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Confirming *merc solubilis* as a *genus epidemicus* in the Evolving Pandemic Using a Mathematical Model Based Upon Machine Learning

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Abstract: Background: Advent of a novel pandemic requires development of faster medicine discovery protocol compared to traditional approach. Normally these are placebo controlled clinical trials, such trials usually involve high risk and a lot of time and money and repetitive exposure of the patients involved. In this study we gathered all the pathognomonic features of COVID-19 and translated them to homeopathic clinical features by using the known technique of *repertorization*, using a software. Top 10 ranked remedies were selected for further exploration. A surrogate model was created for simulation based on real patient data available in which all patients received a random combination of ranked repertorized homeopathic medicine. This output was then fed to a Neural Network. The NN learnt by recognizing patterns that mapped to patients' initial state to the results of remedies administered, fluctuations were averaged out and different patient features were discovered. Thus, enabling the NN to better predict optimum homeopathy remedies than the traditional method stated before. Method: We designed a mathematical model based upon the principles of machine learning and created a virtual clinical trial first of 200 patients and then updated it to 800 in lieu of a real one. The Results of these Surrogate Digital Clinical trial [SDCT] were fed to a neural network. The Neural Network Clinical Learning [NNCL], clearly gave us a list of drugs and a possible genus epidemicus for this covid 19. These results were compared with actual field results to a data of 130 patients of covid like illnesses, covid or pneumonia treated on OPD basic or through tele medicine. Results: The conclusion was reached by comparing the simulated clinical trials, predictions by the NN and findings in the observational studies. Although the model shows reasonable stability, it is presented as a proof of concept, which should be further rigorously studied and tested by other homeopathic practitioners for further optimization if required. In this study *merc sol* merged prominently as a *genus epidemicus*. A further change in the remedy in the reference to a possible second or third wave could be predicted by adding some valuable clinical data to the model. Conclusion: This study could resolve many issues faced by homoeopathic practitioners across the globe and could predict a fairly accurate results making us better prepare in the field.

Keywords: Homoeopathy, Covid19, *merc sol*, *genus epidemicus*, Randomized Placebo Control Clinical Trial, Surrogate Digital Clinical Trial [SDTC], Neural Network Clinical Learning [NNCL]

1. Introduction

COVID 19 has created a kind of turmoil globally. The virus not only has morbidity and mortality but also it is a challenge for global economy. Many scientists and researchers across the globe are working round a clock to find a comprehensive treatment. There are currently no effective specific antivirals or drug combinations introduced for Covid 19 specifically that be supported by high-level evidence [1]. India, with the help of ministry of AYUSH is fighting an extraordinarily strong battle and there are many alternative medicines like Homoeopathy, Ayurveda and yoga which are utilized along with conventional

system of medicine. The Government of India has issued guidelines [2] regarding these adjuvant treatments since the month of March and reviewed them from time to time. Every state in India is also trying natural medicines to lessen the burden on the health care system and the economic burden of the treatment on the patients and community. Similar efforts are also seen in many countries like Brazil as they are also trying to design their own defense strategy against the virus by employing homoeopathic and various alternative medicine [3].

Advent of a novel pandemic requires development of faster medicine discovery protocol compared to traditional approach. Normally these methods investigate various clinical trials, with effects of different known medicine combinations administered to a selected group of affected patients, while giving placebo-medicine to the other set of affected patients defined as control group [4].

Although, Randomized placebo control clinical trials [5] are the gold standard in all kinds of evidence-based medicine the situation becomes difficult when we have such an evolving illness like covid19 that could lead to severe morbidity and mortality. Such placebo trials usually involve high risk and a lot of logistic support, are time consuming and they involve a lot of money. There is a chance of unnecessary repetitive exposure of the people involved.

Mathematical Modeling (MM) [6], enabled by Machine Learning (ML), Neural Network (NN) [7], subset of Artificial Intelligence (AI) have already started to revolutionize the practice of medicine [8]. Although AI is not at a stage to replace the physician or the medical expert, a 'human-in-the-loop' approach could greatly benefit medical fraternity and mankind in general. AI techniques have advanced to a level of maturity that allows them to be employed under real-life conditions to assist human decision-makers AI has the potential to transform key steps of clinical trial design from study preparation to execution towards improving trial success rates [9].

Homoeopathy and homoeopathic practitioners are known to use such newer techniques like computer and Repertory for last two decades. A computer repertory already a great tool that overcomes several constraints as time, to narrow down a group of remedies, employing AI techniques could further enhance this effort and overcome limitations of Randomized Placebo Clinical Trials (RPCT) on emergence of a new disease. This could further validate the narrowed choice of medicines. Some attempts have been made in the recent past in this direction [10].

So, through this article we are recommending use of homoeopathic knowledge alongside Machine learning to estimate and verify the likely remedies in lieu RPCT on advent of a new disease. We validate our results by comparing them with actual on field data of using *'Mercurius solibius'* over other remedies for COVID-19 patients and patients displaying COVID-19 like symptoms in the geographical area of Mumbai, India. This method could be used and compared with other observational case studies around the world and open new dimensions of further research in Homeopathy.

2. Method

A few mathematical functions were created as listed in Appendix A.

