

COVID-19: Monitoring Symptoms and Medication

April 22, 2020



Agenda

- + Introductions
- + BioIntelliSense BioSticker™
- + Medication Safety Considerations with Hydroxychloroquine and Azithromycin in COVID-19
- + Q&A

Introductions

Moderator and Presenters



Mike Ristagno, PharmD, MBA
Chief Client Officer
CareKinesis



Jim Mault, MD, FACS
Founder and CEO
BioIntelliSense



Katie Meyer, PharmD, BCPS, BCGP, CMWA
Pharmacist, Learning and Development
Tabula Rasa HealthCare

Continuous Monitoring FOR COVID-19



BioIntelliSense

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BioIntelliSense Announces FDA Clearance of the BioSticker™, the First Single- Use Medical Device Enabling 30 Days of Continuous Vital Signs Monitoring

An effortless patient experience combined with actionable clinical intelligence to bring medical-grade care to the home

Denver, CO – January 28, 2020 – BioIntelliSense, Inc., a continuous health monitoring and clinical intelligence company, today announces the U.S. commercial launch of its medical grade Data-as-a-Service (DaaS) platform and FDA 510(k) clearance of the BioSticker™ on-body sensor for scalable remote care. BioIntelliSense offers a new standard for Remote Patient Monitoring (RPM) by combining an effortless patient experience with medical grade clinical accuracy and cost-effective data services.



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"We are at the inception of a remarkable new era in healthcare that will employ medical grade sensor technologies to effortlessly capture remote patient data and generate personalized clinical intelligence," said James Maul, MD, FACS, CEO of BioIntelliSense.

The BioSticker is an advanced on-body sensor that allows for effortless continuous monitoring of vital signs and actionable insights, delivered to clinicians from patients in the home setting, thereby creating unique opportunities for early detection of potentially avoidable complications. Through the platform's data sets and analytics, highly-efficient care is now possible at a fraction of the cost of traditional remote patient monitoring.

BioIntelliSense is built on the foundation of a sophisticated team of engineers and data scientists with decades of expertise in wearable sensor development. With these distinctive capabilities and proprietary technologies, the company is poised to help transform care delivery under the leadership of Dr. Maul, an industry veteran who has an accomplished business and clinical career that has culminated in a number of successful connected health ventures.

BioIntelliSense has established a strategic collaboration with UHealth and its CARE Innovation Center to demonstrate the value and clinical applications of the BioSticker device and medical-grade services. This alliance is committed to developing and validating new models of data-driven care that are patient-centered and built for scale.

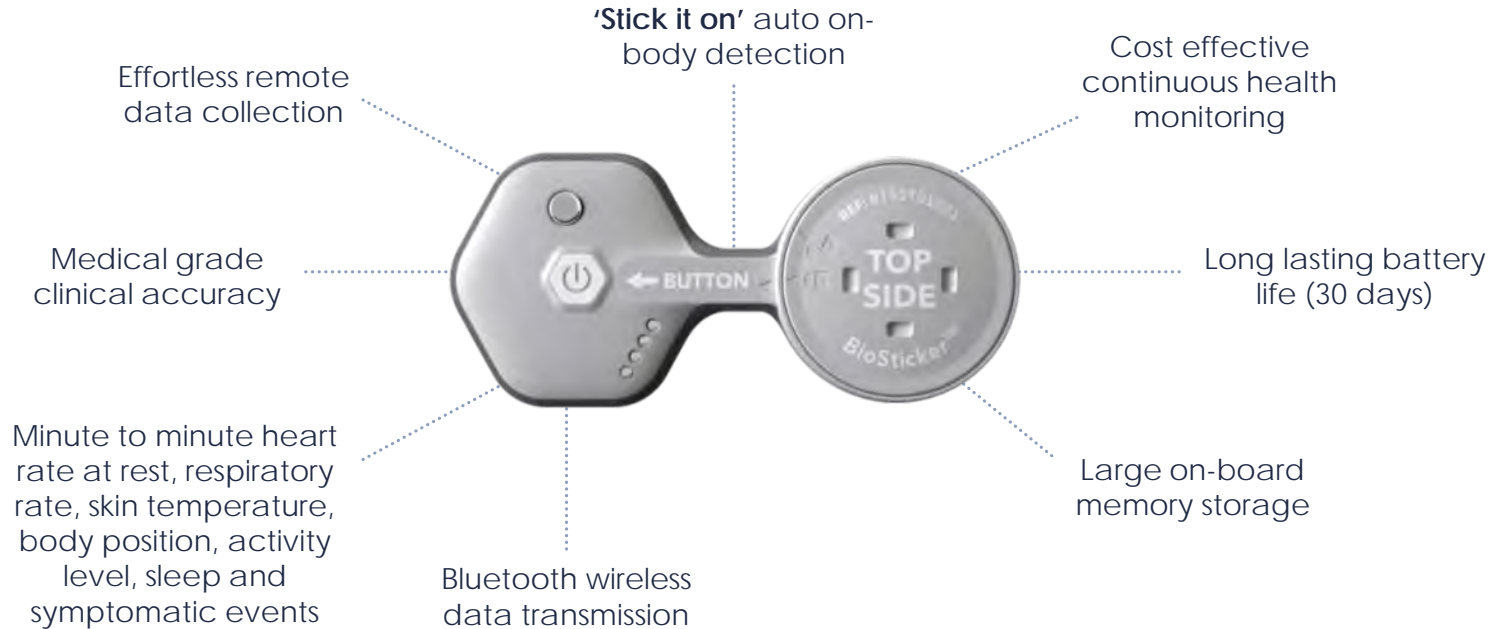
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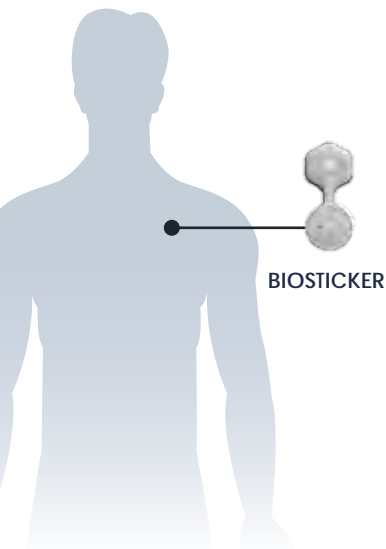
BioSticker

