COVID-19 Clinical Trials

The Intermountain Healthcare Experience

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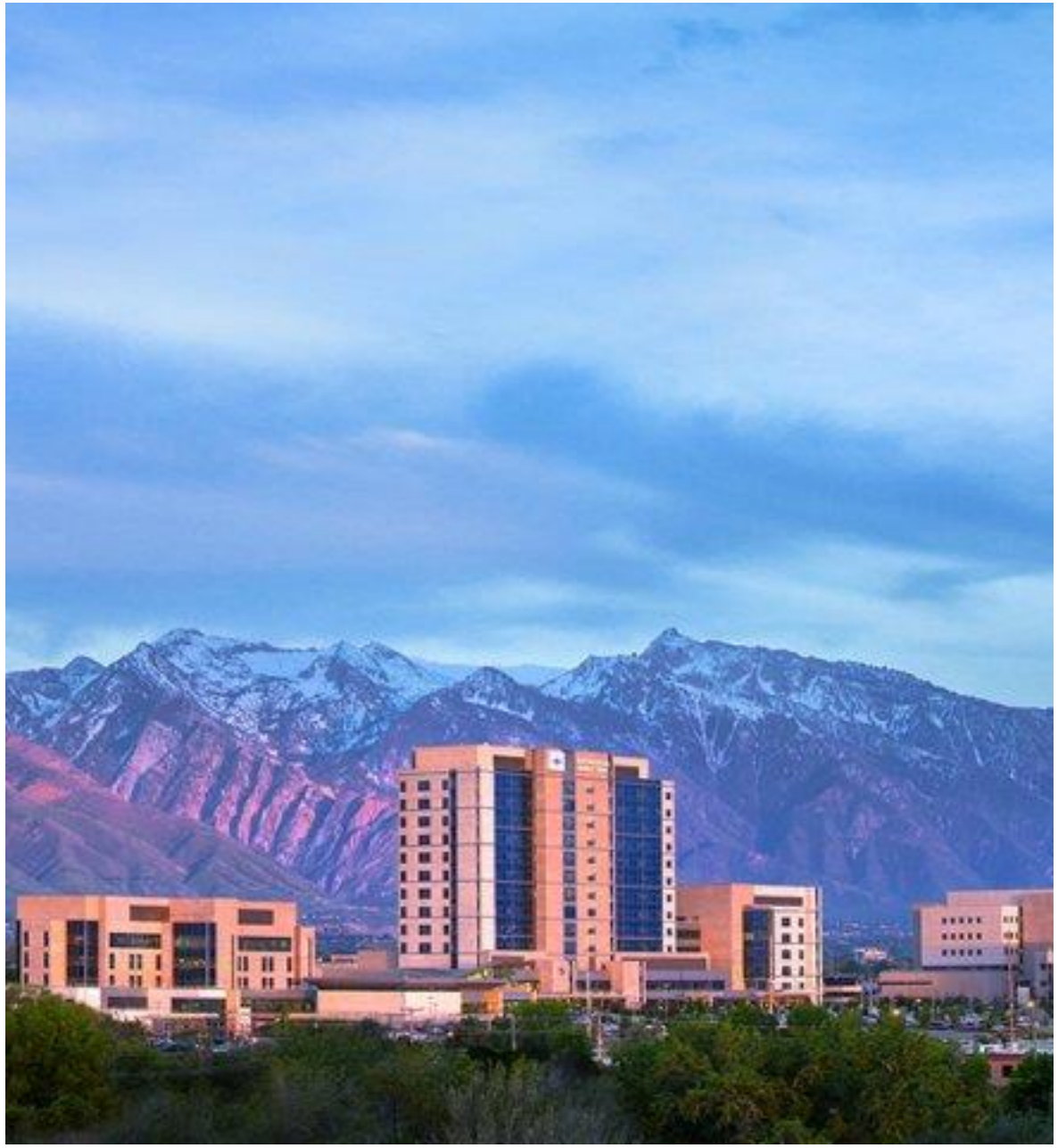
Intermountain Healthcare
Healing for life®



Conflicts

No relevant commercial conflicts (other than trial enrollments for which Intermountain was compensated)

Multiple related government/academic steering/review committees and DSMBs

Multiple unrelated commercial conflicts—DSMBs, steering committees for critical care trials and investigator-initiated research in influenza

