PAKISTAN RANDOMIZED AND OBSERVATIONAL TRIAL TO EVALUATE CORONAVIRUS TREATMENT (PROTECT)

Hydroxychloroquine Phosphate/Sulfate alone and in combination with Oseltamivir and Azithromycin for the Treatment of SARS-Cov2 Infection: A Multiarm Multistage Adaptive Randomized Controlled Clinical Trial (Version 1)

Following are the members of Scientific Task Force notified by the Federal Ministry of Science & Technology, Government of Pakistan vide notification number F.No. 12(6)/2016-Coord dated March 24, 2010. The Task Force is mandated to plan, conduct, and disseminate findings of PROTECT in scientific interest to reduce the impact of devastating pandemic of SARS-Cov-2 in Pakistan

Prof Atta ur Rahman N.I (Chairperson)

Prof Javed Akram, Vice Chancellor UHS, Lahore (Member)

Prof Ghazna Khalid, Visiting Faculty UHS Lahore (Member)

Prof Al Fareed Zafar, Principal Ameeruddin Medical College/PGMI Lahore (Member)

Prof Iqbal Chaudhary, Director ICCBS University of Karachi (Member)

Prof Khalid Saeed Khan, Distinguished Investigator University of Granada Spain (Member)

Prof Maryam Riaz Tarar, Pathologist, Shalamar Medical & Dental College Lahore (Member)

Additional Contributions:

Dr. Shehnoor Azhar Department of Public Health, UHS Lahore

Mr. Waqas Latif (Data-analyst at UHS)

SUMMARY

A scientific taskforce notified by the Ministry of Science and Technology of the Government of Pakistan will oversee a comprehensive cohort study. Within this cohort, a multicenter, adaptive, randomized controlled trial (RCT) that will evaluate, among eligible SARS-Cov-2 infected patients receiving standard supportive care who consent to randomization following a new diagnosis in Pakistan, if a daily active dose Hydroxychloroquine Phosphate/Sulfate alone (control intervention) vs a series of alternatives (comparator interventions) including Oseltamivir and Azithromycin alone and in combination with Hydroxychloroquine Phosphate/Sulfate is effective in clearing the coronavirus (primary outcome). Those not consenting to randomization will be followed up for outcomes of SARS-Cov-2 infection with supportive care only. Findings of this study are expected to inform clinical care and public health protocols and policies for management of SARS-Cov-2.

1. INTRODUCTION

The pandemic of SARS Cov-2 (COVID-19) a condition characterized by array of symptoms leading to Severe Acute Respiratory Illness) began in the Central Chinese city of Wuhan (1). The first case was reported in December 2019 with symptoms resembling Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS). The pathogen was suspected to be from the family of enveloped positive-sense *RNA viruses*, characterized by club-like spikes that project from their surface, an unusually large RNA genome, and a unique replication strategy. As reported by Fehr AR et al in 2015, these viruses cause diseases in other mammals besides lethal respiratory tract infection in human beings. Chinese scientists sequenced the genome of this fast-emerging virus early in 2020 (2). It was named novel Corona virus 2019 causing an array of symptoms now referred to as COVID 19.

Considering the virulence potential and aggressive measures employed by the Chinese authorities to stem this deadly outbreak, World Health Organization has been issuing warnings before declaring it as a pandemic on March 11, 2020 (3). At the time of writing, it has spread to 184 countries with over half a million total infections and 24,000 deaths reported worldwide. The majority of the infected have recovered after showing an array of symptoms characterized by fever, cough and shortness of breath. Understanding of its transmission via droplets is set to modify social codes and human interactions (4). The magnitude of problem is amplified by the absence of pharmaceutical solutions such as drugs and vaccines. For developing countries, the challenge is multifold (5).

A variety of drugs have been tested recently in search for a suitable cure including nafamostat, ribavirin, interferon, corticosteroids etc (2, 6). Chloroquine and hydroxychloroquine have been found to be efficient on COVID-19 and reported to be improving clinical symptoms in Chinese

COVID-19 patients while similar effects have been demonstrated in French patients (6). Combining it with Oseltamivir and Azithromycin has shown further promise in most recent studies (7). However, these findings are yet to be tested for the purpose in Pakistan where COVID-19 is being reported across. The rationale of such drug trial is merited by large population of 220 million and Pakistan's proximity with Iran, one of the countries worst hit by ongoing pandemic.