FDA-510k Class II Medical Device





Medical-grade data services for continuous monitoring of COVID - 19



SKIN
TEMPERATURE



HEART RATE
AT REST



RESPIRATORY RATE
AT REST



COUGHING
FREQUENCY



SLEEP



BODY
POSITION



ACTIVITY LEVEL





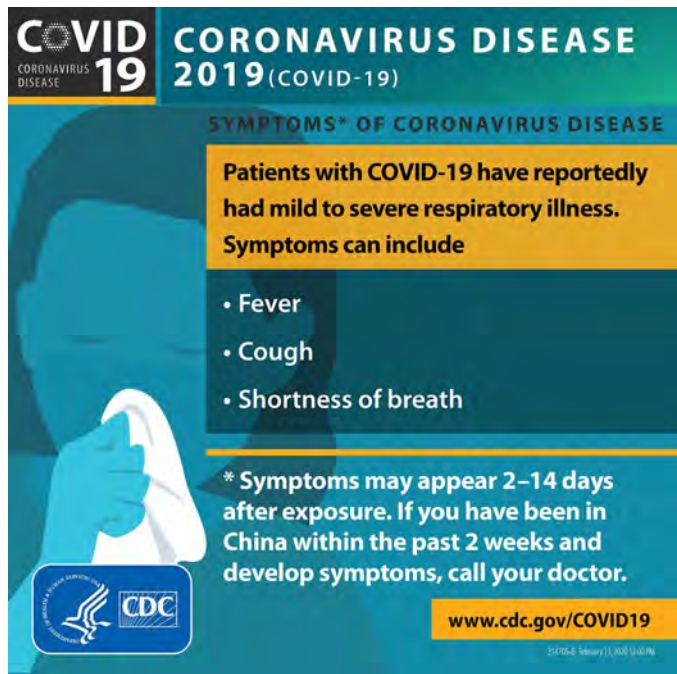
BioHub



- Bluetooth enabled
- Auto-detection of and communication with BioSticker
- Led touch screen and display
- 5G Qualcomm cellular connectivity with built-in ATT data plan
- Captures data from multiple patients and multiple BioSticker devices
- Captures data from select third party blood pressure meters and pulse oximeters (others pending)
- BioHub-Mobile (iOS and Android) may also be used in addition to or instead of the BioHub Device via individual's smartphone or tablet internet connection



BioIntelliSense Vital Sign and Symptomatic Monitoring for COVID-19



BioSticker



Skin Temperature



Coughing Frequency



Respiratory Rate @ Rest



- FDA – cleared multi-parameter vital signs monitor
- Minute to minute skin temperature, respiratory rate at rest, coughing tracker
- 30 – day continuous battery life
- Bluetooth data transmission
- **Stick it on and forget it'** auto on-body detection passive data capture ease of use



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Source: *Tabula Rasa HealthCare, Inc.*

