ORIGINAL PAPER

Prevalence and likelihood ratio of symptoms in patients with good therapeutic response to *Lycopodium clavatum*. A retrospective study

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Background: Assessment of the likelihood ratio (LR) of symptoms has been proposed as a rational means for detecting indicators to homeopathic medicines.
Aims: To investigate the prevalence and LR of symptoms commonly attributed to the homeopathic medicine *Lycopodium clavatum* (Lyc). Secondarily, to answer the question if experienced homeopaths could intuitively infer which the main symptoms of this medicine are.
Methods: The presence of 35 selected symptoms, prescribed medicines and therapeutic response were assessed retrospectively. The symptoms' prevalence in the Lyc responding population and the LR of the symptoms compared to their prevalence in the remainder of the population were calculated.
Results: Two hundred and two Lyc and 550 non Lyc cases (total 752) were included for analysis. Twenty-two symptoms were confirmed as pertaining to Lyc's semiology (prevalence %; LR): contemptuous (3.3; 6.7), urinary stones history (2.7; 5.4), egotism (5.6; 3.6), dictatorial (33.3; 3.4), haughty (8.7; 3.3), sleeps on abdomen (3.3; 3.3), intolerance to clothing in abdomen (12.0; 3.1), reproaches (4.0; 3.0), helplessness (24.0; 2.7), fear of failure (10.7; 2.6), irritability on waking in the morning (16.7; 2.5), constipation alternating with diarrhea (8.7; 2.5), intolerant to contradiction (59.3; 2.3), want of self confidence (30.0; 2.4), abdominal distension after eating (23.3; 2.1); ailments from anticipation (32.0; 1.9), irritability before menses (23.3; 1.8), conscientious (26.0; 1.6), desire of sweets (52.0; 1.6), desire of chocolate (16.7; 1.6), lack of vital heat (41.3; 1.3), and flatterer (1.3; ∞). Surveyed homeopaths' intuitive inferences correlated well with symptoms' prevalence but not with their LR.
Conclusions: Lycopodium's main symptoms are well known by homeopaths, but their knowledge correlates well with the symptoms' prevalence and not with their LR. Retrospective assessment of prevalence and LR of symptoms in good responders might be a means for better selection of symptoms for prospective studies. *Homeopathy* (2016) **105**, 78–83.

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Introduction

Prescription of homeopathic medicines in clinical practice relies on the detection of indicative symptoms and signs in the patients. But knowledge about which symptoms are more significant indicators for medicines'

prescription has grown over time in a mostly unorganized and uncontrolled fashion, turning it into a huge amount of information of sometimes questionable reliability. Just as an example, the 2013 version of the Complete Repertory lists 19,210 entries (including main rubrics and sub-rubrics) for the homeopathic medicine *Lycopodium clavatum* (Lyc), while Kent's repertory accounts for 'only' 6805.[1,2] There is an inevitable tendency to distrust this data as inaccurate as a simple question arises: could a homeopathic drug's picture describe thousands or tens of thousands of different pathogenetic effects, symptoms, and individual characteristics? According to a joke, homeopaths know that half the data in the materia medica and the repertories is right and half is wrong, but don't know which the right and which wrong halves are.

A few years ago the idea that introducing modern epidemiological concepts into the study of homeopathic semiology might contribute to override the aforementioned problem was developed,[3–5] leading to a prospective statistical analysis of six repertory rubrics.[6]

The rationale behind this attempt is quite simple. If a symptom is to be considered as being characteristic of a given medicine, its prevalence should be higher among patients responding to it than in the remainder of the patients. That is to say, its likelihood ratio (LR) should be >1. If the symptom's prevalence is similar or lesser than 1 in the target medicine than in the rest of the patients, it doesn't point to its prescription. The LR of a symptom related to a medicine is calculated as follows: LR = prevalence of the symptom in the population responding to the target medicine/prevalence of the symptom in the rest of patients.   In the present study these epidemiological tools were used, but retrospectively, answering the question if homeopaths know the indicative symptoms of a very commonly used medicine, Lyc, well enough. Preliminary data were published elsewhere.[7]

Materials and methods

Selection of symptoms

On a first step of this research, 110 homeopaths known to be experienced (47 from Argentina and 63 from other countries) were invited by e-mail to answer the following question: "*According to your judgment and experience, which do you think are the 10 most prominent and characteristic symptoms and signs of Lycopodium clavatum, considering their frequency and strength so as to suggest its prescription?*" This survey was not intended to be mandatory for the selection of symptoms to be assessed, but only exploratory of homeopaths' opinions and in order to make a better choice, which fell ultimately on researchers' experience.

