Collecting clinical experience of homeopathic support in COVID-19, newsletter 13

Bayesian analysis of symptoms, 12th issue

LMHI newsletter 16 July 2020

This newsletter has a new title because the other parties involved have completed their preparation. Their findings will be discussed in satellite newsletters. The 'Bayesian analysis of symptoms' issues proceed with constituting new repertory-rubrics for treatment of COVD-19 applying Bayesian statistics. There will be an overlap because high quality data enable better quantitative analysis. In this issue we deal with reliability and reproducibility, also closely related to quality.

The COVID-19 scenery is changing now in several respects. Firstly, the epidemic is reducing in Europe but worsening in India, with over ten thousand new cases each day and still increasing. Secondly, the Indian government recognises homeopathy and promotes co-operation between homeopathic and conventional practitioners. Thirdly, the homeopathic community can now, for the first time, develop a treatment protocol for a new disease based on systematic data collection and statistical analysis of these data, resulting in an app containing a prescription algorithm. This is a unique opportunity for homeopathic practitioners to show that homeopathy is a transparent, systematic and reproducible method. Hitherto, we have frequently been characterised as unreliable scientists by our opponents, but now we can treat a patient together with a conventional doctor and show how we prescribe a homeopathic medicine.

Algorithmic prescribing

In the previous newsletter we showed that the mini-repertory app is able to produce the same results as conventional case-taking with fewer – more common - symptoms. However, the app does not make use of all the information we can derive from our database. There are also symptoms that are less common and provide strong confirmation for specific medicines, such as:

- For *arsenicum*: restlessness; thirst for small sips; less appetite
- For *bryonia*: aversion to motion/lying quietly; wants to be left alone; thirst for large quantities
- For *gelsemium*: cannot keep eyes open; chill back; involuntary urination from coughing

The common factor in these symptoms is that they occur in fewer patients, but are very specific for the particular medicines. Together with the common symptoms in the app, we can obtain a transparent and certain prescription in many cases, even if the app can only give a 'moderate indication'.

Figure 1 shows that the treatment of certain patients can be straightforward if the app indicates a "strong indication" for a specific medicine. A strong indication is given if the combined likelihood ratio (LR) of all symptoms is 10 or higher. Suppose that the prior chance that one of the medicines included in the app will work is 10%, then LR = 10 will result in a posterior chance above 50%. To recap the Bayesian calculation: Prior odds = 0.1/0.9; posterior odds = 10 x prior odds = 1/0.9 = 1.11;

posterior chance = odds/(1+odds)=1.11 / 2.11 = 0.526. Our test of the app described in the previous newsletter showed that it gave the correct advice in 11 out of 18 cases.