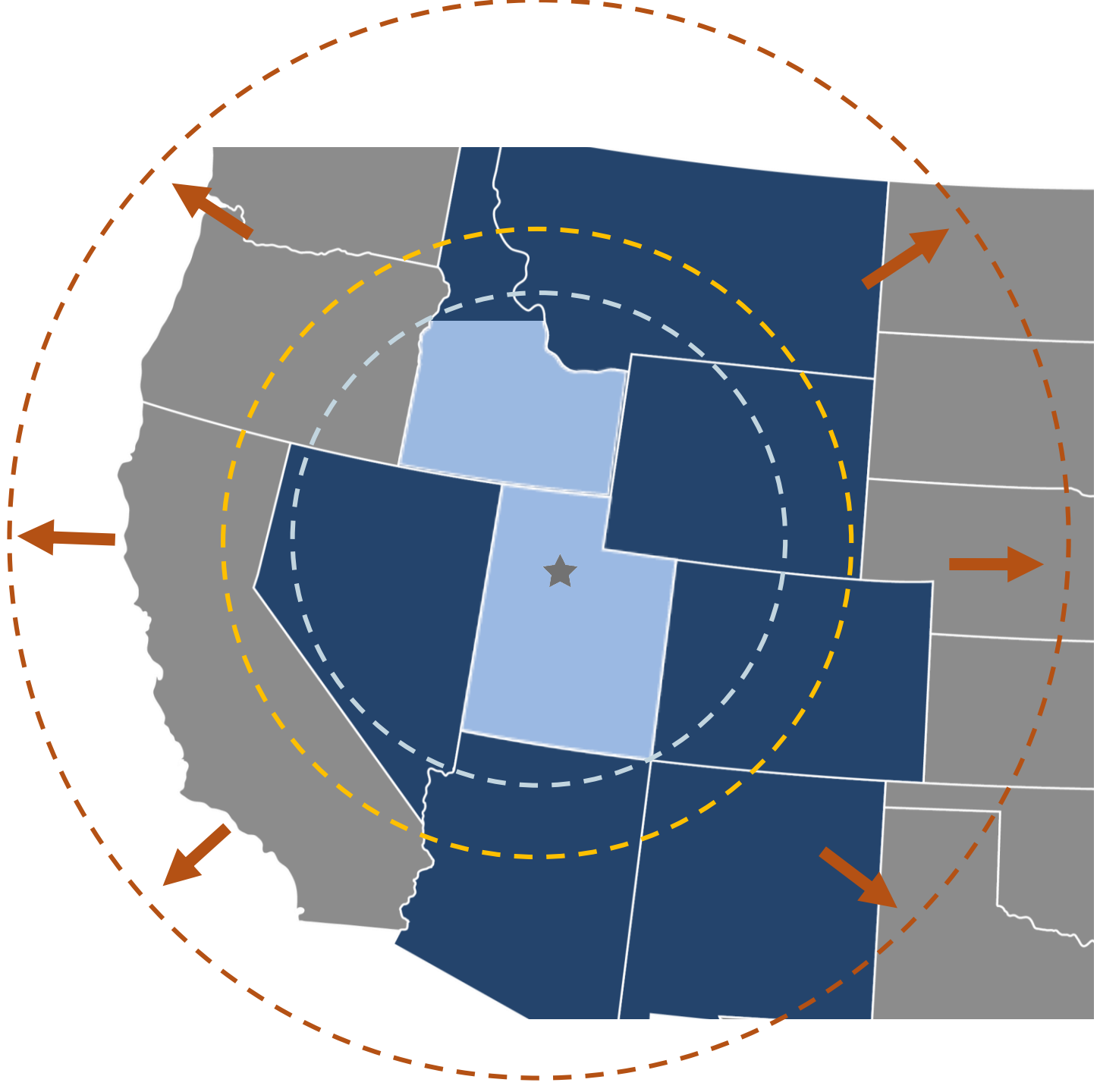
Intermountain's origins

- Non-profit, community-based healthcare system that maintains an academic referral center among multiple other hospital profiles
- Early intimate relationship with the University of Utah
- Founded 1975 when the Church of Jesus Christ of Latter-day Saints donated its hospitals to the communities of the Intermountain West

IHC
INTERMOUNTAIN HEALTH CARE

Intermountain Healthcare
Healing for life®

Intermountain® Healthcare



Intermountain Scope & Stewardship

210 Physician Clinics

TeleHealth in **6** States
~990,000 Interactions

24 Hospitals
(including 1 Virtual Hospital)

41,700
Employees

900,100
SelectHealth Members

$227M Charity Care in 2019

>2M Patient Engagements/Yr.

2,800 Employed Physicians and APPs

~2,800
Lifeflight Patients/Yr.