We will evaluate the role of Hydroxychloroquine Phosphate/Sulfate, Oseltamivir and Azithromycin in COVID-19 infection within a comprehensive multicentre cohort study at the centre of which is a multi-arm, multistage, open label randomised controlled trial. The ongoing pandemic and limited evidence on effectiveness of chloroquine on local population warrant an adaptive trial design so that timely data analyses could promptly inform clinical strategy of containing COVID-19 (8). Hydroxychloroquine Phosphate/Sulfate (200 mg orally thrice a day for 5 days) vs Oseltamivir (75 mg orally twice a day for 5 days) vs Azithromycin (500 mg orally once a day on day 1, followed by 250 mg orally daily on Days 2-5) alone and in combination will be given to patients consenting to take part in the trial (Dosage formulated by Prof Muhammad Shehzad, UHS Lahore). The primary outcome will be clearing of coronavirus nucleic acid (COVID-19) from throat and nasal swabs checked by Reverse Transcription-Quantitative Polymerase Chain Reaction (RT-qPCR). Those not consenting to randomization will be followed up for outcomes of COVID-19 infection with supportive care only.

The comprehensive cohort study will be commenced in four different centers across Pakistan. An independent Data Safety and Monitoring Board (DSMB) will oversee the trial. The Trial will be prospectively registered (clinicaltrials.gov) after ethical committee approval as per requirements of Drug Regulatory Authority of Pakistan (DRAP).

2 OBJECTIVES

2.1 Primary Objective

- To evaluate the effectiveness of Hydroxychloroquine Phosphate/Sulfate (200 mg orally 8hr thrice a day for 5 days) vs oseltamivir (75 mg Orally twice a day for 5 days) vs Azithromycin (500 mg orally daily on day 1, followed by 250 mg orally twice a day on days 2-5) alone and in combination (in all seven groups), in clearing the coronavirus nucleic acid from throat and nasal swab on day 7 of follow-up (primary outcome).

2.1 Secondary Objectives

- To evaluate the effects on secondary outcomes within all randomized participants and in predefined subgroups according to clinical and laboratory features
- To follow up participants not consenting to randomization for the outcomes of COVID-19 infection with supportive treatment only

3 STUDY DESIGN

An adaptive design, set within a comprehensive cohort study, is chosen because it permits flexibility in this fast-changing clinical and public health scenario. The randomized study will be a multicenter, multiarm, multistage, randomized, open label, controlled trial with a parallel design. Participants will be randomized, maintaining concealment of allocation sequence, using a computer-generated random number list of variable block size into multiple intervention groups (and an observation only group will emerge from those not consenting to randomization). Stratification for initial COVID-19 positive status (or days from initial symptoms as a proxy), and age groups will be used to ensure that groups remain balanced in size for each stage of the adaptive design. Furthermore, trained staff will collect oropharyngeal swabs samples as per World Health Organization guidelines. Samples will be maintained at -80 degrees. The groups will be administered their allocated intervention. Investigators will follow up with participants at 3 and 7

days (those positive at day 7 will be followed up further) for monitoring of primary endpoint, measuring time to turn test negative for COVID-19. As per biosafety and personal safety guidelines, nasopharyngeal and oropharyngeal swab samples will be taken by a trained ENT (ear-nose-throat) nurse from the participant at 3 and 7 days (those positive at day 7 will be followed up further) post-treatment. The investigators will also monitor secondary variables including quality of life, symptoms scores, duration it takes to oxygenate and ventilate, duration stayed oxygenated and ventilate, number of hospitals stay days, admission to intensive care, and mortality. This methodology has been peer reviewed by an external expert (see annex 1).

The proposal is being submitted to the Ethical Review Committee at UHS Lahore. To report potential complication associated with a drug regimen, an Adverse Drug Reaction tool of World Health Organization will be used. Trial registration application has already been made with Drug Regulatory Authority of Pakistan (DRAP).

