LWI COVID-19 RESPONSE

STUDY PROTOCOLS FOR COVID-19 RESPONSE IN AFRICA

An African Solution to the Pandemic

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Bisi Bright  FPCPharm, FPSN, MPH, MNIM
CEO, LiveWell Initiative LWI
Exco Member, Healthcare Federation of Nigeria HFN
Founder, Women in Hepatitis Africa WIHA

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WHO WE ARE

**Overview**
- LiveWell Initiative, LWI, is a responsible and goal-focused, self-funded nonprofit organization.

**Our Mission**
- To improve the health status of the people of Africa through wellness promotion and health empowerment and thereby positively influencing their health-seeking behaviour.

**Our Vision**
- To halve health illiteracy in Africa by the year 2030; and to increase the life expectancy of the people to 70 by the year 2030.
EXECUTIVE SUMMARY

**Facts on COVID-19**

- The world is currently experiencing a pandemic of an infectious disease called coronavirus, or COVID-19.
- Nigeria, as of date has been experiencing increase in COVID-19 cases.
- However, the major challenge facing the country COVID-19 response is inadequate test kits.
- Hence, there are a lot of asymptomatic cases out there.

**Our COVID-19 RESPONSE**

LWI has so far responded to the COVID-19 scourge with the following actions:

- Deployment of a Team tagged #LWICOVID19TEAM
- Innovation of a Study Protocol 1, 2, 3
- Co-hosting a webinar with FIP and WHO EMRO to further discuss on our innovation.
OBJECTIVES
Our objective is to work alongside with governments of Africa and other Health Stakeholders in the continent to join hands in reducing and eliminating the spread of the COVID-19 virus through Hypothesis Testing of our Study Protocol, dovetailing into RCTs.
COVID-19 CASE UPDATE

13 NEW CASES CONFIRMED

9:30 p.m. 11th April, 2020

TOTAL CONFIRMED 318
DISCHARGED 70
DEATHS 10

NCDC Toll-free Number: 080097000010
Twitter/Facebook: @NCDCgov/COVID19.NCDC.GOV.NG

https://twitter.com/NCDCgov/status/1249072367000784901
www.livewellng.org
COVID-19 CASE UPDATE

265 NEW CASES CONFIRMED

23rd May, 2020

TOTAL CONFIRMED 7526

DISCHARGED 2174

DEATHS 221

NCDC Toll-free Number: 080097000010
Twitter/Facebook: @NCDCgov/ COVID19.NCDC.GOV.NG
The organization has deployed a **39-man Team** made up of 32 Nurses, 3 Physicians, 2 Pharmacists, 1 Laboratory Scientist, 1 Geneticist and 1 Public Health Officer, to the COVID-19 frontline.

The organization has innovatively drawn up an **Hypothesis Testing of a Study Protocol for COVID-19**. This includes Pre and Post Exposure Prophylaxis PrEP and PEP.

The organization has innovatively initiated the ‘discourse’ among physicians and pharmacists through the Hypothesis Testing, with encouraging results from across the country.
PATHOPHYSIOLOGY:

- Prolonged and progressive hypoxia
- Binding to and Displacing ‘heme’ iron
- Severe haemolysis, hyperoxia and hyperferric ions leading to oxidative stress and cytokine storm
- RBCs useless, cannot carry oxygen anymore
- Liver produces erythropoietin in defence
- Bone marrow ‘stressed’ into producing new RBCs
- Equivalent to carbon monoxide poisoning
- Ground-Glass Opacity in lungs, failure of gas exchange
Cytokine Surge

• With cytokine surge, the lungs are hypoxic even in the presence of oversaturation of oxygen because there is no air exchange at the alveoli due to heme iron displacement, thrombi formation, alveolar interstitial oedema, and alveolar collapse even under the Ventilator

• This must be prevented at all costs

• To achieve this, our Study Protocol introduces PrEP and PEP in a ‘stepped-care’ plan

• The Study Protocol makes a case for Anti-inflammatory and Anticoagulation at this stage due to thrombi formation, alveolar interstitial oedema and alveolar collapse
EMPIRICAL REVERSE LOGIC MODEL

**INPUT**
- STUDY PROTOCOL
  - CQ / HCQS
  - AZI
  - Zn / Vit C
  - Vitamin C

**OUTPUT**
- Debates (Physicians / Pharmacists)
- WhatsApp Platform Health Professionals Debate
- Collaborations
- PrEP and PEP choices

**OUTCOMES**
- Webinars 1, 2, 3
- Randomized Study
- African COVID-19 RESPONSE
- Affordable, Scalable, Replicable, Sustainable COVID-19 Algorithms

**External Influences**
- Related Problems
  - Lack of data
  - Lack of history
  -- Novel virus
- Environment
  - Poverty
    -- Lack of Infrastructure