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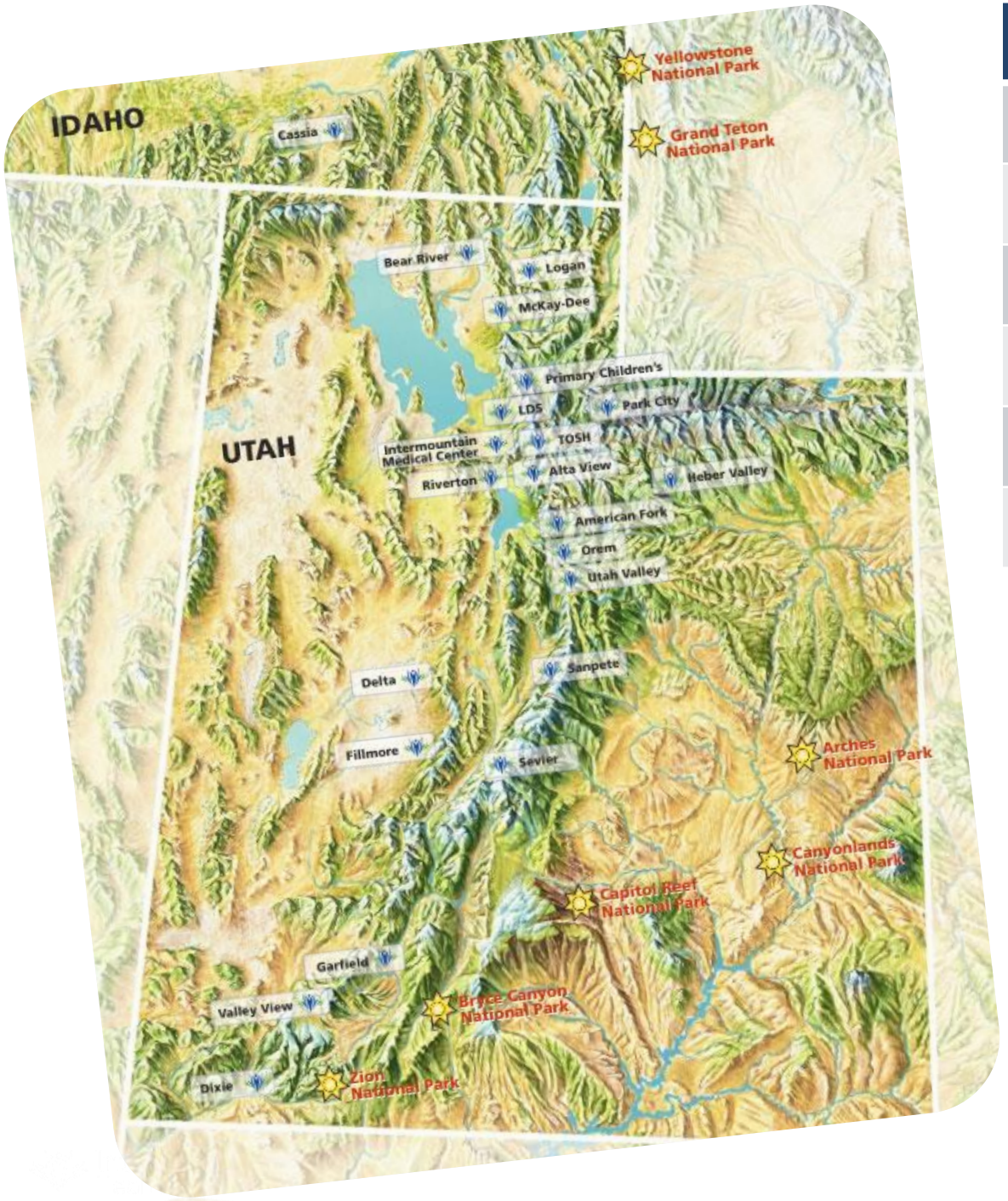


Facility	Beds
Dixie	245
IMC	**510**
LDS Hospital	**250**
McKay Dee	321
Children's	340
Utah Valley	395

Facility	Beds
Cassia	25
Cedar City	48
Layton	43
Orem	24
Park City	37
Sevier	29
TOSH	40

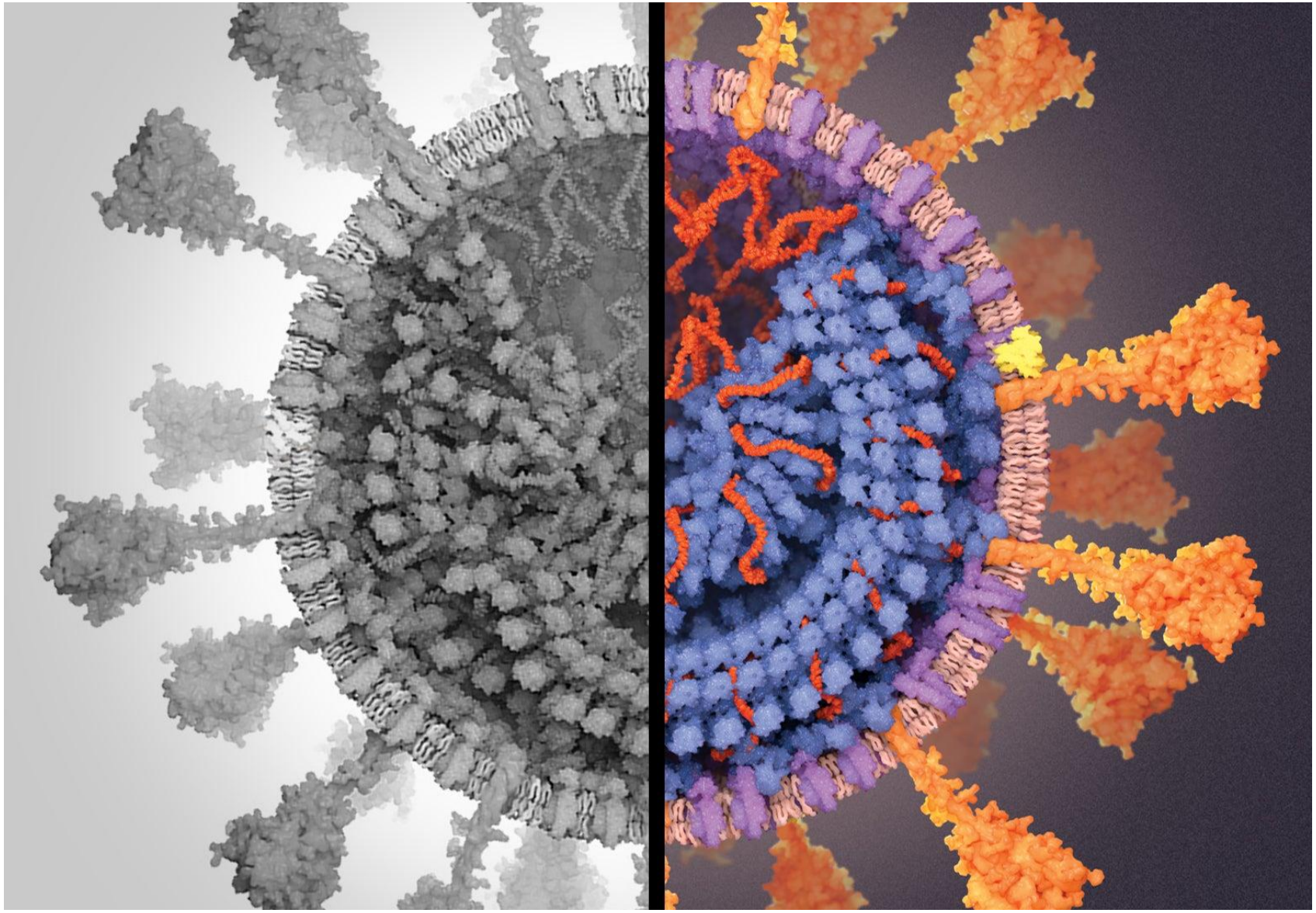
Facility	Beds
Bear River	16
Delta	18
Fillmore	19
Garfield	15
Heber	19
Sanpete	18