4 PARTICIPANTS

Eligible will be newly diagnosed patients without any comorbidities or those with controlled chronic medical conditions, e.g. diabetes mellitus and hypertension. Participants of either gender or age group having tested positive for COVID-19 on RT-qPCR will be invited to take part. Participants who are pregnant or lactating, are already taking any treatment, have liver and kidney failure will be excluded from the study. Each participant will undergo baseline investigation i.e., liver function tests, renal function tests, urinalysis, and Complete Blood Count; before being randomized following informed consent. A case report form (CRF) has been developed for this proposal.

Inclusion Criteria

1. Confirmed SARS-CoV-2 (COVID-19) infection by a positive test result
2. Either gender
3. Symptomatic for example fever, dry Cough, difficulty to breathe

Exclusion Criteria

1. Confirmed absence of SARS-CoV-2 (COVID-19) infection by a negative test result
2. Have chronic conditions such as heart disease, liver and kidney failure
3. Pregnant or currently lactating
4. Immunocompromise and/or systemic disease(s)
5. On other antiviral drugs
6. History of allergy to any of the drugs to be administered in this study

Participant Recruitment

The participants will be recruited by co-investigators at participating clinical trial sites after obtaining informed consent. Nonconsenting patients will be excluded from the randomized study and will be requested to provide consent for inclusion in an observation cohort for outcomes of COVID-19 with supportive care only without medical treatment directed at coronavirus clearance.

4.1 SAMPLING, DIAGNOSIS AND VIRAL LOAD CALCULATION

Trained staff will collect oropharyngeal swabs samples as per World Health Organization guidelines. Samples will be maintained at -80 degrees. The groups will be administered their allocated intervention. Investigators will follow up with participants at days 3 and 7 (and day 14 if patient was positive on day 7) after treatment for monitoring of primary endpoint which is to check the viral load via throat and nasal swab using RT-qPCR (Agilent Real Time PCR System®). In case of any unforeseen event leading to shortage of diagnostic kits, follow-up samples will remain frozen. Since outcome measure is a laboratory test which will be kept blinded, measurement bias

would be avoided. The investigators will also monitor secondary variables including Quality of Life, symptoms score, time taken to require oxygenation, duration of oxygenation and ventilation, number of hospital days stayed, admission to intensive care and mortality. Adherence to protocol will be overseen by quantity of counting leftover drugs corresponding with each patient.

5 OUTCOMES

5.1 Primary outcome

The primary outcome will be turning test negative for COVID-19 on RT-qPCR calculated as viral load of < 150 i.u on day 7 of follow-up. The tests will be performed and results generated blind to the treatment allocation.

5.2 Secondary outcomes

The secondary outcome will be turning test negative for COVID-19 on RT-qPCR calculated as viral load < 150 i.u on day 3. Additional secondary outcome variables will be time taken for patient in requiring oxygen, time taken to ventilation, time on ventilator, quality of life, number of hospitals stay days, symptoms scores, admission to intensive care, and mortality plus other laboratory measurements. For off-label indications, quality of life is one of the ways to reflect patient's lived experience. Therefore, World Health Organization Quality of Life Questionnaire (WHOQoL) will be used. For symptoms scores, WURSS or Wisconsin Upper Respiratory Symptom Survey (with author permission) will also be used.

6 DATA ANALYSIS

All trial data will be analyzed by biostatistician based at the University of Health Sciences, Lahore, using an a priori, approved analysis plan (SPSS 25.0). Interim analyses at each stage (first stage

will be 10% of the total sample size) of the adaptive design will be pre-planned and undertaken confidentially keeping investigators and participants blind till the end of the trial. Primary and secondary outcomes will be analyzed in accordance to the group in which the participants were randomized deploying the intention-to-treat principle. The primary analysis will be expressed as odds ratio (OR) of the comparison between groups for the primary outcome. Interim analyses will be conducted without disclosing groups, thereby maintaining a level of blinding in interpretation of interim results. The results will be reported as point estimates and 95% confidence intervals. Secondary analysis will include in time-to-event data to directly compare the data among groups with survival plots and hazard ratios. This will permit evaluation of the decision to continue beyond Day 3 of treatment upon testing negative with viral load < 150 i.u and relieves patient of potential drug effects besides informing valuable understanding of drug effectiveness. Stratified analyses will be done by baseline COVID-19 positive status upon testing and age groups. Multiple regression and Cox proportional hazards stratified analysis will be used to make adjustments for a small number of covariates taken from stratification factors if there were baseline imbalances. Secondary analyses will deploy multiple regression models as well Chi square, Fisher's exact test and one-way ANOVA to compare groups. The two-sided p-value less than or equal to 0.05 will be taken as significant.

