India's Fight against COVID-19
Role of ICMR

Prof. (Dr.) Balram Bhargava

Secretary DHR & DG, ICMR

COVID-19 Pandemic

Why??

This century has witnessed several exotic viral infections more frequently and more complex

- SARS
- MERS
- EBOLA
- YELLOW FEVER
- ZIKA
- NIPAH

Possible reasons:

- Change in environment and ecology
- Rapid urbanization
- Extreme connectivity
- Neglected public health
- Inadequate spending on health

COVID-19 Pandemic

India's Response

Largest democracy with respect to peoples voices to recalibrate its intervention measures:

- Serious from the beginning
- Whole of government approach
- Calibrated, proactive, pre-emptive, graded RESPONSE
- Science driven with best practices and evidence based
- Strong leadership with excellent communication
- 5T strategy: Test-Track-Trace-Treat-Technology
- Resisted concept of herd immunity!

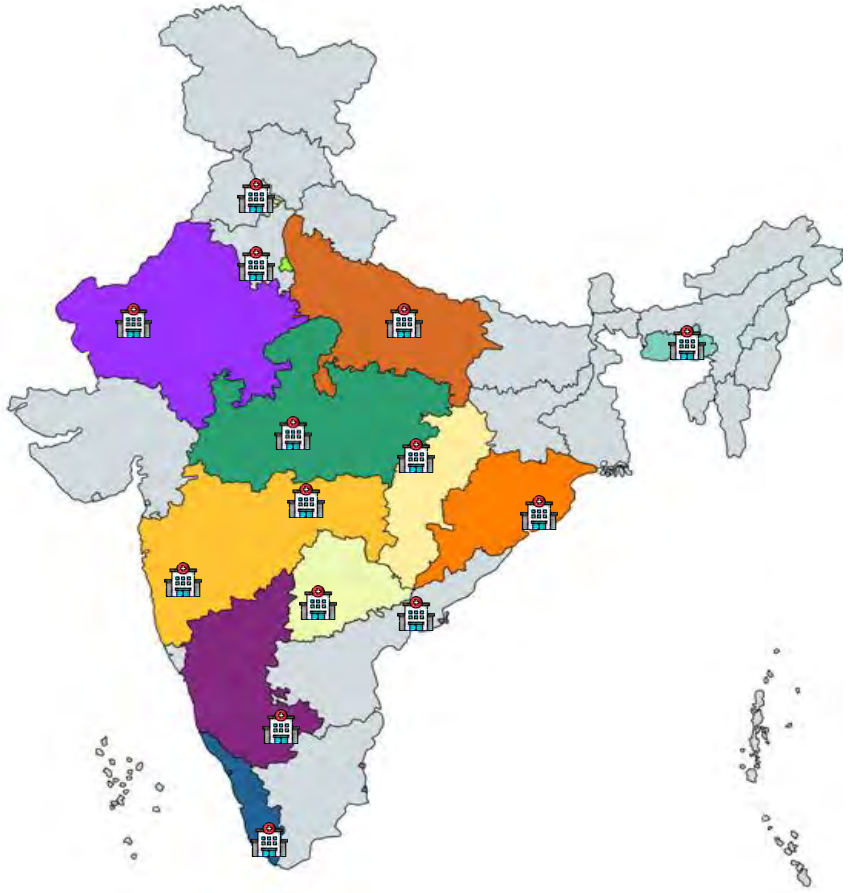
Testing

1st Wave & 2nd Wave

Upscaling Testing Facilities

'Laboratory in Every District of India'

14 Mentor Institutes

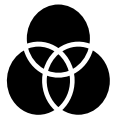


Basic pre-requisites

Calibrated & Functional RT-PCR

Calibrated & Functional BSL-2

Biomedical Waste Disposal Policy



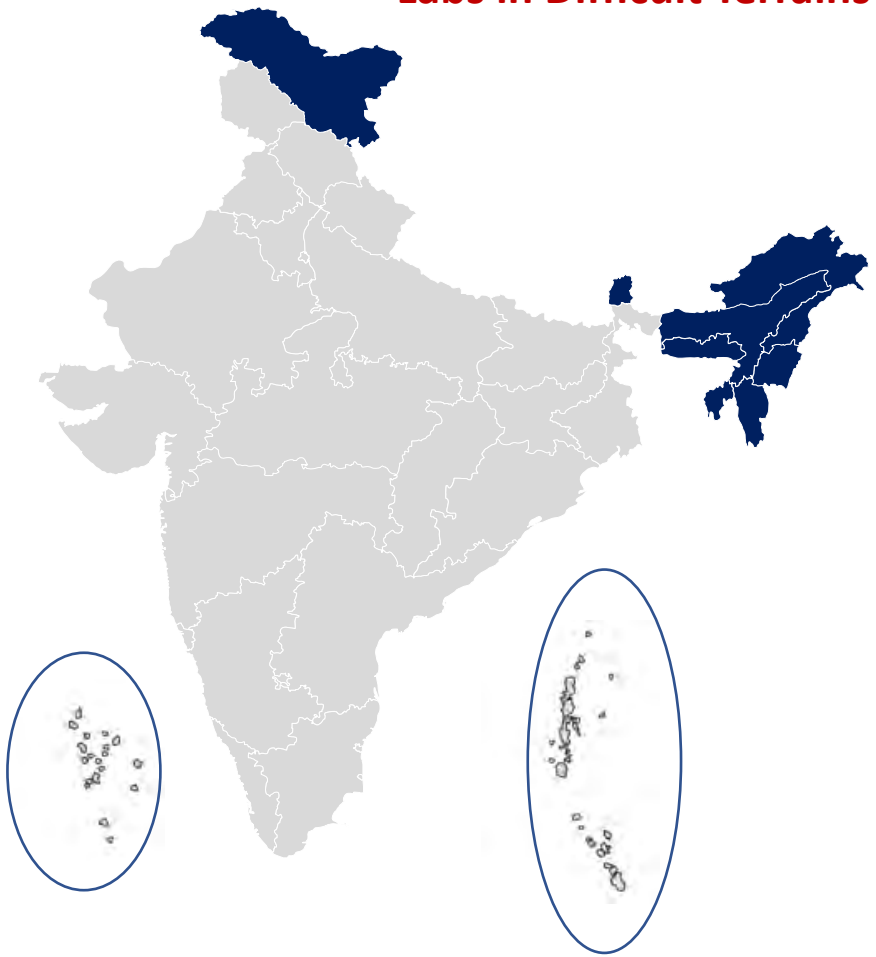
Cold Centrifuge

Staff Trained in Molecular Virology

Functional Autoclave

Pipettes, consumables

Labs in Difficult Terrains



- 522/542 Medical Colleges equipped
- 664/741 districts have RTPCR testing labs
- All districts have RAT testing facility.

Indian J Med Res. 2020 Feb & Mar;151(2 & 3):216-225

Gazette Notification

Equipped BSL-2 Mandatory for MCI Registration

रजिस्ट्री सं. डी.एल.-33004/99

REGD. No. D. L.-33004/99

भारत का राजपत्र
The Gazette of India

सी.जी.-डी.एल.-अ.-08062020-219821
CG-DL-E-08062020-219821

असाधारण
EXTRAORDINARY
भाग III—खण्ड 4
PART III—Section 4
प्राधिकार से प्रकाशित
PUBLISHED BY AUTHORITY

सं. 185] नई दिल्ली, सोमवार, जून 8, 2020/ज्येष्ठ 18, 1942
No. 185] NEW DELHI, MONDAY, JUNE 8, 2020/JYAISTHA 18, 1942

भारतीय आयुर्विज्ञान परिषद् के अधिक्रमण में शासी बोर्ड

अधिसूचना

नई दिल्ली, 3 जून, 2020

सं. भा.आ.प.-34(41)/2020-मेडि./103234.—भारतीय आयुर्विज्ञान परिषद् अधिनियम, 1956 (1956 का 102) की धारा 33 द्वारा प्रदत्त शक्तियों का इस्तेमाल करते हुए, "प्रतिवर्ष एम.बी.बी.एस. में 50 दाखिलों के लिए न्यूनतम शर्तें विनियमावली, 1999" में पुनः संशोधन करने हेतु भारतीय आयुर्विज्ञान परिषद्, केंद्रीय सरकार के पूर्व अनुमोदन से

ई-मेल /E-mail : mci@bol.net.in
वेबसाईट /Website : www.mciindia.org

Pocket 14, Sector-8, Dwarka, Phase – I, New Delhi-110077

भारतीय आयुर्विज्ञान परिषद के अधिक्रमण में शासी बोर्ड
BOARD OF GOVERNORS IN SUPERSESSION OF MEDICAL COUNCIL OF INDIA

No. MCI(34)(41)(Gen)-Med/2020 104795 Date: 16-06-2020

MOST URGENT
BY-EMAIL / MCI WEBSITE

To

The Principal/Dean of all Medical Colleges

Subject:- Inclusion of BSL-2 level laboratory testing facility for infectious pathogens in the Department of Microbiology in all Medical Colleges by amending the Minimum Standard Requirements for 50/100/150/200/250 MBBS Admissions Annually Regulations – Reg.

Madam/Sir,

This in continuation of Council letter bearing nos. MCI (34) (41) (Gen)-Med/2020/030203 dated 02.06.2020 and MCI-7 (9) SG/2019-Md./201873 dated 10.04.2020 on the above mentioned subject.

2. The aforesaid amendments have been notified in the Official Gazette and is applicable for all Medical Colleges as also applicants seeking to establish a new Medical College from the academic year 2020-21. Copies of the same are available on MCI website and are enclosed for ready reference.

Accordingly, (a) Medical Colleges awarding recognised MBBS degrees; (b) Medical Colleges that are in any phase of renewal (first/second/third/fourth/recognition); (c) Medical Colleges that are in the phase of seeking increase in intake of MBBS, and (d) All applicants who have applied to BoG, MCI for grant of permission to establish a new Medical College from the academic year 2020-21; are required to

Molecular Tests for COVID-19

Existing Molecular Tests

Standard RT-PCR

COBAS 6600/8800

TrueNat

CBNAAT

Abbott machines

+ Other USFDA Approved Closed Platforms

New Molecular Tests/ Methods

CRISPR/FELUDA Test

RT-LAMP Assays

Dry Swab Method

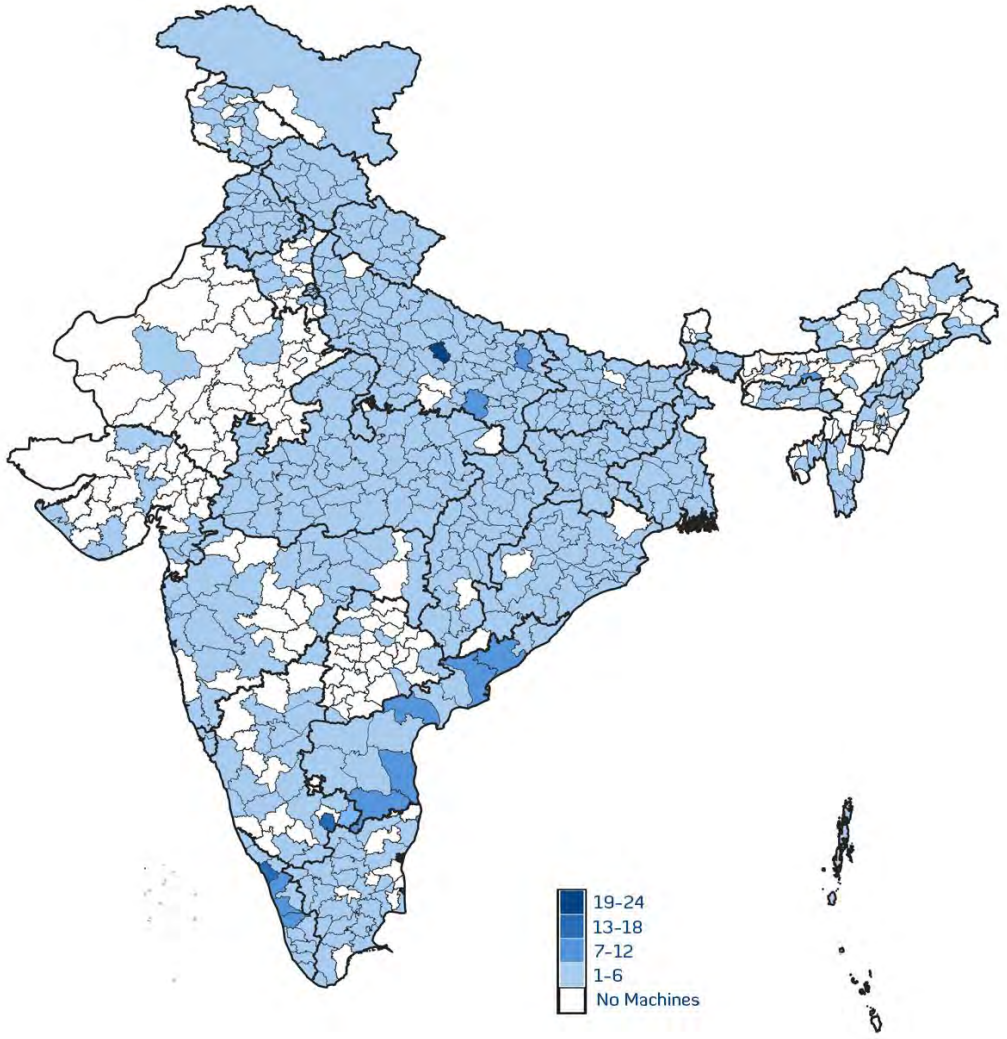
SARS-CoV-2 in saliva

Point-of-care Molecular ‘TrueNat’

‘Laboratory in a suitcase’

- Portable, battery operated, fully automated chip-based RT-PCR system, weighing ~3kg
- Remote areas, network data transfer & automated reporting
- Sample collected in viral lysis buffer
- Minimum biosafety & biosecurity requirements
- Results available in 45 minutes

- WHO approved & used for TB diagnosis since 2018
- Repurposed for COVID-19 testing since April 2020
- Repurposed for Nipah & Leptospirosis



2530 Truelab™ workstations operational
1008 sites in 530 districts of India

- *thelancet.com/journals/lanmic/article/PIIS2666-5247(20)30164-6/fulltext*
- *Indian J Med Res Epub ahead of print DOI: 10.4103/ijmr.IJMR_2363_20*
- *https://www.who.int/tb/areas-of-work/laboratory/en/*

High Throughput Laboratories

Minimum Human Intervention

Tests: 1500-4000 samples/day

State of Art High Throughput Machines

- *Regional Medical Research Centre, Bhubaneswar*
- *Rajendra Memorial Research Institute, Patna*
- *National Centre for Disease Control, Delhi*
- *National Institute for Research in Reproductive Health, Mumbai*
- *National Institute for Cholera & Enteric Disease, Kolkata*
- *MLN Medical College, Allahabad*
- *National Institute for Research in Tuberculosis, Chennai*

- *National Institute for Cytology & Preventive Research, Noida*
  (Multiple RT-PCR platforms)

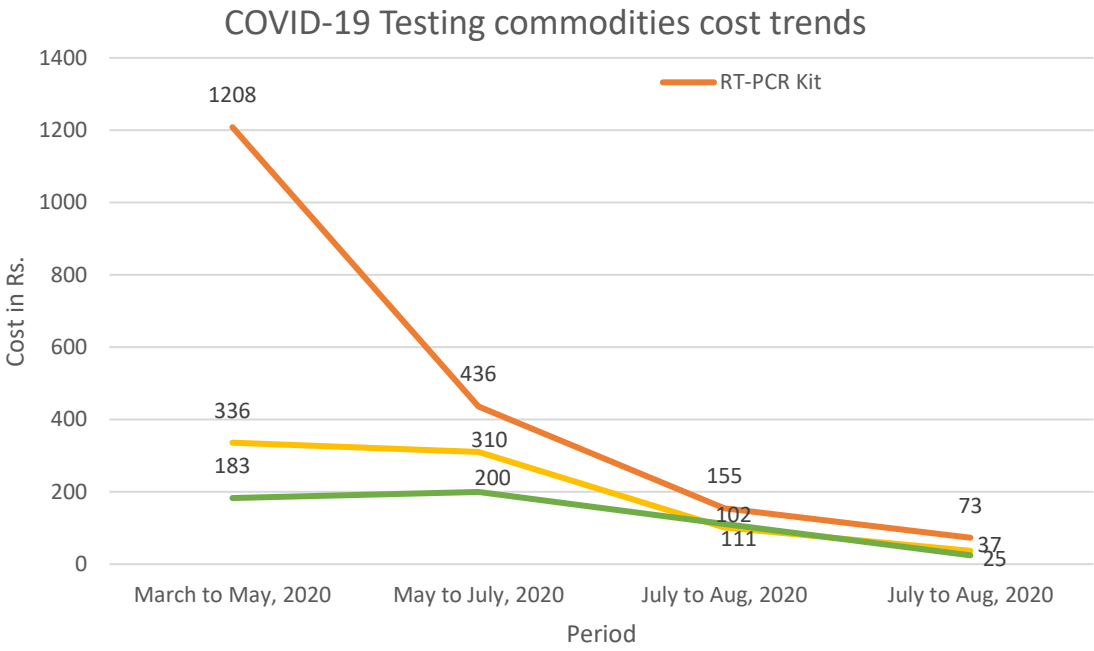
Mobile RTPCR COVID-19 Testing

- Joint initiative of Spice-Health & ICMR
- Inaugurated by Hon’ble HM on Nov. 23, 2020
- Testing capacity upto 2,000 samples/day
- 10 labs deployed. Target - 100