Facility	Beds
Alta View	71
American Fork	89
Logan	146
Riverton	97

Intermountain Research, before the pandemic

- Pioneers in Medical Informatics
- Early ARDS trials: ECCO$_2$R RCT; founding member of ARDS Network, then PETAL
- PCORnet site; CTSA partnership with Utah and Stanford
- General focus on QI, big data, population genomics, trial enrollments, structural heart disease devices
- A handful of R01s/equivalents, K awards, and CDC contracts
- A dozen active investigators in PCCM, and a handful in each of ID, thrombosis, cardiology, oncology, MFM, health services, and transplant

Then came the awful virus



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COVID Research Dashboard (Year 1)

20 Hospitals with any trial

3 Hospitals with traditional trials

15 Randomized clinical trials

>1600 Patients enrolled

4 Regulatory liaisons

6 Research managers

15 Research Coordinators

3 Home Health Nurses

11 AMS and **2** IDS pharmacists

8 COVID trial PIs

15 COVID coinvestigators

50 TeleHealth Access points for research staff

Intermountain® Healthcare

Enrollments in first pandemic year

Trial	Status	Sponsor	Intermountain enrollment	Enrolling hospitals
HAHPS	Published; in IPMA	Intermountain	75	12
HyAzOUT	In IPMA	Intermountain	177	central
ORCHID	Published	NHLBI	21	2
CCP EAP	Published	Mayo Clinic	550	12
REGN2040	Manuscript in preparation	Industry	18	2
Ibrutinib	incomplete	Industry	20	1
COVACTA	Published	Industry	30	1
REMDACTA	Manuscript in preparation	Industry	30	2
REGN2066	Completed	Industry	43	2
ACTIV3	3 trials completed; 1 published	ACTIV	49	2
PASSITON	Recruiting	NCATS	17	1
ACTIV4b	Recruiting	ACTIV	136	central
RDVOUT	Completed	Industry	27	central
APICS-COVID	Recruiting	DoD	8	2
RED CORAL	Completed	NHLBI	70	3
BLUE CORAL	Recruiting	NHLBI	54	3
BCIR	Completed	NIAID	10	2
IVY epidemiology	Published	CDC	41	2
IVY HCW serology	Published	CDC	250	2
IVY2 VE	Recruiting	CDC	40	2
IVY Echo	Analysis	CDC	25	1

Intermountain® Healthcare

Integrate research to serve multiple needs simultaneously

- Clinical
- Operational
- Public health

Overcommunicate

- Communicate up channels, repeatedly
- Communicate laterally, repeatedly
- Communicate outward, repeatedly

Organizing an Entire System for a Public Health Emergency

Incident Command

Research Enterprise

Clinical Operations

COVID Trial Executive Committee

COVID-19 Therapeutics Committee

Cardiovascular	Investigational Drug Pharmacy
Maternal Fetal Medicine	Bioinformatics
Acute Care / Transplant	Regulatory Staff
Oncology	IRB