7 SAMPLE SIZE AND POWER ANALYSIS

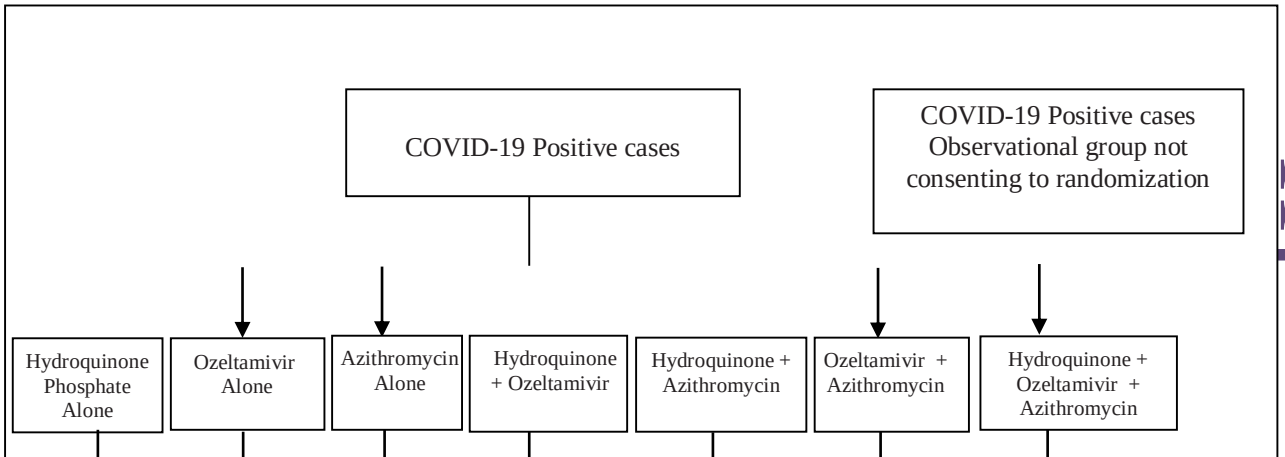
This is an adaptive design and parameters for formal sample size calculation in a new disease of a previously unknown virus are not available. Then the sample size and power analysis are indicative

for review at each stage of adaptive design. In a standard two arm, head-to-head trial, the sample size would have been as follows: in order to detect a difference in primary outcome of 10%, assuming a 50% efficacy of Hydroxychloroquine Phosphate/Sulfate in turning the test at day 7 and expected rates in comparator groups 60% at a significance level 5%, and a power of 90%, a sample size of approximately 520 subjects in each group will be required for a standard trial. (7, 8, 9) Additional considerations will need to make for the interim analysis at every stage of the adaptive design. Interim analysis will review sample size according to time to clearance also. Planned blinded sample size re-estimations will need to be undertaken in which we will constantly re-examine the original sample size assumptions. We will aim to maintain the trial power at 90% even if the original sample size assumptions turn out to be far from the observed data. The adaptation at each stage will allow us to drop out less promising interventions and will prevent an underpowered trial for the most promising interventions. As the planned modifications will be undertaken in a blinded fashion, there will be no increase in the type I error rate.

8 DATA SAFETY AND MONITORING

The independent data safety and monitoring board (DSMB) has been notified (Annex II). it will act according to Good Practice Guidelines. In line with well-established editorial standards, the interim analyses will be done independently of the authors of the paper. To achieve that, DSMB will establish an interim analysis sub-committee of independent individuals who will be named in acknowledgment section of the paper. The study statistician will be part of this committee and will keep that interim findings blind from the clinical investigators. The DSMB meeting agenda will have an open and a closed part, the latter part will only by attended by interim analysis sub-committee.