Setting. Patients' records assessment. Inclusion/ exclusion criteria

On the second step, all the patients' records at the Out-patients Clinics of the Department of Homeopathy, School of Health Sciences, Maimonides University, were assessed once by one of three experienced homeo-paths, two of whom were teachers at the Department of Homeopathy and the third was a tutor at the Medical School of Medicine of the same University. All the examiners were mostly unaware of the aims and methods of the present study. At the homeopathic outpatient clinics, the patients are seen by an experienced homeopathy teacher with the assistance of students at the postgraduate medical course of homeopathy.

Only patients with 2 or more visits, chronic ailments, between 18 and 65 years old and only one prescribed homeopathic medicine were included. The reason to exclude acute cases, children and older adults, was to obtain a more homogeneous and comparable sample of patients, while it did not seem appropriate to compare the LR of symptoms between medicines mostly used in acute and chronic cases, and between children and older patients.

The following information was extracted from the patients' records: first visit age, sex, date of consultation, main complaint (classified according to World Health Organization's International Classification of Diseases 10, ICD-10), prescribed medicine, and presence of symptoms under scrutiny; second visit date and presence of positive changes attributable to treatment, with 3 possible answers: *yes, no, in doubt/can't say.* In order to be conservative, only patients with a *yes* for an answer were considered to be respondents to the medicine. Patients with *no* or *in doubt/can't say* as answers were considered not to be respondents to the medicine.

The data was collected into an Epi Info 7 database (http://wwwn.cdc.gov/epiinfo/).

Statistical analysis

A comparison was held between 2 groups: patients responding well to Lycopodium and the remainder of the patients. As proposed by Rutten, among the latter were included patients not responding to Lyc and patients prescribed with any other medicine.[6] For each of the assessed symptoms, the following were calculated: prevalence and 95% confidence interval (CI) for each group; LR and 95% CI between groups. Correlations between surveyed homeopaths' suggestions with prevalence and LR of symptoms were also calculated. Calculations were done with the aid of MS Excel® and Vassar Stats statistical computation website (http://vassarstats.net/).

Results

Selection of symptoms

A total of 25 homeopaths fulfilled the requirement, suggesting 34 symptoms as characteristic of Lyc. From these, 24 were selected and 10 were discarded for being too general, difficult to assess, known to be not regularly assessed in our setting or considered to be rarely seen in our clinical practice. Additional 11 symptoms were arbitrarily added by researchers according to their clinical experience (Table 4).

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Records assessment

A total of 2110 records were assessed, from which 1358 were excluded due to multiple reasons (Figure 1, Flow-chart).

Patients' characteristics

The patients were seen for the first time between 23/1/1992 and 1/11/2013. Cases were taken by several different physicians who worked over time as teachers at the Department of Homeopathy. The time elapsed between the first and the second visit was, range: 7 to 3680 days; median: 49 days. Lycopodium was prescribed very frequently, in 26.9% of cases, and significantly much more frequently in females (29.6% of women) than in males (18.8% of men). Almost 70% of cases were considered to have exhibited a good therapeutic response attributable to treatment, with an almost significant better response to Lyc than to the other medicines as a whole (Table 1).

Main complaints

Lycopodium responding cases were more likely to suffer from digestive troubles than the remainder of the population. No additional significant differences were found between groups for the other ICD-10 categories (Table 2).

Medicines prescription

Thirty-three different homeopathic medicines were indicated. Of these, 6 accounted for 80% of prescriptions: Lyc, Sulph, Puls, Nat-m, Phos and Nux-v. Fourteen medicines were prescribed only once each: Bar-c, Bell, Chel, Con, Kali-bi, Kali-br, Kali-c, Merc-c, Nat-c, Nat-s, Ph-ac, Stram, Thuj and Verat. When comparing the frequency of medicines' prescription in all cases to the frequency of medicines' prescription in patients exhibiting a good therapeutic response, no appreciable difference could be noticed. Six medicines, accounting to 10 cases, resulted ineffective: Arg-n, Rhus-t, Kali-c, Nat-c, Nat-s and Thuj (Table 3).