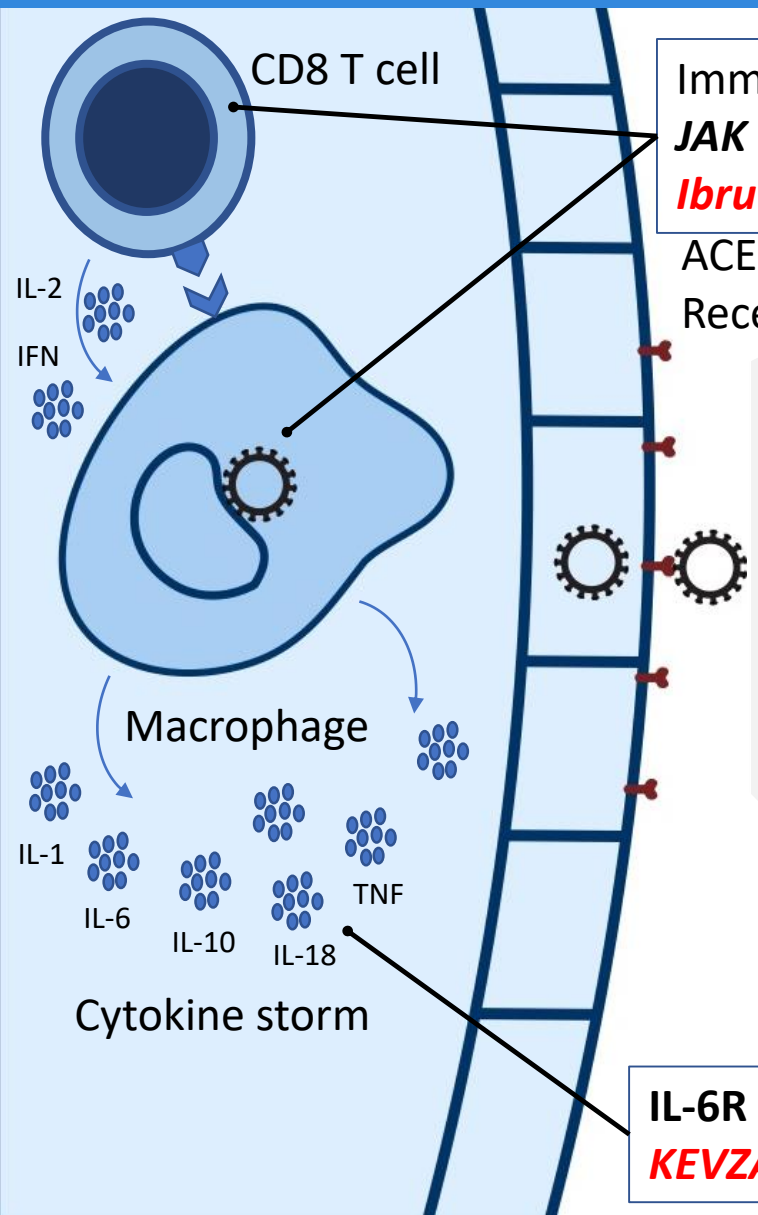
Infectious Diseases	Pharmacy	Hematology
Critical Care	Research	Rheumatology
Hospitalists	Transfusion	Trauma Surgery

Inter-divisional collaborations

COVID-19 Rounds

Immunologic Therapies

Virologic Therapies

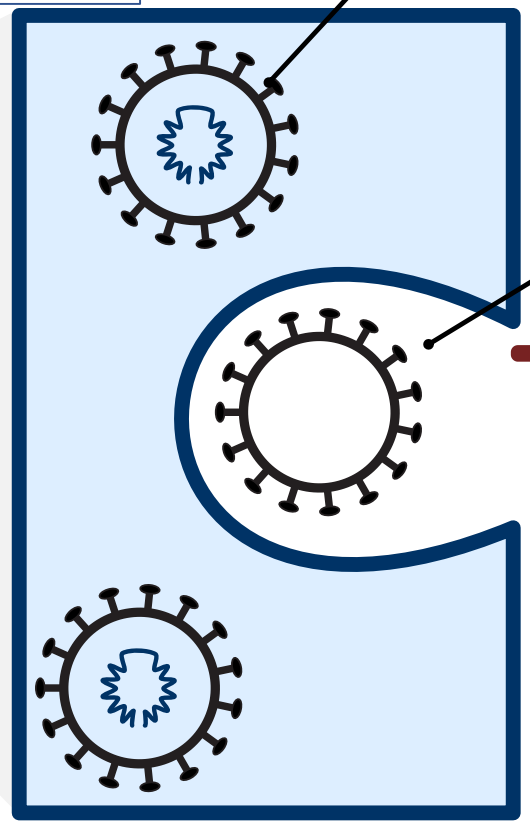


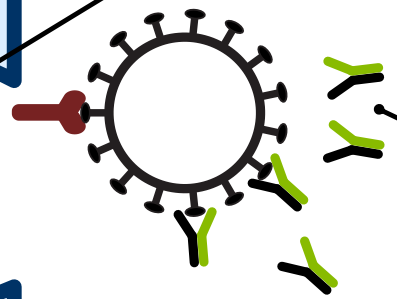
Immune signaling
JAK and BTK Target
Ibrutinib Trial

ACE2
Receptor

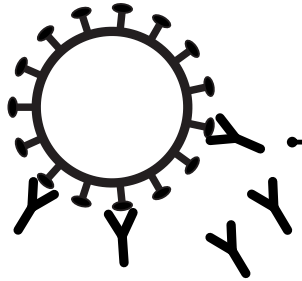
RNA Replication
Remdesivir
REMDACTA

Hydroxychloroquine
changes the pH of the endosome, impairs cell entry
HAHPS, HyAzOUT