Self Reliance '*Atmanirbhar Bharat*'

Products validated at 24 ICMR Approved Validation Centres

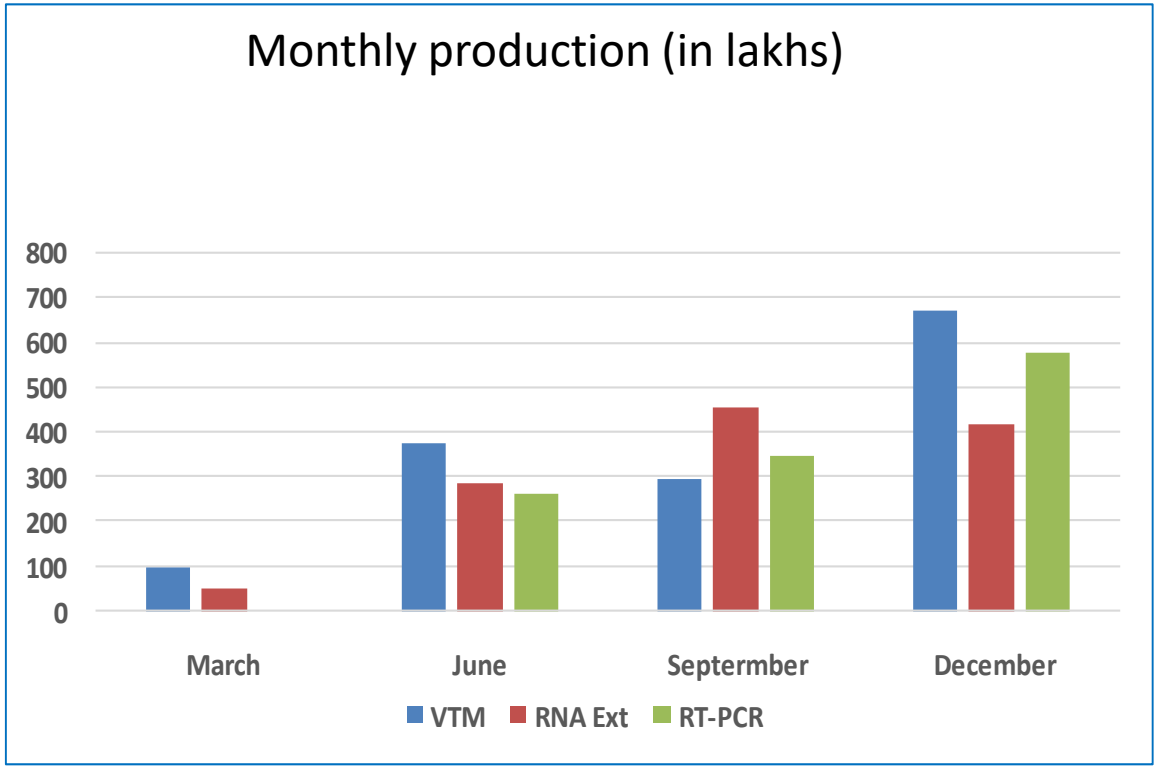
Validated by ICMR				Availability on GeM	
	Evaluated	Approved	Indigenous	Product	Vendor
VTM	260	220	208	871	88
RNA kits	277	174	114	669	56
RTPCR kits	365	165	95	564	63
RAT	118	42	34	78	13
Rapid Ab	209	26	19	76	22
ELISA kit	107	30	21	39	18
PCR Machines	-	-	-	375	29
RNA Extractors	-	-	-	47	21

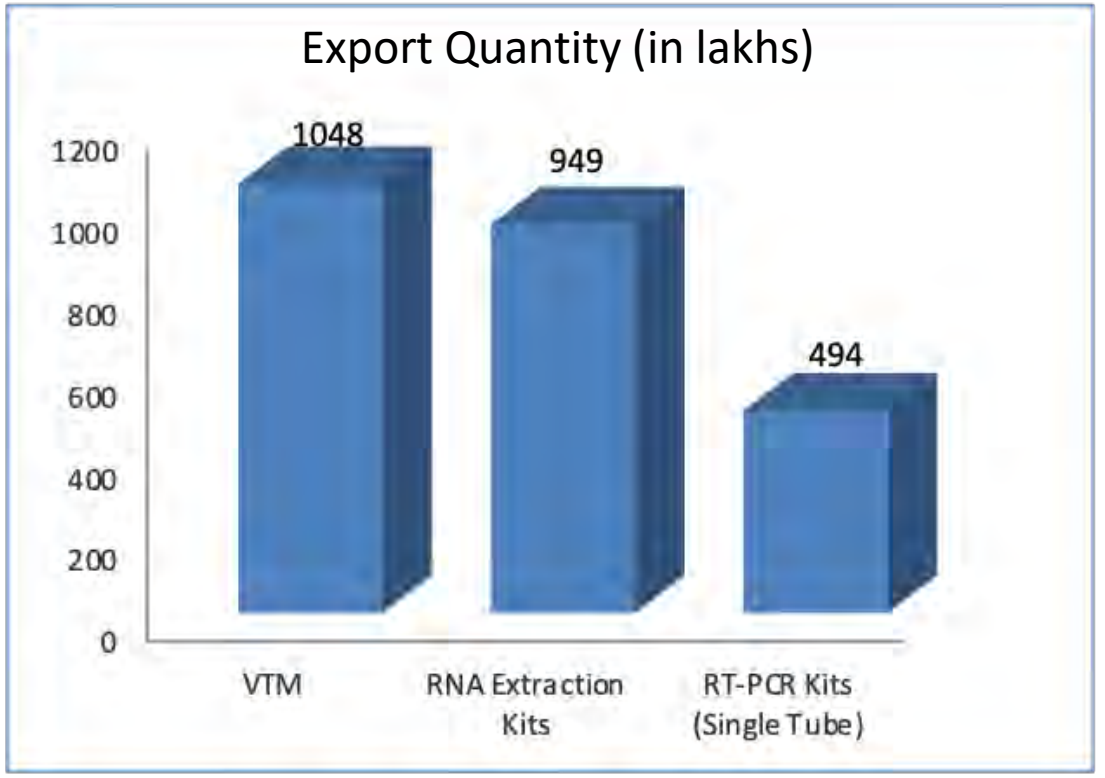


27th May 2021: 1336 diagnostic commodities evaluated

Total cost of one RTPCR test is INR 135 today as compared to INR 1727 in May 2020

Import Dependence to Export Surplus





Mission '*Lifeline Udaan*'

- **During the lockdown** (*March 24 to May 31, 2020: 4 phases*) Ministry of Civil Aviation, Indian Air Force, GOI implemented a special mission

- The 24X7 mission launched to carry consumables, testing commodities, medical supplies to various parts of the country

- Special flights commissioned to ensure timely delivery of testing commodities to various parts of the country

Partners

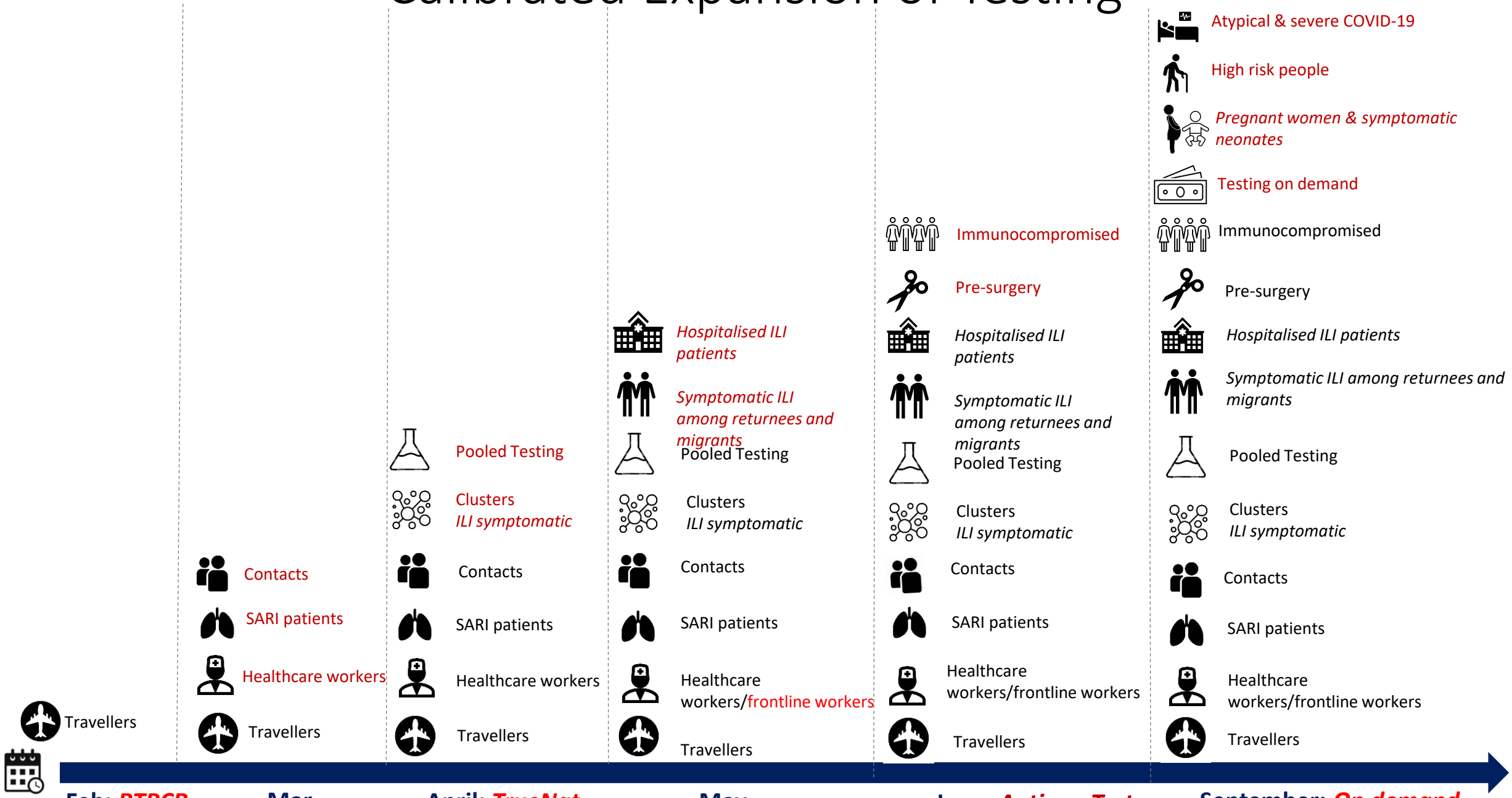
Civil Aviation

India Post

Indian Railway

Indian Airforce

Calibrated Expansion of Testing



Testing Laboratory at Iran

- Shia pilgrims (>6,000) stranded in Iran in Feb. 2020
- ICMR-NIV, Pune set-up RTPCR lab in Embassy of India, Tehran

- 2,028 samples collected from 5 cities
- 308 (15%) samples tested positive for SARS-CoV-2
- Special flights operated by Indian Air Force & Iranian Airlines for repatriation

ICMR-NIV Lab at Indian Embassy in Tehran

Coronavirus: NIV scientist goes to Iran to help stranded citizens

TNN | Updated: Mar 4, 2020, 08:15 IST

Some of the pilgrims from the state stuck in Tehran

MUMBAI: The National Institute of Virology (NIV) in Pune has sent one of its scientists to Iran to help the Indian citizens who are stranded there with the testing and diagnosis of novel coronavirus, or Covid-19.

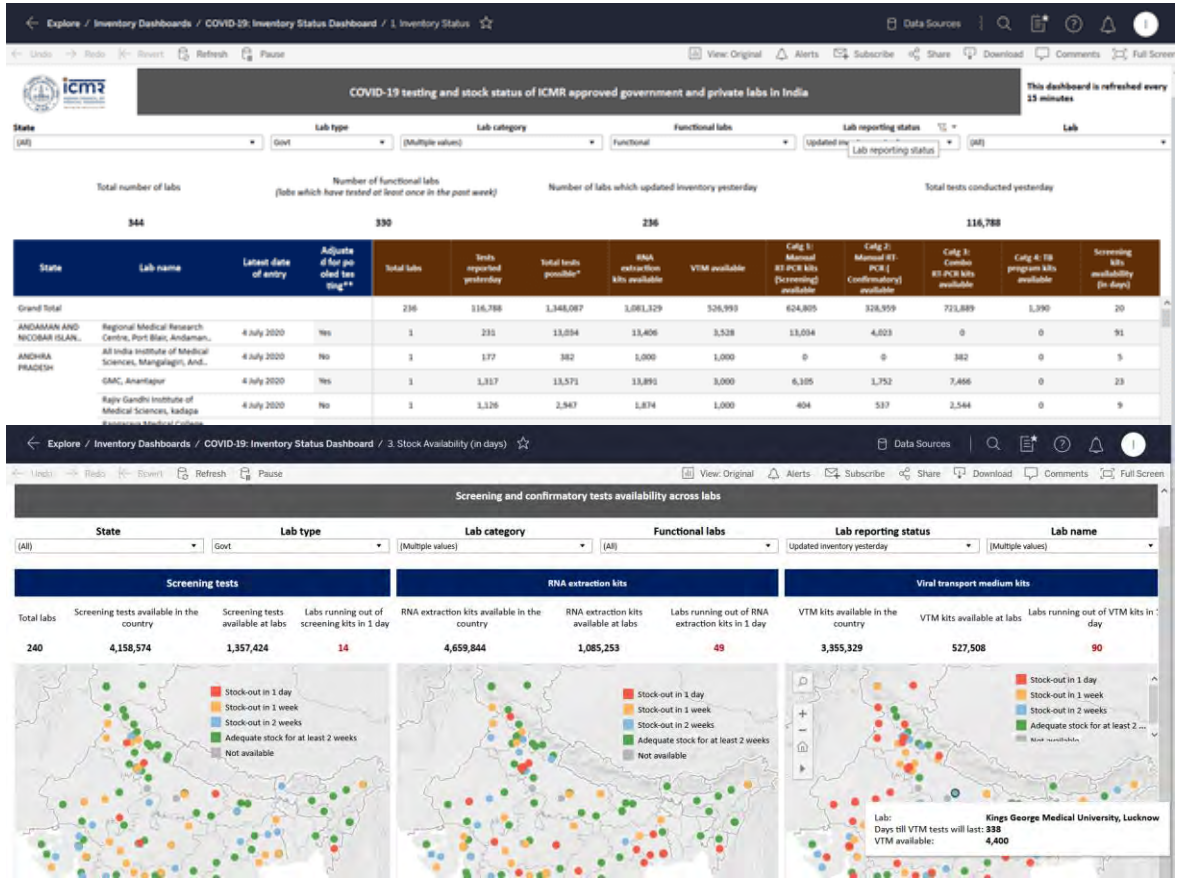
"There are about 1,200 Indians from Kargil in different parts of Iran," a top official from the Indian Council of Medical Research (ICMR) said. "The medical testing facilities for Covid-19 in Iran are not adequate. The scientist will help facilitate the medical evaluation of our citizens stranded there."