March 17, 2020 08:01 ET

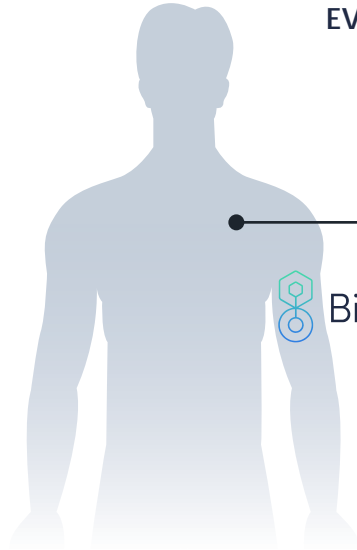
Tabula Rasa HealthCare Named Principal Distributor of the BioIntelliSense BioSticker™ for Programs of All-Inclusive Care for the Elderly (PACE)

Tabula Rasa HealthCare and BioIntelliSense Partnership enables remote monitoring including symptoms of COVID-19

MOORESTOWN, N.J., March 17, 2020 (GLOBE NEWSWIRE) -- **Tabula Rasa HealthCare, Inc. (TRHC) (NASDAQ: TRHC)**, a healthcare technology company advancing the field of medication safety, enters into an agreement with BioIntelliSense to distribute its BioSticker™, the first FDA-cleared, single-use device enabling 30 days of continuous vital sign monitoring.

BioIntelliSense RPM Platform for COVID19

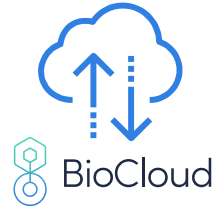
REAL-TIME PHYSIOLOGICAL,
VITAL & SYMPTOMATIC
DATA TRANSMITTED WIRELESSLY
EVERY 10 MINUTES



 BioSticker



 BioHub



BioCloud



 BioReport
(via .pdf viewer)

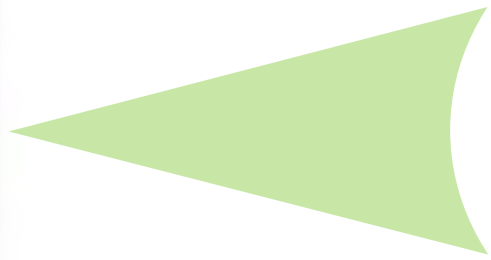
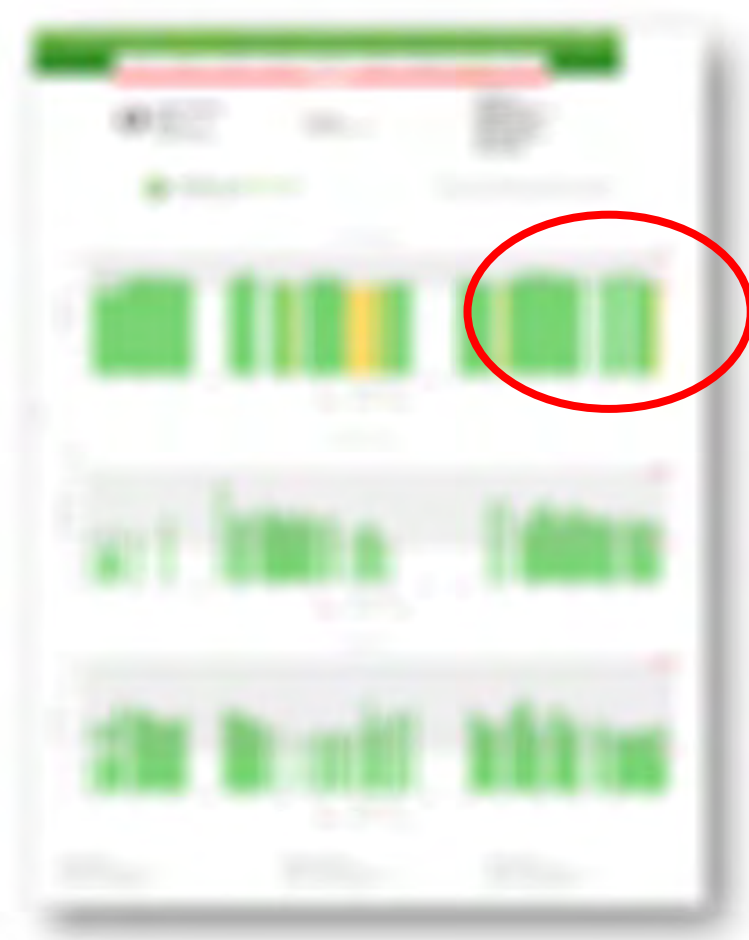
SCALABLE RULES LOGIC &
EXCEPTION-BASED VIRTUAL CARE

- BioCloud API's deliver data and insights into CareKinesis application
- Active Monitoring via Clinical Call Center