Monoclonal Antibodies
Bind glycoprotein spike and neutralize the virus
REGN2066, ACTIV3



Natural Antibodies
Convalescent Plasma
Hyperimmune IgG
FDA-Mayo Study

IL-6R antagonists: Selective cytokine blockade
KEVZARA, COVACTA, REMDACTA

Inpatient COVID-19 Treatment Guidelines

3/2/2020 updates red and/or bolded

General Principles

- **Encourage enrollment in clinical trials:** Trials are critical for defining best practice, protecting patient safety, and are an important pathway for access to investigational therapies (click here for more info).
- Clinicians and patients/families should discuss current evidence, weigh risks and benefits, and employ appropriate safety monitoring with any COVID-19 treatments. **See Appendix for more information.**
- Treatment for bacterial pneumonia and other comorbidities remains per clinician judgment.

Intensive Care Management of COVID-19

Ithan Peltan, MD, MSc and Eliotte Hirshberg, MD, Intermountain Healthcare

Updated January 4, 2021 (version 9.1)

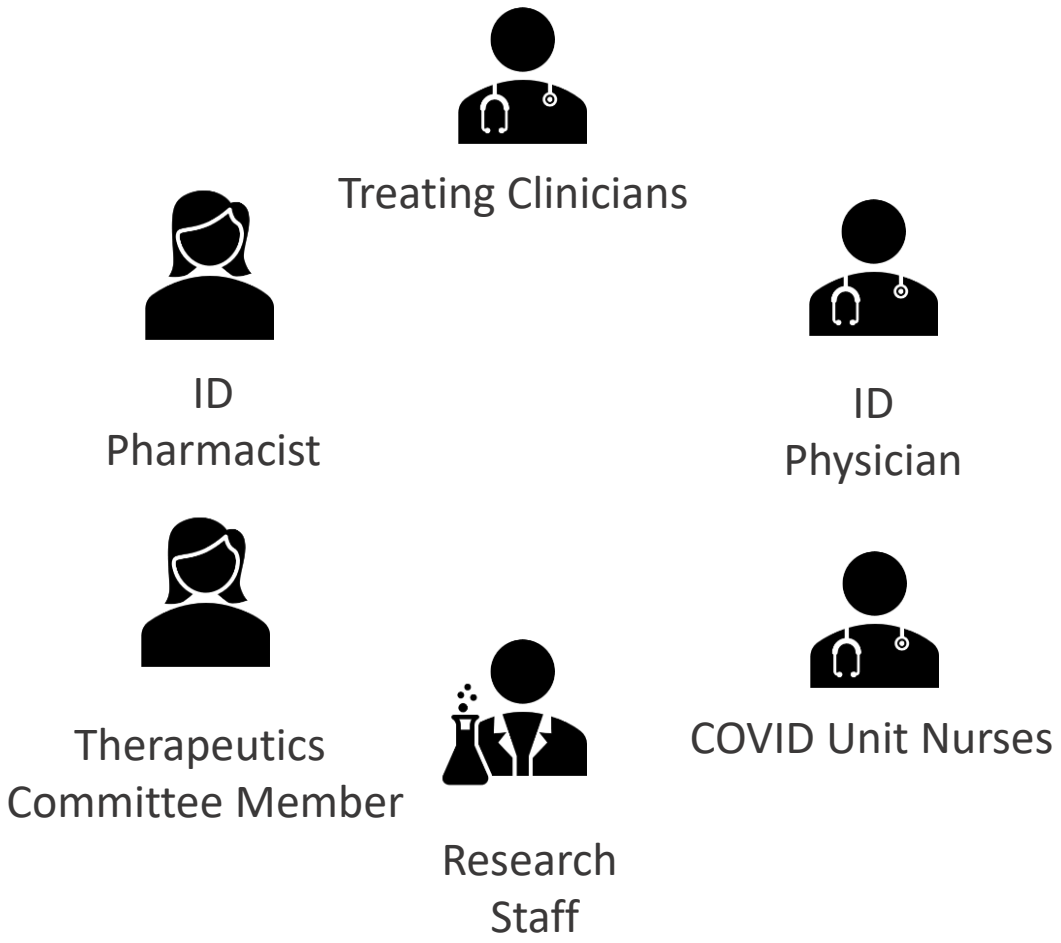
WHAT HAS CHANGED IN THIS UPDATE COMPARED TO VERSION 8.4?

- ***Treatment:*** Evidence continues to rapidly evolve. See NIH and Intermountain recommendations for the most recent recommendations.
- ***Trials:*** Current information on active trials is available here.

WHAT HAS CHANGED IN THIS UPDATE COMPARED TO VERSION 9.0?

- ***Fluid management:*** Clarification that specific recommendations regarding fluid management and diuresis apply to confirmed COVID-19 cases.