Back home: Indian nationals after they were brought to India by Indian Air Force's C-17 Globemaster aircraft from COVID-19-hit Iran, at Hindon airbase on Tuesday. Fifty-eight Indians were airlifted in the military transport aircraft. | Photo Credit: PTI

Image courtesy: The Hindu

Inventory: Demand Forecasting

(National / State / Depot)

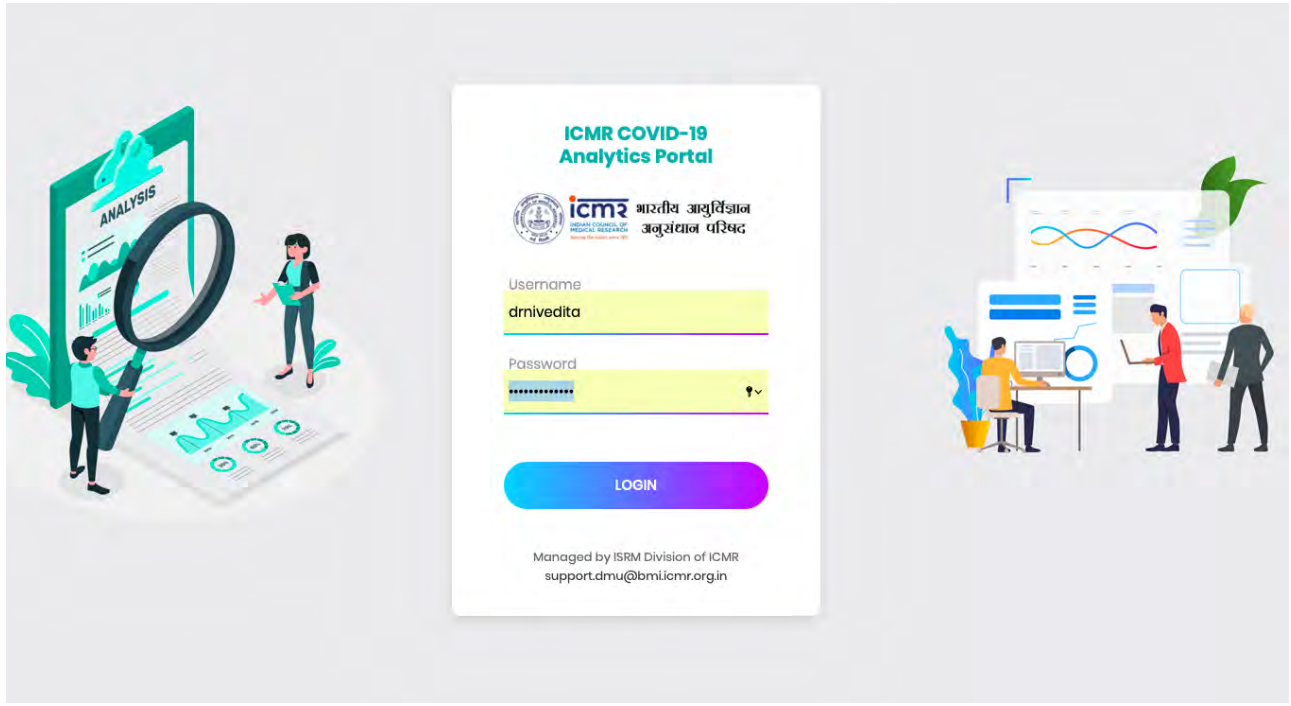


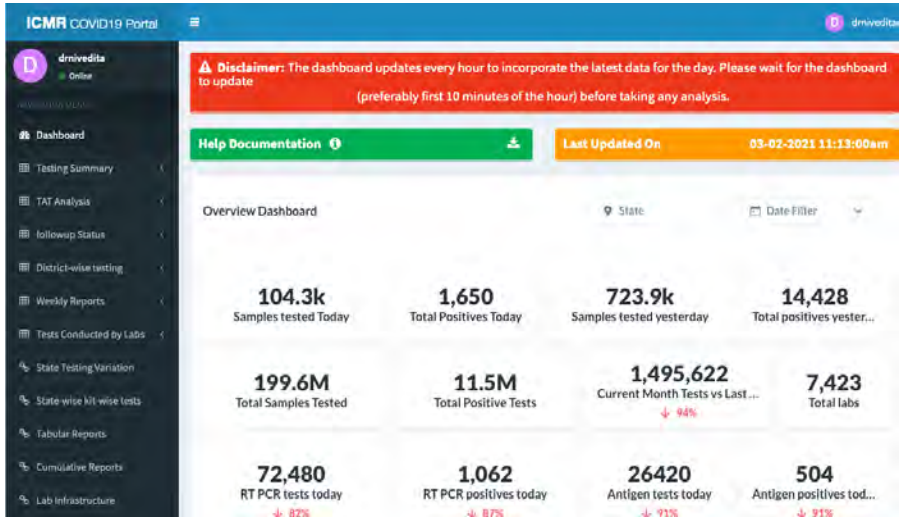
To enable information on stock-out status, lab requirements & suggestive dispatch quantities: ***Launched in April 2020***

20 ICMR depots for seamless distribution of testing commodities

CV Analytics: Testing Data Portal

Dashboard

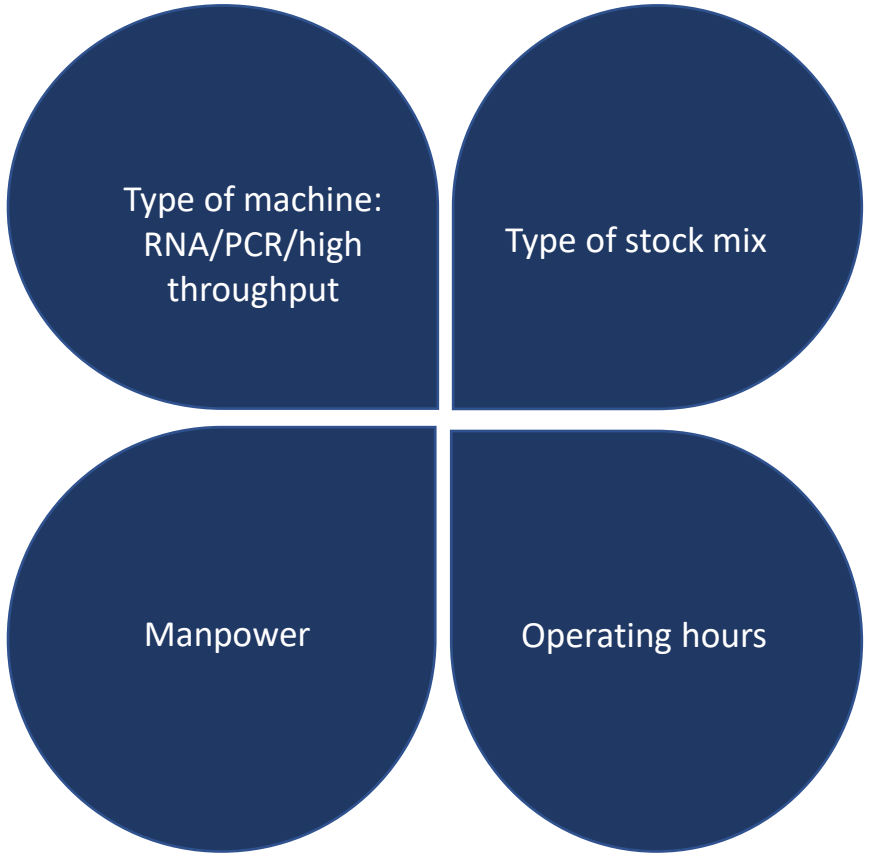




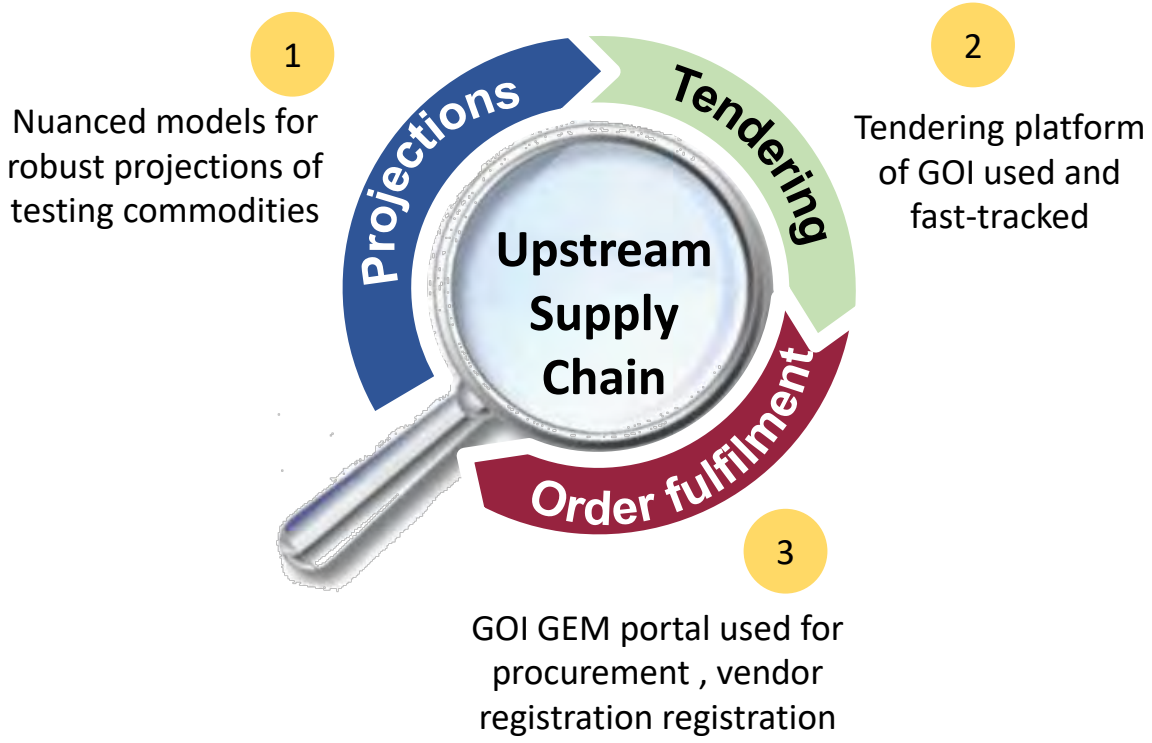
- One of the largest testing database in the world
- Hosted by ICMR

Capacity Assessment: Matching Procurements

Capacity Assessment



Streamlining procurement process



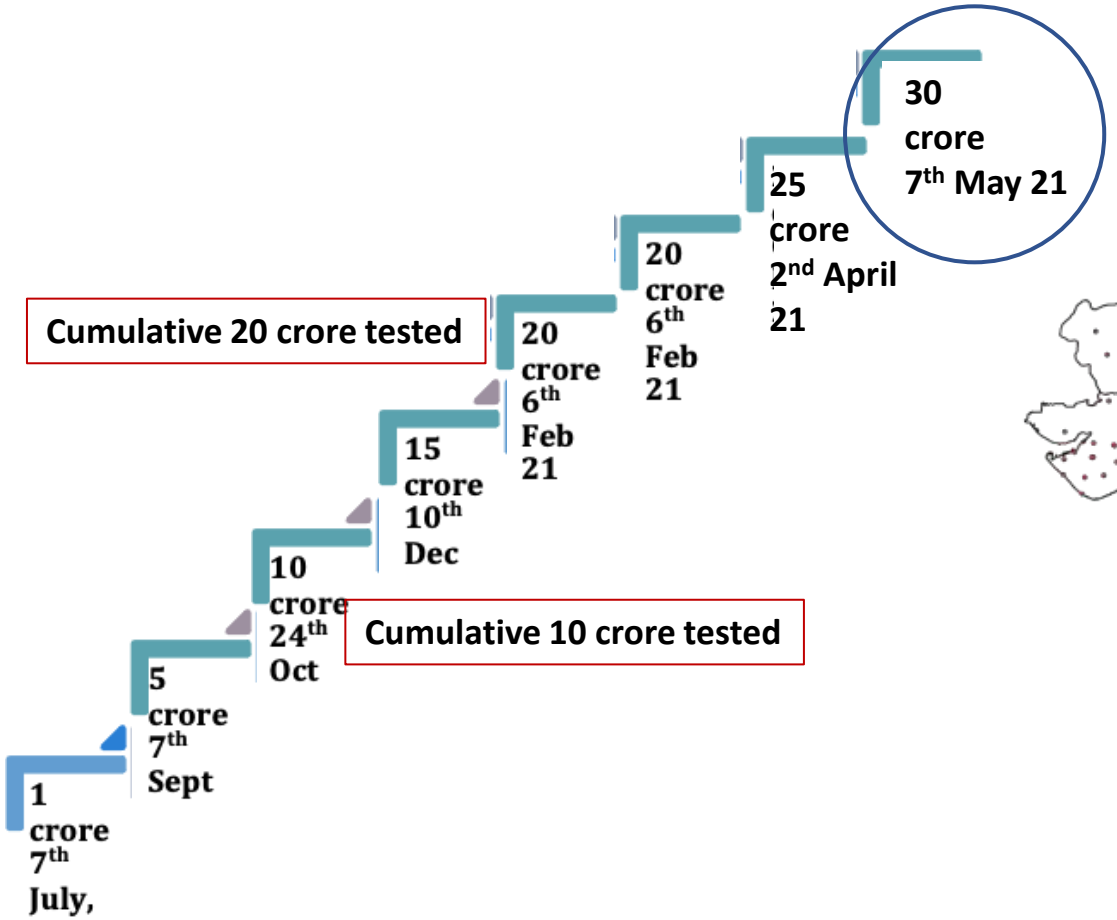
Indian J Med Res. 2020 Feb & Mar;151(2 & 3):210-215

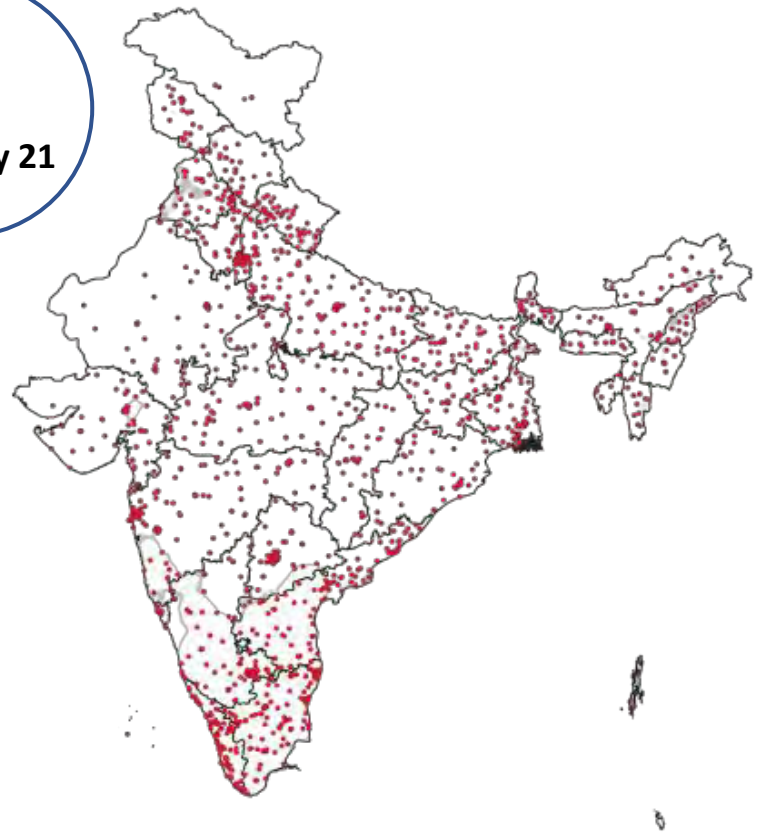
COVID-19 Testing Network

2589 COVID-19 Govt & Private Molecular Testing Labs

>7000 RTPCR and >3800 TrueNat & CBNAAT machines

12 high throughput COBAS 6600/8800 machines





Testing

Second Wave

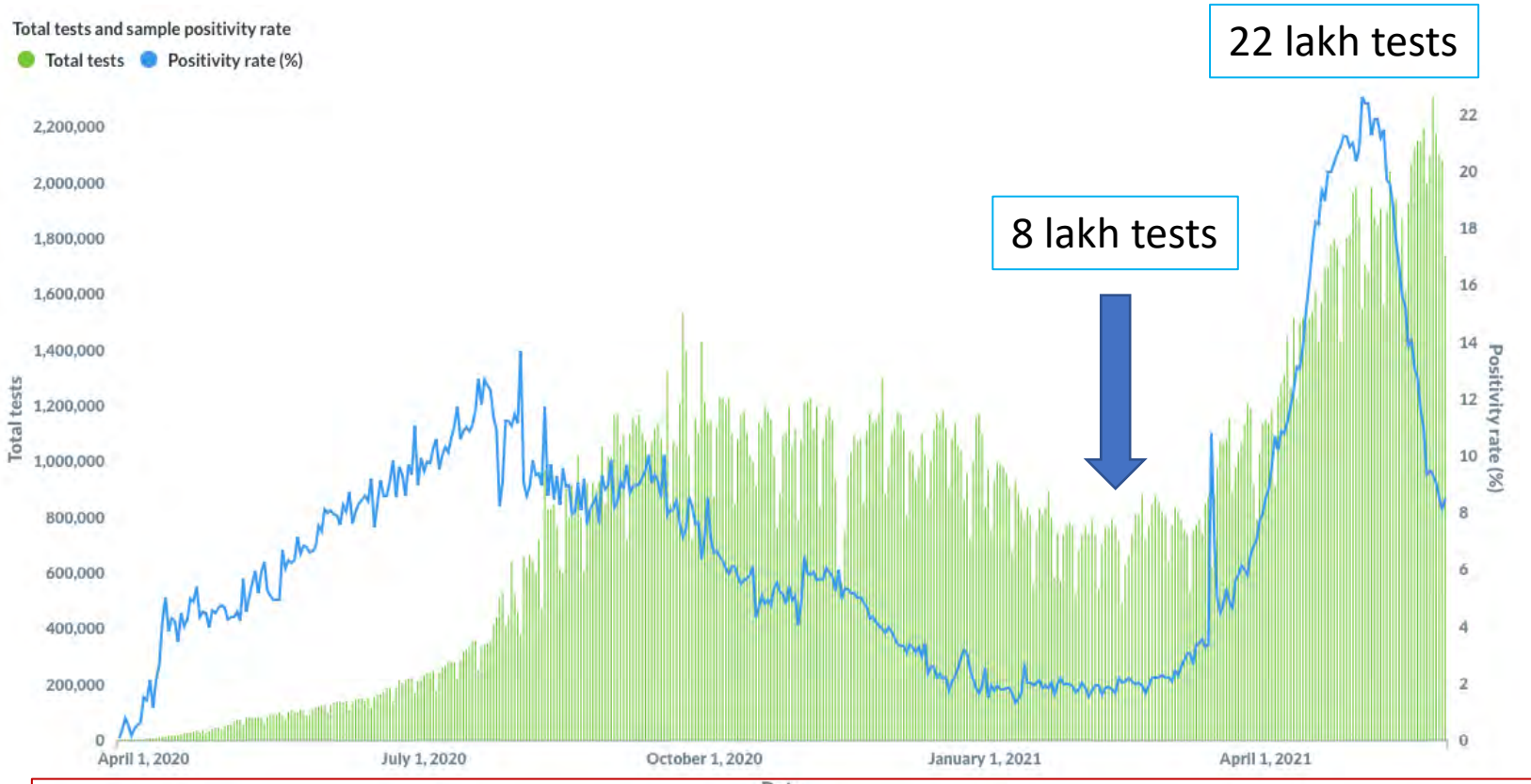
COVID-19 Testing: Challenges

- India facing a massive upsurge in COVID-19 cases
- Weekly (May 22-28) test positivity rate is 9.3%
- Early testing, isolation and home-based care key to control transmission