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Therapy Design - The LWI Example

• **Empirical Reverse Logic** Model
• We Looked at *All component parts* of the disease
• Healthcare Professionals – *PrEP / Travelers*
• Early Exposure / Asymptomatic Stages (*URA*)– *PEP*
• Early Disease (*MRA* - Trachea) – *Ambulatory Care*
• Advanced Disease – (*LRA* – Bronchi) – *Inpatient Care*
• Intensive Disease – (*LRA* – Aveoli) – *Critical Care, glass-ground opacity resultant from Cytokine Surge, Platelet aggregation, Displaced Heme Iron, Hyperoxia and Hyperviraemia*
• Post – Treatment *IPT - Intermittent Preventive Therapy*
Incidence of Risk Factors – CQ /HCQ

- CQ and HCQ retinopathy screening recommendations of AAO stated that high-risk patients were those who used CQ longer than 5 years.

- Those who had a cumulative dose >460 g or 2.3 mg/kg real weight/d, or

- Those who were elderly or had concurrent liver or renal dysfunction.

- QT wave prolongation in patients after 4-5 years of abuse.
EXCLUSION CRITERIA

MODERATE TO HIGH RISK:
• Cardiovascular Disease with recent travel abroad and without post-travel self isolation
• Acute Respiratory Airway Disease with or without recent travel
• Ageing Patients >65 years
• Hepatitis B or C patient in remission

HIGH RISK:
• History of Diabetes with recent travel
• Renal Disease
• Chronic Airways Disease – COPD, Emphysema
• Ageing Patients >75 years
• Hepatitis B or C patient not in remission
• Elevated Liver Enzymes
CQ/HCQ ARE 4-AMINOQUINOLINES

- **PROPERTIES**
  - Antiinflammatory
  - Antiviral
  - Antiprotozoal
  - Antiparasitic
  - Haemozoin Inhibitors
  - Zinc Ionophore
  - PCR Inhibitor

CQ / HCQ – MODES OF ACTION

• CQ/HCQ has a multiple modes of action on the virus
• It prevents the virus from penetrating the host cell using its S protein and Protease
• It breaks the polymerase chain and prevents viral replication
• It is a zinc ionophore and ensures penetration of zinc into the viral cell, altering the pH
• Zinc also potentiates CQ action, and CQ has a good safety profile in therapeutic doses
4-AMINOQUINOLINES:

• Suppress exaggerated Immunoglobulin response IgG and IgM through Immunomodulation and therefore also exerts

• Antiinflammatory action

• A highly soluble and more potent 8-Aminoquinoline, Quinine, will cross the BBB

• Will therefore penetrate the Alveoli and displace the viruses, disseminate the glass ground opacity, restore heme iron and noormalcy

• Haemozoin Inhibitor – starves the virus of its food vacoules
CQ / HCQ TOXICITY???

WRONG - OVERDOSE

- 450mg bd x 5
- 600mg bd x 10
- 600mg dly x 10
- 450mg tds x 5

RIGHT – LWI PROTOCOLS

- Within Therapeutic Margins
- Total loading dose less than 3.5g
- Safety Profiling and Risk Profiling assured

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SUCCESS

• Uvais NA. The risks of prescribing hydroxychloroquine in COVID-19–infected patients with schizophrenia.
  • Prim Care Companion CNS Disord. 2020;22(3):20com02635
• Jay Rathod BS, Joel Gernsheimer MD
• https://doi.org/10.4088/PCC.20com02635

FAILURE

• OBSERVATIONAL STUDY published in Lancet, May 22,2020 96,000 subjects; No dosage, No named COUNTRIES, No description of study population, hurriedly published, unscientific
  https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31180-6/fulltext
Hydroxychloroquine rated ‘most effective’ coronavirus treatment, poll of doctors finds

By Natalie O’Neill
April 2, 2020 at 11:30 PM • 2 MIN READ

| **Emerging prophylaxis strategies against COVID-19.**
Agrawal S, Goel AD, Gupta N |
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong><a href="https://www.ncbi.nlm.nih.gov/pubmed/32231348">https://www.ncbi.nlm.nih.gov/pubmed/32231348</a></strong></td>
</tr>
<tr>
<td>A summary of ongoing clinical trials for chemoprophylaxis of COVID19 show CQ and HCQ as a number of pre exposure and post exposure prophylaxis</td>
</tr>
</tbody>
</table>