The fact that children, elderly, and acute cases were excluded form this research should be taken into consideration in assessing frequency of prescribed medicines.

Prevalence and LR of symptoms. Correlation between surveyed homeopaths suggestions, prevalence and LR of symptoms

According to the LR results, 22 symptoms could be confirmed as pertaining to Lycopodium's semiology and to be indicators of its employment, because of having a LR and a lower end of LR's 95% CI >1. Additional 5 symptoms had a LR ≥1.5 but with the lower end of the 95% CI below 1. So they were classified as probable. Three symptoms were considered to be possibly attributed to Lycodium, because of a LR >1 and <1.5 and a lower end of the 95% CI below 1. Finally, 5 symptoms had a LR ≤1, suggesting they should not be considered as pertaining to Lycopodium, though this should be assessed with caution because in these cases the upper limit of the of LR's 95% CI was above 1. Symptoms with low prevalence need greater amount of cases to be able to establish a statistically significant LR. All these results should be considered as provisory and need confirmation through prospective research (Table 4).

Surveyed homeopaths' suggestions on Lyc's characteristic symptoms correlated well with observed symptoms' prevalence, (R = 0.77, 95% CI = 0.54, 0.90, P < 0.0001), but did not correlated at all with symptoms' LR (R = −0.03, 95% CI = −0.43, 0.39) (Table 4).
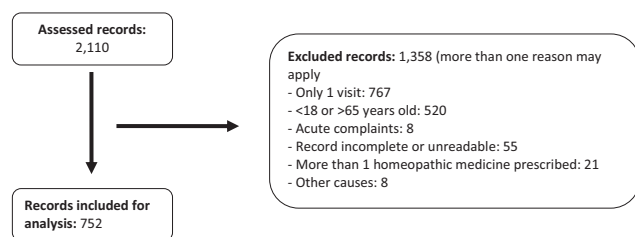
Discussion

Several weaknesses should be taken into account when considering the results of this research. Several sources of bias could influence the figures. In a retrospective work of this kind, it is quite difficult to assess when a patient has had a positive evolution and it is much more difficult to attribute it to the treatment. Although it should be

Figure 1 Flow-chart.

Table 1 Patients' characteristics. N = 752

	Lyc cases	*Other medicines cases*	*Total*
Total (n and %)	202 (row% 26.9; col.% 100)	550 (row% 73.1; col.% 100)	752 (row & col.% 100)
Females (n and %)	166 (row% 29.6)*	394 (row% 70.4)	560 (row% 100%; col.% 74.5)
Males (n and %)	36 (row% 18.8%)*	156 (row% 81.2)	192 (row% 100%; col.% 25.5)
Age (mean ± SD)	42.3 ± 12.7	42.3 ± 12.8	
Therapeutic response			
Yes	150 (74.3%)#	376 (68.4%)#	
In doubt	25 (12.4%)	59 (10.7%)	
No	27 (13.4%)	115 (20.9%)	

* P = 0.003 (Chi-Square).
\# P = 0.063 (Chi-Square).

Table 2 Frequency of main complaints in cases responding to Lycopodium and in the remainder of the population, classified according to WHO's ICD-10. N = 752

ICD-10	Lycopodium responding cases. N (%)	Remainder of the population. N (%)	LR (95% CI)
I Certain infectious and parasitic diseases	1 (0.7%)	2 (0.3%)	
II Neoplasms	1 (0.7%)	3 (0.5%)	
III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1 (0.7%)	18 (3.0%)	0.22 (0.03−1.66)
IV Endocrine, nutritional and metabolic diseases	15 (10.0%)	65 (10.8%)	
V Mental and behavioral disorders	35 (23.3%)	147 (24.4%)	
VI Diseases of the nervous system	5 (3.3%)	29 (4.8%)	0.69 (0.27−1.76)
VII Diseases of the eye and adnexa	1 (0.7%)	7 (1.2%)	
VIII Diseases of the ear and mastoid process	0	2 (0.3%)	
IX Diseases of the circulatory system	2 (1.3%)	10 (1.7%)	
X Diseases of the respiratory system	15 (10.0%)	99 (16.4%)	0.61 (0.36−1.02)
XI Diseases of the digestive system	36 (24.0%)	55 (9.1%)	2.62 (1.80−3.84)
XII Diseases of the skin and subcutaneous tissue	14 (9.3%)	86 (14.3%)	0.65 (0.38−1.17)
XIII Diseases of the musculoskeletal system and connective tissue	11 (7.3%)	38 (6.3%)	1.16 (0.61−2.22)
XIV Diseases of the genitourinary system	12 (8.0%)	35 (5.8%)	1.38 (0.73−2.59)
XV Pregnancy, childbirth and the puerperium	0	1 (0.2%)	
XVIII Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	0	2 (0.3%)	
XIX Injury, poisoning and certain other consequences of external causes	0	1 (0.2%)	
XXI Factors influencing health status and contact with health services	0	1 (0.2%)	
Not specified	1 (0.7%)	1 (0.2%)	
Total	150 (100%)	602 (100%)	752