- RTPCR testing capacity ~12-13 lakhs/day
- RAT testing capacity also ~17 lakhs/day
- Laboratories working 24X7 to meet the increased testing demand

- *Despite infection among laboratory staff test performance still maintained*

COVID-19 Testing & Positivity Rates



May 2021: Total tests / day: 19-22 lakhs (11.5 lakh RTPCR + 10.5 lakh RAT)

May 19, 2021: 22,17,320 (Highest ever in the world)

ICMR: Testing in Second Wave

- Rationalize RTPCR tests
- Increase RAT testing for early detection, isolation and home care
- COVID-19 tests approved by reputed global agencies accorded marketing permission by DCGI
- Home testing

Testing During Second Wave

PHASE I: Large cities / Urban areas

RT-PCR is the standard test

RT-PCR

PHASE II: District Level

Molecular assays with short turn-around-time

TrueNat

CBNAAT

Abbott machines

PHASE III: Field Level / Rural areas

Rapid Antigen tests to increase access & availability

Antigen Tests

 # Important to upscale field testing to detect cases early & isolate them to reduce transmission

Second Wave: Increase RAT Testing

- Multiple 24X7 RAT booths to be set up in cities, towns and villages
- RATs to be allowed at all government and private health care facilities (**No accreditation required)**

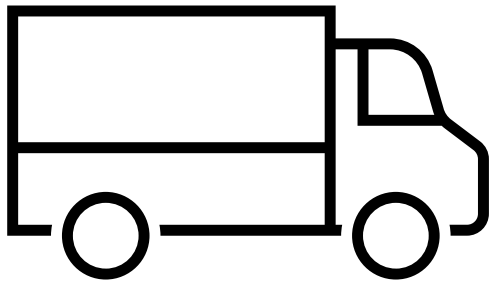
- RAT booths to be set up with the community in schools, colleges, community centers, RWA offices etc
- All RTPCR and RAT test results should be uploaded on ICMR portal

- Social distancing norms to be ensured at all RAT & RTPCR testing centers

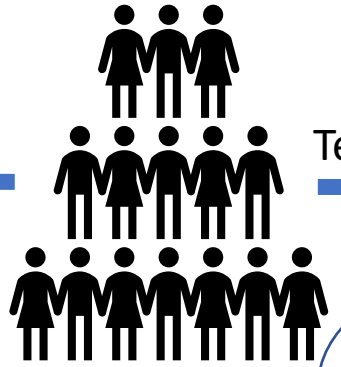
Augmenting Testing in Rural India

- **One mobile testing van /10 villages**
- **Testing modality: RAT**

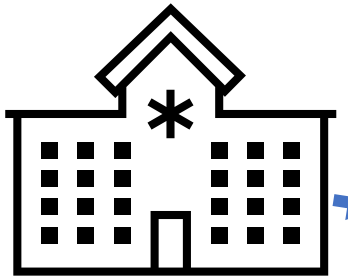
- **Testing at PHCs/CHCs/subcenters (N=1,87,601)**
- **Testing modality: RAT + Primary COVID care**



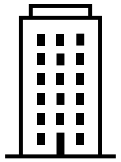
Testing option 1



Testing option 2



Symptomatic:
Collect sample for testing at nearest RTPCR facility

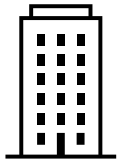


Test -
Link with

Test +
Link with

Jan Aushadhi Kendra

Symptomatic
Collect sample for testing at nearest RTPCR facility



Data Capture Modalities into ICMR portal to be ensured

Home Testing

1
Buy test kit from Chemist shop

2
- Download mobile app
- Register
- Read user manual

- Ensured patient confidentiality
- Data stored in secure server
- Linked with ICMR database

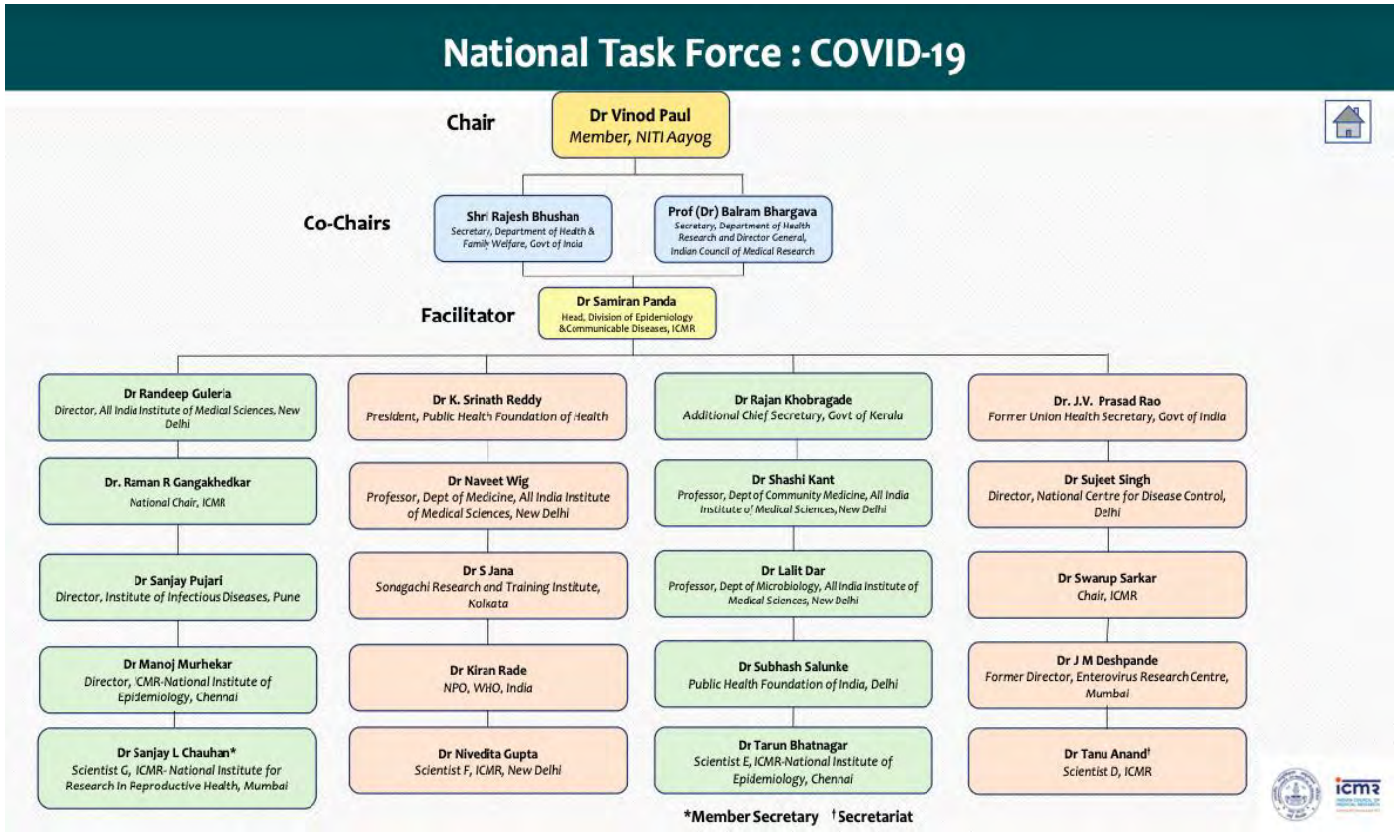
3
Conduct the test

4
- Click mobile image and upload
- Mobile phone gives test result

Research

National Task Force on COVID-19

Notified 18th March 2020



Calibration: of testing strategy

Advise: Govt. on lockdown & containment strategies

Develop: Advisories: Discharge policy etc.

Provide: Oversight for all ongoing research

Recommend: Required clinical trials (drug/vaccine)

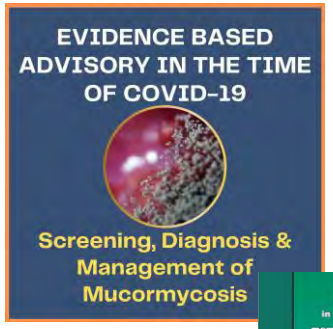
Explore: Newer, re-purposed treatment options

