PCOR Building Data Capacity
It Is Feasible, and Worthy of our Best Efforts!

Laura Esserman MD MBA
Director UCSF Breast Care Center
Professor of Surgery and Radiology UCSF
Alfred A. de Lorimier Endowed Chair in General Surgery

EHRs Are An important Step Forward, but learning health systems require another layer

What They Accomplish

- Organize all information in one place
- Enable a way to bill for services in real time
- Orders and messages collated

What They Do NOT Accomplish

- Do not facilitate reuse of data in real time for multiple purposes
- Do not currently facilitate sharing of tools and processes across institutions
- Decision Support is challenging
- Unstructured data makes QA/QI challenging
- Do not support registries or trials

In Order to Realize The Vision of Shared Data

We have to reimagine the process of generating clinical data

CERSI
UCSF-Stanford

OneSource Phase III: Demonstration of EHR/eCRF integration in the COVID-19 critical care environment

OneSource: SMART on FHIR for I-SPY COVID-19 trial

Adam Asare, PhD (UCSF, QLHC)
Anna Northrop (UCSF)
Heidi Collins, MS (UCSF)
Laura Esserman, MD, MBA (UCSF)

Lisa Weiss, MS
Noha Lim, PhD
Andrew Robinson (UCSF)
Julia Wallace (UCSF)

Call Collins (OpenClinica)
Mark Wheeldon (Formeidx)

Mitra Roca, PhD (FDA)
Scott Gordon, PhD (FDA)

June 11th , 2021

Source Data Capture from EHRs to Improve Quality and Efficiency

2019

U.S. FOOD & DRUG ADMINISTRATION

Source Data Capture from EHRs: Using Standardized Clinical Research Data

Mitra Rocca[1], Adam Asare[2,3], Laura Esserman[2], Sue Dubman[2], Gideon Gordon[1]

[1]Center for Drug Evaluation and Research, Food and Drug Administration
[2]University of California - San Francisco (UCSF)
[3]Quantum Leap Healthcare Collaborative

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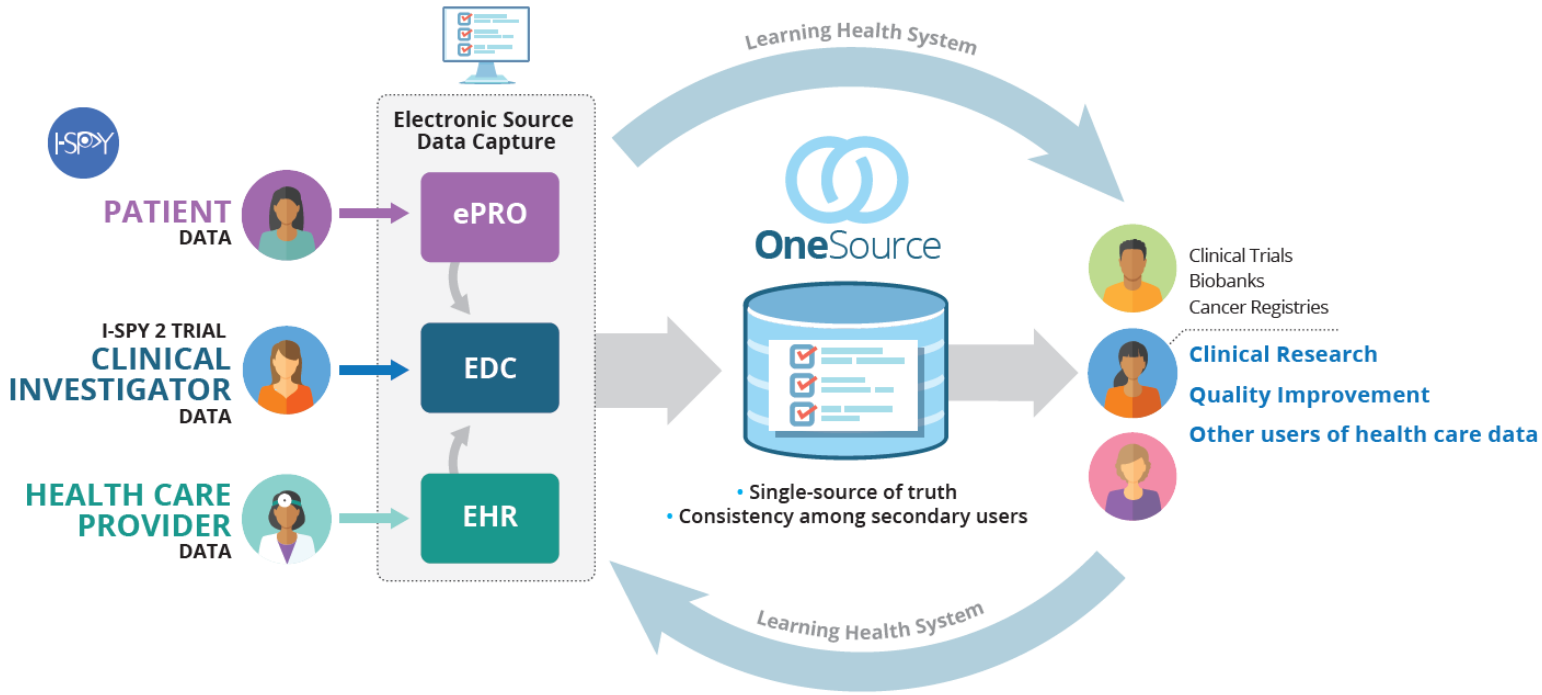


ePRO: Electronic Patient Reported Outcomes
EDC: Electronic Data Capture
EHR : Electronic Health Record