noticed that knowledge of homeopathic drugs has grown mostly by means of clinical response of few or unique cases, or even more vague appreciations by diverse authors. Theoretical work supporting the idea of 'cure as gold standard for likelihood ratio assessment' has been published.[8]

Another possible source of bias is the difficulty in assessing the presence of symptoms in patients' records, because the mere mention of the symptoms in them doesn't mean necessarily that they were really present in the patients nor that they were strong enough to be considered as medicine indicators. Even more problematic are the false negative results. Symptoms could have been present in the cases without the assisting physician noticing or recording them. During patients' anamnesis, some symptoms are systematically inquired, as desire and aversion to foods or sensitivity to external temperatures. Others, like flatterer, haughty or contemptuous, rely completely on the physician's observational skills. Still others remain hidden unless a third person reveals them, like 'hard with subordinates, agreeable to superiors.' Past health troubles not currently present at the moment of consultation can be completely ignored. 'Gallstones history' could be an example of this.

Finally, some circular reasoning or confirmation bias could be argued against this work. If homeopaths believe in a set of symptoms as typical of Lyc, they will surely give this medicine to the patients presenting with them, and the same set will be found in patients who have been prescribed with that drug. But it should be noticed that most of the assessed symptoms were not suggested by the attendant homeopaths.

Nevertheless, some strengths could be also highlighted. The relative importance of symptoms of a particular homeopathic medicine has been assessed in a numerous series of cases in the real world of normal clinical work. In this sample of adult patients with chronic complaints we could identify a set of very prevalent symptoms and of high LR in a Lyc responding population. Looking at them, one can 'get the medicine's picture' (Figure 2). Moreover, the fact that surveyed homeopaths intuitive inference correlated well with symptoms' prevalence and not with their LR, is probably highlighting that the usual way of thinking of homeopaths is to give greater

Table 3 Medicines prescribed in all included cases (N = 752) and in cases responding to treatment (N = 526)

Medicine	All included cases N (%)	Cases with response to treatment
Lyc	202 (26.9%)	150 (28.5%)
Sulph	124 (16.5%)	85 (16.4%)
Puls	85 (11.3%)	60 (11.4%)
Nat-m	77 (10.2%)	48 (9.1%)
Phos	62 (8.2%)	44 (8.4%)
Nux-v	57 (7.6%)	43 (8.2%)
Calc-c	28 (3.7%)	22 (4.2%)
Ars	27 (3.6%)	18 (3.4%)
Sep	22 (2.9%)	12 (2.3%)
Lach	17 (2.3%)	12 (2.3%)
Ign	10 (1.3%)	7 (1.3%)
Sil	8 (1.1%)	5 (1.0%)
Arg-n	4 (0.5%)	0
Aur	4 (0.5%)	2 (0.4%)
Staph	3 (0.4%)	2 (0.4%)
Caust	2 (0.3%)	1 (0.2%)
Merc	2 (0.3%)	2 (0.4%)
Plat	2 (0.3%)	2 (0.4%)
Rhus-t	2 (0.3%)	0
Other (see text)	(14 medicines) N = 14 (1.9%)	(10 medicines) N = 10 (1.9%)
Total	752 (100%)	526 (100%)

Table 4 Prevalence of symptoms in Lyc responding cases (N = 150). LR of Lyc symptoms calculated as: LR = prevalence of the symptom in the Lyc responding cases/prevalence of the symptom in the remainder of the population