Various symptoms of COVID-19 published by various medical sources [11-13] Were gathered. These symptoms were translated to homeopathy-based symptoms using the method of repertorization by state of art homeopathy software.

Repertorisation Table

Patient Name : *Mr. NHS m covid* **Reg_No. :** *3135* **Rep_Date :** *16/10/2020*

Normal Repertorisation

	Puls	Nat-m	Merc	Sulph	Bell	Hep	Calc	Sil	Phos	Ars	Hyos	Bry	Rhus-t	Apis	Chin
Totality	35	35	33	30	30	29	28	27	27	26	25	24	23	23	23
Symptoms Covered	15	14	14	15	13	13	12	12	11	11	13	12	14	12	11
[KR] [Fever]Fever:Lungs:Pneumonia, in, high:			3												
[C] [Cough]Coughing agg.:					2	2									
[GN] [Chest, Lungs, Bronchia and Cough]Old people:Spasmodic cough											1				
[KR] [Cough and Expectoration]Cough:Hacking:Continuous, almost, wc															
[C] [Cough]Dry:	3	3	2	3	3	2	3	2	3	3	3	3	1	1	3
[C] [Smell]Diminished:	2	3	2	1	3	2	3	3	1		3		1		
[C] [Smell]Diminished:Taste, and diminished:	2	2						1							
[C] [Smell]Wanting, lost:	3	3	3	2	3	3	3	3	3	2	2	2	2		
[C] [Smell]Wanting, lost:Taste, with loss of:	2	1									1				
[AL] [S]Smell:Loss:	1	2	1	1	2	1					2				
[BN] [Nose]Smell:Weak (diminished or lost):With loss of taste:	3	2									1				
[C] [Taste]Wanting:Loss of taste:	3	3	2	2	3	2	2	3	3	1	2	2	1	2	1
[C] [Taste]Wanting:Tastelessness of food:	3	3	1	1	1	1	2	1		1		1	1	1	3
[KT] [Skin]Eruptions:Urticaria:Fever,during:				2									3	3	
[BN] [Skin and exterior body]Scarlet fever:And scarlatinoid eruptions:			4	3	4	2			2	3	3	3	2	2	1
[PH] [Phatak A-Z]Urticaria, hives, wheals:Fever during:													1	1	
[C] [Respiration]Difficult:Forenoon:				1								1			1
[C] [Respiration]Difficult:	3	2	2	3	2	3	2	3	3	3	1	3	2	3	3
[C] [Throat]Inflammation, sore throat:	2	2	3	2	3	3	2	1	2	2		2	2	2	2
[C] [Nose]Obstruction:	3	3	2	2	1	2	3	3	3	3		1	2	1	2

Symptoms 1 to 20 Total Symptoms : 26 Remedies 1 to 15 Total Remedies : 766

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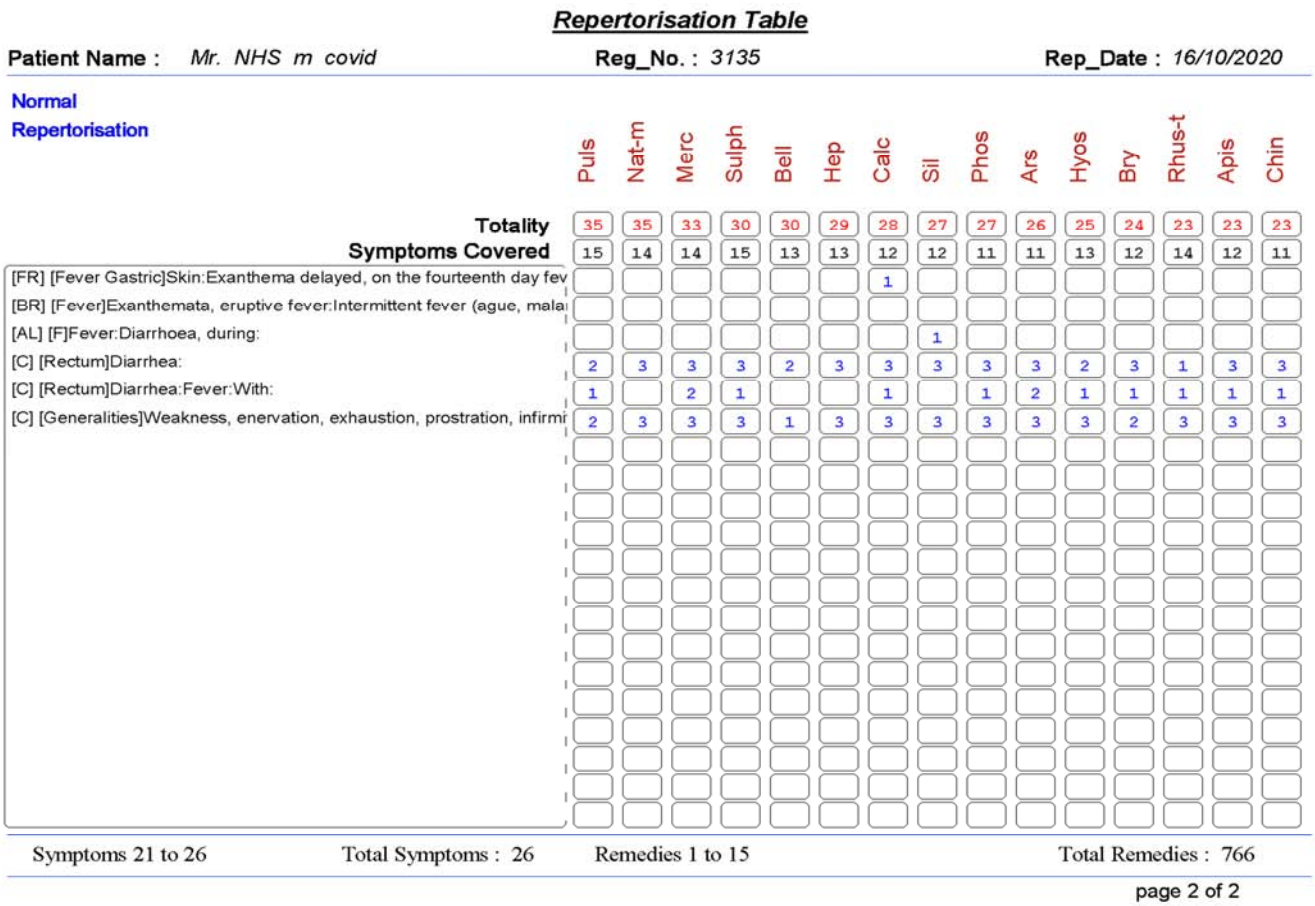
Figure 1. *Hompath repertorization of Covid-19 Symptoms (a).*