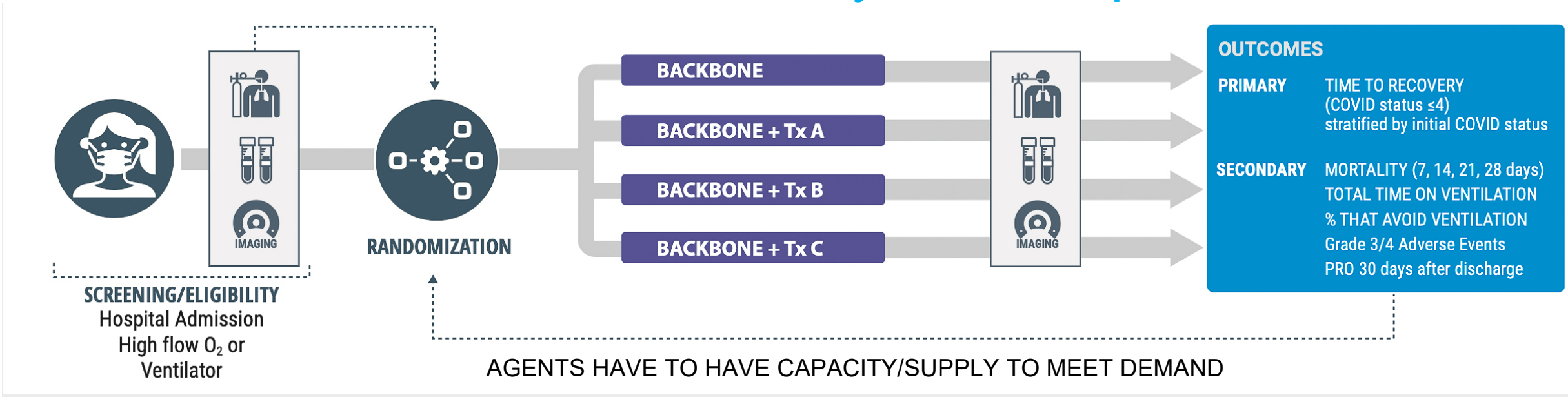
CRFs ask for data that is not in or easy to find in the notes

QL HC Quantum Leap Healthcare Collaborative

Key challenges

- Focus on the data that is mission critical
  - Working as a team to identify the key elements to collect, and when to collect them
  - Design work-flow so that teams can function together for data collection
- Enter Once use Many
  - Acquiring data in the course of care
  - Having structured data elements in place
  - Ensuring that there is an audit trail in place
  - Ability to use the data acquired for multiple purposes
- Visualization of data for individual and population management

I-SPY COVID TRIAL: Enrollment started July 30; 1200+ patients to date



BACKBONE : All patients will get **best standard of care** (optimal ventilatory management) + Remdesivir + steroids
every patient gets some treatment with proven efficacy. Backbone updated as

GOAL: Rapidly screen agents for a BIG IMPACT

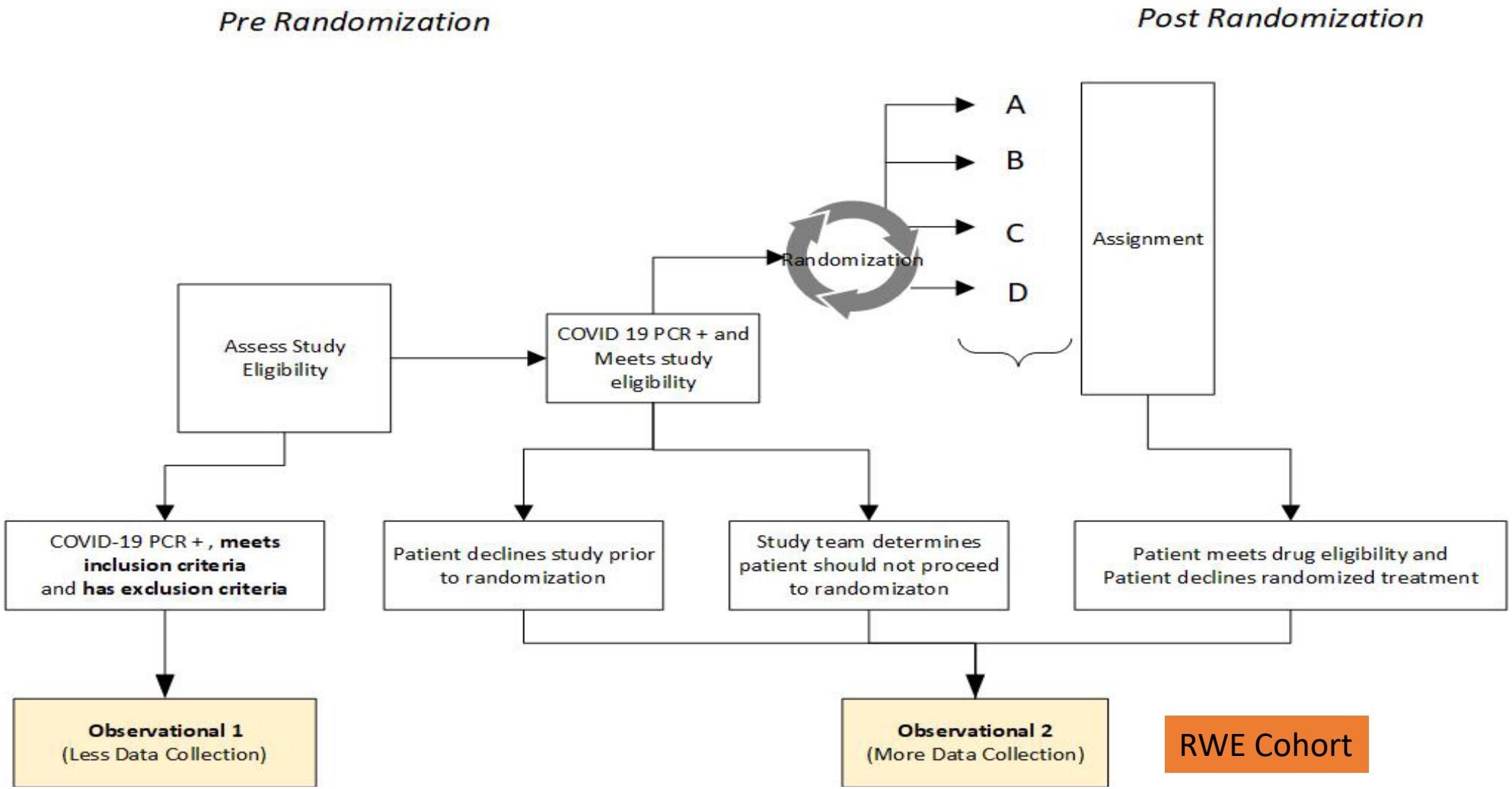
TRIAL will EVOLVE over time:

- Agents that reach target for faster recovery (~ 30%)
- Agents can drop for futility, hit maximum accrual without graduating, or graduate by hitting the efficacy target
- *Agents that graduate . . . Confirmation of signal could lead to an EUA*

Note:

- ***Day 1 for study patients:*** *first day patient requires high-flow oxygen (6L or more) or intubated—not day of diagnosis.*
  - *From the time a patient is put on high-flow oxygen (6L or more) or intubated, there is* ***120 hour (+/- 6 hours) window*** *to enroll patients*

Observational Arm: Real World Evidence Cohort



Processes	May-July 2020	Aug- Oct	Nov -December	January-February	March	April-June 2021
Data	Develop Checklists of Essential structured data elements-Capture Disease outcomes; Streamline AE reporting; Approval from FDA July	Implement EDC, Automated reporting Central IRB requirement implemented Weekly investigator, agents review	Refined edit checks, DMC reports; Death Summary Reports; Automated Safety Review triggers (DILI); Safety Working Group Review Process UPDATES: Revision of data elements based on user feedback; as needed per FDA and new agents	Add CRC resources to sites unable to keep up with data collection; Add central CRC to support for new sites or those with issues Query capability to respond to FDA on dose holds and reductions; standardizing process for assessing renal toxicity from disease vs. drug UPDATE	Risk based monitoring instituted UPDATE	
OneSource	Landscape scan to understand impediments to good quality data	Landscape scan to understand workflow and requirements	OneSource grant from FDA to streamline data capture, integrate care and research processes BARDA OneSource	FHIR tools developed; EHR integration with EDC (Open Clinica); Mapping Patient ID to Medical Record number; Develop change management process	Designed Automated labs, demographics, Con Meds	Moved to Production for lab, demographic process; Design Clinician Source for Checklist
Achievements	FDA Approval for Master Protocol and 3 agents FAST grant awarded	EDC system launched across 7 sites in August without error Remote SIVs Central IRB	Automated Death Summaries; AE adjudication standards Pharmacist joins QLHC to manage agents Pharmacy checklist Agent activation checklist BARDA, DTRA support	Local CRCs hired (7) First central CRA hired (1/25) Expand to meet non-traditional research site needs **Every death, AE, AESI, SAE reviewed by Safety Working Group (>40% of all patients)**	Lab automation tested UCSF First study arm lock in data base	Lab, demographic, and conmed in production UCSF Harmonize reporting requirements across FDA, IRB, BARDA, HRPO

Daily Check List

Standardized Check List Integrated with EHR
CMS could Support Completion of a Daily Check List

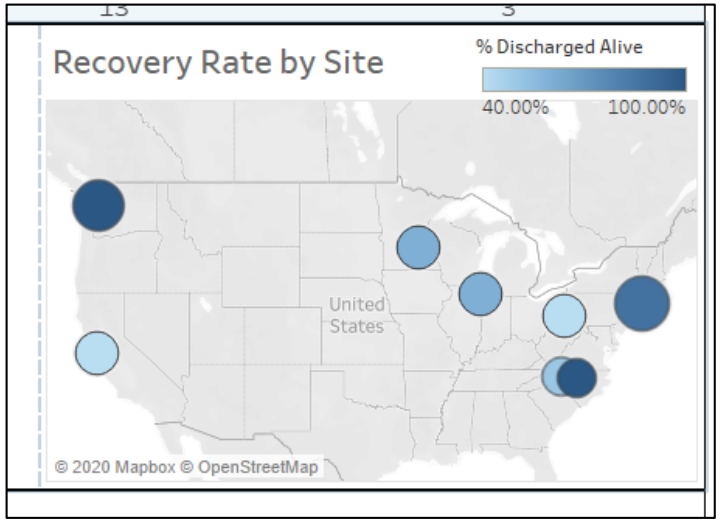
- COVID WHO Scale (FDA standard)
  - If level 5
    - FiO2
  - If level 6/7 (intubation), standard ventilator settings:
    - paO2/Fio2 OR sp02
    - use of proning
    - Tidal volume
    - Volume control (plateau pressure)
    - PEEP
  - If level 7
    - Vasopressors
    - ECMO
    - Dialysis (Kidney Replacement Therapy)
- Major Adverse Event over previous 24 hours
  - MI
  - Pneumothorax
  - PE
  - Stroke
  - Dialysis (if not ventilated)
  - Bleed requiring transfusion
  - Positive culture / date (pull culture result and sensitivity)
    - Blood
    - Urine
    - lung

- Daily
  - Off Study drug (reason) (proceed to early discontinuation)
  - Continue study drug
  - Dose modification. (reason)
  - Dose Hold (reason)
- Labs/ site reference range
  - Creatinine, AST, ALT, Bilirubin, CBC/ Differential, PT, PTT, D-Dimer, CRP, BNP, troponin, bicarbonate
  - directly pulled from EMR and
  - programmed with Reference Ranges for automated adverse event grading)
- Short list of concomitant medications
  - Steroids
  - Convalescent plasma
  - Inhaled NO (nitric oxide)
  - Flolan
  - Vasopressors (1-3)
  - Antibiotics (1-3)
  - Anticoagulation (prophylactic, therapeutic , intermediate)
  - Neuromuscular blockade

Clinicians entering data
At the point of care

Seamless ability to enroll on trials

Automated feedback:
ICU at a glance



Creatinine, AST, ALT, Bilirubin, CBC/ Differential, bicarbonate, PT, PTT, D-Dimer, CRP, BNP, troponin

Early Discontinuation, Discharge or Death, Electronic Patient Reported Outcomes

Automated Toxicity and Safety Reporting

AE Reports for Safety Committee Review

Click save button when finished. Save

Report1_SAE_AESI | Report2_AESI | Report3_AESI

Close out or not?
- ○ Information complete
- ◉ Ongoing review required

Expected with COVID/ARDS?
- ○ Yes
- ○ No

Expected for ?
- ○ Yes
- ○ No

Relationship to ?
- ○ Unlikely
- ○ Unrelated
- ○ Possible
- ○ Probable
- ○ Definite

