

# Effectiveness of a Treatment Team on Adherence to Health System Guidelines for Hydroxychloroquine Use During Two Phases of the COVID-19 (SARS-CoV-2) Pandemic

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## Background

- During the early phase of COVID-19 pandemic, optimal therapeutic approach was unclear
- Some experimental COVID-19 therapeutics were FDA approved for other indications
  - These were on existing hospital formularies
- The UPMC hospital system organized a multi-disciplinary treatment team of physicians and pharmacists to:
  - Review** literature on COVID-19 therapeutics
  - Create** guidelines for use of agents across 24 hospitals
  - Restrict and monitor** agents not recommended of treatment of COVID-19
- Prior to April 13, 2020, no randomized controlled trials (RCTs) were enrolling for hydroxychloroquine (HCQ) in the UPMC system
  - HCQ was not restricted in treatment of COVID-19 during this period (**Phase 1**)
  - HCQ use was up to provider discretion but limited to inpatients for 5 days without combination therapy
    - Concomitant azithromycin was not
- Once RCTs started enrolling for our hospital sites April 13, 2020 (**Phase 2**), HCQ was restricted to patients either:
  - Enrolled in RCTs (for HCQ) or
  - Ineligible for RCT due to vulnerable status (e.g. incarcerated)
- In order to monitor the safety and efficacy of these policies, a quality improvement project was approved to ensure the guidelines were being followed across the hospital system

## Methods

**Design:** Retrospective chart review

**Setting:** 24 UPMC system hospitals

**Aims:**

- Monitor effectiveness of treatment team during both phases of treatment guidelines to ensure compliance with guidelines
- Evaluate treatment outcomes of patients admitted with COVID-19

## Methods

**System approach:**

- Prospective review of all patients on HCQ across 24 hospitals
- Daily evaluation for appropriateness, dosing, drug-drug interactions, indication, duration based on treatment guidelines (Phase 1)
- Daily evaluation for appropriateness based on enrollment in RCT or ineligibility (Phase 2)
- Feedback to local pharmacists to stop non-recommended HCQ therapy
- Phase 1** Admitted before April 13, 2020
- Phase 2:** Admitted on or after April 13, 2020

**Inclusion:** Admission to a UPMC hospital with symptomatic COVID-19

**Exclusion:** Emergency room visit only, asymptomatic SARS-CoV-2 infection, no definitive outcome

**Primary Outcome:** Adherence rate to system guidelines for use of HCQ for Phase 1 and Phase 2

**Secondary Outcomes:**

- Rate of HCQ use in Phase 1 and Phase 2
- Rate of morbidity and mortality
- Rate of bacterial superinfection

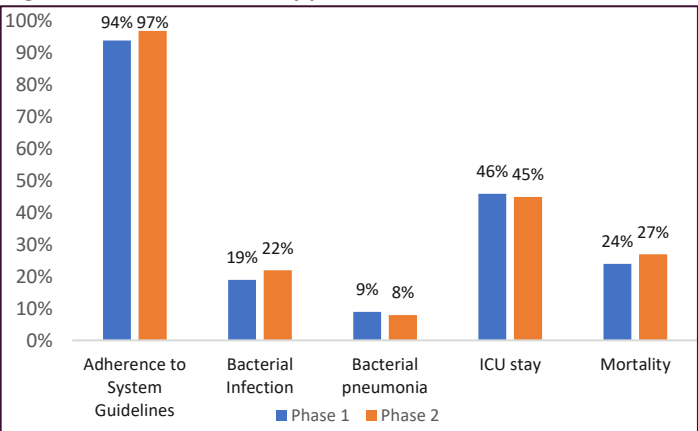
## Results

Table 1. Patient characteristics by phase

	Phase 1, n=127		Phase 2, n=134		p value
Age, median (IQR)	68	(56-78)	67	(57-77)	0.89
Male, n %	72	57	60	45	0.06
BMI, median (IQR)	29	(25-36)	29	(25-34)	0.80
Diabetes mellitus, n %	37	29	46	35	0.36
Hypertension, n %	86	37	93	69	0.79
Coronary artery disease, n %	31	24	23	17	0.17
Heart failure, n %	17	13	13	10	0.44
Chronic obstructive pulmonary disease, n %	15	12	26	19	0.13
Asthma, n %	11	9	15	11	0.54
Chronic kidney disease, n %	18	14	19	14	1.00
End stage renal disease, n %	2	2	7	5	0.17
Cirrhosis, n %	2	2	2	1	1.00
Active malignancy, n %	4	3	9	7	0.26
Immune suppression, n %	17	14	17	13	0.86

## Results

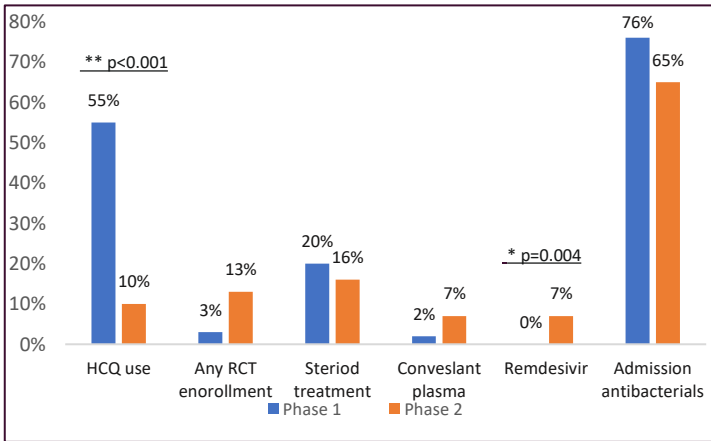
Figure 1. Patient outcomes by phase



### Types of non-adherence to guidelines

- Phase 1:**
  - Azithromycin/HCQ combination therapy (67%)
  - Incorrect dose/setting for HCQ (33%)
- Phase 2:**
  - HCQ receipt outside of RCT (67%)
  - Azithromycin/HCQ combination therapy (33%)
  - Other non-recommended therapies (33%)

Figure 2. Treatments by phase



## Risk Factors for Mortality

- Hospital mortality in this study was 25%
- Receipt of HCQ, adherence to system guidelines, and phase of epidemic were not associated with increased risk of death univariate analysis
- Multivariate logistic regression analysis identified four independent risk factors death (Table 2).

Table 2. Independent risk factors for mortality

	Odds Ratio	95% CI	p-value
ICU stay	6.3	3.1-13.1	0.0001
Heart Failure	4.6	1.9-11.5	0.001
Abnormal CXR	4.0	1.5-10.9	0.006
Age (per year)	1.1	1.03-1.09	0.0001

## Discussion

- In a large healthcare system, a multi-disciplinary treatment team created treatment guideline during a rapidly-evolving landscape of new data, experimental therapeutics, and availability of RCT enrollment
- System physicians and pharmacists worked with local hospitals to help optimize adherence to guidelines
- Adherence to treatment guidelines was high during both phases studied
  - Mortality and superinfection did not differ significantly during the two phases studied
  - Mortality risk factors identified were related to patient status, rather than treatment effects
- Analysis of inter-hospital variability, regional variability, and racial/socioeconomic variability in outcomes are ongoing
- Implementation of rapid changes to practice in the setting of pandemic, with unproven medications, can be managed successfully over a diverse group of hospitals in a large system

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