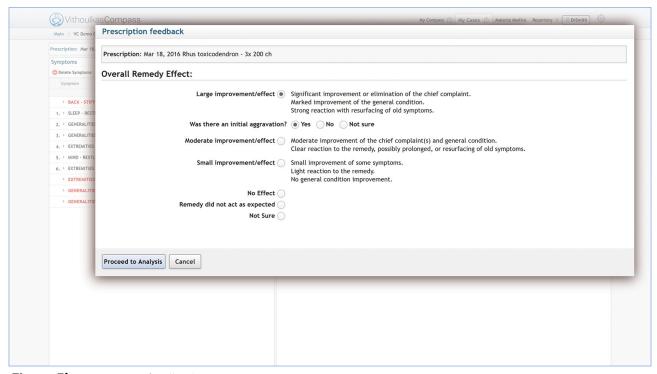


Figure 5b: Prescription feedback



c. Supporting Technologies - a valuable toolbox

Multivariable repertory search engine

• More important frequent symptoms, synonyms

Suggest remedies decision support system

- Multidimensional scoring function
- Suggested remedies important symptoms
- Quality checks

Suggest Symptoms Differential analysis

- Algorithms (frequency, degree, rubric size)
- Symptoms hierarchy
- Keynote symptoms
- Polar symptoms
- Likelihood ratios

Comparative Repertory Metadata

- Remedy differentiation in the same rubric
- Subtle behaviours of remedies

Synapse dynamic templates

- Themes with pathology
- Aetiology themes
- Generic Themes

Repertorisation quality checks and heuristics

Online resources

- Medical Dictionaries
- Thesaurus
- Translation

Collaboration tools

- User generated content
- User feedback
- Send / receive cases (including to lists of users)
- Community based improvements

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Research and Development



Vithoulkas Compass Research and Development

Principal areas of research include:

- New and innovative ways to systematize case-taking
- Tools for more effective usage of the repertory and rubric selection
- Knowledge management of homeopathic source materials
- Advanced data statistics
- Homeopathic studies and experiments
- Homeopathic educational tools

The VC team is always open to cooperate with practicing or research parties for the purpose of exchanging data and to participate in projects which promote well-founded homeopathic practice.

Notes

To receive more information and apply for a free trial, please visit our website.

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4 Agias Varvaras street 152 31 Chalandri, Athens, Greece e-mail: info@vithoulkascompass.com