FLOW CHART OF TRIAL LAYOUT BY GROUPS



طبی علاج کے لئے منظوری فارم

(Consent Form For Medical Treatment)

MR NO; ……. Date; ……..

Patient Name and age; ……..

Father/husband Name;……..

I, here by allow/give full consent to my doctor for online consultation including the History taking and online medical examination and prescription.
I, here by declare that I will not do any legal proceedings in future in any circumstances.

میں رضامندی دے رہا ہوں کہ میرے ڈاکٹر میری بیماری کے بارے میں سوال پوچھ سکتے ہیں اورآن لائن انٹرنیٹ ویڈیو مشاورت کے ذریعے علاج کر سکتے ہیں میں کسی بھی صورت میں میں نے کسی بھی قانونی کارروائی کے لیے مجاز نہیں ہو گا

Patient signature/thumb impression and CNIC Number

Relative/family member signature and CNIC Number

COMBINED RESEARCH FORM: ADAPTIVE TRIAL FOR COVID 19

DRUG REGIMEN

A- Hydroxychloroquine Phosphate/Sulfate (200 mg orally thrice a day for 5 days)

B- Oseltamivir (75 mg orally twice a day for 5 days)

C- Azithromycin (500 mg orally once on Day 1, followed by 250 mg orally twice a day on Days 2-5)

D- Hydroxychloroquine Phosphate/Sulfate (200 mg orally thrice a day for 5 days) + Oseltamivir (75 mg orally twice a day for 5 days)

E- Hydroxychloroquine Phosphate/Sulfate (200 mg orally thrice a day for 5 days) + Azithromycin (500 mg orally once on day 1, followed by 250 mg orally twice a day on Days 2-5)

F- Oseltamivir (75 mg orally twice a day for 5 days) + Azithromycin (500 mg orally once on day 1, followed by 250 mg orally twice a day on days 2-5)

G- Hydroxychloroquine Phosphate/Sulfate (200 mg orally thrice a day for 5 days) + Azithromycin (500 mg orally once on day 1, followed by 250 mg orally twice a day on days 2-5) + Oseltamivir (75 mg Orally twice a day for 5 days)

H- Supportive care only

A- DEMOGRAPHIC INFORMATION:

1. ID: _____
2. Age: _____ years
3. Gender: Male / Female
4. Domicile:
5. Marital Status:
6. Study Center:
7. Income group: 0 – 10,000/- | > 10, 000 – 25,000/- | > 25,000 – 50,000/- | > 50,000/-

8. Number of Household Members:
9. Living as: Combined family / Single Family
10. Overseas travel history within last 3 months:
11. Highest level of Education achieved:

B. PREEXISTING CONDITIONS

CONDITION	YES/NO	STATUS (CONTROLLED/UNCONTROLLED)	COMMENTS
Diabetes Mellitus			
Hypertension			
Tuberculosis			
Heart Disease			
Liver Disease			
Kidney Disease			
Any other			
Drug Use			
Tobacco Use		**Average number of cigarettes a day:**	
Radiograph Chest			

C. BASELINE INVESTIGATIONS: COMPLETE BLOOD COUNT

MEASURE	COUNT/VALUES	REFERENCE RANGE (MAYO CLINIC)
Red Blood Cells		**Male:** 4.35-5.65 trillion cells/L* (4.32-5.72 million cells/mcL**) **Female:** 3.92-5.13 trillion cells/L (3.90-5.03 million cells/mcL)
White Blood Cells		3.4-9.6 billion cells/L (3,400 to 9,600 cells/mcL)
Platelets		**Male:** 135-317 billion/L (135,000 to 317,000/mcL) **Female:** 157-371 billion/L (157,000-371,000/mcL)
Hemoglobin		**Male:** 13.2-16.6 grams/dL*** (132-166 grams/L) **Female:** 11.6-15 grams/dL (116-150 grams/L)
Hematocrit		**Male:** 38.3-48.6 percent **Female:** 35.5-44.9 percent

