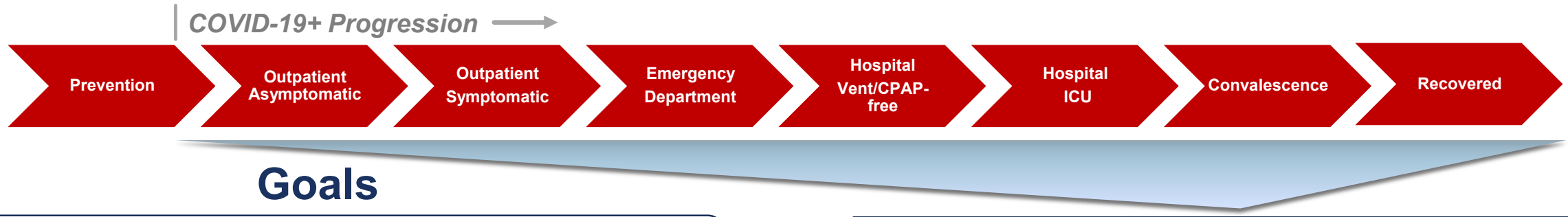
NHLBI COVID-19 Clinical Research Framework



Goals

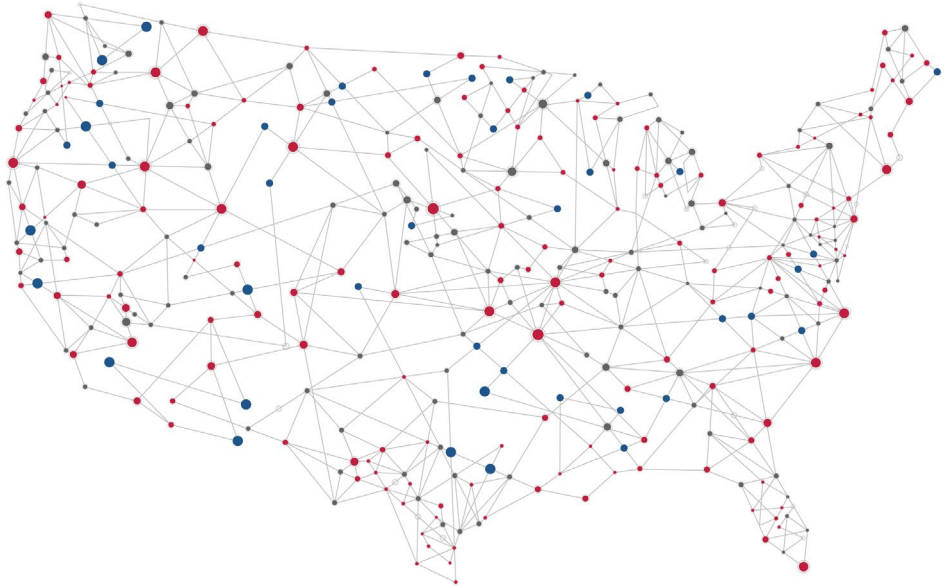
Reduce case severity/fatality, speed recovery	→ Host-Directed Therapeutics Clinical Trials
Understand short- and long-term trajectory	→ Cohort of Cohorts for Long-Term Follow up
Enable risk stratification, precision interventions	→ Screening, Referral and Registries
Identify biomarkers and therapeutic targets	
Target populations most severely affected	→ Community-Engaged Research Consortium