Daily COVID Rounds: effector arm for integrated research-clinical activity

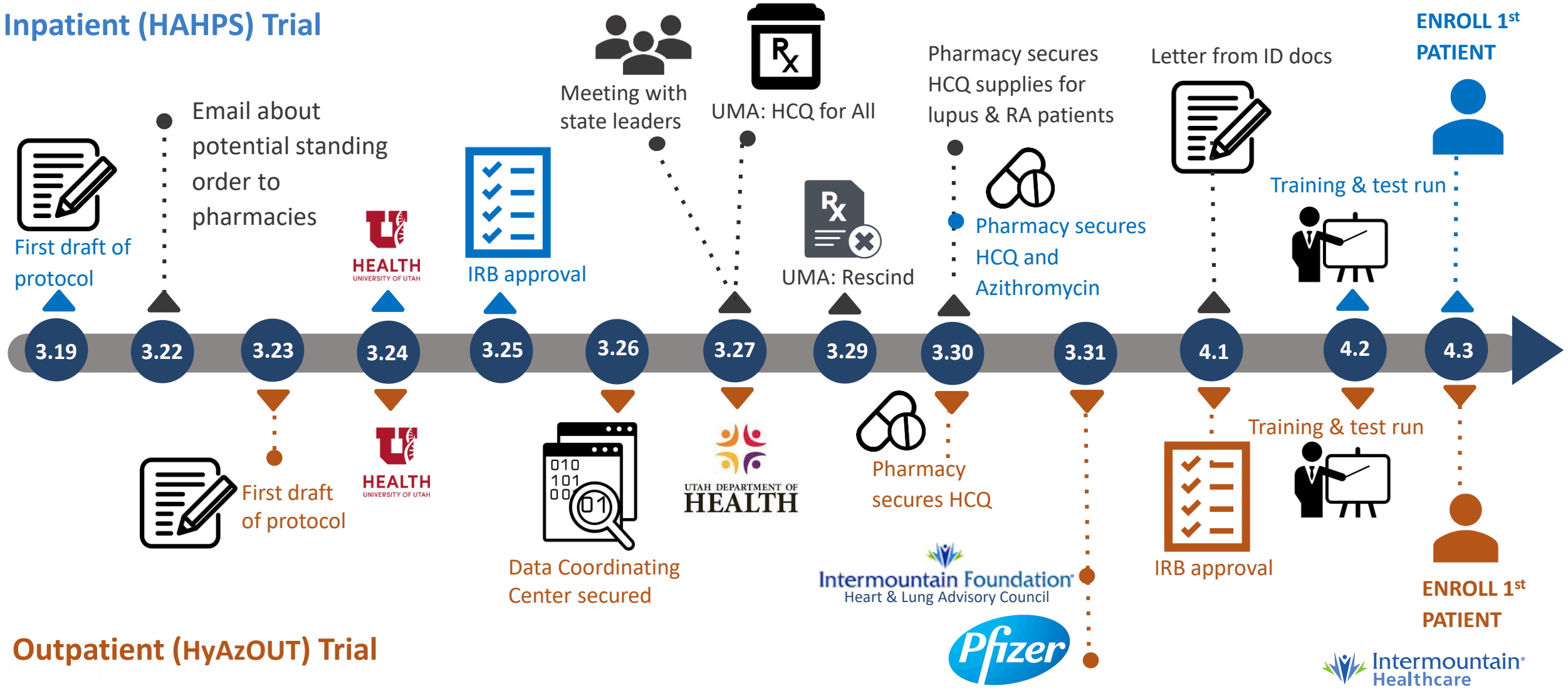


- Quick review of current trials, new admits, and complex cases
- EMR worklist tracked labs, enrollments, etc
- Synchronized care, education, and feedback; saved time for clinical ID service and research staff
- Per major hospital plus tele-rounds for smaller hospitals combined
- Facilitated load leveling procedures across Intermountain

The Salt Lake Tribune

Utah has already ordered $800K of malaria drugs, could spend millions more on unproven COVID-19 treatment

Intermountain COVID-19 trials: the pandemic begins



Intentional Adaptation

Considerations

- What should we do and for whom should we do it?

Initiatives

- Clinical trial design and selection
- IPOC COVID registry for trial design and epi research
- IS support for EMR adaptations and Clinical Decision Support

Attribute	N in IPOC
COVID patients	171,288
Inpatients	12,917
Inpatient days	77,875
Data elements	1,033