Develop: Clinical Management Protocols

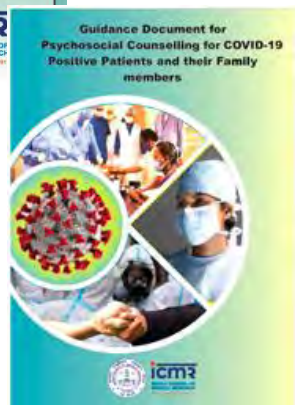
Research/Guidelines /Advisories

Letters to States/ Stakeholders

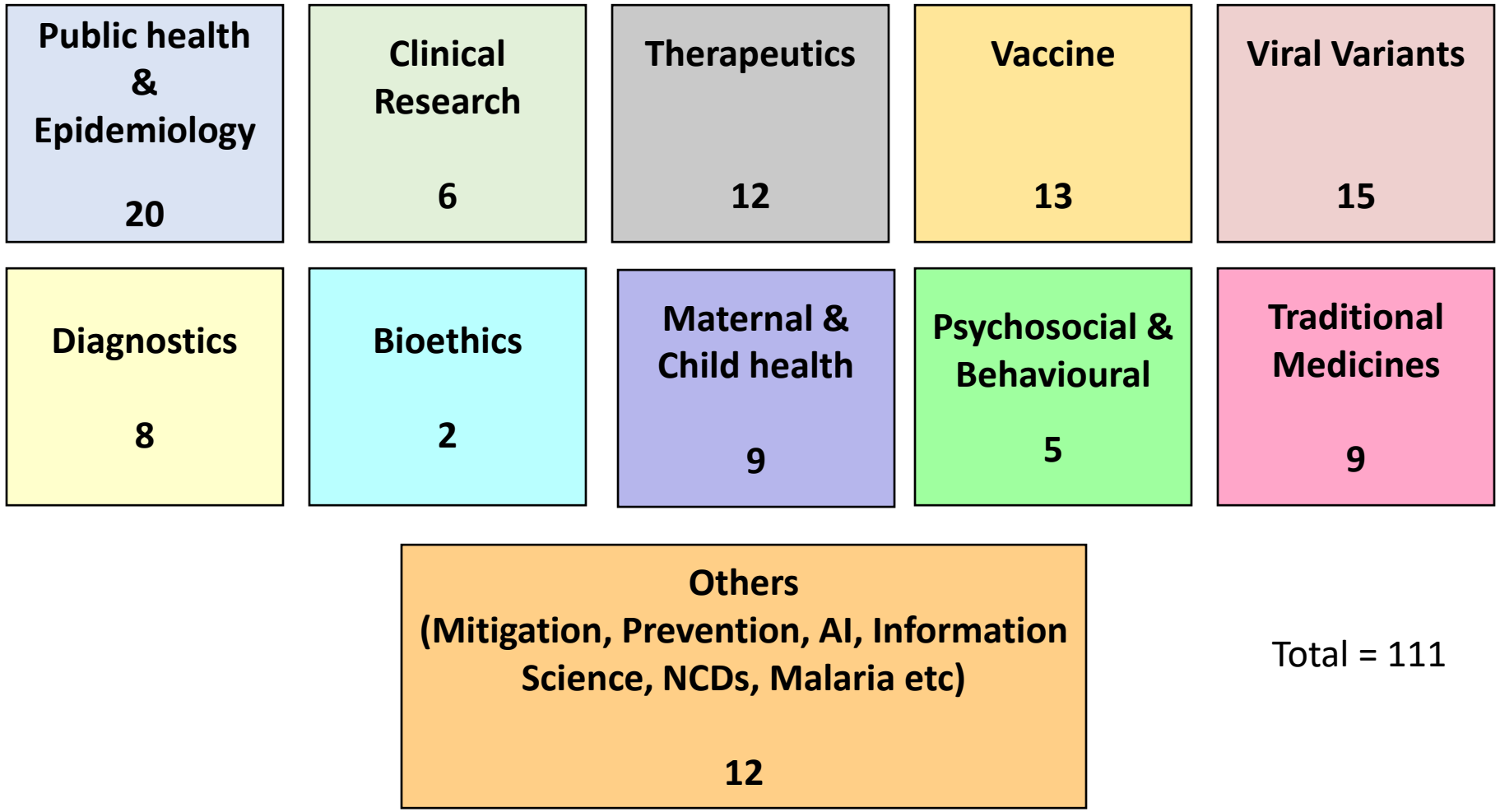
Press Briefing



Advisories on ICMR website



ICMR's Global Scientific Publications

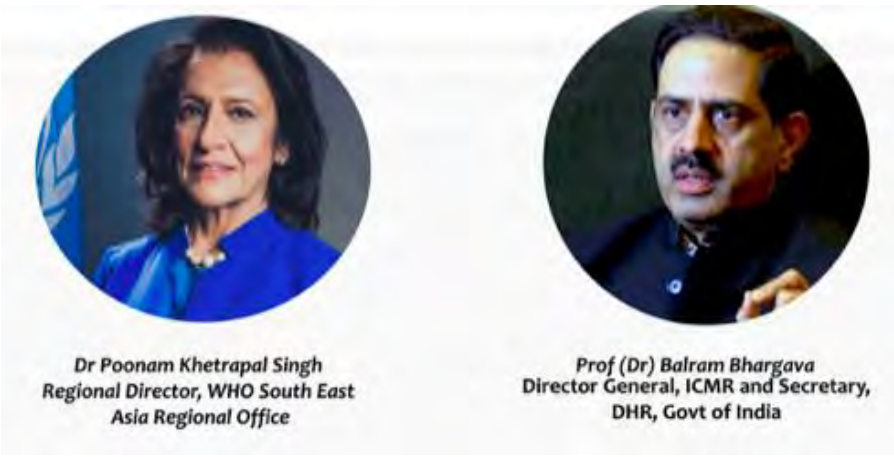


Total = 111

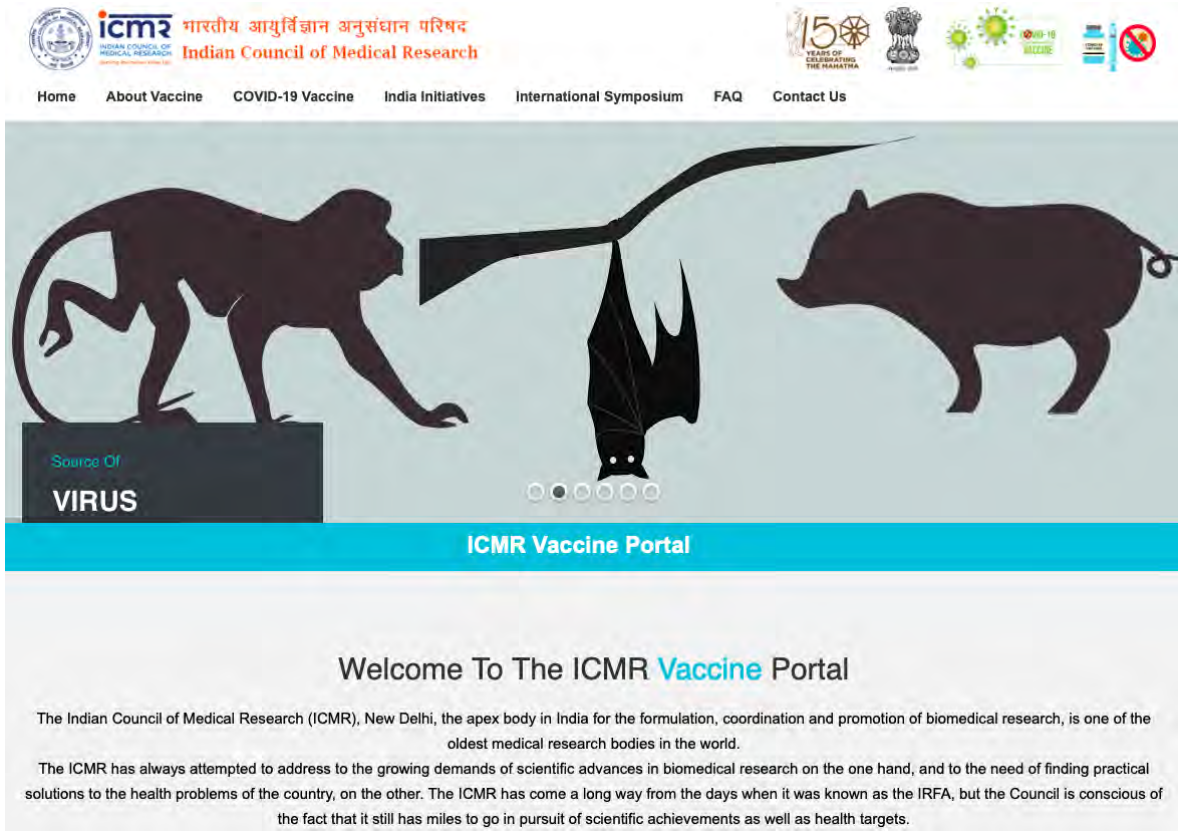
International Symposium

Science and Ethics of Vaccines

July 30, 2020



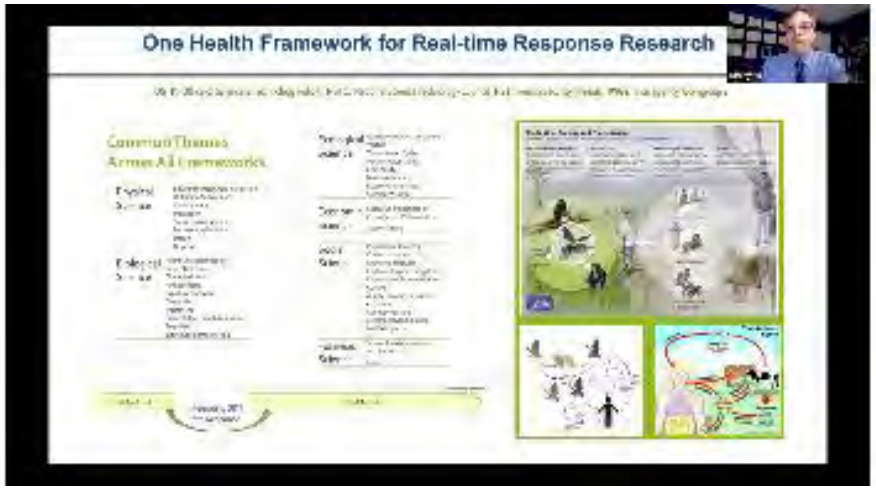
Vaccine Portal of India



https://vaccine.icmr.org.in

International Symposium on One Health

April 12, 2021

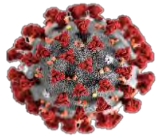


Discussion on research informing biosafety, preparedness and response

Therapeutics

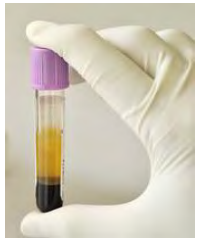
Equine Hyperimmune Globulin

ICMR-NIV, Pune & Biological Evans/Serum Institute of India/CRI Kasauli

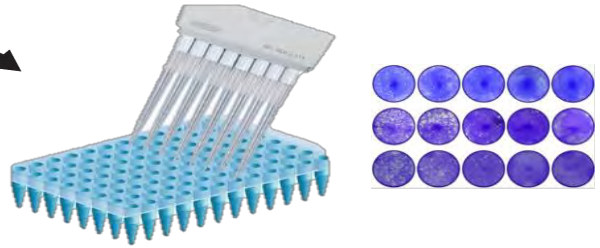


SARS-CoV-2 Inactivated whole antigen

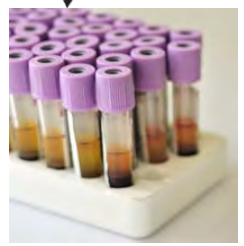
Horse inoculation



Collection of plasma after 21 days



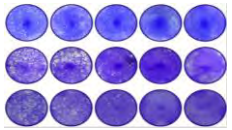
Testing for presence of antibodies by PRNT and ELISA



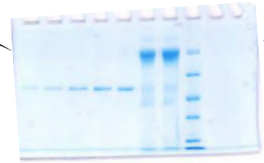
Pooling of plasma for purification

Purification of IgG antibodies

Pepsin digestion for purification of F(ab')2 fragments



Antibody titration of purified bulk samples by PRNT



Purity check of antiserum by SDS-PAGE

Anti-serum for SARS-CoV-2

Next steps:

- Preclinical studies
- Human studies

Immunotherapy, Vol.7 Iss.2 No:1000172

Human Monoclonal Antibodies

ICMR (HQ/NIMR/NIV)
Funding/Technical/Field Support

** ICGEB*
Implementing site

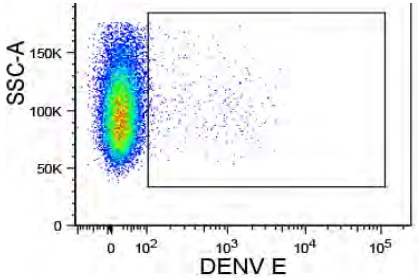
EMORY VACCINE CENTRE(USA)
Technical support/ Antibody characterization

DBT
Technical Support

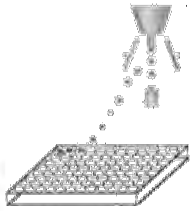
1. Samples (May) from 42 Exposed/Recovered Individual

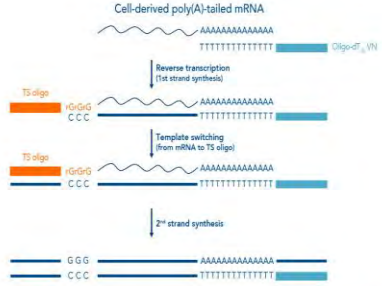
2. Isolation of PBMCs

3. Ag-specific memory B cell single cell sorting

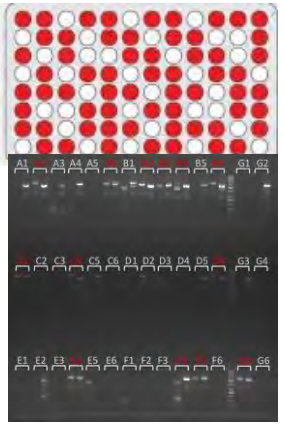


4. cDNA synthesis followed by 5' RACE and antibody gene amplification

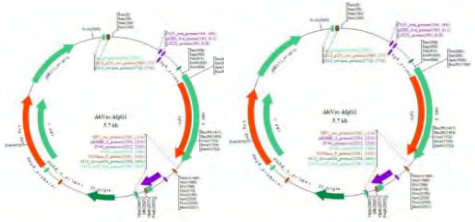




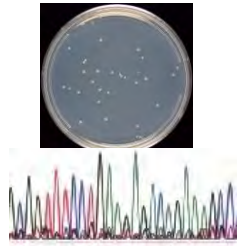
5. High throughput Ab cloning



6. Co-transformation Heavy chain and Light chain vectors

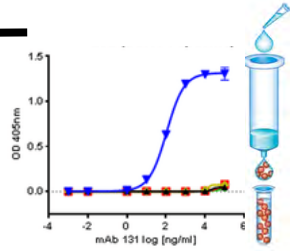


7. Colony PCR & sequencing



8. Co-transfection for mAbs expression

9. mAbs purification, Analysis of specificity



10. Neutralizing potential & affinity analysis

Steps 1-10
Work Completed

Next Steps:
- 3D structural analysis
- Final formulation for delivery
- Technology Transfer
- Preclinical testing
- Commercial manufacture
- Clinical Trials

Protocol adopted from Emory Vaccine Center (Rafi Ahmed, Murali Kaja, Carl Davis) Optimized protocol

Convalescent Plasma: (PLACID Trial)

39 public/private hospitals

Inclusion criteria:
- **Adults ≥18 years of age with confirmed moderate COVID-19**
- **PaO_2 /FiO_2: 200 - 300 mm Hg;**
- **Respiratory rate > 24/min;**
- **O_2 saturation ⩽93%.**

22 April to 14 July 2020
During lockdown

Total number of patients ***(n=464)***

Intervention with convalescent plasma

Interventional arm *(n=235)*
2 doses of convalescent plasma (200 ml in each dose) and best standard of care

Control arm *(n=229)*
Best standard of care

Results: Outcome at 28 days of enrolment

19% progressed to severe disease/all cause mortality (n=44)

18% progressed to severe disease/all cause mortality (n=41)

risk difference 0.008 (95% confidence interval −0.062 to 0.078); risk ratio 1.04, 95% confidence interval 0.71-1.54

Convalescent plasma did not lead to reduction in progression to severe covid-19 or all cause mortality

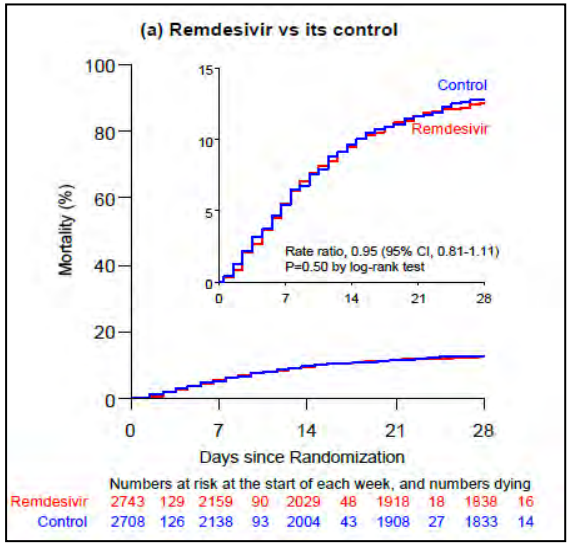
BMJ. 2020 Oct 22;371:m3939

WHO SOLIDARITY Trial

- Multi-country, RCT, Adaptive design, Remdesivir and Interferon
- Globally: 30 countries, 405 hospitals, 14,029 randomized
- In India: ICMR-NARI, April 2020, 26 hospitals, 1,048 adults

- Interim Analysis: (n=11,266)

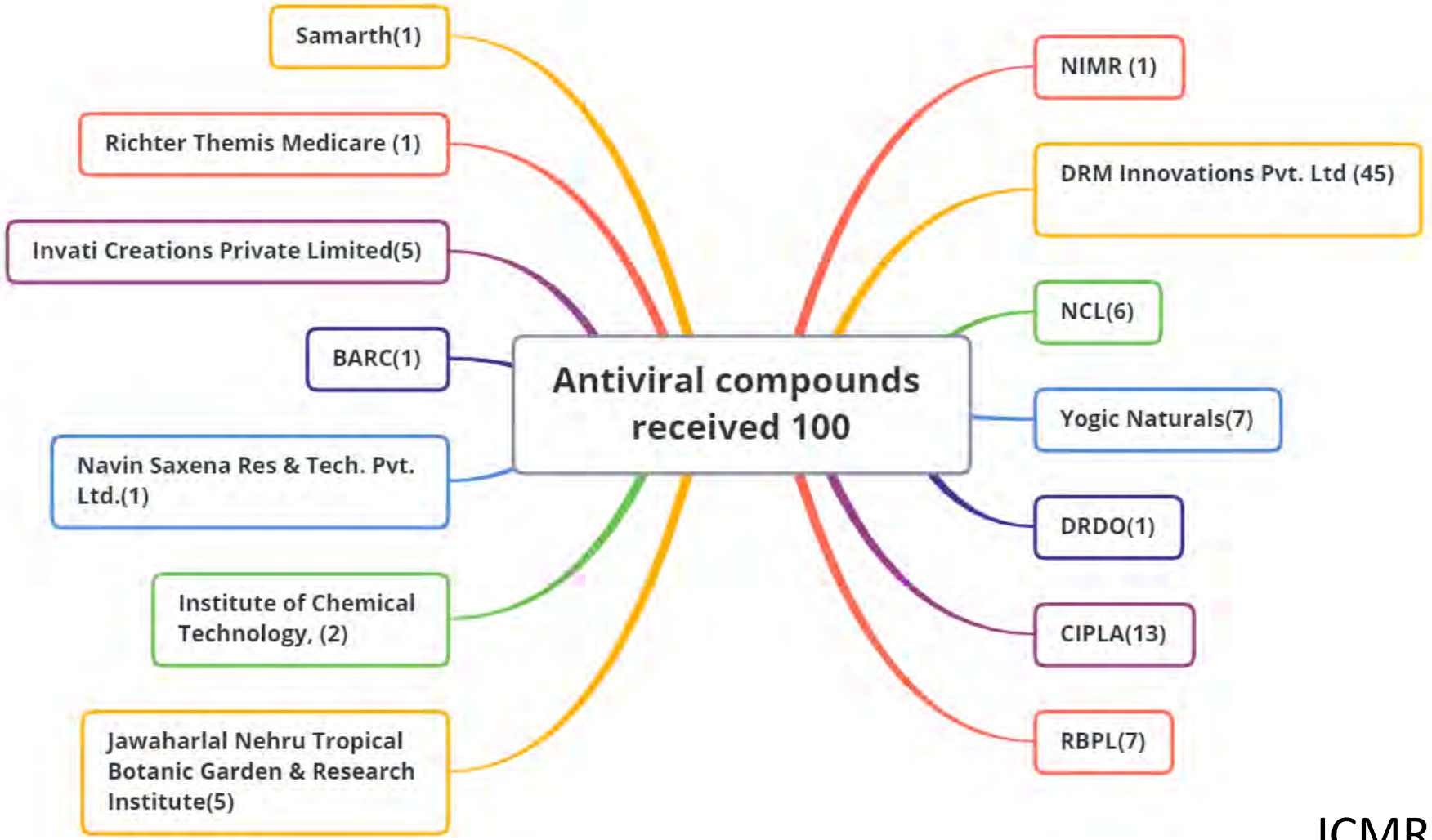
  Remdesivir, Hydroxychloroquine, Lopinavir and Interferon - little or no effect on *overall mortality, initiation of ventilation and duration of hospital stay*



NEJM; 2021; 384:497-511 DOI:10.1056/NEJMoa202318

Screening Antiviral Property

Natural/Synthetic Compounds & Repurposed Drugs



Clinical Studies

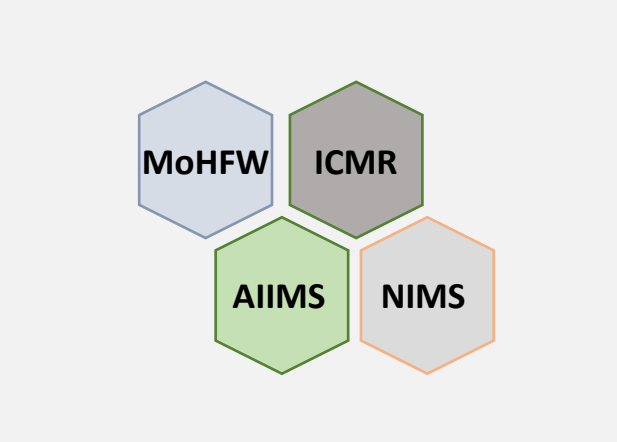
National COVID-19 Clinical Registry

Ministry of Health & Family Welfare

ICMR INDIAN COUNCIL OF MEDICAL RESEARCH

Department of Medicine (AIIMS Delhi)