BioReport and BioCloud Trending Alerts

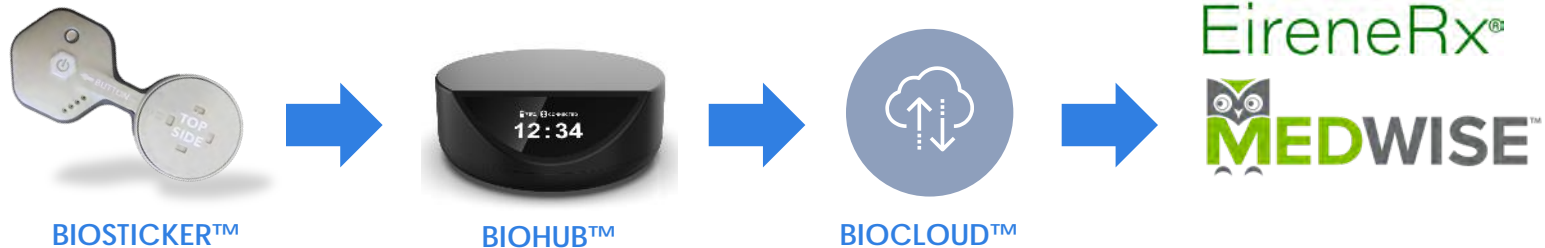






Combining Forces for a Scalable RPM Solution

- **MedWise BioInsights™**, a proprietary and proven clinical solution, for Remote Patient Monitoring (RPM)
- Seamless integration with **BioIntelliSense medical grade data services** (BioSticker, BioHub, BioCloud)
- Near-real-time receipt and evaluation of biometric data feeds to **monitor indications of side effects and adverse events** associated with medication therapies
- Clinically-actionable alerts to facilitate **timely interventions** and promote best patient outcomes
- **MedWise medication safety has been proven to reduce** ER visits, hospitalizations, lengths of stay, readmissions that are associated with serious medication side effects and adverse drug events



MedWise BioInsights™ Call Center Monitoring

- **At scale, seven clinical call centers** across the US, supporting RPM monitoring across all US time zones
- For PACE, RPM to be performed adjacent to the **PACE Pharmacy Clinical Call Center** in New Jersey
- Staffed with over **1,000** clinicians comprised of **Board-Certified Physicians, Pharmacists and Nurses**
- **Over 20 million outbound calls** made annually to support patient interventions and outcomes
- **Unique competitive advantage** through decades of remote clinical call center management experience
- Now, being deployed to **monitor patients at-risk of COVID-19 infection and those recovering from the virus**

LEVERAGING TECHNOLOGY TO IMPROVE HEALTHCARE

Led by Carlos F. Perez, MSN, RN-BC,
Executive Vice President



BioIntelliSense COVID19 RPM Use Cases

- At-home continuous vital-signs monitoring of patients who tested COVID positive in ER/Ambulatory Clinic but not admitted
- At-home continuous vital-signs monitoring of patients discharged from hospital after COVID in-patient treatment
- At-home and workplace continuous vital-signs monitoring of employees
- Continuous vital-signs monitoring of high-risk individuals





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Thank You

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CLIENT LIAISON TODAY!

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Questions?



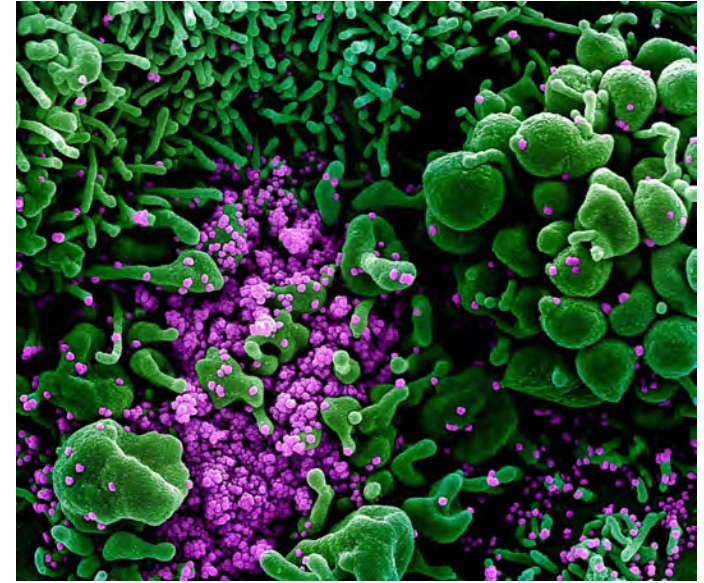
TRHC
University

Medication Safety Considerations with Hydroxychloroquine and Azithromycin in COVID-19

Katie Meyer, PharmD, CMWA, BCPS, BCGP
Pharmacist, Learning and Development

Objectives

- Describe the mechanism of action of hydroxychloroquine and azithromycin for the treatment of COVID-19
- Recognize key pharmacokinetic and pharmacodynamic concerns with hydroxychloroquine and azithromycin in patients with COVID-19
- Given a patient case, evaluate a regimen for pharmacokinetic and pharmacodynamic concerns in a patient undergoing treatment for COVID-19