Expected for ?
- ○ Yes
- ○ No

Relationship to ?
- ○ Unlikely
- ○ Unrelated
- ○ Possible
- ○ Probable
- ○ Definite

AE Event: Sepsis Grade 4

Investigator's Attribution:

Study Drug	Relationship	Action Taken
	Unrelated	
	Possible	

Committee's Consensus:

Ongoing review required and

Committee's note:

Patient No.: 634821

Site:

Demographics: 51.8-year-old fem

Treatment Arm:

▼ **Notes**

PCR positive date:	
Date screened:	
COVID-19 scale at screening:	
Date consented:	
Date started study:	
Days on ventilator (COVID scale>=6):	0
AE start date:	2021-05-03
Event description:	On 03 May 2021 patient presented with epig failure and shock, evidenced by leukocytosis secondary to transient cholangitis from gallst antibiotics. On 06 May 2021, patient was dow

▼ **Daily log table**

Date (Days from start)	COVID-19 Scale	ARDS Event	Lab CTCAE v5.0 Grade 3 or 4	AE status
2020-10-05 (1)	5	Antibiotics Prophylactic anticoagulation	Lymphocyte count decreased	
2020-10-06 (2)	5	Antibiotics Prophylactic anticoagulation	Lymphocyte count decreased	AE start
2020-10-07 (3)	4	Prophylactic anticoagulation	Lymphocyte count decreased	
2020-10-08 (4)	4	Prophylactic anticoagulation		
2020-10-09 (5)	4			AE resolved
2020-10-10 (6)	4	Prophylactic anticoagulation		
2020-10-11 (7)	4	Prophylactic anticoagulation		
2020-10-12 (8)	4	Prophylactic anticoagulation		Discharged

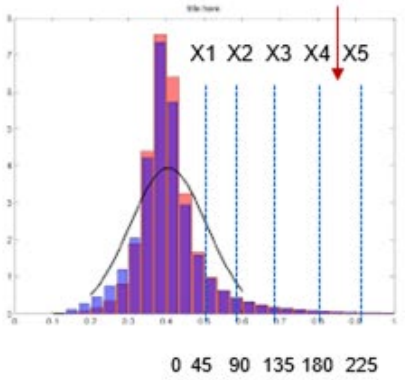
Automated scoring of CTCAE 5.0 laboratory toxicity grading

CTCAE 5.0 Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Alanine aminotransferase (ALT) increased	• **>ULN - 3.0 x ULN** if baseline was normal; • **1.5 - 3.0 x baseline** if baseline was abnormal	• **>3.0 - 5.0 x ULN** if baseline was normal; • **>3.0 - 5.0 x baseline** if baseline was abnormal	• **>5.0 - 20.0 x ULN** if baseline was normal; • **>5.0 - 20.0 x baseline** if baseline was abnormal	• **>20.0 x ULN** if baseline was normal; • **>20.0 x baseline** if baseline was abnormal	-

- ALT: 192.0 U/L on treatment visit
- Reference range: 7-45 U/L
- Baseline: Pt was normal
- Grade determination: 192.0 / 45 = 4.27, which is between 3-5 x ULN
- **Grade is 2**

Reference range from Laboratory Y's validation approved by FDA

Automate Grading



Automating comparison of adverse events across arms

Data Monitoring Committee (DMC) View

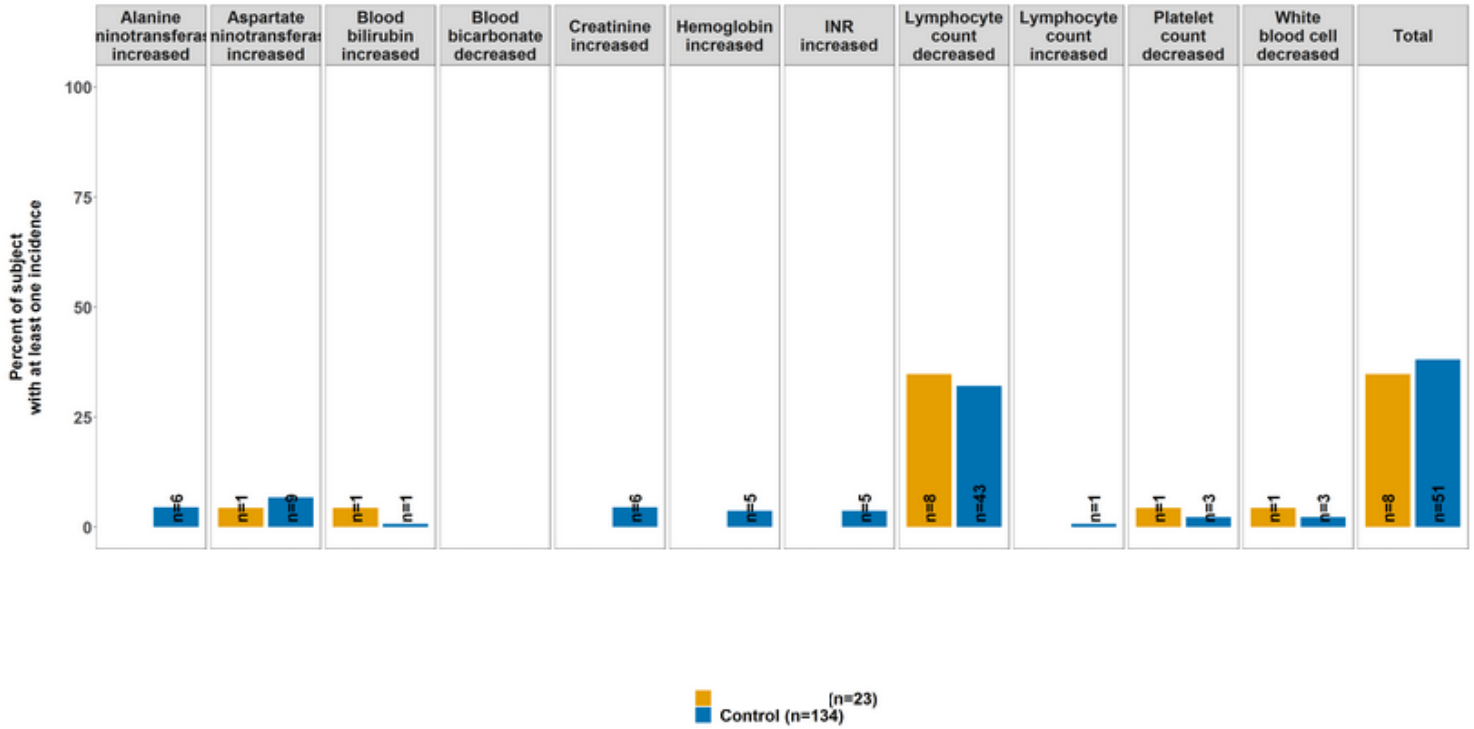
Laboratory Events (Grade 3-4)