| **Uvais NA. The risks of prescribing hydroxychloroquine in COVID-19–infected patients with schizophrenia.**
*Prim Care Companion CNS Disord.* 2020;22(3):20com02635
Jay Rathod BS, Joel Gernsheimer MD |
<table>
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<tbody>
<tr>
<td>There are currently 7 completed clinical trials and 29 registered clinical trials focusing on HCQ or CQ as a therapeutic avenue for COVID-19. Of these, 5/7 trials have shown favorable outcomes for patients using CQ or HCQ and 2/7 have shown no change compared to control.</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th><strong>Chloroquine, Zithromax, Zinc usage by Bauchi State Government</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong><a href="https://www.vanguardngr.com/2020/05/no-apology-for-saying-i-recovered-by-taking-chloroquine-zithromax-zinc/">https://www.vanguardngr.com/2020/05/no-apology-for-saying-i-recovered-by-taking-chloroquine-zithromax-zinc/</a></strong></td>
</tr>
<tr>
<td>The bauchi state governor used Chloroquine, Zithromax and Zinc to recover from Covid-19.</td>
</tr>
<tr>
<td>CHLOROQUINE STUDIES UPHeld</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td><strong>1A</strong> Efficacy of chloroquine and hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial</td>
</tr>
</tbody>
</table>

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# SUMMARY OF CLINICAL TRIALS – CQ / HCQ – Evidence of Overdoses – in red


Table 1: Summary Of Clinical Trials On CQ & HCQ

<table>
<thead>
<tr>
<th>Authors</th>
<th>Participants (Treatment/Control)</th>
<th>Treatment</th>
<th>Control</th>
<th>Additional Therapy</th>
<th>Primary Objective</th>
<th>Trial Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gao J et al.</td>
<td>100+</td>
<td>Chloroquine Phosphate</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Treatment was found to be superior to control in terms of inhibition of pneumonia exacerbation and disease mitigation.</td>
</tr>
<tr>
<td>Gautret P et al.</td>
<td>36 (20/16)</td>
<td>Hydroxychloroquine (200mg) t.i.d. 10 days 6G cumulative dose</td>
<td>Patients not receiving HCQ</td>
<td>6 patients received an additional therapy of azithromycin</td>
<td>Results of the naso-pharyngeal swab (Day 6)</td>
<td>Around 70% of patients in the treatment group were virologically cured. (P&lt;0.001)</td>
</tr>
<tr>
<td>Chen J et al.</td>
<td>30 (15/15)</td>
<td>Hydroxychloroquine (400mg) q.d. 5 days 8G cumulative dose</td>
<td>Patients on conventional treatment</td>
<td>–</td>
<td>Results of the naso-pharyngeal swab (Day 7)</td>
<td>Disease cure rate in the treatment group was found to be insignificant when compared to that of control. (P&gt;0.05)</td>
</tr>
</tbody>
</table>
THE PROTOCOLS

• STUDY PROTOCOL 1 – ‘Smart’ Protocol

• STUDY PROTOCOL 2 – The ‘Generic’ Protocol along with ancillary and symptomatic remedies

• STUDY PROTOCOL 3 – Easy to understand, easy applicability...Written for Community Health Workers, CHW, in Low income settings

• Includes Intermittent Preventive Therapy IPT
LWI Study Protocols recommend:

- **PrEP** Pre Exposure Prophylaxis
- **PEP** Post Exposure Prophylaxis
- **Ambulatory Regimen** for COVID-19 Outpatients
- **Inpatient Regimen** for COVID-19 Patients on admission
- **Critical Care Regimen** for ICU Patients and
- **Post-Recovery IPT** (Intermittent Prophylactic Therapy) for post-discharge patients
RISK MODIFICATION
– Pre-Testing

- LFT for Hepatitis with or without remission
- BUN, Urea and Creatinine for Renal History
- Electrolytes and ECG for severely Hypertensive patients and above 75 years
- Visual acuity before and after intervention for patients with Chronic Eye Disease
- Baseline BP, for continuous monitoring
- Dosage Calibration below 4G for all patients as much as is possible
# STUDY PROTOCOL

**SUGGESTED TREATMENT PROTOCOLS FOR DEBATE - CORONAVIRUS COVID-19 - Emergency Preparedness**

## 1. PrEP - Pre Exposure Prophylaxis

### i) HealthCare Workers / Healthcare Professionals

- Chloroquine 500mg stat daily x 3 days or Hydroxychloroquine 400mg stat daily x 3 days
- Azithromycin 250mg dly x 3 days

### ii) Self-Isolated Persons

- Chloroquine 250mg stat then 250mg weekly x 3 weeks or Hydroxychloroquine 200mg stat then 200mg weekly x 3 weeks

### iii) Self Quarantined Persons Post-Travel or Persons in an Epicenter

- Chloroquine 500mg stat then 250mg daily x 7 days or Hydroxychloroquine 400mg bd then 400mg daily x 7 days
- Azithromycin 250mg dly x 5-7 days