Repertorisation Table

Patient Name : Mr. NHS m covid Reg_No. : 3135 Rep_Date : 16/10/2020

Normal Repertorisation

	Puls	Nat-m	Merc	Sulph	Bell	Hep	Calc	Sil	Phos	Ars	Hyos	Bry	Rhus-t	Apis	Chin
Totality	35	35	33	30	30	29	28	27	27	26	25	24	23	23	23
Symptoms Covered	15	14	14	15	13	13	12	12	11	11	13	12	14	12	11
[FR] [Fever Gastric]Skin:Exanthema delayed, on the fourteenth day fev							1								
[BR] [Fever]Exanthemata, eruptive fever:Intermittent fever (ague, mala															
[AL] [F]Fever:Diarrhoea, during:								1							
[C] [Rectum]Diarrhea:	2	3	3	3	2	3	3	3	3	3	2	3	1	3	3
[C] [Rectum]Diarrhea:Fever:With:	1		2	1			1		1	2	1	1	1	1	1
[C] [Generalities]Weakness, enervation, exhaustion, prostration, infirmi	2	3	3	3	1	3	3	3	3	3	3	2	3	3	3

Symptoms 21 to 26 Total Symptoms : 26 Remedies 1 to 15 Total Remedies : 766

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Figure 2. *Hompath repertorization of Covid-19 Symptoms (b).*

In $\vec{x}$ patient features are mapped from general symptoms of COVID-19 translated in the form of generalised homeopathic rubrics. Since $\vec{x}$ is a multidimensional vector other co-morbidity could be added.

Table 1. *Mappings COVID-19 symptoms of multi-dimensional patient vector $\vec{x}$.*

COVID-19 Symptoms	Homeopathic Rubrics	Vector $\vec{x}$
a high temperature	[Fever, Heat] Heat in general	$\overrightarrow{x_1}$
a new, continuous cough	[Cough] Constant	$\overrightarrow{x_2}$
a loss or change to your sense of smell or taste	[Smell] Wanting, lost: Taste, with loss of: [Taste] Wanting: Loss of taste	$\overrightarrow{x_3}$
Nausea	[Stomach] Nausea	$\overrightarrow{x_4}$
Diarrhoea	[Rectum] Diarrhoea:	$\overrightarrow{x_5}$
Joint Pain	[Extremely Pain] Joints:	$\overrightarrow{x_6}$
Headache	[Head Pain] General:	$\overrightarrow{x_7}$
Extreme Tiredness	[Generalities] Weakness, enervation, exhaustion	$\overrightarrow{x_8}$

Vector $\vec{y}$ is mapped to the repotrised remedies/medicines from state of art homeopathy software used by professional homeopathy practitioners. Out of 766 remedies top ranking remedies were selected.

Table 2. *Mappings of Homeopathy remedies to vector $\vec{y}$.*

Homeopathic Remedies	Vector $\vec{y}$
Ars. Albunz	$\overrightarrow{y_1}$
Phosporus	$\overrightarrow{y_2}$
Chelidonium	$\overrightarrow{y_3}$
Merc sol	$\overrightarrow{y_4}$
Antim Ars	$\overrightarrow{y_5}$
Bry	$\overrightarrow{y_6}$
Ant-t	$\overrightarrow{y_7}$
Cal-c	$\overrightarrow{y_8}$
Nux-v	$\overrightarrow{y_9}$
No remedy	$\overrightarrow{y_{10}}$

The mathematician designed a mathematical model to create a surrogate Digital clinical trial in lieu of actual clinical trial first of 200 virtual patients then of 800 virtual patients.