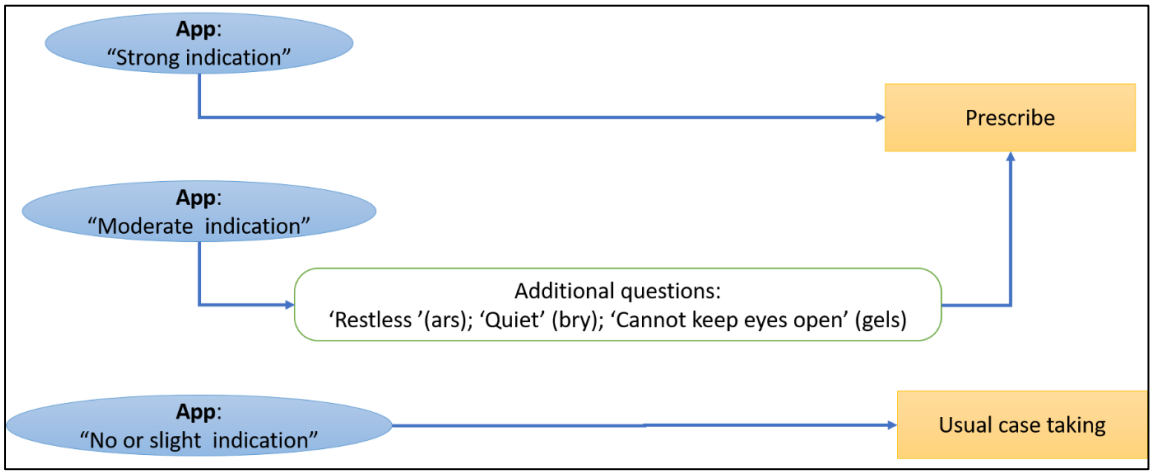

Figure 1: algorithm for prescribing in COVID-19 cases, restricted to included medicines (at the moment ars, bry and gels)

Of course, if an experienced homeopathic practitioner recognises a very peculiar symptom (not in the app) in a particular patient, indicating a medicine that cannot be recommended by the app, the practitioner's judgement should prevail. The app, however, makes its homeopathic prescription based on a mathematical principle. The major difficulty in the practice of homeopathy lies in the large variety of symptoms and recognising the patterns in these symptom.

Cure and causality

An example: my neighbour had visited a busy shopping mall the previous day, at the height of the Dutch COVID-19 epidemic, and developed fever, chills, headache and fatigue. In the Netherlands it was not possible to test for COVID-19, but based on the symptoms I prescribed *Gelsemium C30*. The medicine arrived the following day. However, the patient was already much better by then, before the medicine was taken.

The placebo effect is greatly under-estimated and this is often shown in randomised controlled trials (RCTs). A Cochrane analysis of the RCT efficacy of Oxycodone – one of the strongest painkillers - for neuropathic pain showed a moderate improvement by the real medicine in 44% of the patients.[1] However, 27% of the patients taking placebo had the same improvement. Apparently, the placebo effect contributes more than half of the effect in actual practice, as is the case for many medicines. As well as the placebo effect there is also spontaneous recovery, as we see in the majority of COVID-19 cases.[2]

I cannot say if my neighbour was cured by the placebo effect or spontaneously recovered, but I would certainly not claim that *Gels* cured this patient. To do so to a conventional doctor would undoubtedly cause him to lose all faith in me. Moreover, he would not ask my advice in treating COVID-19 patients. The credibility of any homeopathic practitioner would be seriously undermined if he stated that every patient with mild COVID-19 was cured by his medication.

Even more detrimental would be the effect of falsely attributing positive causality to the effectiveness of our app. The strength of this app is that it is based on precise estimates of the LRs of

common symptoms. Such LRs are often small, say around 2, but the combination of four symptoms with LR=2 would render a combined LR=2x2x2x2=16.

Let us suppose that a symptom with a LR=2 for medicine A has a prevalence of 20% in those who respond well to the medicine, whilst the prevalence of the same symptom in the remainder of the population is 10%. What would be the influence on the LR if half of our supposedly responsive population were actually cured by the placebo effect or spontaneously recovered? This latter half of the population will in fact have the same prevalence of the symptom as the remainder of the population, i.e. 10%. The result is that the prevalence in our population of supposed responders to medicine 'A' becomes 15%, and the LR=1.5, as shown in Figure 2. Four symptoms with LR=1.5 would then produce a combined LR=1.5x1.5x1.5x1.5=5.06. The recommendation of the app would then not be "Strong indication for medicine A", but "Slight indication for medicine A".