	Kent (1)	Complete 2013 (1)	Suggested by surveyed homeopaths. % (2)	Prevalence in Lyc responding cases % (95% CI)	LR (95% CI)
Confirmed Lycopodium symptoms					
Contemptuous	2 (21)	3 (109)	8	3.3 (1.2–8.0)	6.7 (1.6–27.7)
Urinary stones history	3 (17)	4 (119)	(R)	2.7 (0.9–7.1)	5.4 (1.2–23.7)
Egotism	0 (8)	3 (56)	8	5.3 (2.5–10.6)	3.6 (1.4–9.1)
Dictatorial	2 (9)	4 (83)	52	33.3 (26.0–41.6)	3.4 (2.4–4.7)
Haughty	3 (37)	4 (108)	4	8.7 (4.9–14.7)	3.3 (1.6–6.6)
Sleeps on abdomen	0 (16)	3 (50)	(R)	3.3 (1.2–8.0)	3.3 (1.03–10.8)
Clothing, intolerance (abdomen)	3 (28)	4 (74)	16	12.0 (7.5–18.6)	3.1 (1.7–5.7)
Reproaches	2 (20)	3 (126)	8	4.0 (1.6–8.9)	3.0 (1.1–8.5)
Helplessness	0 (6)	4 (121)	32	24.0 (17.6–31.8)	2.7 (1.9–4.0)
Fear of failure	0 (1)	1 (88)	12	10.7 (6.4–17.0)	2.6 (1.4–4.7)
Irritability, morning, on waking	3 (38)	4 (66)	12	16.7 (11.3–23.8)	2.5 (1.6–4.0)
Constipation alternating with diarrhea	2 (81)	3 (138)	(R)	8.7 (4.9–14.7)	2.5 (1.3–4.8)
Contradiction, intolerant to	3 (35)	4 (118)	36	59.3 (51.0–67.2)	2.3 (1.9–2.8)
Self confidence, want of	2 (48)	3 (269)	52	30.0 (22.9–38.1)	2.4 (1.7–3.3)
Abdominal distension after eating	3 (58)	4 (126)	(R)	23.3 (17.0–31.1)	2.1 (1.5–3.1)
Anticipation, ailments from	1 (6)	4 (222)	24	32.0 (24.8–40.2)	1.9 (1.4–2.5)
Irritability before menses (women <51 y.o., n = 371, 90 responding to Lyc)	2 (11)	3 (71)	8	23.3 (15.3–33.7)	1.8 (1.05–2.9)
Desire of sweets	3 (37)	4 (249)	56	52.0 (43.7–60.2)	1.6 (1.3–1.9)
Conscientious	2 (35)	4 (133)	8	26.0 (19.3–33.9)	1.6 (1.2–2.2)
Desire of chocolate	0 (2)	3 (169)	(R)	16.7 (11.3–23.8)	1.6 (1.02–2.4)
Lack of vital heat	2 (108)	4 (288)	(R)	41.3 (33.4–49.7)	1.3 (1.1–1.6)
Flatterer		4 (7)	4	1.3 (0.2–5.2)	∞
Probable Lycopodium symptoms					
Contrary	1 (44)	1 (106)	8	1.3 (0.2–5.2)	4.0 (0.6–28.3)
Censorious, critical	2 (53)	3 (156)	(R)	5.3 (2.5–10.6)	2.3 (0.98–5.4)
Worse at 4 pm	3 (19)	4 (225)	20	1.3 (0.2–5.2)	2.0 (0.4–10.9)
Suspicious	3 (75)	4 (171)	4	8.0 (4.4–13.9)	1.8 (0.9–3.4)
Nose obstruction during night	3 (27)	4 (75)	8	2.0 (0.5–6.2)	1.5 (0.4–5.6)
Possible Lycopodium symptoms					
Hard with subordinates, agreeable to superiors		1 (4)	8	0.7 (0.0–4.2)	1.3 (0.1–12.8)
Easy satiety	3 (68)	4 (142)	12	0.7 (0.0–4.2)	1.3 (0.1–12.8)
Hurry	1 (72)	1 (267)	(R)	4.0 (1.6–8.9)	1.05 (0.4–2.5)
Possible not Lycopodium symptoms					
Desire of open air	3 (84)	4 (203)	(R)	11.3 (6.9–17.8)	0.8 (0.5–1.2)
Aversion to onions	0 (1)	1 (13)	(R)	0.7 (0.0–4.2)	0.8 (0.1–6.8)
Reserved	1 (47)	1 (179)	12	12.7 (8.0–19.3)	0.7 (0.4–1.1)
Gallstones history	3 (35)	4 (131)	(R)	2.0 (0.5–6.2)	0.7 (0.2–2.4)
Fear of narrow places	0 (4)	4 (71)	8	2.0 (0.5–6.2)	0.6 (0.2–2.1)
Symptoms suggested by surveyed homeopaths but not assessed					
Digestive troubles			52		
Urinary troubles			24		
Irritability			20		
Cowardice			8		
Weeping when thanked			8		
Affectionate			8		
Fear arising from the stomach			8		
Right sided symptoms			8		
Ailments from suppressed anger			8		
Timidity, shyness			8		