CONNECTS

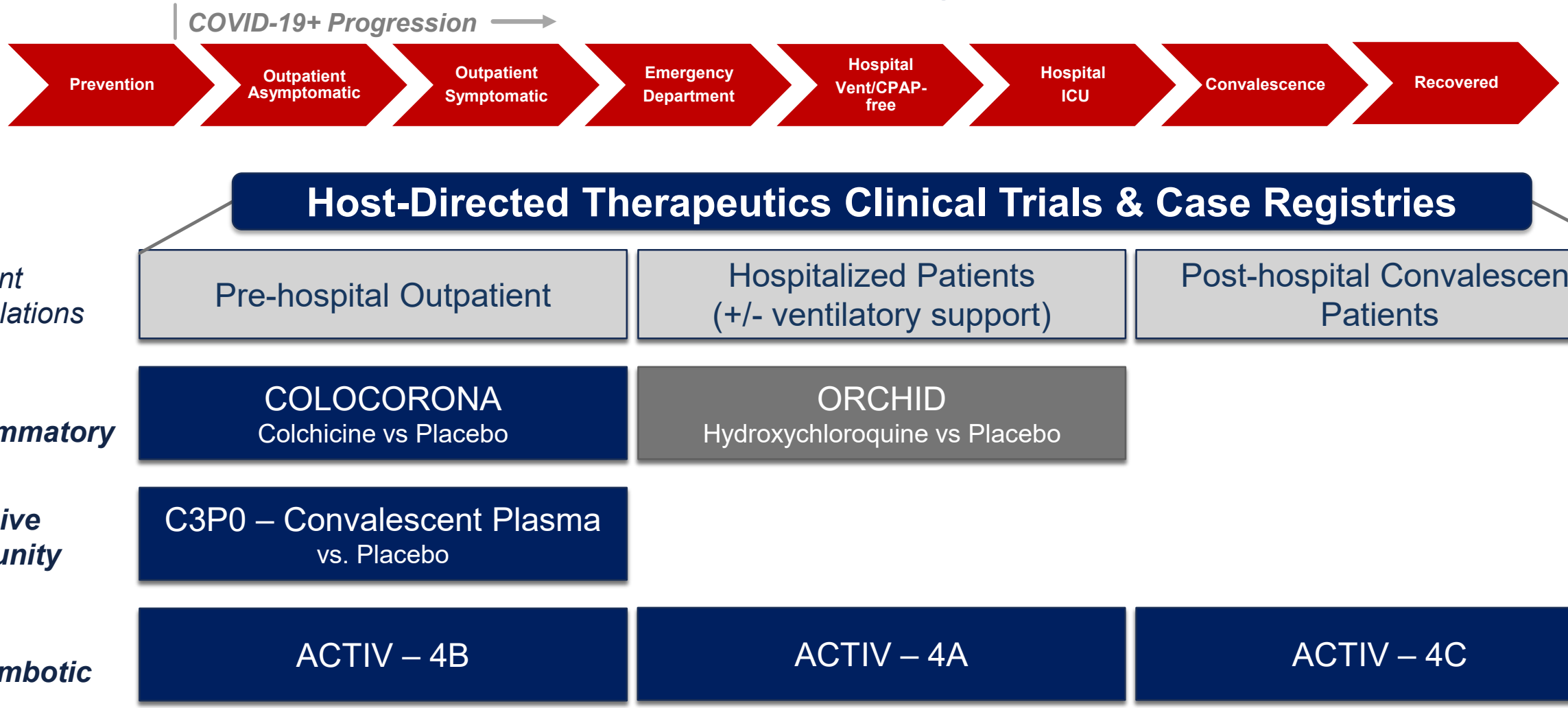
"Collaborating Network of Networks for Evaluating COVID-19 and Therapeutic Strategies"

Goal: Leverage and expand NHLBI's national clinical research networks to rapidly and nimbly respond to emerging research and clinical needs for COVID-19

- **Leveraging existing assets**, data and studies
- Comprehensive, **expandable platform** linking trial network, registries and cohorts
- Facilitating case finding, **clinical trial accrual**, **longitudinal studies, and community engagement**



CONNECTS Clinical Trial and Registries Platform: Driving Toward COVID-19 Host-directed Interventions Before, During, and After Hospitalization