Includes CTCAE v5.0 events that may not be drug related and per protocol nor reported as a formal AE, SAE, AESI or IRAE

Listing

All Interventions | Agent A vs Control | Agent B vs Control | Agent C vs Control | Agent D vs Control

Percent Subject

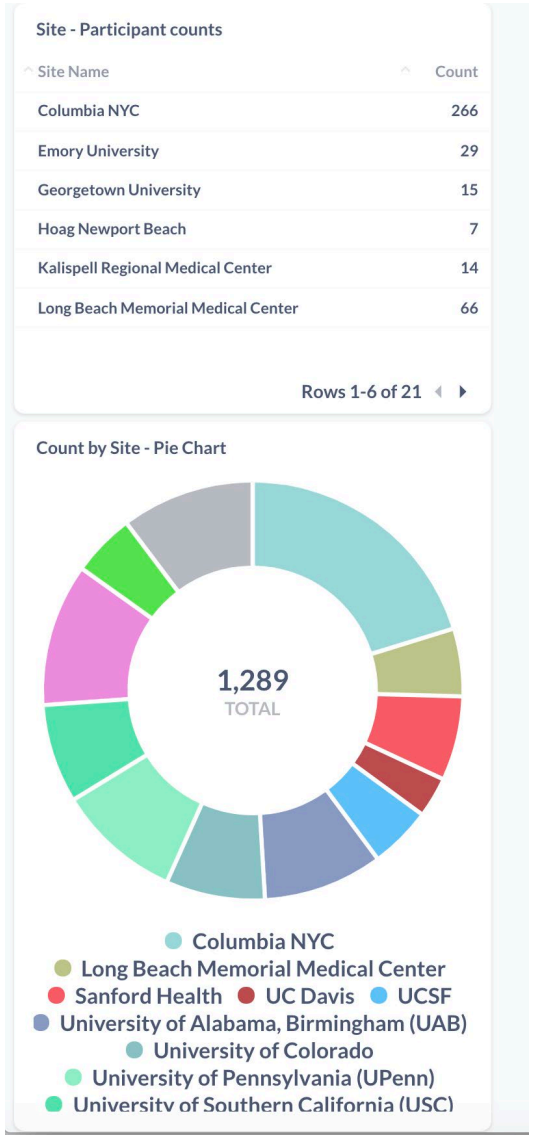


Results reported out bi-weekly

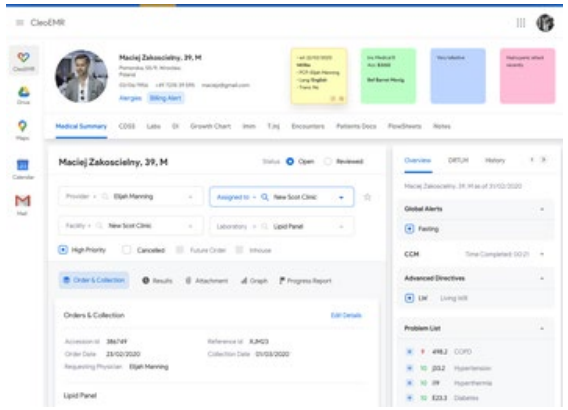
Trial at a Glance

Could also be your ICU at a Glance

I SPY COVID TRIAL: Accessible to all Investigators



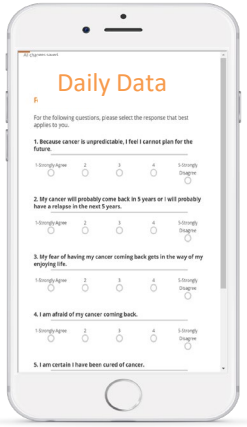
EHR Integration for Rapid Entry and Data Capture