## 2. PEP - Post Exposure Prophylaxis

### i) Contact with a person who has tested Positive (without symptoms)

- Chloroquine 500mg bd stat then 500mg daily x 3 days or Hydroxychloroquine 400mg bd stat then 400mg daily x 3 days
- Azithromycin 250mg dly x 3 days

### ii) Person with Dry Cough or Any throat Symptoms

- Chloroquine 500mg bd stat then 500mg daily x 3 days or Hydroxychloroquine 400mg bd stat then 400mg daily x 3 days
- Azithromycin 500mg dly x 3 days

### iii) Family members in a home with a self isolated member

- Chloroquine 500mg bd stat then 500mg daily x 3 days or Hydroxychloroquine 400mg bd stat then 400mg daily x 3 days
### 3. INPATIENT - Admitted in Hospital or Isolation Centre

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinine p.o.</td>
<td>600mg tds x 5 days</td>
<td>Generous Fluids</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500mg dly x 7 days</td>
<td>Vitamin C 1000mg daily x 10 days</td>
</tr>
<tr>
<td>Zinc Sulphate</td>
<td>220mg daily x 7 days</td>
<td>Respirator</td>
</tr>
</tbody>
</table>

### 4. ICU PATIENT - INTENSIVE CARE UNIT

#### i) Patient with Severe Symptoms

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinine I.V.</td>
<td>with dextrose tds</td>
<td>Vitamin C 1000mg daily x 10 days</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500mg i.v.</td>
<td>BLS</td>
</tr>
<tr>
<td>Zinc Sulphate</td>
<td>220mg daily x 7 days</td>
<td>Respirator / Ventilator</td>
</tr>
<tr>
<td>Generous Fluids</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### ii) Patient in Critical State

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dosage</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive Care in isolated IUC Bunker</td>
<td></td>
<td>Generous Fluids</td>
</tr>
<tr>
<td>Quinine I.V.</td>
<td>with dextrose tds</td>
<td>Vitamin C 1000mg daily x 10 days</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500mg i.v.</td>
<td>ALS / Critical Pulmonary Care</td>
</tr>
<tr>
<td>Zinc Sulphate</td>
<td>220mg daily x 7 days</td>
<td>Respirator / Ventilator</td>
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</table>

*The information in this STUDY PROTOCOL is shared for the purpose of professional debates among physicians and pharmacists and not for treatment. The above listed Protocols are subject to the discretion of Prescribing Clinicians and they are as recommended in a compilation of recent findings on COVID-19. LiveWell Initiative LWI, a nonprofit organisation, takes no liability for damage from the use of the above suggested STUDY PROTOCOL FOR DEBATE. This document is not intended for non-physicians and non-pharmacists. It is strictly meant for research, as we look towards a cure for the Pandemic.*
**EMPIRICAL DATA**

- **Kaduna State** — *Positive feedback from State Government, adopting the protocol for trial*


- **Chevron** - *Self isolated Traveller recovered after PEP upon displaying symptoms and advised by the physician*

- **Canada** - *an ICU patient discharged after fully recovering on quinine i.v. Instituted by her physician*

- **United Kingdom** — *Self Quarantined Nurse fully recovered after PEP*

- **Lagos cohorts** — *Group PrEP, Self PrEP, PEP*
contd

- Oyo State Isolation Center – 11 patients all fully recovered and discharged
- Lilly Hospital, Warri
- FMC Keffi
- Faith Multiplex Hospital, Benin City
- Babcock University, Ilishan
- Plateau State Government, Jos
- Lagos University Teaching Hospital LUTH
- FMC, Owerri
- ....and a host of others
Patient Monitoring

• Patients who present with moderate to high risk, should be monitored before, during and after intervention

• In particular, such patients’ liver function, electrolytes and urea, or visual acuity may be monitored before and after intervention

• This is aligned with risk modification
NEXT STEPS

• Collate the Data
• Call for Partner Institutions and Sponsors
• Collaborate with Governments
• Institute RCTs
• Drive Data and Publications
• More Research and
• Validation / Authentication
CONCLUSION

• As a responsible organization, we have escalated the Hypothesis to government, public and private sector physicians and pharmacists, with a view to gathering data for a future Randomized or Adaptive Study.
• After the webinar series, we shall progress into a formal Randomized Study with willing partners.
• This is a Study by Africans for Africa.
Bibliography


Thank You for listening


LWI Research Team Lead:

Bisi Bright  FPCPharm, FPSN, MPH
CEO, LiveWell Initiative LWI
Exco Member, Healthcare Federation of Nigeria HFN
Founder, Women in Hepatitis Africa WIHA
Former Secretary General, West African Postgraduate College of Pharmacists

Twitter: @bisibright  @L_W_I  @WIHA_NG  @WIHA_NG2
Linkedin: Bisi Bright
Website: www.livewellng.org  wiha.livewellng.org
Tel: +234 7018001787; +234 8091769289

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