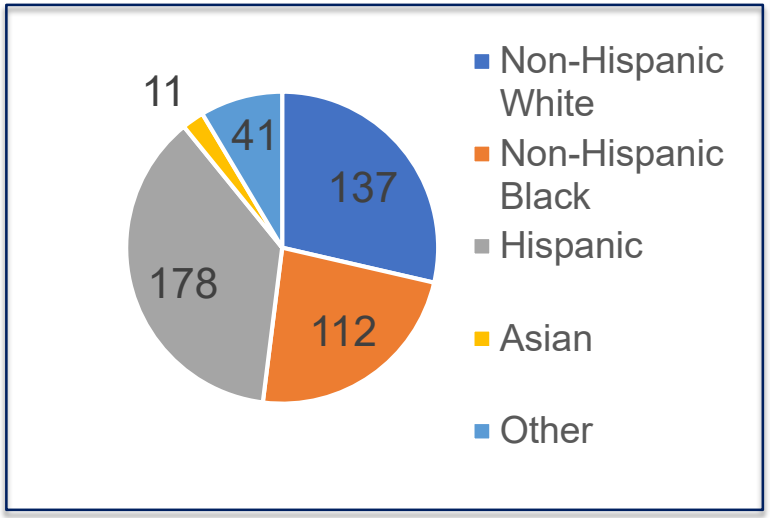


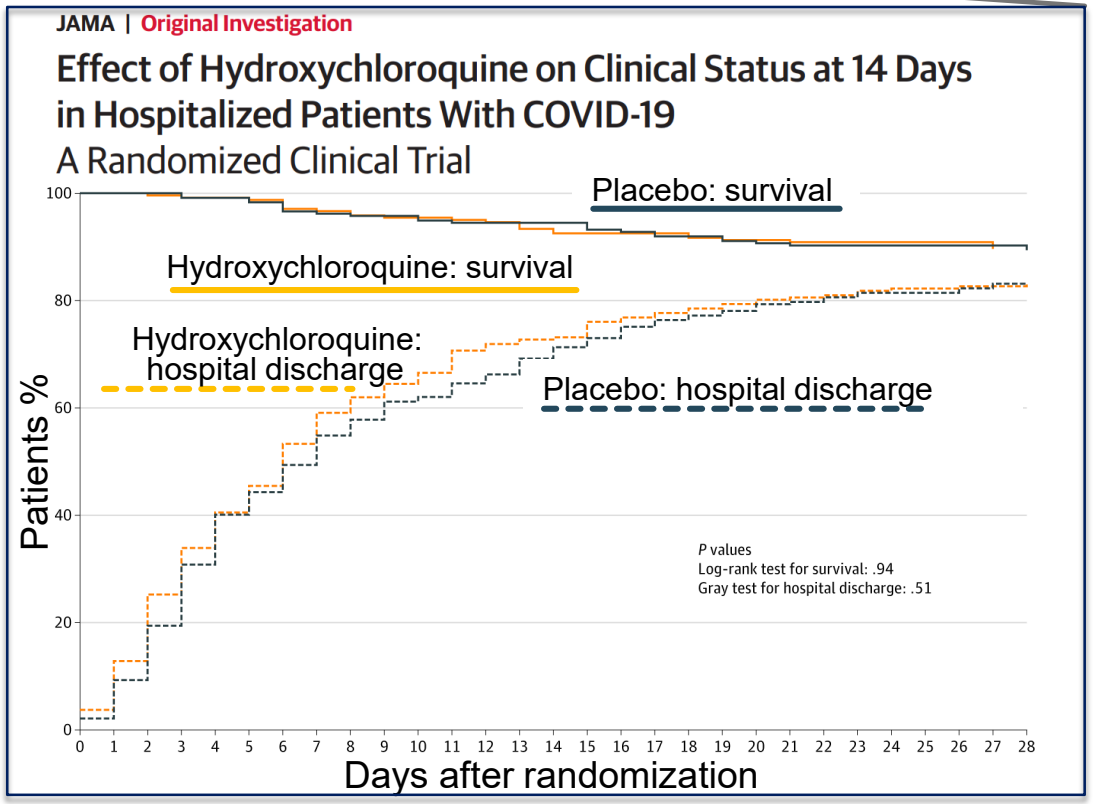
Outcomes Related To COVID-19 Treated With Hydroxychloroquine Among In-patients With Symptomatic Disease (ORCHID) Trial

Prevention → Outpatient Asymptomatic → Outpatient Symptomatic → Emergency Department → **Hospital Vent/CPAP-free** → Hospital ICU → Convalescence → Recovered

Hospitalized Patients
(+/- ventilatory support)

Patient Demographics





Addressed early question about Hydroxychloroquine effectiveness.
Study was stopped on June 19 because there was no benefit or harm.