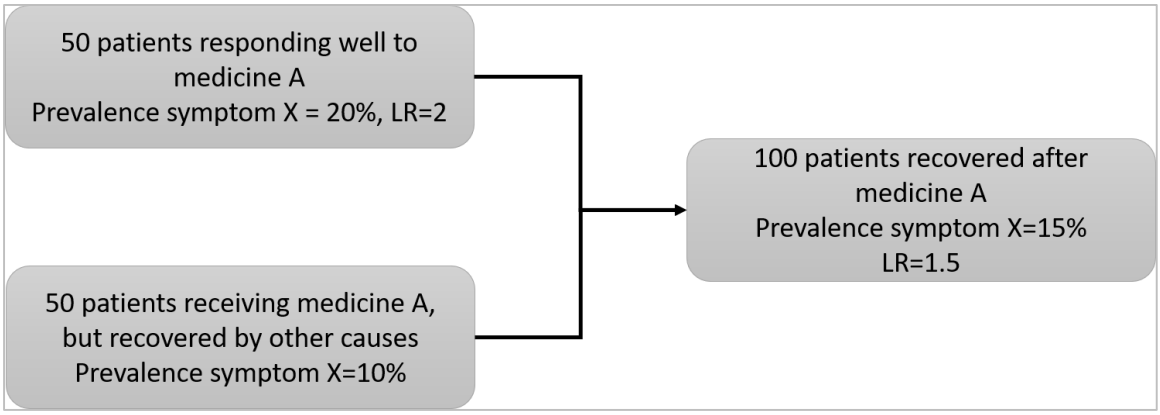

Figure 2: the influence of false positive outcome of treatment on LR calculation

If we acknowledge, and we should, that about half of the recoveries of our patients are not caused by the prescribed medicine, it becomes apparent that the calculated LRs are underestimates. However, we should not fatalistically assume that we can never know which half of our patients recover from the medicine, as we may observe developments in the healing process that indicate an increased probability that the medicine actually caused the cure, such as:

- A development that seems typical for response to homeopathic medicine: shortly after the first dose of the medicine the patient shows a mental and/or functional improvement, such as undertaking things he could not before the medicine was given. After that we the improvement building up in other respects
- After some time, the improvement stops and is resumed after repeating the medicine

These indications of causality are part of the modified Naranjo criteria and will be explained further in one of our newsletters about qualitative research.[3] Of course, there much subjectivity in these observations and doctors tend to be over-optimistic about the influence of their therapy. No practitioner can escape bias, but if you think that all of your patients improved because of your treatment, you are certainly biased! By carefully describing the healing process, it should be possible to select 50-70% of your cases which are more likely to have been cured by the medicine. Such

selection of cases generates higher LRs and this will produce a better performance of the algorithm based on these LRs.

Credibility and co-operation

For a long time, the medical scientific community believed in a dichotomy in research: RCTs were reliable, whilst individual cases or case-series were unreliable. As a consequence, the RCT was seen as very much better than observational research because it was considered the only way to assess causality. This opinion has altered since the turn of the century, as the RCT has been found to be much more biased than expected.[4] On the other hand, there is a growing awareness that we can learn from experience.[5] Observational research has become more important, especially in individualised medicine.[6]

We are now in the unique situation that we can show conventional colleagues how we learn from experience and demonstrate the transparency of our method. At the same time, we must show our conventional colleagues that we are well aware of bias, placebo effects and spontaneous recovery. This can be evidenced by a careful selection of the cases that are used for LR calculations, which at the same time will improve our results.

Table 1 shows the present status of the database underlying the mini-repertory app. With the information provided above, you may suspect that many of the lower LR values are underestimates. However, you can also see some high LR values, like for 'heaviness eyelids' and *gels*, 'thirst for large quantities' and *bry*, 'chill back' and 'involuntary urination from cough' for *gels*. Here, the opposite has happened: confirmation bias resulting in over-estimated LRs.

Confirmation bias is likely to occur with keynote symptoms. 'Heaviness of eyelids' is a keynote symptom for Gels and therefore practitioners will have a preference for this medicine if this symptom is present. It may also happen that the practitioner is more likely to observe heaviness of eyelids when he thinks of *Gels*, lowering the cut-off value for observing the symptom. These keynote symptoms are not used in the app because they would influence the outcome too greatly.

Conclusion

Placebo effects and spontaneous recovery are greatly under-estimated causes of cure. False causal attribution of cures to medicines causes both under-estimation of LR in common symptoms and over-estimation of LR in keynote symptoms. A case description should be completed by a description of responses to the medicine that do or do not indicate a causal relationship between the prescribed medicine and the improvement. Describing all cases as if the medicine caused the cure will harm the credibility of homeopathy.