The values were bounded between 0 and 1 where 0 indicates death, and 1 indicates excellent health.

The initial model was normalised as shown Figure 2 between 0 and 1 and taking placebo (no remedies) as a comparator tending towards 0.

Neural Network Clinical Trial [NNCT] was set up to learn from Surrogate Digital Clinical Trial [SDCT].

The network was trained on the results obtained in SDCT to generate the best distribution of homeopathic remedies over a set of fixed virtual patients based on covid 19 symptoms. This would enable homeopathic practitioners to arrive at a set of best possible homeopathic remedies for patients displaying covid 19 like symptoms.

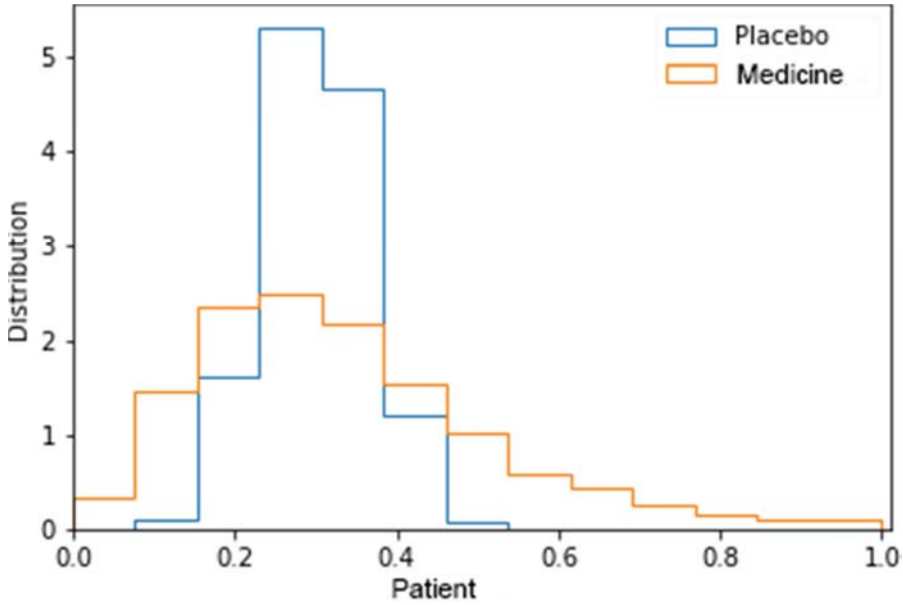

Figure 3. *Normalization of the mathematical function (a).*

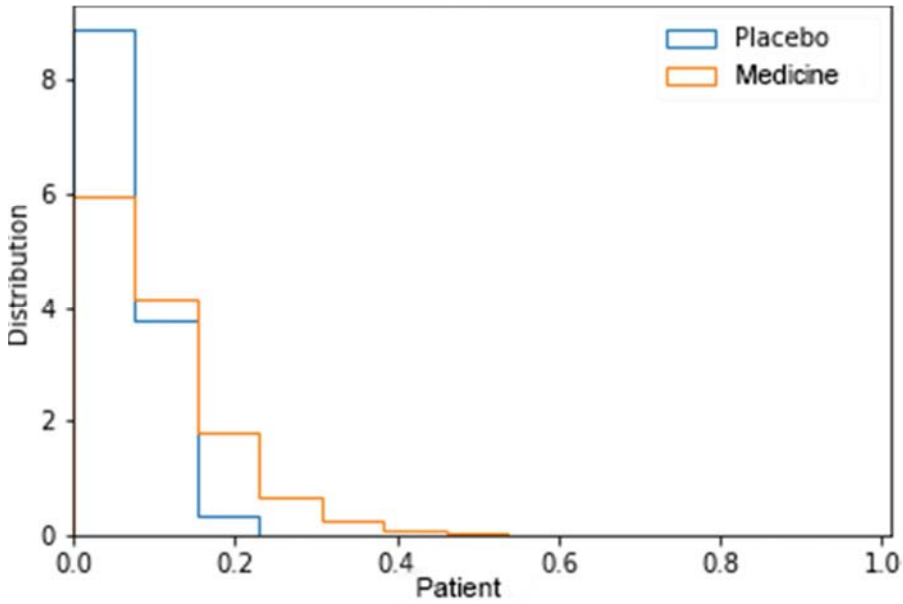

Figure 4. *Normalization of the mathematical functions (b).*

Results for the analysis are shown for N=200 and N=800 patients. In the real world there are many 'unknown factors' such as unknown co-morbidities or any other health conditions that would interfere with actual controlled clinical trials. These 'unknown factors' are modeled as 'stochastic noise'.