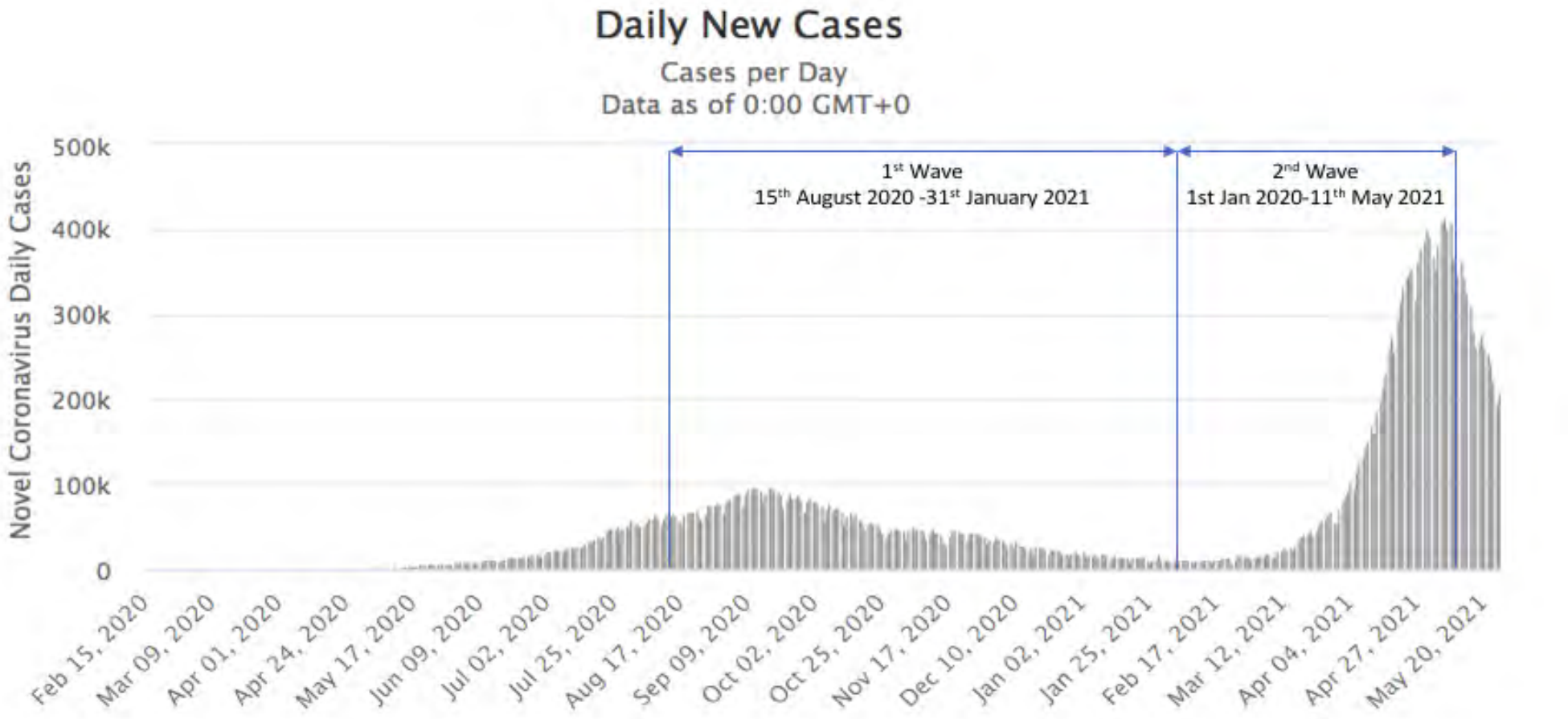
ICMR INDIAN COUNCIL OF MEDICAL RESEARCH NIMS



http://icmrcovidregistry.nic.in/

2nd Wave: What Has Changed?

Data available for hospitalized patients from 40 hospitals across the country from 1 Sep 2020 to 11 May 2021

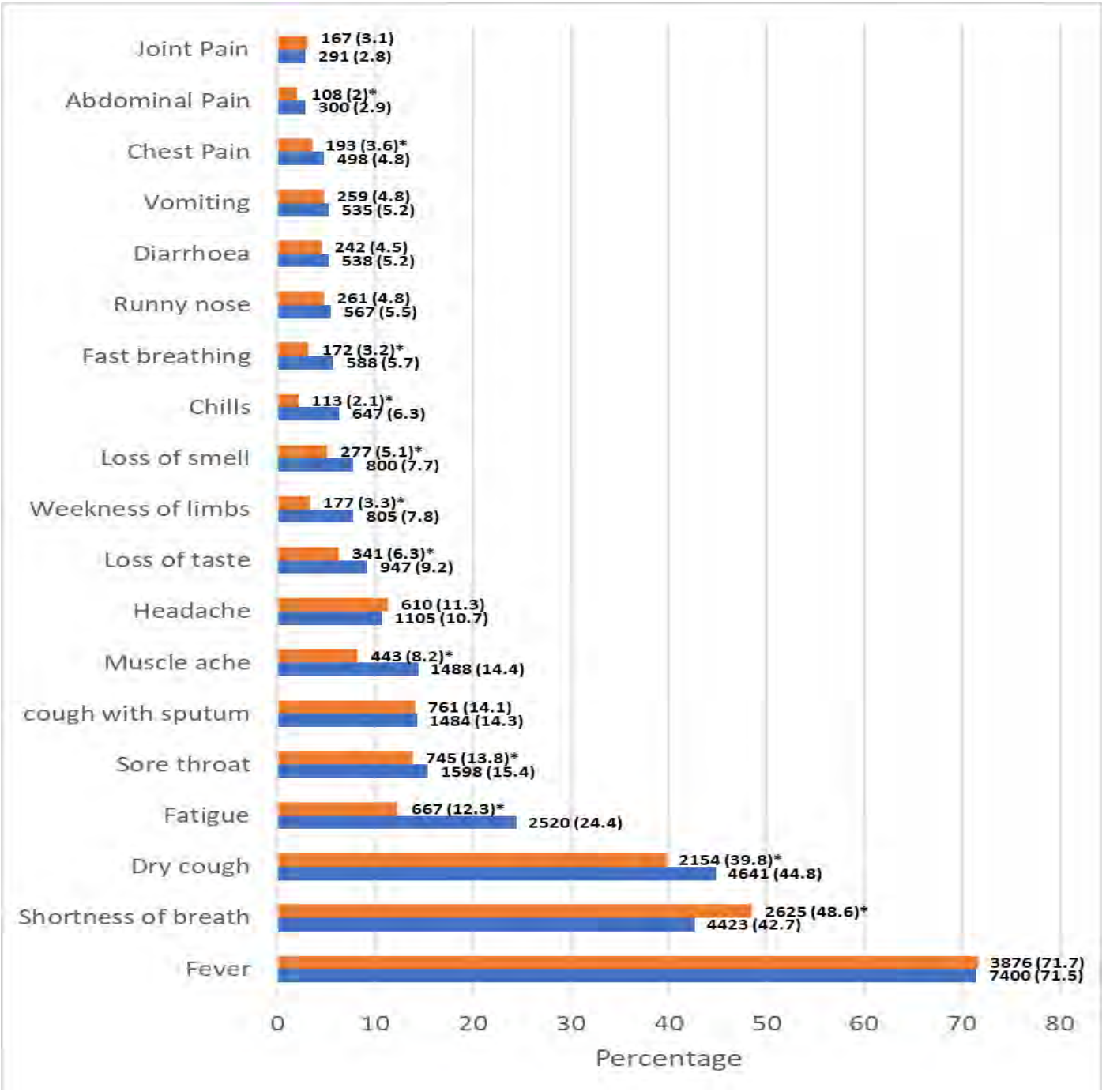


Source: https://www.worldometers.info/coronavirus/country/india/

(Note: Worldometer sources the number of COVID-19 cases, as provided by the state bulletins)

1st Vs 2nd Wave N=18,985

	2nd Wave n=6903 1 Feb to 11 May 2021	1st Wave n=12082 1 Sep 2020 to 31 Jan 2021	P
Age in years, Mean (SD)	48.7 (18.1%)	50.6 (18.0%)	<0.001
Age categories 0-19 years (n=763) 20-39 years (n=4,697) 40-60 years (n=7,691) >60 years (n=5,843)	 304 (4.4%) 1,829 (26.5%) 2,853 (41.3%) 1,917 (27.8%)	 459 (3.8%) 2,868 (23.7%) 4,838 (40%) 3,917 (32.4%)	 <0.001
Male (n=12,302)	4,401 (63.8%)	7,901 (65.4%)	0.02
Days: Symptom onset to admission, median (IQR)	3 (1,5)	4 (2,6)	<0.001
One or more comorbidities (n= 9,925)	3,171 (47.4%)	6,754 (56.2%)	<0.001
Symptomatic (n=15,756)	10,351 (85.7%)	5,405 (78.3%)	<0.01



Presenting complaints in patients of 1st (n=10351) *vs.* 2nd wave (n=5405)

*Statistically significant comparisons
Data labels are n(%)

1st Vs 2nd Wave N=14,448

	2nd Wave n=3,259	1st Wave n=11,189	P
Requiring supplemental oxygen, n(%)	1,638 (50.3 %)	4,777 (43.2%)	<0.001
Requiring mechanical ventilation n(%)	260 (15.9%)	530 (11.1%)	<0.001
Duration of hospital stay in days, median (IQR)	6 (4,9)	7 (5,10)	<0.001

1st Vs 2nd Wave

70% of admitted patients ≥ 40 years of age in both waves

There were some increase patients in younger age groups

- 0-19 years (3.8% to 4.4%),
- 20-39 years (23.7% to 26.5%)

In 2nd wave

- Lower proportion of admitted patients had comorbidities
- Higher proportion had shortness of breath
- Higher proportion developed ARDS
- Higher proportion required oxygen & subsequently mechanical ventilation

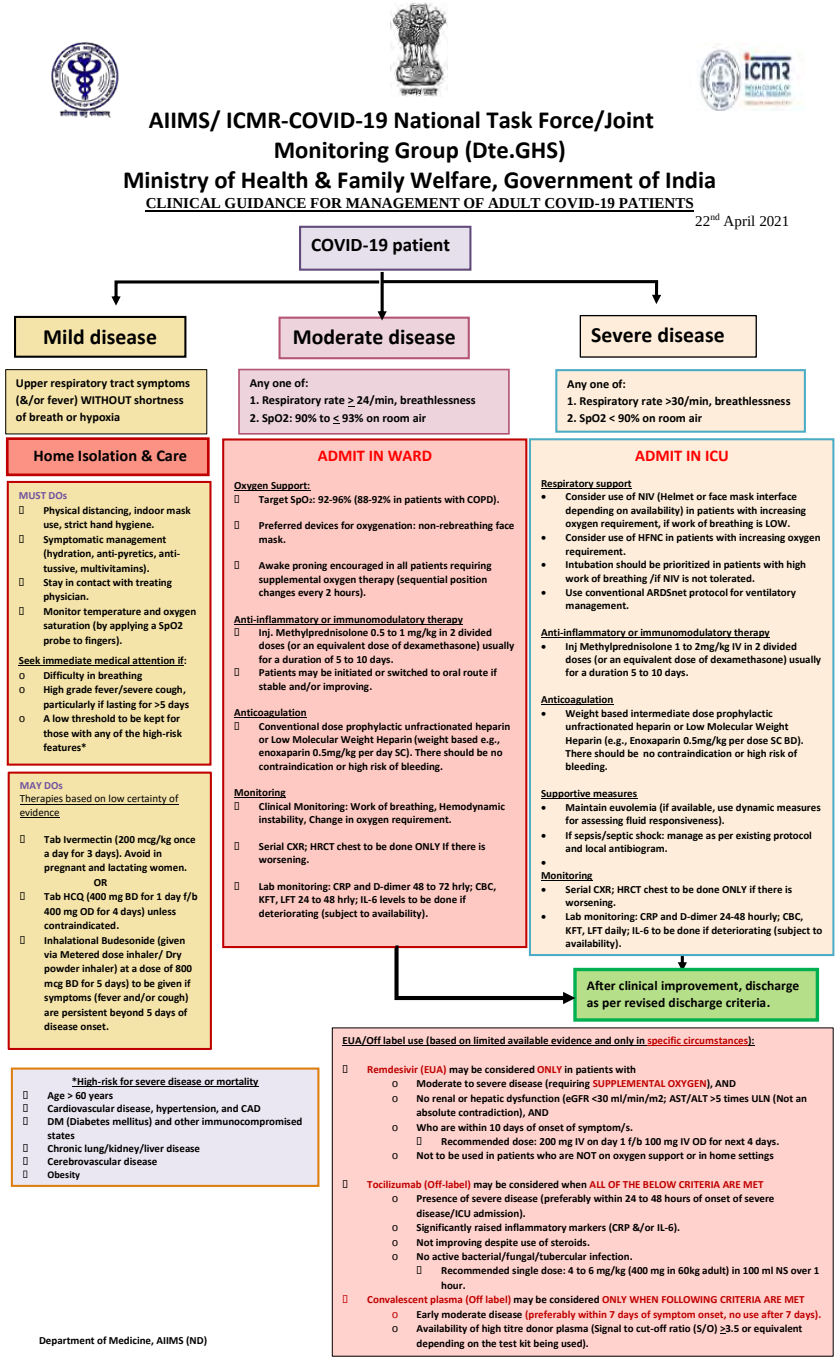
In 2nd wave, mortality in admitted patients was higher (13.3% vs.10.2%)

- Mortality higher in 2nd wave in all age groups except 0-19 years
- Mortality in younger age group lower than the >60 years age group

Outreach

Management Protocol

National Task Force



HOME CARE FOR COVID-19

SUSPECT COVID-19
(If you have any one of the following)


Fever


Cough


Headache


Sore throat


Breathlessness


Bodyache


Recent Loss of smell


Recent Loss of taste

WHILE CARING FOR SELF
- Get COVID19 test
- Consult your doctor for admission if oxygen saturation below 93%
- Blood tests to be decided as needed by your doctor

DOs


Stay home


Sanitize hands


Isolate & take rest


All family members should wear mask


Cross-ventilation in rooms – open windows

Monitor


Body temperature


Oxygen saturation (by Oxymeter)

Treatment


Drink water, pulses, juice, coconut water etc.