Colorized scanning electron micrograph of an apoptotic cell (green) heavily infected with SARS-CoV-2 virus particles (purple), isolated from a patient sample. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. NIAID Source: nih.gov



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Patient case introduction

Patient case

- CV is a 78-year-old-female with a past medical history (PMH) of congestive heart failure (CHF), gastroesophageal reflux disease (GERD), major depressive disorder (MDD), hyperlipidemia, osteoarthritis, and seasonal allergies
- She was recently admitted to her local hospital and diagnosed with COVID-19
- After five days in the hospital, she was discharged on her inpatient COVID-19 regimen, hydroxychloroquine and azithromycin



Patient case (continued)

Subjective

- The patient states that she has been feeling better since her hospitalization; however, she complains of shortness of breath, fatigue, and a dry cough.

Objective

- Temperature 98.6°F
- BP 130/89 mmHg
- HR 89 bpm
- QTc 466 msec at discharge

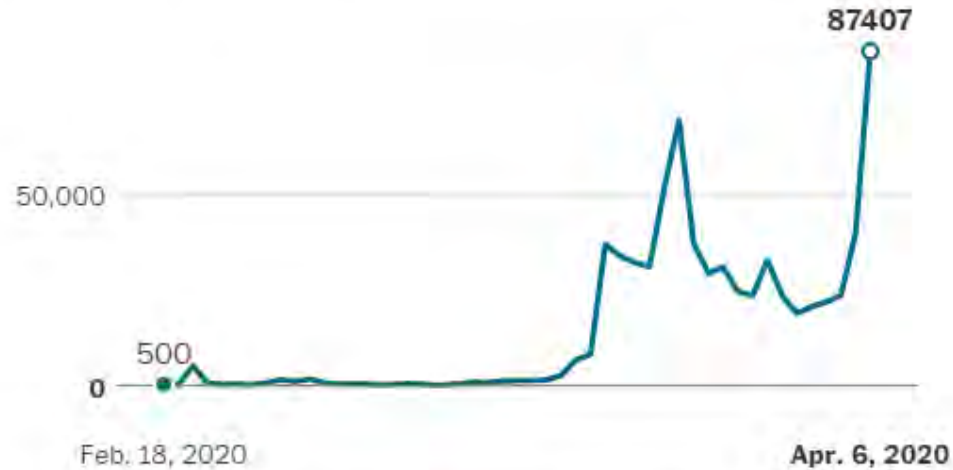
141	101	9	86
3.4	25	0.7	



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Hydroxychloroquine and azithromycin mechanism of action in COVID-19

Social media mentions of hydroxychloroquine



Claims about hydroxychloroquine and chloroquine as a treatment for covid-19 surged on social media in the second half of March and early April.

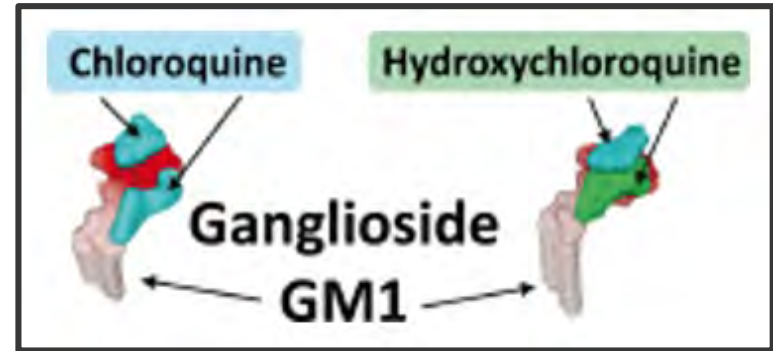
Source: Brandwatch, Crowdtangle

THE WASHINGTON POST

Hydroxychloroquine (CLQ-OH) and COVID-19

Mechanism of action

- Direct antiviral activity
- Immune modification
- Zinc ionophore



CLQ-OH and COVID-19 (continued)

Dosing (not FDA approved)

- 400mg PO BID x 2 doses, then 200mg PO BID on days two to five
- 200mg PO BID for 7-10 days
- 400mg PO BID for five days

*No current dosage adjustment recommended for renal/hepatic dysfunction

Adverse drug reactions (short term)

- Gastrointestinal disturbances
- **ECG abnormalities, prolonged QTc**
- Hypoglycemia
- Extrapyrimal reactions