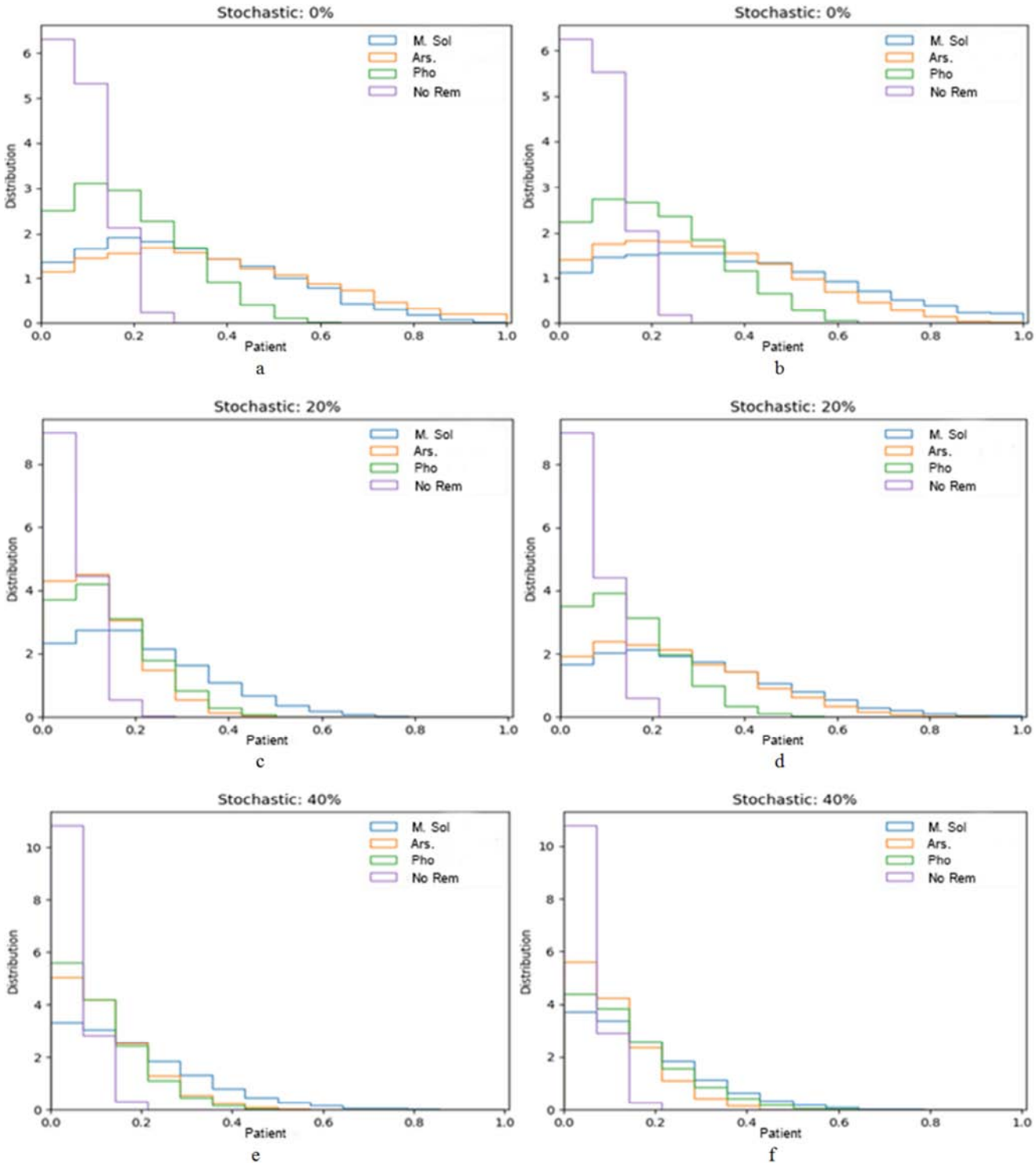

Figure 5. *Running function G_0N=200 (a, c, e) and N=800 (b, d, f).*

Even after the stochastic is notched upto to 40%, starting from 0% three remedies showed highest distribution of multidimensional vector $\vec{y}$ over mutlidimensional vector $\vec{y}$ in data of N=200 and then N=800 patients.