- * L = liter
- ** mcL = microliter
- *** dL = deciliter

D. LIVER, KINDNEY FUNCTION TESTS & ELECTROLYTES

MEASURE	COUNT/VALUES	REFERENCE RANGE (MAYO CLINIC)
Alanine Transaminae (ALT)		7 to 55 units per liter (U/L)
Aspartate Transaminase (AST)		8 to 48 U/L
Alkaline Phosphatase (ALP)		40 to 129 U/L
Albumin		3.5 to 5.0 grams per deciliter (g/dL)
Total Protien		6.3 to 7.9 g/dL
Bilirubin		0.1 to 1.2 milligrams per deciliter (mg/dL)
Gamma Glutamyl Transferase (GGT)		8 to 61 U/L
Lactate Dehydrogenase (LD)		122 to 222 U/L
Prothrombin Time (PT)		9.4 to 12.5 seconds
Serum Creatinine		0.84 to 1.21 milligrams per deciliter (74.3 to 107 micromoles per liter)
Blood Urea Nitrogen (BUN)		7 to 20 mg/dL (2.5 to 7.1 mmol/L)
Potassium		3.6-5.2 mmol/L
Bicarbonate		22-29 mmol/L
Sodium		135-145 mmol/L
Calcium		8.6-10.2 mg/dL
Total Protein		6.3-7.9 g/dL

These results are typical for adult men. Normal results vary from laboratory to laboratory and might be slightly different for women and children

E. PRIMARY OUTCOME VARIABLES:

DRUG REGIMEN A - G	**Day 1**	**Day 3**	**DAY 6** *(N/Aif -ve on Day 3)*	**Tested -ve or +ve**	**Days taken to for viral load < 150 i.u**	**RTPCR KIT ORIGIN**

Days stayed at hospital:_____

Secondary outcome

1. Not hospitalized with resumption of normal activities
2. Not hospitalized, but unable to resume normal activities
3. Hospitalized, not requiring supplemental oxygen
4. Hospitalized, requiring supplemental oxygen
   Duration took to require oxygenation: _____ hours/days
   Duration stayed oxygenated: _____ hours/days
5. Hospitalized, requiring mechanical ventilation
   Duration took to require ventilation: _____ hours/days
   Duration stayed ventilated: _____ hours/days
6. Death

WHOQOL-BREF

The following questions ask how you feel about your quality of life, health, or other areas of your life. I will read out each question to you, along with the response options. Please choose the answer that appears most appropriate. If you are unsure about which response to give to a question, the first response you think of is often the best one. Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life in the last four weeks.

		Very poor	Poor	Neither poor nor good	Good	Very good
1.	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2.	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last four weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3.	To what extent do you feel that physical pain prevents you from doing what you need to do?	5	4	3	2	1
4.	How much do you need any medical treatment to function in your daily life?	5	4	3	2	1
5.	How much do you enjoy life?	1	2	3	4	5
6.	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
7.	How well are you able to concentrate?	1	2	3	4	5
8.	How safe do you feel in your daily life?	1	2	3	4	5
9.	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last four weeks

		Not at all	A little	Moderately	Mostly	Completely
10.	Do you have enough energy for everyday life?	1	2	3	4	5
11.	Are you able to accept your bodily appearance?	1	2	3	4	5
12.	Have you enough money to meet your needs?	1	2	3	4	5
13.	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14.	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither poor nor good	Good	Very good
15.	How well are you able to get around?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16.	How satisfied are you with your sleep?	1	2	3	4	5
17.	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18.	How satisfied are you with your capacity for work?	1	2	3	4	5
19.	How satisfied are you with yourself?	1	2	3	4	5

20.	How satisfied are you with your personal relationships?	1	2	3	4	5
21.	How satisfied are you with your sex life?	1	2	3	4	5
22.	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23.	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24.	How satisfied are you with your access to health services?	1	2	3	4	5
25.	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last four weeks.

		Never	Seldom	Quite often	Very often	Always
26.	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	5	4	3	2	1

Do you have any comments about the assessment?