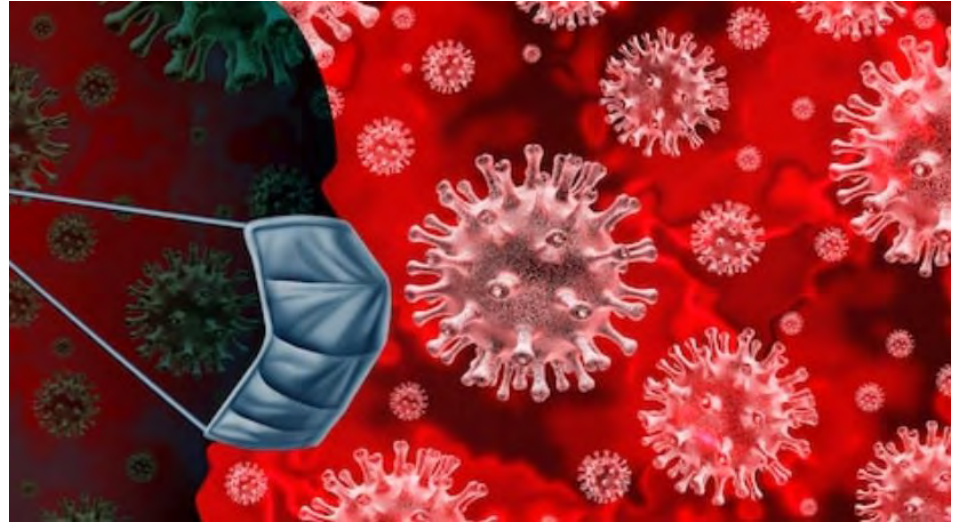
<https://www.livescience.com/coronavirus-chloroquine-study-stopped-early.html>

<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/>

Azithromycin and COVID-19

Mechanism of action

- Active against Zika and Ebola in vitro
- Immunomodulatory properties



Azithromycin and COVID-19 (continued)

Dosing (not FDA approved)

- 500mg IV/PO on day one, followed by 250mg IV/PO daily for four days
- 500mg PO daily for seven days

*No current dosage adjustment recommended for renal/hepatic dysfunction

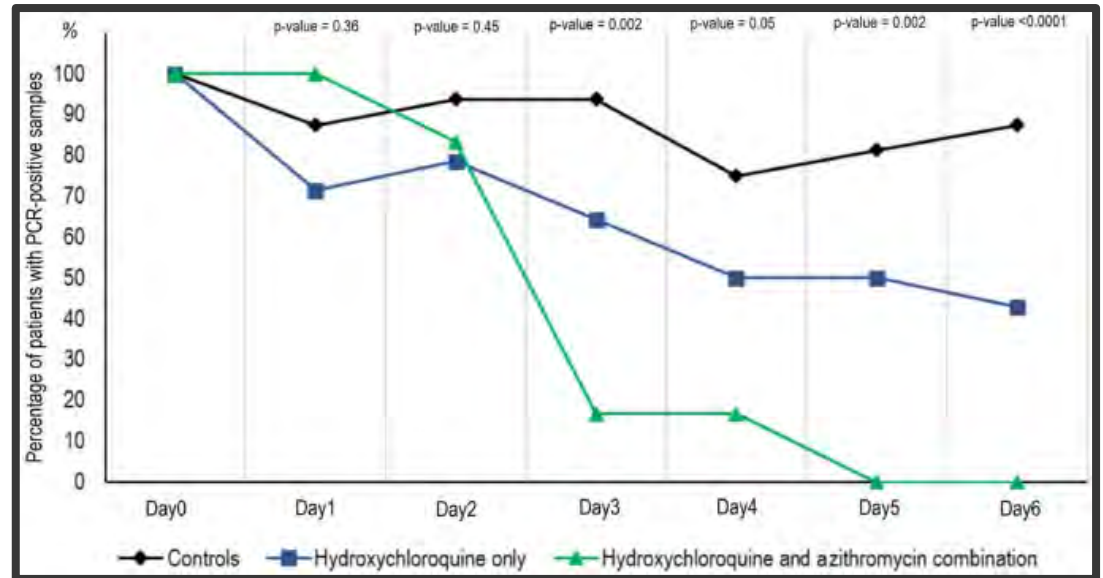
Adverse drug reactions (short term)

- Gastrointestinal disturbances
- **ECG abnormalities, prolonged QTc**
- *Clostridium difficile* associated diarrhea

Hydroxychloroquine and azithromycin

Open-label, non-randomized clinical trial

- 36 hospitalized patients
- Viral suppression at six days
- Methodological problems with this study





Pharmacokinetic (PK) and pharmacodynamic (PD) concerns with hydroxychloroquine and azithromycin in COVID-19

PD concerns

Hydroxychloroquine

- Increased risk of hypoglycemia when given in conjunction with anti-diabetic medications
- Increased risk for hemolytic reactions when given in combination with dapsone
- Increased risk of QT prolongation and Torsade de Pointes (TdP)