Lie on your chest and breathe deeply to improve oxygenation


Paracetamol at 6 hrs interval & cough syrup if required


Multivitamins & mineral


Steam inhalation & warm water gargle thrice a day


Budesonide via Metered Dose Inhaler (MDI)/Dry Powder Inhaler (DPI) advised by treating physician– ONLY if symptoms persist beyond 5 days

DON'Ts

- ✕ Do not use oral steroid without advise of medical practitioner
- ✕ Do not use remdesivir in home care setting
- ✕ Do not use nebulizer for budesonide
- ✕ Do not use oxygen cylinder without advise of medical practitioner

Treatment not routinely advised unless indicated

1. Ivermectin
2. Hydroxychloroquine
3. Azithromycin
4. Doxycycline
5. Favipiravir
6. Remdesivir
7. Tocilizumab
8. Convalescent plasma

सत्यमेव जयते

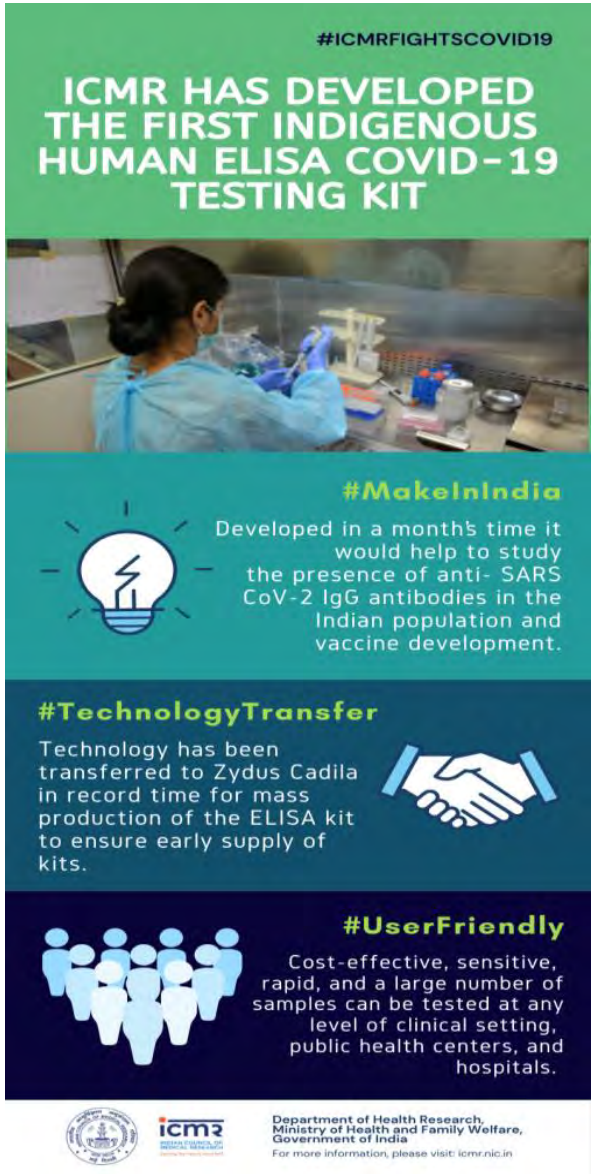
AIIMS/ ICMR-COVID-19 National Task Force/ Joint Monitoring Group

Ministry of Health and Family Welfare

Government of India

Surveillance Studies

Indigenous ELISA



- **Covid 'Kawach' Elisa**
- **Used for Serosurveys starting April 2020**
- Developed by NIV, Pune
- Technology transferred to Zydus Cadila & seven other companies
- To check presence of IgG (determine past SARS-CoV-2 exposure)

Indian J Med Res. 2020 May; 151(5):444-449

National Serosurveys

1
May/June, 2020

Age: ≥ 18 yrs

Seroprevalence: 0.73%

2
Aug/Sept, 2020

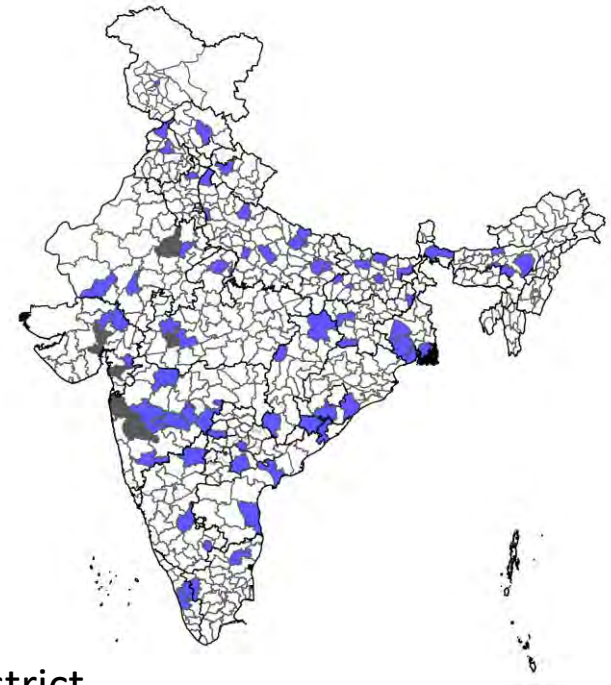
Age: ≥ 18 yrs

Seroprevalence: 7.1%

3
Dec/Jan, 2021

Age: ≥ 10 yrs + HCWs

Seroprevalence: 24.1%



- 70 districts, 700 villages/wards
- From 21 states
- Multistage cluster sampling
- 10 villages/wards from each district
- Selected based on Population Proportionate to Size (PPS)

- *Indian J Med Res; 2020 Jul & Aug;152(1 & 2):48-60*
- *Lancet Glob Health, January 27, 2021*
- *Int J Infect Dis. 2021 May 19;S1201-9712(21)00442-2*

Indian SARS-CoV-2 Genomic Consortium
(INSACOG)

Ministry of Health & Family Welfare
Government of India

NCCS Pune

NIV Pune

NIBMG Kalyani

CCMB Hyderabad

INSACOG
Central Coordination:
NCDC, MoH&FW

ILS, Bhubaneshwar

CDFD Hyderabad

InSTEM Bengaluru

IGIB Delhi

NIMHANS Bengaluru

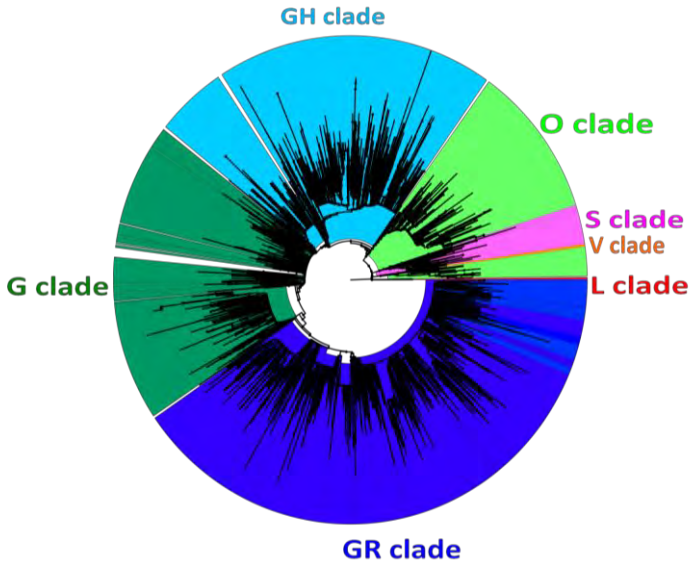
ICMR INDIAN COUNCIL OF MEDICAL RESEARCH
Serving the nation since 1911

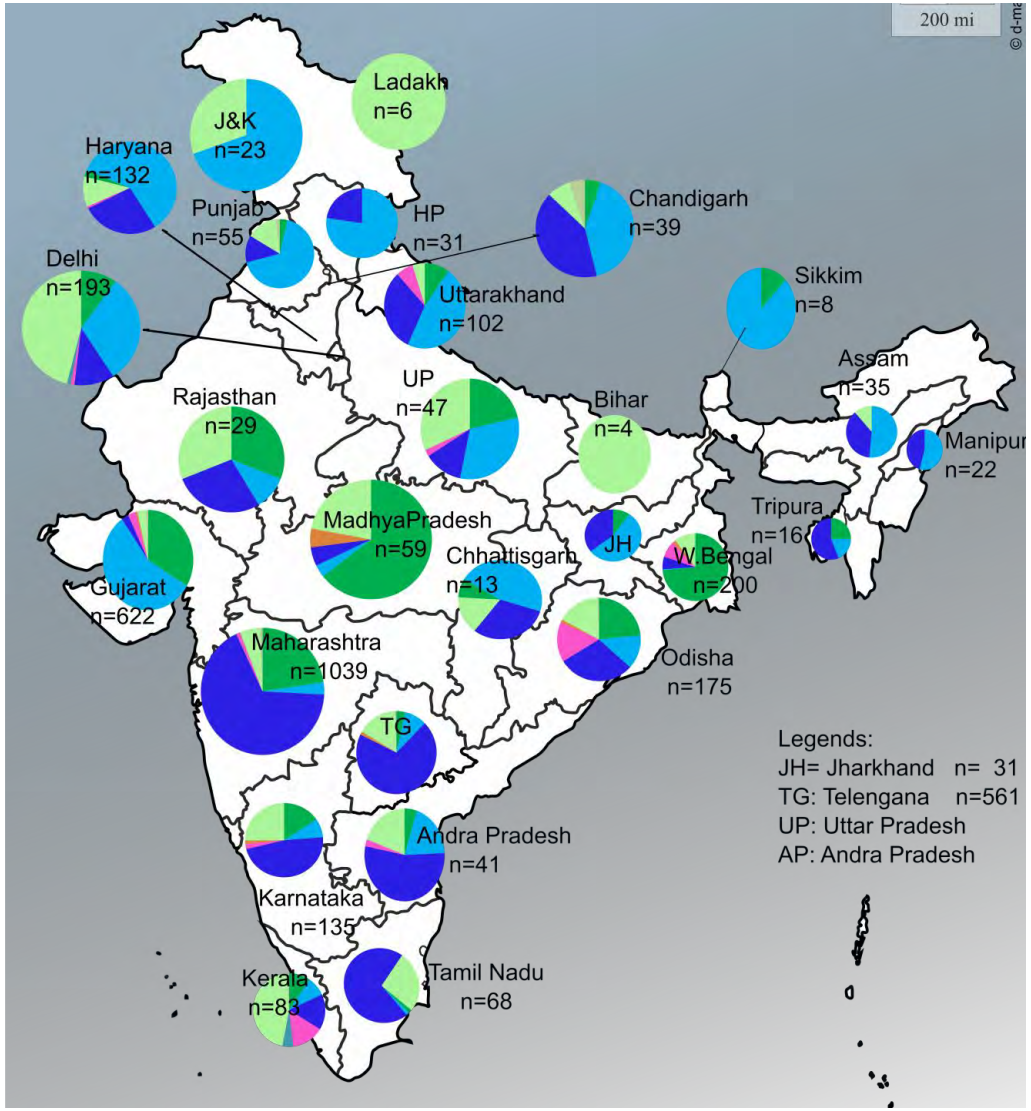
भारत सरकार GOVERNMENT OF INDIA
विज्ञान और प्रौद्योगिकी मंत्रालय MINISTRY OF SCIENCE AND TECHNOLOGY
जैवप्रौद्योगिकी विभाग
DEPARTMENT OF BIOTECHNOLOGY

- Sentinel surveillance for early detection of variants of concern of SARS-CoV-2
- Determine the circulating strains of SARS-CoV-2 in unusual events (high mortality, super-spreader)

Genetic Sequencing

GR clade (n=1513)
GH clade (n=859)
G clade (n=816)
O clade (n=477)
(unclassified)
S clade (n=102)
L clade (n=24)
V clade (n=07)
GV-GR clade (n=1)





March – August 2020

- 10 Nasal/throat swab samples/month collected from COVID-19 positive patient each state/UT
- Seven clades circulating: G, GR & GH, O; S, L&V in minimal circulation
- <1% nucleotide divergence observed among different clades

Viruses 2021, 13, 925

VOC of SARS-CoV-2

B.1.1.7 (Alpha)
Dec 2020
UK returnees
Chennai

Infection 2021 (In press)

P.1 (Gamma)
Feb 2021
UAE returnees
Mumbai

B.1.351 (Beta)
Feb 2020
SA returnees
Mumbai

Travel Medicine and Infectious Disease 41 (2021) 102023

B.1.617 (Delta)
Feb 2021
Maharashtra
Mumbai, Pune, Akola

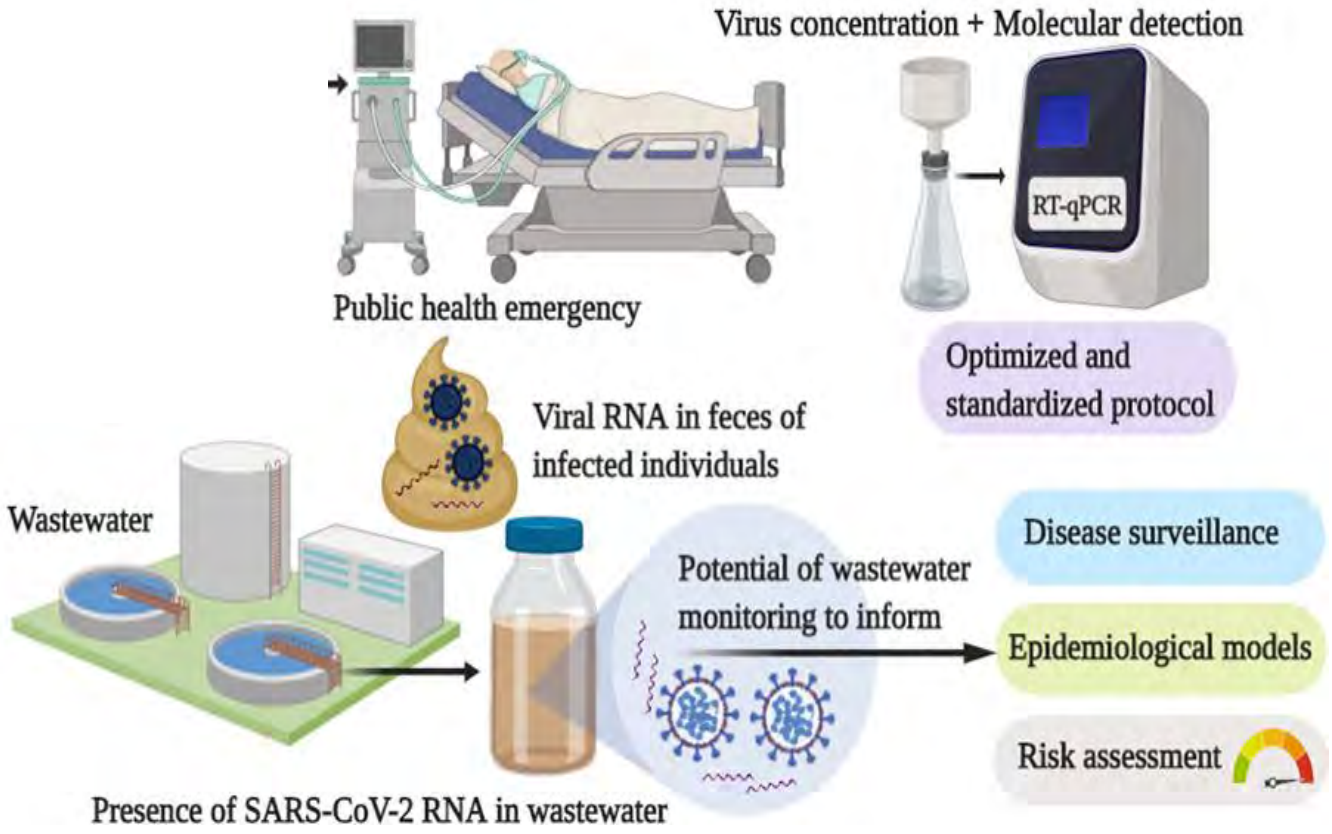
Microorganisms 2021 (In press)

Cold Spring Harbor Laboratory

bioRχiv
THE PREPRINT SERVER FOR BIOLOGY

Sewage Surveillance:

Detection of SARS-CoV-2

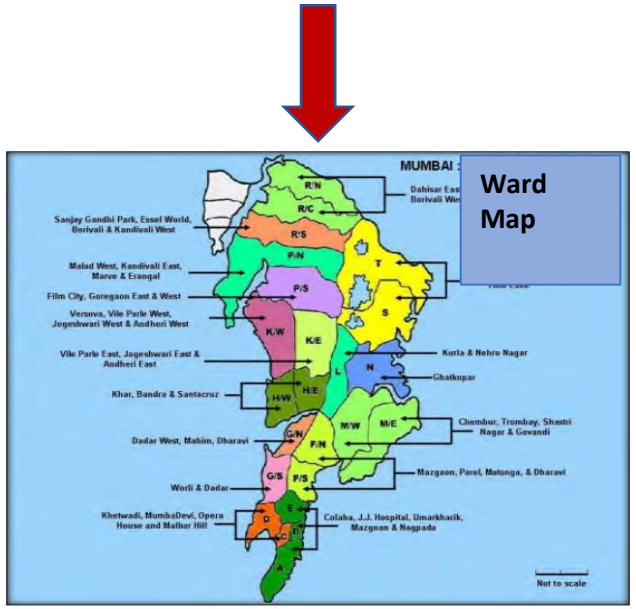


- Method for sample collection & processing standardized by ICMR-NIV, Mumbai
- Implemented at 20 sites in Mumbai
- Phased expansion with WHO-India at Polio sewage surveillance sites

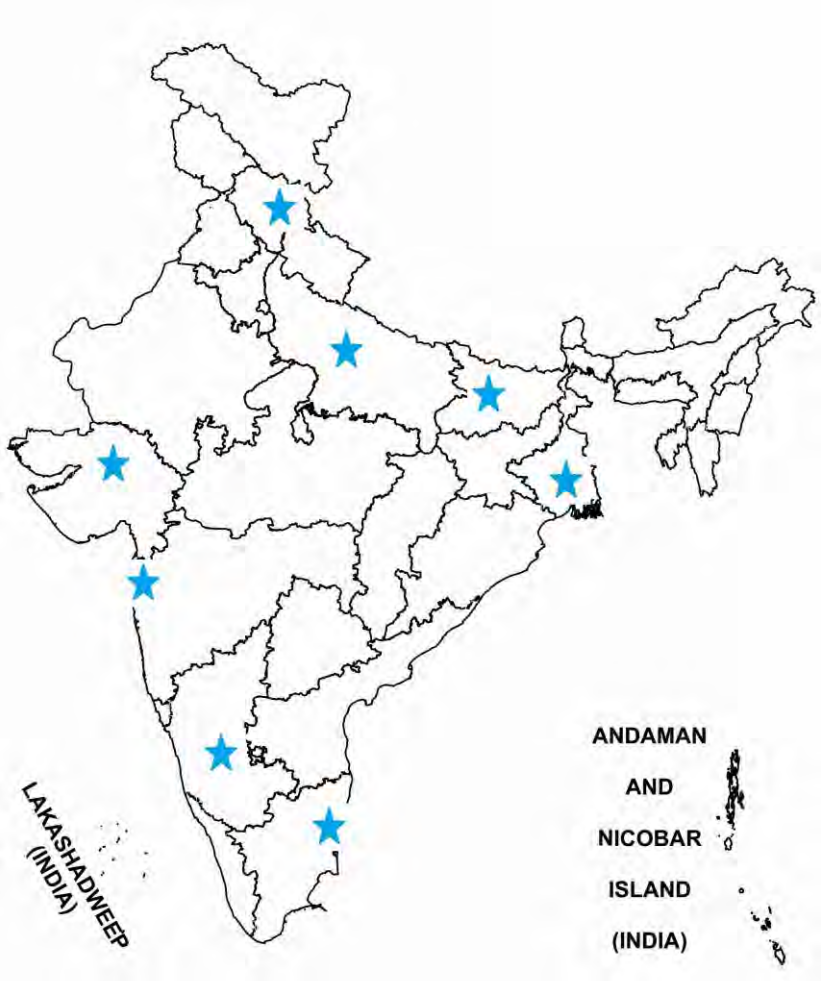
Indian J Med Res. *2020 Dec 15; doi: 10.4103/ijmr. IJMR_3541_20.*

Sewage Surveillance

Pilot study undertaken at Mumbai city in 19 wards



- Surveillance initiated at 3 Polio sewage sample collection sites
- Expansion to 9 sites (June 2021)



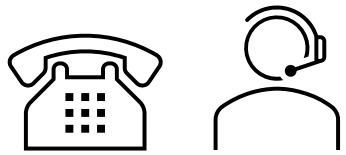
Indian J Med Res. 2020 Dec 15; doi: 10.4103/ijmr. IJMR_3541_20.