PETAL NETWORK
Prevention & Early Treatment of Acute Lung Injury

The Clinical Trial of COVID-19 Convalescent Plasma of Outpatients (C3PO)

COVID-19+ Progression →

Prevention | Outpatient Asymptomatic | Outpatient Symptomatic | Emergency Department | Hospital Vent/CPAP-free | Hospital ICU | Convalescence | Recovered

Patient Populations

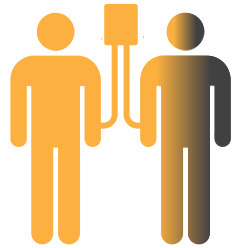
Passive Immunity

Pre-hospital Outpatient

C3P0: Convalescent Plasma vs. Placebo

- **Population**: Adults presenting to the ED:
  - Mild, symptomatic, lab confirmed COVID-19
  - High risk for progression to severe/critical illness
  - Clinically stable for outpatient management at randomization
- **Planned Enrollment**: 600 in total (300 per arm)
- **Intervention**: A single dose of convalescent plasma (CP) or saline placebo

CONNECTS



SIREN

C3PO
Clinical Trial of COVID-19 Convalescent Plasma in Outpatients

Evaluating the use of **convalescent plasma** to treat non-hospitalized patients with mild COVID-19.

Accelerating COVID-19 Therapeutic Interventions and Vaccines 4 (ACTIV-4)

Host-Directed Therapeutics Clinical Trials

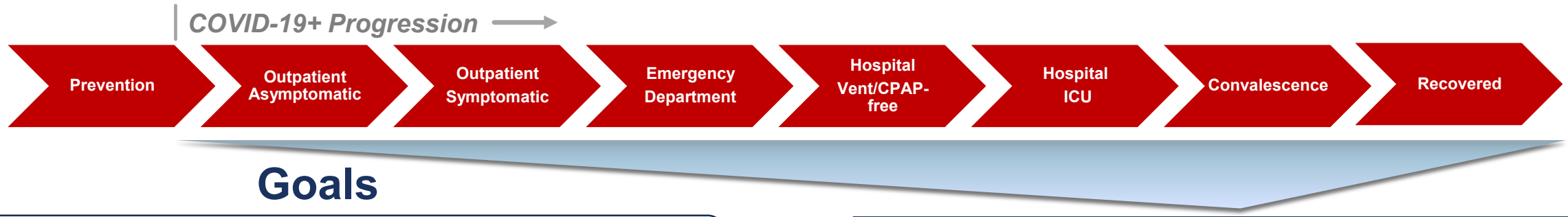
	Pre-hospital Outpatient	Hospitalized Patients (+/- ventilatory support)	Post-hospital Convalescent Patients
Patient Populations			
Anti-Thrombotic	ACTIV – 4B	ACTIV – 4A	ACTIV – 4C
	• **Anticoagulation (apixaban)**: prophylactic *or* therapeutic dose • **Antiplatelet agent**: low dose aspirin • **Placebo**	• **Prophylactic dose** of heparin • **Therapeutic dose** heparin	• **Prophylactic dose** anticoagulant (apixaban) • **Therapeutic dose** anticoagulant (apixaban)

Evaluating effectiveness of antithrombotic drugs to reduce life-threatening blood clots.

CONNECTS

ACTIV-4

NHLBI COVID-19 Clinical Research Framework



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ACTIV-4

CONNECTS

C3PO
Clinical Trial of COVID-19 Convalescent Plasma in Outpatients

ORCHID Trial