Azithromycin

- Increased risk of QT prolongation

Plaquenil (Hydroxychloroquine) Package Insert. Last Revised 2017. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/009768s037s045s047lbl.pdf
Zithromax (Azithromycin) Package Insert. Last Revised 2019. <http://labeling.pfizer.com/ShowLabeling.aspx?id=511>
<https://www.medpagetoday.com/infectiousdisease/covid19/85552>

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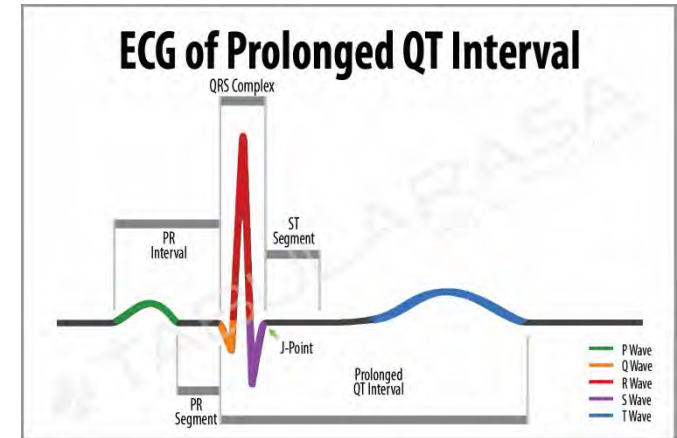
CLQ-OH, azithromycin, and Long QT Syndrome (LQTS)

CLQ-OH: has been implicated in increasing the QT interval leading to fatal TdP

- Risk of TdP may be increased with additional risk factors present, or in patients taking multiple QT prolonging medications

Azithromycin: has been implicated in increasing the QT interval

- Evidence is currently conflicting regarding the risk of fatal TdP



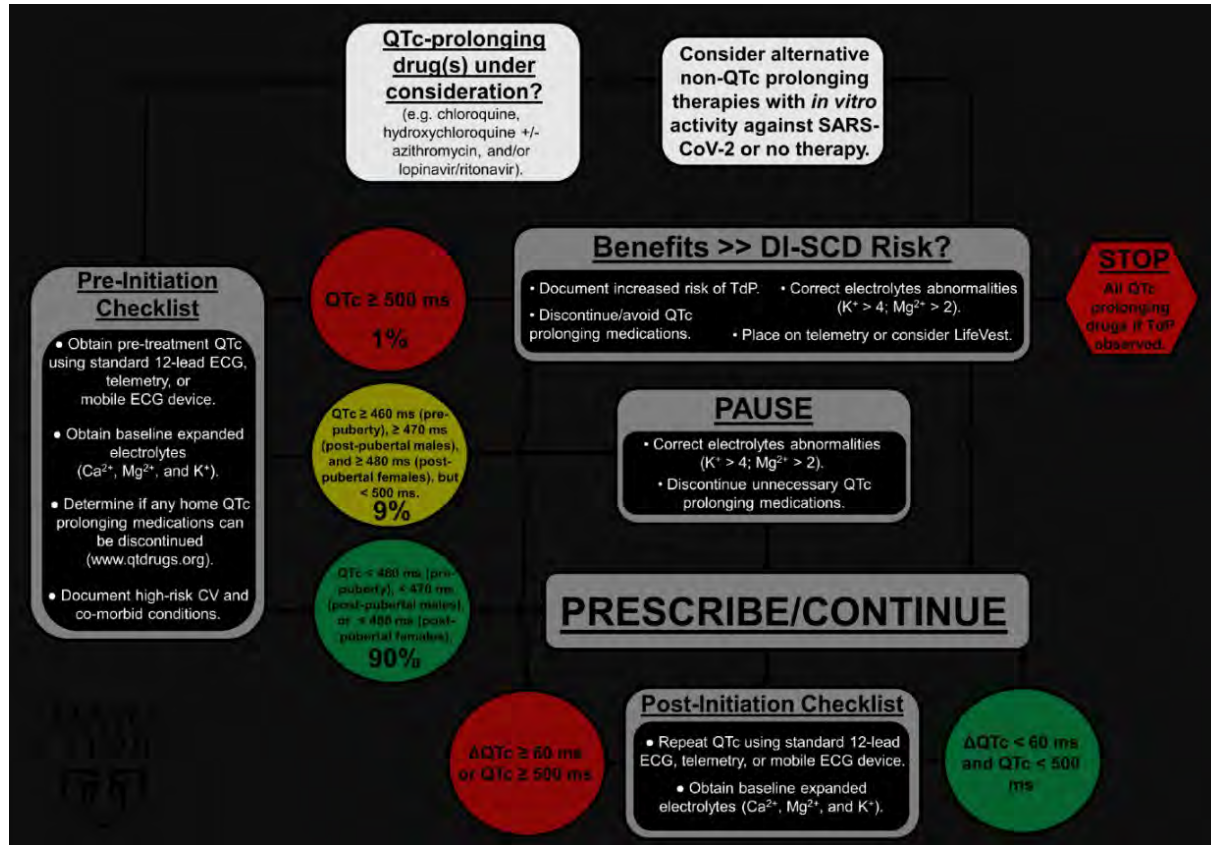
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Ohara H et al. *Cardiovasc Toxicol*. 2015;15(3):232-40.