Table 1: count of symptoms and resulting LR calculations for ars, bry, gels and phos. Status 18-06-2020.

Symptoms	Total	ars	LRars	bry	LRbry	gels	LRgels	phos	LRphos
n=	**272**	49		76		36		16	
fatigue	**152**	33	1.26	34	0.74	31	1.68	10	1.13
dry cough	**123**	18	0.78	44	1.44	15	0.91	9	1.26
fever	**106**	19	0.99	31	1.07	15	1.08	10	1.67
muscle/bone pain	**99**	25	1.54	30	1.12	9	0.66	4	0.67
headache	**97**	13	0.70	34	1.39	18	1.49	5	0.87
throat pain	**82**	20	1.47	24	1.07	10	0.91	3	0.61
dyspnea	**72**	6	0.41	21	1.06	7	0.71	9	2.29
chill	**70**	9	0.67	19	0.96	23	3.21	3	0.72
chest discomfort	**65**	8	0.64	18	0.99	8	0.92	8	2.25
anxiety	**58**	28	4.25	9	0.47	3	0.36	4	1.19
diarrhoea	**50**	14	1.77	12	0.81	7	1.07	5	1.78
thirst	**47**	17	2.58	22	2.27	2	0.29	2	0.71
cough	**44**	12	1.71	13	1.08	3	0.48	2	0.76
loss of taste and/or smell	**51**	5	0.49	13	0.88	1	0.13	4	1.36
dry mouth/throat	**54**	16	1.92	23	1.91	3	0.39		
chest pain	**27**	3	0.57	11	1.77	3	0.82	3	2.00
thirstless	**27**	1	0.18	6	0.74	9	3.28	3	2.00
nausea	**20**	7	2.45	4	0.64	3	1.16	1	0.84
chest pain < cough	**18**	1	0.27	10	3.22	5	2.52	2	2.00
back pain	**17**	1	0.28	11	4.73	1	0.41	1	1.00
productive cough	**16**	4	1.52	2	0.37	1	0.44	4	5.33
heaviness eyelids	**15**			2	0.40	13	42.61		
cough < talking	**13**	2	0.83	6	2.21				
perspiration	**13**	2	0.83	4	1.15	2	1.19	1	1.33
chill back	**13**			4	1.15	9	14.75		
desire cold drinks	**12**			5	1.84	1	0.60	3	5.33
cough < deep respiration	**11**	2	1.01	8	6.88				
> open air	**11**	1	0.46	4	1.47	1	0.66		
thirst large quantities	**11**			10	25.79				
desire warm drinks	**11**	3	1.71	4	1.47	1	0.66		
desire fresh air	**10**	1	0.51	5	2.58	1	0.73		
restless	**10**	7	10.62	2	0.64				
taste bitter	**10**	3	1.95	2	0.64	1	0.73		
loss of appetite	**10**	10	3.50			3	0.98	1	0.73
Involuntary urination during cough	**9**			2	0.74	7	22.94		

At the moment the medicine *phosphorus (phos)* is the first candidate to be added to the app, but we like to have more cases for more precision of the outcome.

Resuming requisites for case descriptions

We resume the minimal necessary data for this project. We already had:

- Severity of COVID-19 illness: Mild – Moderate – Severe – critical
- Is COVID-19 confirmed?
- Medicine, with date of first intake
- Number of hours until onset of improvement and/or until absence of fever
- If possible at least 3-5 symptoms that were characteristic for the case
- Pneumonia on X-ray or CAT

Also check:

- Number of days between first symptoms and deteriorated condition
- Prostration/exhaustion; where is the weakness seated
- Fear/anxiety
- Confusion
- Restlessness
- Fever, chill, or chill alternating with fever
- Thirst
- Pain; where
- Cough dry or moist
- Dyspnea
- Throat pain
- Loss of taste and/or smell
- diarrhoea

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