_____

_____

_____

_____

Wisconsin Upper Respiratory Symptom Survey – 21 --- *Daily Symptom Report*

Day:	*Date:*	*Time:*	*ID*:

Please fill in one circle for each of the following items:

	Not sick	Very mildly		Mildly		Moderately		Severely
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**
How sick do you feel **today**?	O	O	O	O	O	O	O	O

Please rate the **average severity of your cold symptoms over the last 24 hours** for each symptom:

	Do not have this symptom	Very mild		Mild		Moderate		Severe
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Runny nose	O	O	O	O	O	O	O	O
Plugged nose	O	O	O	O	O	O	O	O
Sneezing	O	O	O	O	O	O	O	O
Sore throat	O	O	O	O	O	O	O	O
Scratchy throat	O	O	O	O	O	O	O	O
Cough	O	O	O	O	O	O	O	O
Hoarseness	O	O	O	O	O	O	O	O
Head congestion	O	O	O	O	O	O	O	O
Chest congestion	O	O	O	O	O	O	O	O
Feeling tired	O	O	O	O	O	O	O	O

Over the last 24 hours, how much has your cold interfered with your ability to:

	Not at all	Very mildly		Mildly		Moderately		Severely
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**
Think clearly	O	O	O	O	O	O	O	O
Sleep well	O	O	O	O	O	O	O	O
Breathe easily	O	O	O	O	O	O	O	O
Walk, climb stairs, exercise	O	O	O	O	O	O	O	O
Accomplish daily activities	O	O	O	O	O	O	O	O
Work outside the home	O	O	O	O	O	O	O	O
Work inside the home	O	O	O	O	O	O	O	O
Interact with others	O	O	O	O	O	O	O	O
Live your personal life	O	O	O	O	O	O	O	O

Compared to yesterday, I feel that my cold is…

Very much better	Somewhat better	A little better	The same	A little worse	Somewhat worse	Very much worse
O	O	O	O	O	O	O

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ANNEX 1

COVID adaptive trial

Javier Zamora <javierza@gmail.com> 27 March 2020 at 14:54
To: Khalid Khan <profkkhan@gmail.com>

Dear Khalid,
I have read the protocol. It is really interesting and worthy to do in this critical moment of the pandemic.
Please find attached the document with some comments.
If you need further advice from me, don't hesitate to contact me
Kind regards
Javier

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Javier Zamora
Head of the Clinical Biostatistics Unit. Hospital Ramón y Cajal. IRYCIS. Madrid. Spain
Senior Lecturer - Queen Mary University London
CIBER Epidemiology and Public Health
http://www.hrc.es/investigacion/inves_unidadbio.htm
Phone: +34 91 3368103
Fax: +34 91 3369016

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ANNEX 2

No. UHS/VC-20/705
Date: March 27, 2020

Professor Javed Akram
MRCP (UK), FRCP (London), FRCP (Glasgow),
FRCP (Edin), FACC (USA), FACP (USA), FASIM (USA)
Vice Chancellor

University of Health Sciences
Lahore - Pakistan

OFFICE ORDER

In the wake of recent outbreak of Corona Pandemic, a Data Safety and Monitoring Board is hereby established with immediate effect.

The members of the Board are as below:

(i)	**Prof. Aziz ur Rehman,** *MBBS, FCPS* Professor of Medicine Rashid Latif Medical & Dental College, Lahore	**Chairman**
(ii)	**Dr. Asma Kazi,** *MBBS, FCPS* Associate Professor of Medicine Rashid Latif Medical & Dental College, Lahore	**Member**
(iii)	**Dr. Anjum Razzaq,** *MBBS, DTCD, MCPS, MPH* HoD Epidemiology Institute of Public Health, Lahore	**Member**
(iv)	**Mr. Faisal Mushtaq,** *MSc (Biostat), M. Phil (Public Health)* Demonstrator Biostatistics	**Member**
(v)	**Mr. Muhammad Umer Farooq,** *MSc (Biostat), M. Phil (Public Health)* Demonstrator Biostatistics	**Member**
(vi)	**Dr. Usman Saleem,** *R.Ph, Pharm D* Chief Pharmacist Arif Memorial Teaching Hospital, Lahore	**Member**
(vii)	**Dr. Syeda Kissa Fatima Zaidi,** *MBBS* House Officer Arif Memorial Teaching Hospital, Lahore	**Member**

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Vice Chancellor
University of Health Sciences, Lahore

CC:
1. All members of the Committee
2. Registrar, UHS
3. Director Admin & Coord, UHS
4. PSO to VC