(1): Points in Kent and Complete 2013 repertories' entries and number of medicines in the rubrics.
(2): % of surveyed homeopaths suggesting the symptom.
(R): Symptoms added by researchers.
∞: For the symptom *flatterer* the LR was not possible to be calculated because its prevalence in the remainder of the population was = 0.

importance to more prevalent symptoms than to those with higher LR. From an epidemiological point of view, a highly prevalent symptom should serve to discard a medicine when the symptom is absent in the patient, while a symptom with high LR should lead to confirm the medicine when it is present in the case.[9]

Prospective multicentre research of real prevalence and LR of symptoms should be carried on in order to tune homeopathic medicines' knowledge and more important, to improve prescription accuracy and clinical results.

Conclusions

Main homeopathic symptoms and indicators of the homeopathic medicine Lyc are well known by experienced homeopaths, but their knowledge correlates with the
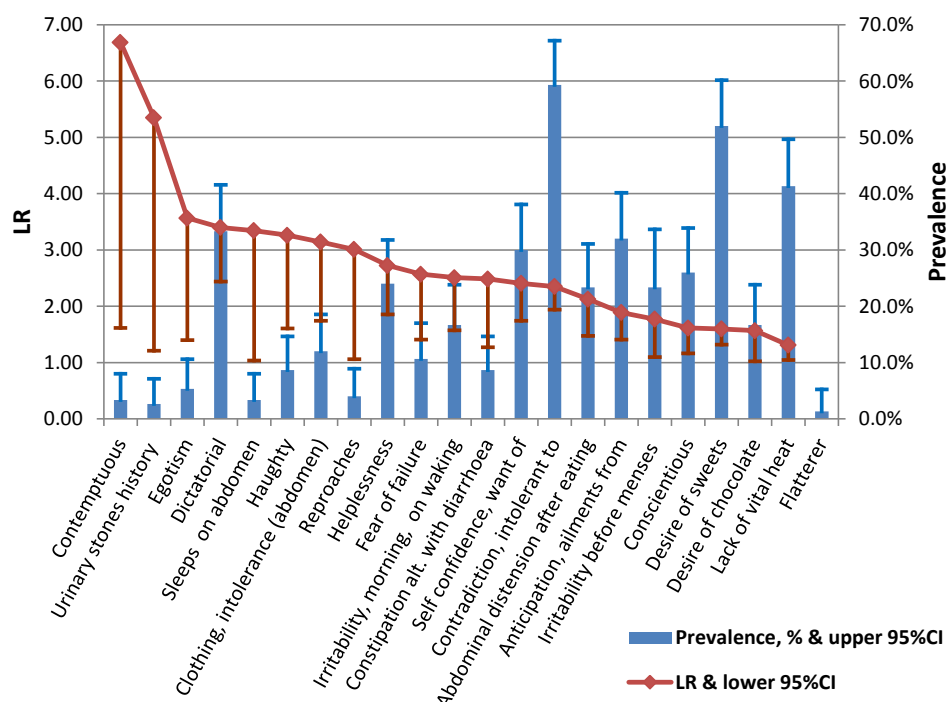
Figure 2 Confirmed Lyc symptoms' prevalence and LR.

symptoms' prevalence and not with their LR. Retrospective assessment of prevalence and LR of symptoms in good responders could be a means for better selection of symptoms for prospective research.

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Conflict of interest statement

No conflict of interest is declared.

Acknowledgments

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