CLQ-OH, azithromycin, and LQTS



Pharmacokinetic concerns

Hydroxychloroquine

- Absorption decreased by antacids
- CYP450 metabolism

The image shows a Medication Risk Mitigation Matrix for Hydroxychloroquine. The matrix is a table with columns for various CYP450 enzymes and rows for different medications. The enzymes listed are CYP2D6, CYP2C19, CYP2C8, CYP2C9, CYP2C18, CYP2C19, CYP2C19, CYP2C19, and CYP2C19. The medications listed are Hydroxychloroquine, Naproxen, Metoprolol, and Simvastatin. The matrix shows the percentage of inhibition for each combination. For example, Hydroxychloroquine inhibits CYP2D6 (10%), CYP2C8 (10%), and CYP2C9 (10%). Naproxen inhibits CYP2C9 (10%) and CYP2C19 (10%). Metoprolol inhibits CYP2C19 (10%) and CYP2C19 (10%). Simvastatin inhibits CYP2C19 (10%).

Medication (NDC #)	CYP2D6	CYP2C19	CYP2C8	CYP2C9	CYP2C18	CYP2C19	CYP2C19	CYP2C19	CYP2C19	Notes
Hydroxychloroquine	10	0	0	0	10	0	10	10	0	
Naproxen	0	0	0	0	10	10	0	0	0	⚠️
Metoprolol	0	0	0	0	0	0	10	10	0	⚠️
Simvastatin	0	0	0	0	0	0	0	10	0	



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Patient case evaluation

Patient case - medication list

Aspirin 81mg PO daily
Atorvastatin 40mg PO daily
Escitalopram 10mg PO daily
Furosemide 40mg PO daily
Ibuprofen 600mg PO q6h as needed
Loratadine 10mg PO daily
Losartan 50mg PO daily
Metoprolol tartrate 25mg PO BID
Montelukast 10mg PO daily
Omeprazole 40mg PO daily



COVID-19 Regimen

Hydroxychloroquine 200mg PO BID
x ten days
Azithromycin 500mg PO daily x
seven days

Patient case - safety evaluation



Patient case - LQTS evaluation

Patient risk factors

- Age
- Female gender
- Hypokalemia

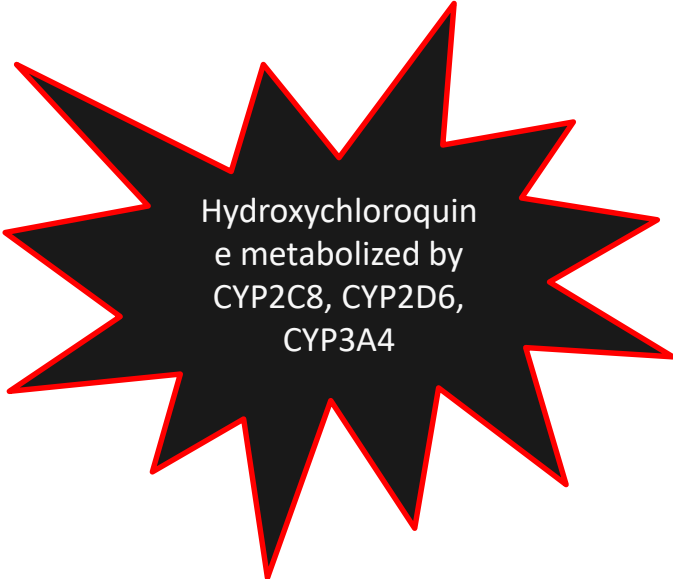
Medication risk factors

- Azithromycin, escitalopram, furosemide, hydroxychloroquine, and omeprazole contributing to risk for LQTS



Patient case - PK interactions

- Simultaneous, multi-drug analysis



Hydroxychloroquin
e metabolized by
CYP2C8, CYP2D6,
CYP3A4



The image shows a blurred screenshot of a clinical data table. The table has multiple columns and rows. Two rows are highlighted with red boxes, and several other cells are highlighted in yellow. The text is illegible due to blurring.

Patient case - recommendations

- Potassium supplementation
- Change omeprazole to pantoprazole or histamine 2 receptor antagonist (H2RA)
- Discontinue ibuprofen or change to alternative
- Monitor ECG, magnesium, potassium

References

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Questions?



Thank You!

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