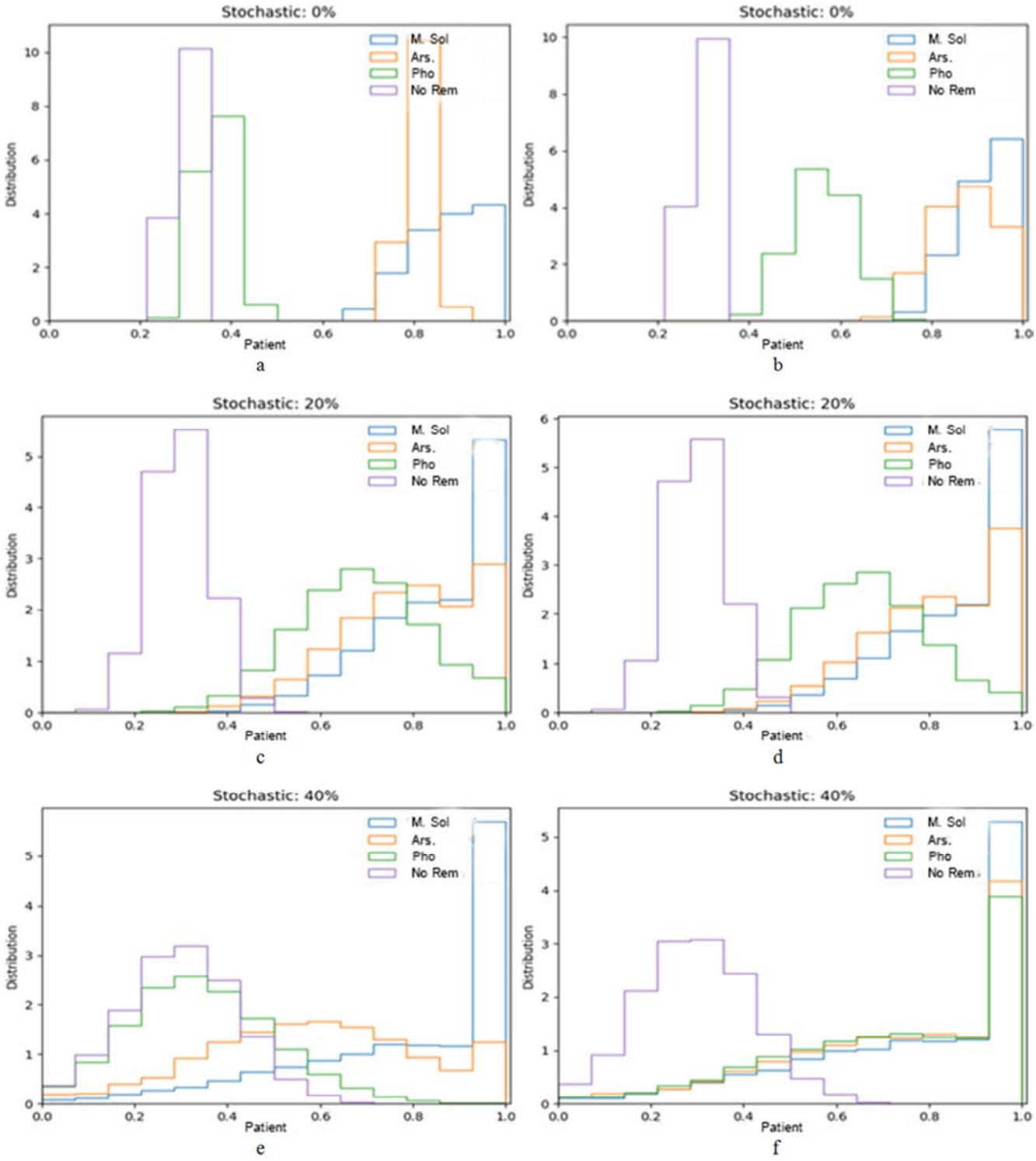

Figure 6. *Shows function G_1 N=200 (a, c, e) and N=800 (b, d, f).*

Clearly the most optimum remedy seems to be '*merc sol'* after the NN is run.

Thus, the result generated by this neural network indicates '*Merc sol* 'as a *Genus epidemicus.*

These results are then compared, verified, and validated by observational case studies presented by Dr. Vaisampayana's team of Homeopathic Doctors.

In this observational study of 130 patients treated by Dr Vaisampayana's team at his clinic on OPD basis and through tele medicine corroborates that '*merc sol'* is an invaluable remedy for covid 19/ covid like symptoms / pneumonias. This could also be considered as a preventive medicine for vulnerable group of patients exposed to other covid infected people.

Total number of cases seen for acute respiratory infections or viral infections prescribed merc sol 200C were130.

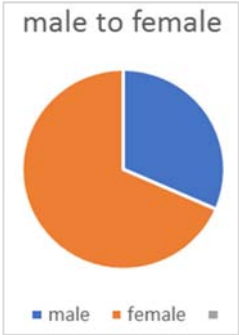

Figure 7. *Gender Distribution/Sex Ratio/Male: Female 41:89.*

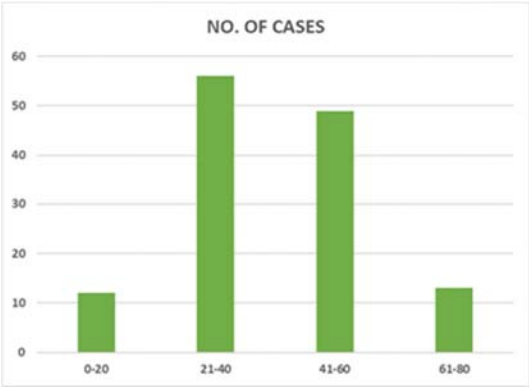

Figure 8. *Age Distribution.*

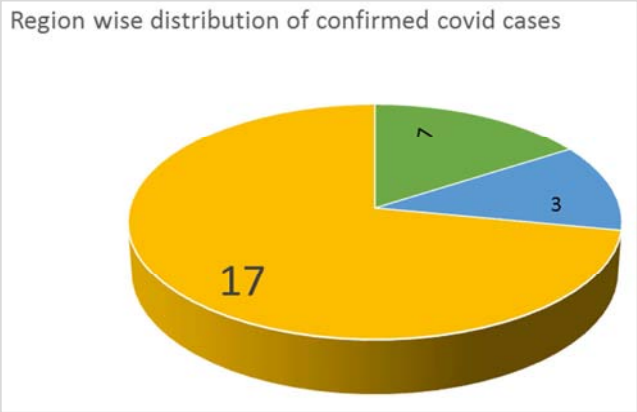

Figure 9. *Geographical Distribution.*

Table 3. *Age Distribution.*

0-20	12
21-40	56
41-60	49
61-80	13

Twenty-seven people were confirmed COVID-19 treated through online consults out of which 7 were from India 3 from Europe and 18 from the united states Here are a few examples from the above cases:

Table 4. *Example cases on field in Mumbai, India.*

Mode of consult	Case	Region	Protocol	Results
Tele medicine	F/6 months grandfather died of Covid	India	Merc sol 200 TDs for 5 days	Asymptomatic in 5 days
Tele Medicine	Female 45 schoolteacher fever, anosmia, Taste loss of with exhaustion and nervousness	USA	Merc Sol TDS for 5 days	Asymptomatic in 3 days
Clinical examination	Male/ 56 Psychiatric history covid like symptoms	India	Merc sol 200 TDs for 3 days	Admitted although asymptomatic due to h/o psychiatric illness was Covid Positive on pathological examination
Clinical examination	Male /54 mild fever, loss of smell and test mostly asymptomatic h/O exposure	India	Merc sol TDS for 7 days	Admitted to institutional quarantine facility due to the presence other high-risk members at home

Eight people had confirmed pneumonia were asymptomatic. COVID-19test was not recommended by government authorities.

Two cases were admitted in institutional quarantine as there were many high-risk people in the surrounding. One was admitted due to not obeying social distancing and high anxiety and other person was admitted due to previous history of psychiatric illness and difficult to manage at home. 4 people had twenty contacts altogether and these 20 contacts were covid negative and were treated only with standalone homoeopathy

People who had relapses, 10 people had relapsing infection 21 to 30 days after the first one was diagnosed, 5 people had history of Koch's in the past, 3 people had auto immune / endocrinal history and 2 people had high level of anxiety.

3. Discussion

Mathematics and Natural medicine although are diverse subjects a mathematical model and the modern technology could work hand in hand and produce some good results when paired together.

Machine learning and neural network could be useful in the field of homeopathic medicine where the accuracy of the action enhances, and it could save a lot of time energy and money.

Although single blind or double-blind placebo controlled RCT is still considered gold standard it is practically difficult to work in some acute or sudden illnesses where a life and death situation is occurring on the field. A double blind RTC could work when an epidemic / pandemic is stabilized and the actual dimensions of the clinical presentations are known like in an epidemic of chicken pox or any known viral illness where actual risk and the other risk factors involved are known for several decades so that any critical situation arising at a sight could be handle with a sound knowledge of good ethical research practice.

However, in an evolving epidemic like covid19 where the

total depth is unknown and there is a high chance of infection to the treating physician and the staff as exact nature of the disease and the depth is still unknown to the medical world. It could not replace the RCT, but it could make us better prepared in comparison with the theoretical preparation based upon assumptions.

The results obtained by the software in homoeopathy could be further validated by employing Machine Learning Models in lieu of gold standard-controlled trials, as seen in this experiment we estimated 3bestpossible drugs, '*arsenic album'*, '*phosphorus'* and *'Mercurius solubilis'* which were further validated by the observational case studies mentioned above.

According to Dr Hahnemann's organon Q99 [14]. the disease although will be called as covid next wave and next presentation may differ so will be the next genus epidemicus. So, any new symptoms added / subtracted from the list could give us robust estimates about the probable list of homeopathic medicines that could be potentially viable for use as the pandemic evolves.

4. Conclusion

The mathematical model created in this study is a simulated placebo control trial with ten best possible homeopathic solutions demonstrated merc sol clearly emerging as a '*genus epidemicus'* of COVID-19 19 till this time. The observational study of 130 patients also confirmed use of merc sol as a remedy in COVID-19 like cases/ pneumonias and diagnosed covid cases. This also confirms the preposition published in Thieme about our article published in the month of July. The accuracy of the above model could be further tested and improved as more varied data is made available in context of the current pandemic. Further data is being sanitized by other Doctors [15] to be used to test this model.

Highlights

Clinical symptoms of COVID-19 were repertorized by a mathematician with state of art software

Best 10 homoeopathic actions with 9 remedies and a placebo were identified

Designed a mathematical model to create a surrogate Digital clinical trial in lieu of actual clinical trial of 200 and then 800 virtual patients

The result indicated that homoeopathic medicines are working better than a placebo

The results of this study were fed to a neural network

The neural network was trained to run further trials

The above mathematical endeavor confirmed merc sol as a genus epidemic of this pandemic

The findings of machine learning were verified by an observational study of 130 patients of COVID-19 like illness, diagnosed COVID-19 and pneumonias of merc sol treated during this time frame.

Machine learning is giving accurate estimates that could be verified on the field.

5. Appendices

5.1. Appendix A: Mathematical Model and Functions

Functions

Three functions are created, with minor differences to capture the proposed hypothesis.

Generalized function G

This general function $G(\vec{x},\vec{y})$ models the behaviour of a physical system and consists of general set of hypotheses.

To perform a practical test of the techniques proposed we use a set of functions $g(\vec{x},\vec{y})$ which aim to capture the following hypotheses:

Highly non-linear multi-variable function

This function can take values between [0, 1]

Consists of a stochastic component

$G(\vec{x},\ 0)$represents no remedies outcome

$G(\vec{x},\vec{y})$ represents reaching higher or lower values than $G(\vec{x},\ 0)$ signifying remedies $\vec{y}$ in homeopathy which have a positive or negative effect for health.