EHR Systems

Pull discrete data from EHR

Study reports sent back



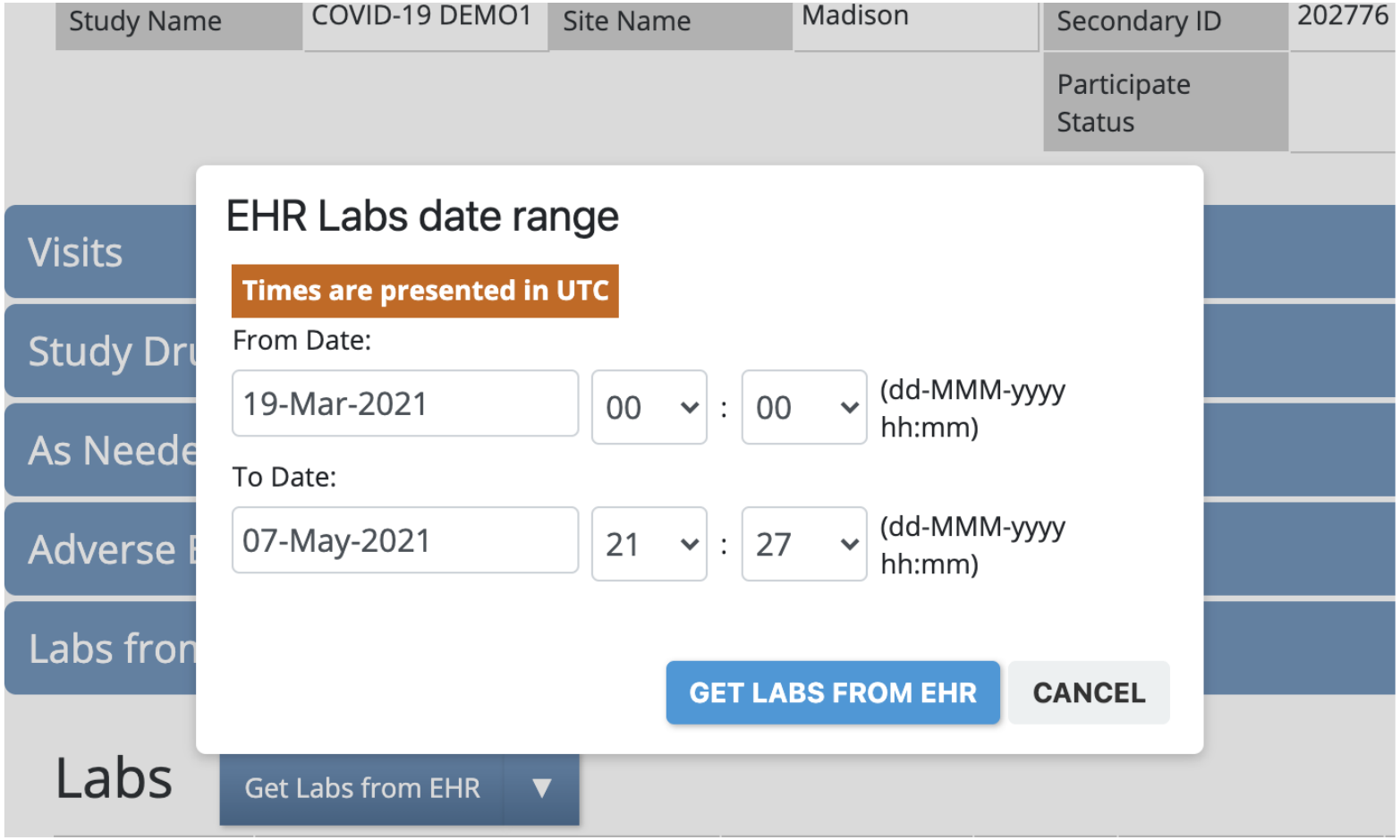
I-SPY COVID Study System

Receive alerts; monitor participants

Focus Is On Clinical Care

- **EHR Integration**
  - Automates capture of demographics, medications, and labs
  - Supports decisions for both clinical care and research
  - Sends daily check list and trial reports back to EHR system
- **Generalizable approach across sites and EHR systems**

Labs, Meds, and Demographics Pulled from EHR



EHR Labs and Meds Data Returned

Labs

Get Labs from EHR ▼

Search:

Study Day	Effective Date of Lab (UTC-00)...	Test Name	Value	Ref. Range Text	Lab Interpretation	Lab Status	Status	Last Updated	Updated By	Actions
Day -2685	2013-11-11 08:53 PM	Hemoglobin A1C	5.0	4.0 - 6.0 %	Not Available	Final	completed	14-Apr-2021	nanwar	
Day -3988	2010-04-18 08:40 PM	Hemoglobin A1C	5.0	4.0 - 6.0 %	(NONE)	Final	completed	14-Apr-2021	nanwar	
Day -2685	2013-11-11 08:52 PM	Cholesterol	231	0 - 200 mg/dL	Abnormal	Final	completed	14-Apr-2021	nanwar	
Day -3988	2010-04-18 08:40 PM	Cholesterol	231	0 - 200 mg/dL	Abnormal	Final	completed	14-Apr-2021	nanwar	
Day -2685	2013-11-11 08:52 PM	LDL Calculated	118	0 - 160 mg/dL	Not Available	Final	completed	14-Apr-2021	nanwar	
Day -3988	2010-04-18 08:40 PM	LDL Calculated	118	0 - 160 mg/dL	(NONE)	Final	completed	14-Apr-2021	nanwar	
Day -2685	2013-11-11 08:52 PM	HDL	51	35 - 70 mg/dL	Not Available	Final	completed	14-Apr-2021	nanwar	
Day -3988	2010-04-18 08:40 PM	HDL	51	35 - 70	(NONE)	Final	completed	14-Apr-2021	nanwar	

Results 1-8 of 8 Show 50 per page

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Meds from EHR

Meds

Get Meds from EHR ▼

Search:

Category	Medication Name	Effective Period Start	Dose Quantity	Dose Unit	Dose Delivery Method	Status	Last Updated	Updated By	Actions
Community	NALOXONE 4 MG/ACTUATION NASAL SPRAY	25-Feb-2021	1	spray	Nasal	completed	13-May-2021	IPMD	
Community	FENTANYL 200 MCG LOZENGE ON A HANDLE	25-Feb-2021	200	mcg	Buccal	completed	13-May-2021	IPMD	
Patient Specified	MULTIVITAMIN TABLET	Not Available	1	tablet	Oral	completed	13-May-2021	IPMD	
Community	DIAZEPAM 2 MG TABLET	25-Feb-2021	2	mg	Oral	completed	13-May-2021	IPMD	