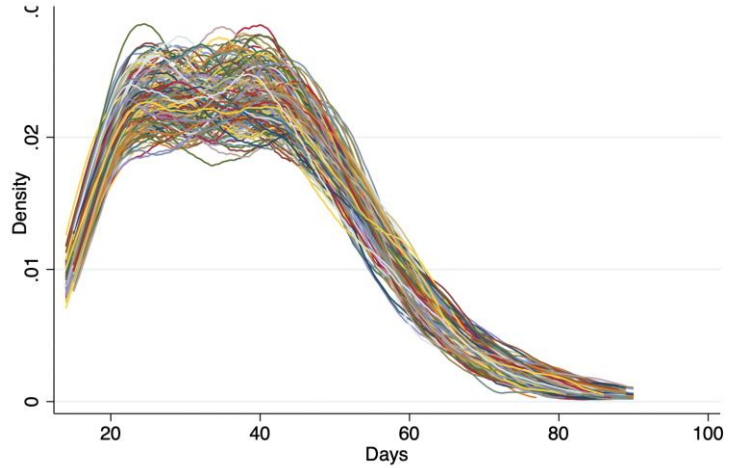
	Patients (n=299)	Mechanical ventilation			Mortality	
		Sensitivity (95% CI)	Specificity (95% CI)	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
r	231 (77%)	0·93 (0·85–0·98)	0·28 (0·23–0·35)	0·61 (0·54–0·68)	0·88 (0·68–0·97)	0·24 (0·19–0·29)
rferritinaemia	73 (24%)	0·57 (0·45–0·68)	0·87 (0·81–0·91)	0·72 (0·64–0·79)	0·56 (0·35–0·75)	0·78 (0·73–0·83)
natological dysfunction	98 (33%)	0·76 (0·65–0·85)	0·82 (0·76–0·87)	0·79 (0·73–0·86)	0·84 (0·63–0·95)	0·72 (0·66–0·77)
tic inflammation	100 (33%)	0·64 (0·53–0·75)	0·77 (0·71–0·82)	0·71 (0·64–0·78)	0·72 (0·50–0·87)	0·70 (0·64–0·75)
ulopathy	65 (22%)	0·50 (0·38–0·62)	0·88 (0·83–0·92)	0·69 (0·61–0·77)	0·44 (0·25–0·65)	0·80 (0·75–0·85)
kinaemia	105 (35%)	0·82 (0·71–0·89)	0·81 (0·75–0·86)	0·81 (0·75–0·87)	0·76 (0·54–0·90)	0·68 (0·63–0·74)
score ≥2	161 (54%)	0·95 (0·88–0·99)	0·59 (0·52–0·65)	0·92 (0·88–0·96)	0·96 (0·78–1·00)	0·49 (0·43–0·55)
score ≥3	99 (33%)	0·87 (0·77–0·93)	0·81 (0·75–0·86)	0·92 (0·88–0·96)	0·80 (0·59–0·92)	0·68 (0·62–0·73)
score ≥4	61 (20%)	0·71 (0·59–0·81)	0·92 (0·87–0·95)	0·92 (0·88–0·96)	0·64 (0·42–0·81)	0·80 (0·74–0·84)

C=area under the receiver operating characteristic curve. cHIS=COVID-19-associated hyperinflammatory syndrome.

4: Association with outcomes by individual cHIS components

	Sig.	Exp(B)	95% C.I.for EXP(B) Lower	Upper
FEVER	.000	1.944	1.876	2.016
COUGH	.000	1.779	1.718	1.842
BODY_ACHES	.000	1.564	1.509	1.622
DECR_SMELL	.000	2.469	2.373	2.570
COVID_CONTACT	.000	2.588	2.501	2.678
Non-White Race/ Ethnicity	.000	3.333	3.225	3.444
Male	.000	1.247	1.206	1.288

Figure 12 B. Days to recovery among surviving patients (requires home *and* not on supplemental oxygen)



The struggles

Barriers	Solutions
Compliance concerns	FDA, OCR, OHRP guidance helped some; pandemic commitment on part of our compliance office
PPE limitations	Telepresence technologies
Financial shortfalls	USG COVID payments; better capitation; redeployed staff
Political pressures	Flexibility, support of top executives, frequent meetings
Staff exhaustion/burnout	We hired up but often failed to manage exhaustion; fought with monitors to decrease “busy work”
Premature loss of equipoise	We built and ran relevant trials quickly

Successes

Achievements	Reasons
Collaboration across divisions	Smaller faculty; central leadership; civic-mindedness; integrated clinical-research structure
Hiring up	Better capitation for the trials; activating stewardship pharmacists
Smooth prioritization	Integrated committees; use of ACTIV to aid prioritization; other research stopped; COVID Rounds
Touchless consenting	Excellent IS support; preexisting telemedicine infrastructure; FDA guidance; COVID Rounds
Contracting	Buy-in from legal and research admin; simultaneous calls with investigators and lawyers
National trial engagement	PETAL Network/NHLBI; CTSA and PCORnet; IPOC registry

Unresolved difficulties

Problems	Hopes for the future
Trial monitoring	Simplification and regulatory reform
Staff exhaustion	Better training and pay for research coordinators; better pipeline (similar to, e.g., “Teach for America”)
Tensions about status and workload	Better incentives for clinicians to help with research; better management of other research programs
Exhaustive AE/con med reporting	Regulatory reform
Rigid and clunky consent documents and processes	Regulatory reform, including no more two-part consents, allowance for modular complexity
Running trials at extended sites	Modular HR packages; strike teams; merging hospitals administratively

Extra wish lists

- Comprehensive risk management solutions
  - Indemnification and simple/stock contracts
  - HR management (eg. modular workforce including clinical buy-down for MDs and pharmacists)
  - OCR and other agencies buffering non-malicious actors
- Regulatory reform
  - Simplify consent and bureaucratic paper trails
  - “Learning EUA” or equivalent for promising therapies (e.g. CCP)
  - Allow sites within a system flexibility in their preferred structure
- Inter-PHE infrastructure for extended clinical sites

Questions?