May contain noise features like other interference or cancellation, dependency like $x_k(\ y_i - y_j)$

Factorizable function G_0 based on general function G

Function G_0 is factorized such that P represents patient specifics, m_0 is remedies specific, m_1 as a function of patient and remedies and a stochastic S dependency on η parameters:

$$G_0(\vec{x},\ \vec{y}\ ) =\ \mathrm{P}(\vec{x}\ )m_0(\vec{y})m_1\left(\overrightarrow{x,\vec{y}}\right)\mathrm{S}$$

With,

$$P(\vec{x}) = \left|\frac{\sum(\alpha_k - 2\alpha_k x_k)}{\sum\alpha_k}\right|^{\psi}$$

$$\begin{aligned} d_0(\vec{y}) = \exp(-|&\tilde{\alpha}_1 y_9 + \tilde{\alpha}_2 y_1 + \tilde{\alpha}_3 y_2 + \tilde{\alpha}_4 y_3 + \tilde{\alpha}_5 y_4| \\ &+|\tilde{\alpha}_6 y_5 + \tilde{\alpha}_7 y_2 + \tilde{\alpha}_8 y_6 + \tilde{\alpha}_9 y_7| \\ &+|\tilde{\alpha}_{10} y_8 + \tilde{\alpha}_{11} y_9 + \tilde{\alpha}_{12} y_1 + \tilde{\alpha}_{13} y_{10}|/10) \end{aligned}$$

$$d_1(\vec{x},\vec{y}) = 1 + 0.1\sin(\beta_1 y_1 - |(\beta_2 y_4 + \beta_3 y_5 + \beta_4 y_6)(\beta_5 x_1 y_3 - \beta_6 x_3 y_9)|)$$

The patient function $P(\vec{x})$ dependence on a coefficient ψ which controls how easily patients recover in the absence of medicines. If ψ<1 then function $P(\vec{x})$ tends to higher values, and ifψ>1, it tends to zero. The medicine function m_0 has an exponential dependence over a combination of medicine parameters y_i . Function m_1 adds an oscillation which depends on a specific combination of medicine and patient features, which allow certain combinations to affect an increase or decrease of the whole value of the function. For instance, the second term inside the sin function it is observed that there is a factor that contains the combination $(x_1 y_3 - x_3 y_9)$ that takes into account medicine/remedies

interaction between y_3 and y_9, weighted by features X_1 and X_3. Other parameters are random selected, in the range. A certain function G_0 exists for every set of specific parameters. The equations above therefore describe a family of functions such as G_0. Function G_0 distributions are checked with different parameter values, with and without medicines as displayed in Figures 3 and 4.

To reproduce the behavior parameter values are fixed. The noise is handled by a Gaussian function centered at 1, using standard deviation (sigmoid) and non-interdependent x and y. Since the output of function G0 needs to be in the range of [0, 1]:

negative values are not taken, and S is centered around 1

maximum value attained by P(x) m0, m1 is calculated

possible fluctuations are considered up to two standard deviations.

The function is divided by the value maximum value $G_0^{(0)} \equiv \max_{\vec{x},\vec{y}}\big(P(\vec{x})m_0(\vec{y})m_1(\vec{x},\vec{y})\big)(1+2\eta)$. The value of the function is bounded to [0, 1]. If any fluctuation of the noise is beyond the two standard deviations and the function is higher than 1, an assumption is made that the function evaluates to 1.

Non Factorizable Function G1

Function G1 inherits all the characteristics described in previously, such as:

Non-linearities

Medicine related noise interference/cancellation.

Although the function inherits the above features it is compact and unfactorizable. The distributions of function G1 are visualized in Figure 5 which show results with and without placebo. In this observation distribution with medicines takes smaller values as compared to distribution without medicines. This means there is a certain combination of medicines which are detrimental for patients' health.

$$G_1 = \frac{1}{15}\left|x_1 + (y_1 + 3y_2 - y_3)(x_5 - x_3) + \sinh(y_7 - y_6) - 5e^{-(y9-y_3)}\right|S_\eta$$

5.2. Appendix: B: OPD Patient Form

Consent for Homoeopathy as Adjuvant therapy

Patients Name:
A/S:
DOA:
Reported positive on:
Contact no :

COVID- Merc sol protocol by Dr Shailendra Vaishampayan/Dr Kirti Mutreja/ Dr Abhay Chheda

Sr no	Merc sol	None	I+	2+	3+
1	Restless sleep				
2	Night fever				
3	Diarrhoea before/ with fever				
5	Dirty tongue				
6	Indented tongue				
7	Salivation				
8	Perspiration/ oily				
9	Body warm/cold				
10	Aversion sweet				
11	Ulcers in mouth				
12	Trembling in upper extremities				
13	Cough 2-3 paroxysm				

Patients signature:

Figure 10. *OPD Patient Form.*

Declaration of Conflict of Interests

The author (s) declare no potential conflict of interest with respect to the research, authorship and/or publication of this article.

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