Results 1-4 of 4 Show 10 per page

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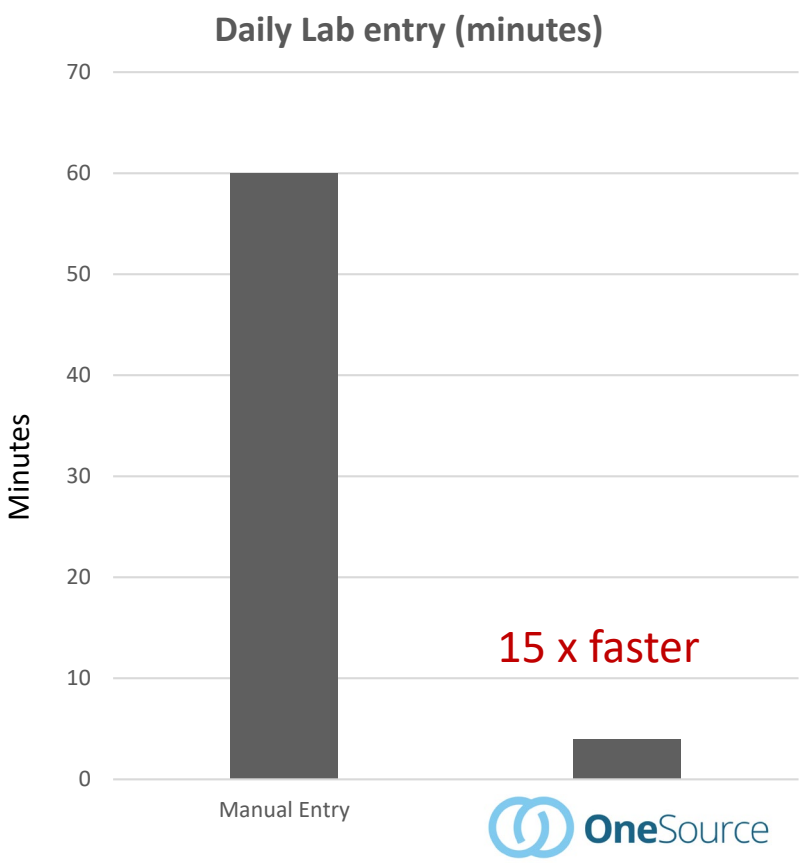
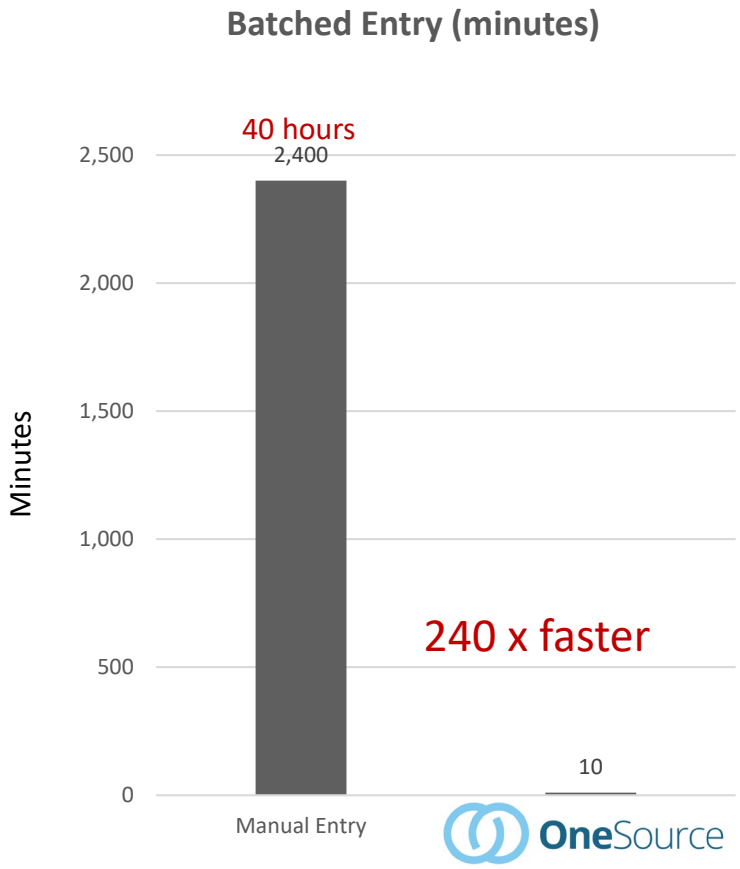
Data Capture Improvements (UCSF)

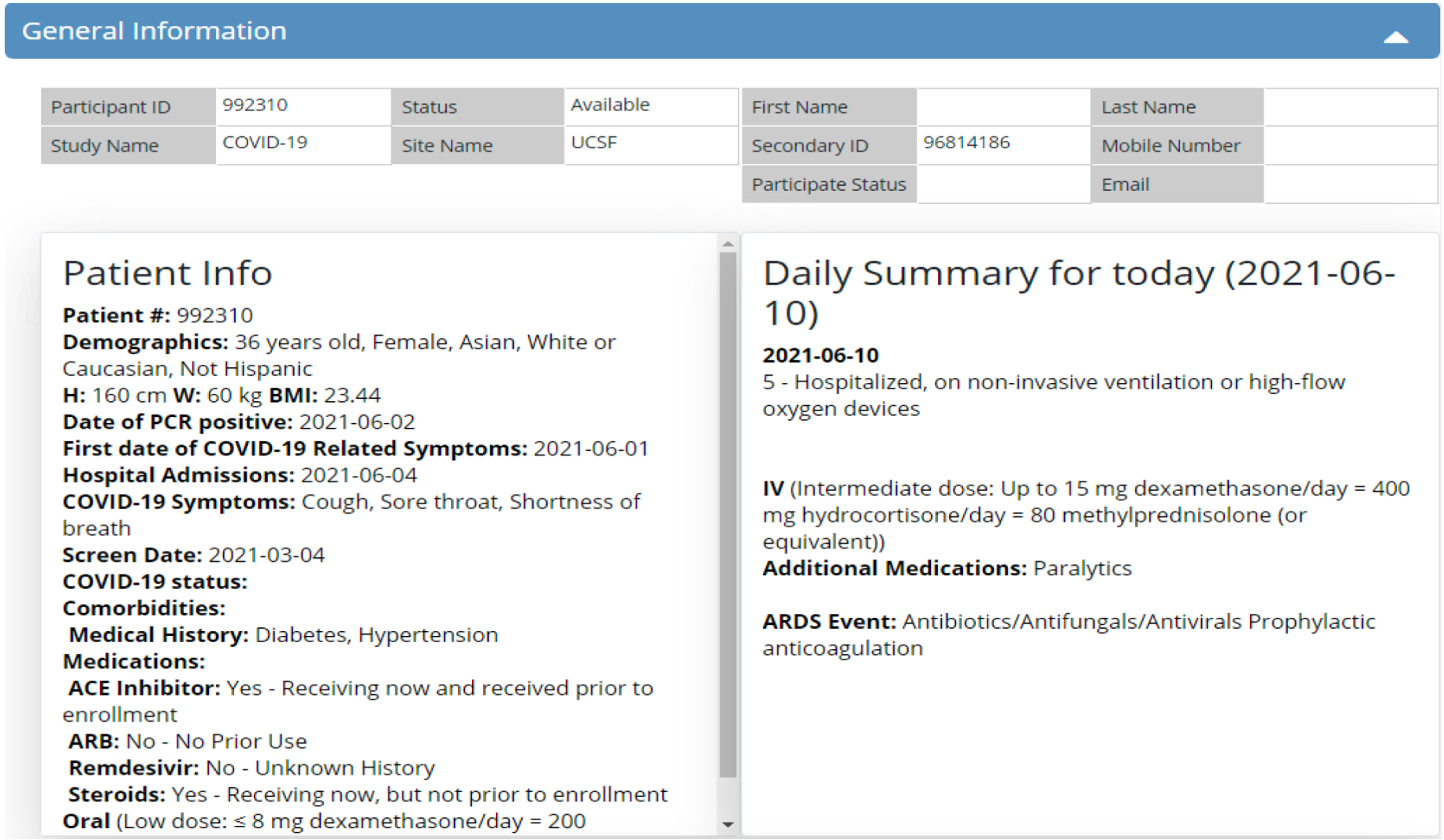




5 subjects daily (Labs for the Daily Check List)
(20 Labs each for 5 patients)

Batching subjects over the course of 20 days
(200 labs/CRFs - to catch up on data entry)

OneSource Tools Support Real Time Data Capture



General Information

Participant ID	992310	Status	Available	First Name		Last Name	
Study Name	COVID-19	Site Name	UCSF	Secondary ID	96814186	Mobile Number	
				Participate Status		Email	

Patient Info

Patient #: 992310
Demographics: 36 years old, Female, Asian, White or Caucasian, Not Hispanic
H: 160 cm **W:** 60 kg **BMI:** 23.44
Date of PCR positive: 2021-06-02
First date of COVID-19 Related Symptoms: 2021-06-01
Hospital Admissions: 2021-06-04
COVID-19 Symptoms: Cough, Sore throat, Shortness of breath
Screen Date: 2021-03-04
COVID-19 status:
Comorbidities:
Medical History: Diabetes, Hypertension
Medications:
ACE Inhibitor: Yes - Receiving now and received prior to enrollment
ARB: No - No Prior Use
Remdesivir: No - Unknown History
Steroids: Yes - Receiving now, but not prior to enrollment
Oral (Low dose: ≤ 8 mg dexamethasone/day = 200

Daily Summary for today (2021-06-10)

2021-06-10
5 - Hospitalized, on non-invasive ventilation or high-flow oxygen devices

IV (Intermediate dose: Up to 15 mg dexamethasone/day = 400 mg hydrocortisone/day = 80 methylprednisolone (or equivalent))
Additional Medications: Paralytics

ARDS Event: Antibiotics/Antifungals/Antivirals Prophylactic anticoagulation

I SPY 2 (BREAST CANCER) Forms for data collection: Structured and available for repurposing in Clinical Care

Enter Once→ Use Many

Screening

Patient Demographics

Menopausal Status

Tests:

- MRI Volume
- Blood Specimen
- Tissue Specimen
- Pre-Treatment Pathology
- Disease Assessment
- Non-Study Lesions
- Labs
- Cardiac & Other Tests
- MammaPrint
- SET Index (EOP)

On-Study Eligibility

Randomization Results

Baseline Health

- Conditions & Symptoms

ePRO Patient Quality of Life

Treatment

Treatment:

- Chemo/EOP Treatment
- GnRHa Treatment
- Non-Study Treatment
- Early Discontinuation
- Post-Surgery Summary

Tests:

- Labs
- Cardiac & Other Tests
- MRI Volume
- Blood Specimen
- Tissue Specimen

Assessments:

- Response Evaluation
- PreRCB Assessment
- Adverse Events

Protocol Violation

ePRO Patient Questionnaires

Post-Op

Treatment:

- Follow-Up / Adjuvant Therapy
- Subsequent Surgeries

Tests:

- Blood Specimen
- Labs
- Cardiac & Other Tests

Adverse Events

ePRO Patient Questionnaires

Outcomes

- Event Free Survival
- Distant Recurrence Free Survival

Treatment spans 7 months, followup 10 years
5 specialties
Legacy data had to be migrated

Centralized agreements can drive quality and efficiency

Platform Trials Facilitate Collaboration around Common Approaches to Data Collection- Investment for many studies, not just one . . .

- Common contract
- Central IRB
  - IREX
- Centralized and automated billing based on milestones direct through EDC
  - Sites complete data forms which automatically triggers payment
- OneSource integration : Read and write capability through FHIR
  - Read: Automated pull of demographics, concomitant meds, and labs
    - Leverages ONC rules for “read” from EHRs
  - Write back:
    - eligibility, initial Dx summaries, daily checklists, Pt Summaries
    - notify care team about trial participation by patients
    - notify care team about patient reported toxicity
  - Enables workflow to drive decision support
    - Prediction of residual disease at 12 weeks (B CA) for de-escalation; adverse event grading, reporting and ***patient care***
- Standard order sets for meds (every site does not have to do their own build)

This Change Will Enable us to Generate Practice Changing Data

- **Allows practice to improve**
  - Not just practice
- **We can know what we are doing and what the consequences are**
  - Assessing Outcomes does not have to be the heroic effort of chart review
  - Outcomes assessment can be a routine of care
- **Clinical research is just a special case of clinical care**
  - Trial summaries should be visible to clinicians
  - Trials often create more discipline about process, which should then be applied to all patients
- **The clinical care team can assemble mission critical data to better support decisions and care**
  - ***Integrate clinical care and research to produce better outcomes for all patients***

HHS can drive a transition to learning healthcare systems

- Create alternate payment systems using checklists and time spent

- Why Is this so important?
  - Removes incentive to duplicate data entry and note creation for every provider
  - Can foster the creation of a trusted “single source of truth” about clinical conditions of patients
  - Supporting the data collection with Structure on the back end makes data analyzable and shareable in real time
  - Critical for a pandemic
  - Critical for a learning health care system