SARS-CoV-2 Re-infection

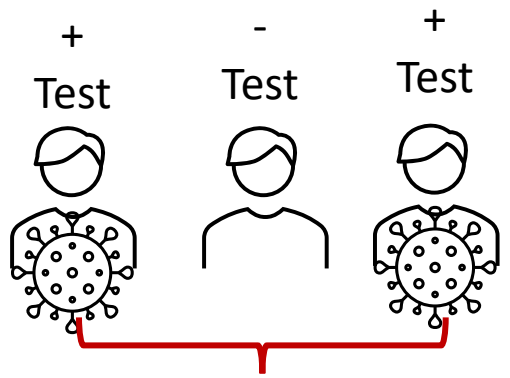
Epidemiological case definition of SARS CoV-2 re-infection and assess its magnitude in India

COVID-19 testing database

Archive based telephonic survey



Reinfection

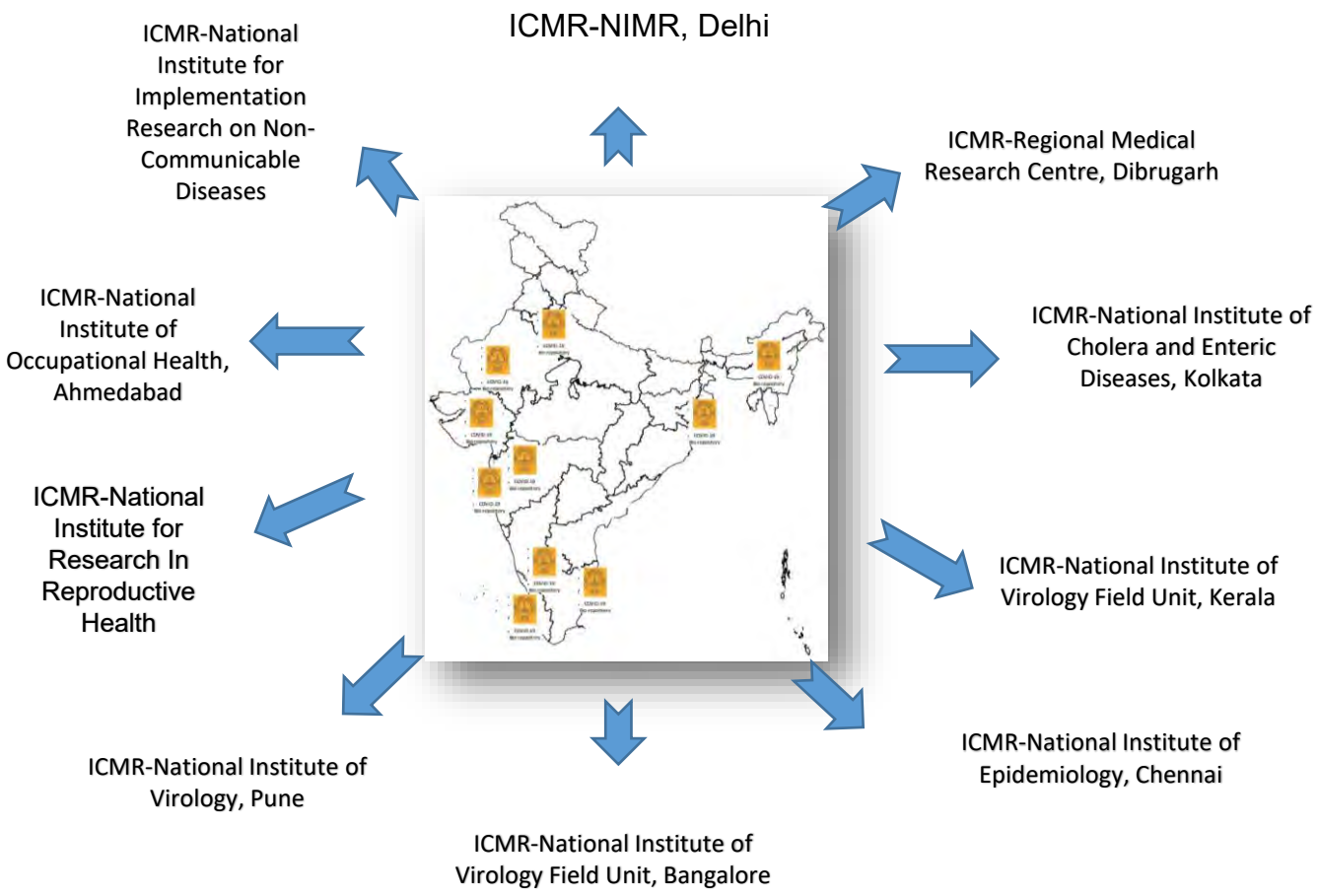


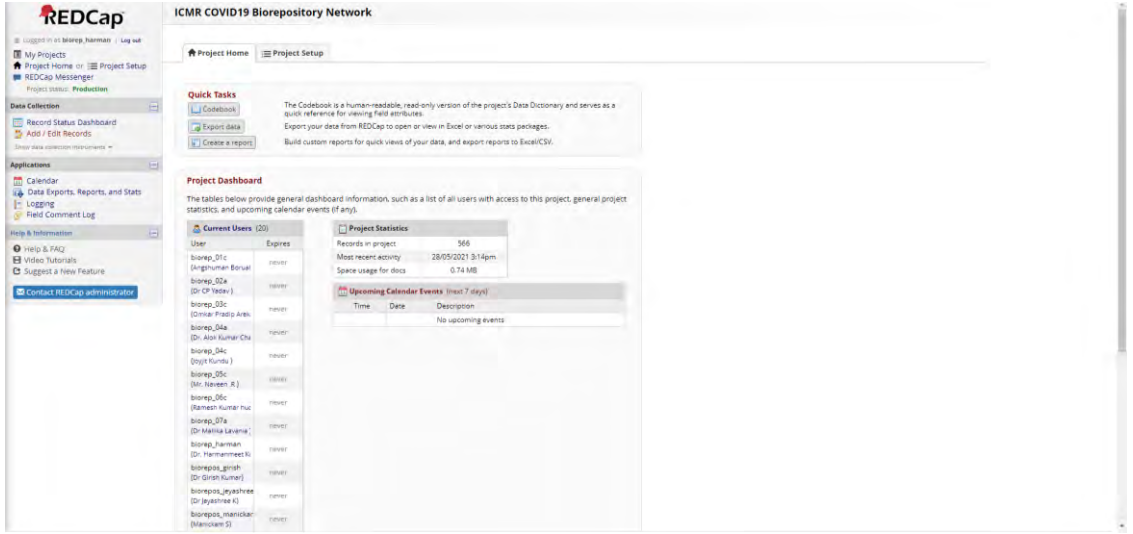
New Definition:

- Re-infection was defined when an individual tested positive on two separate occasions (by RTPCR/RAT) at least 102 days apart with one negative RTPCR test in between
- 58 out of 1,300 individuals (4.5%) were classified as reinfection cases based on the above criteria

Epidemiology & Infection; https://doi.org/10.1017/S0950268821000662

ICMR-Bio-Repositories



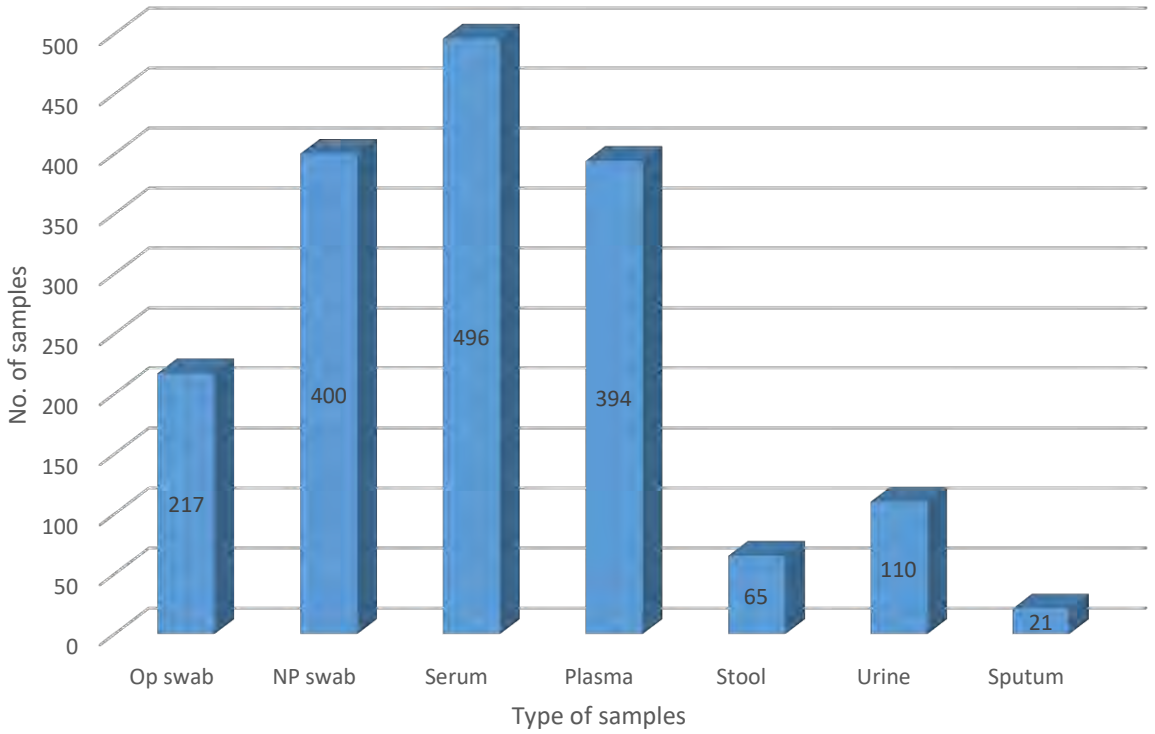


Glimpse of an online portal for collection of data

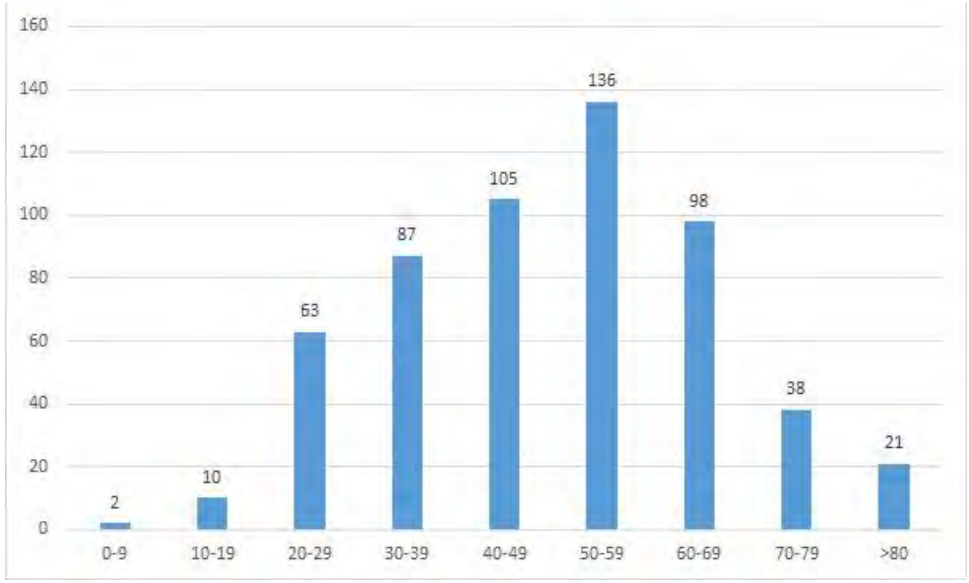
Information for the samples is collected in 3 modules:

- Module 1 to be completed on the day of enrolment for the day of admission to the hospital
- Module 2 to be completed for the days/s of sample collection
- Module 3 to be completed at discharge or death or transfer (for follow-up patients only)

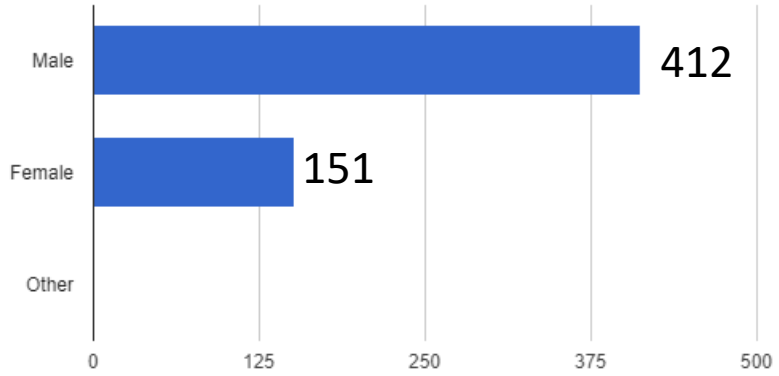
Biorepositories



Type of sample collected



Age distribution

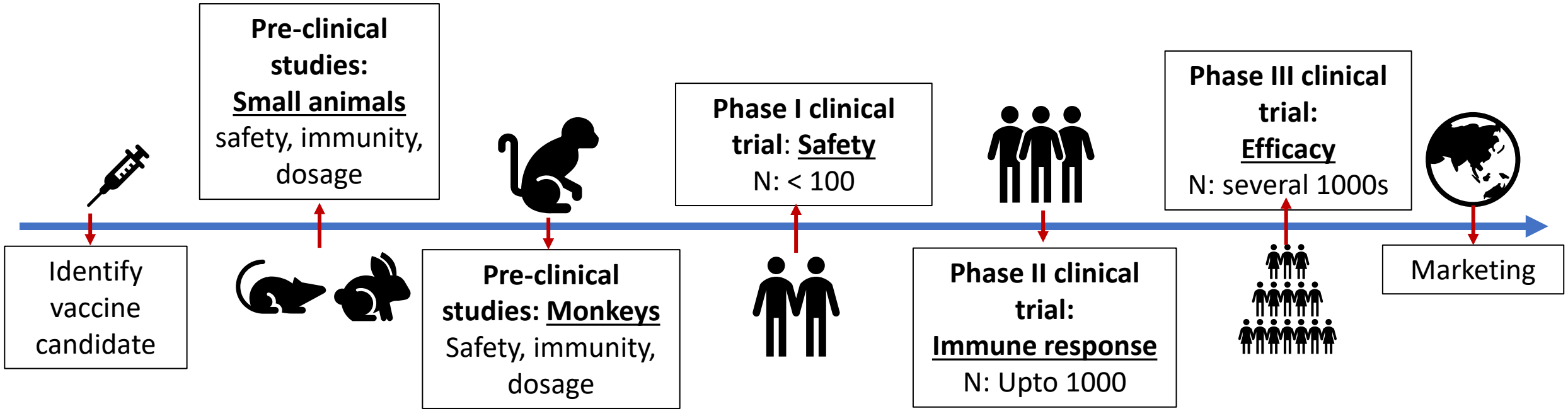


Sex distribution

- 1703 well characterized samples from 563 individuals have been collected by the network
- Comprehensive clinical information available

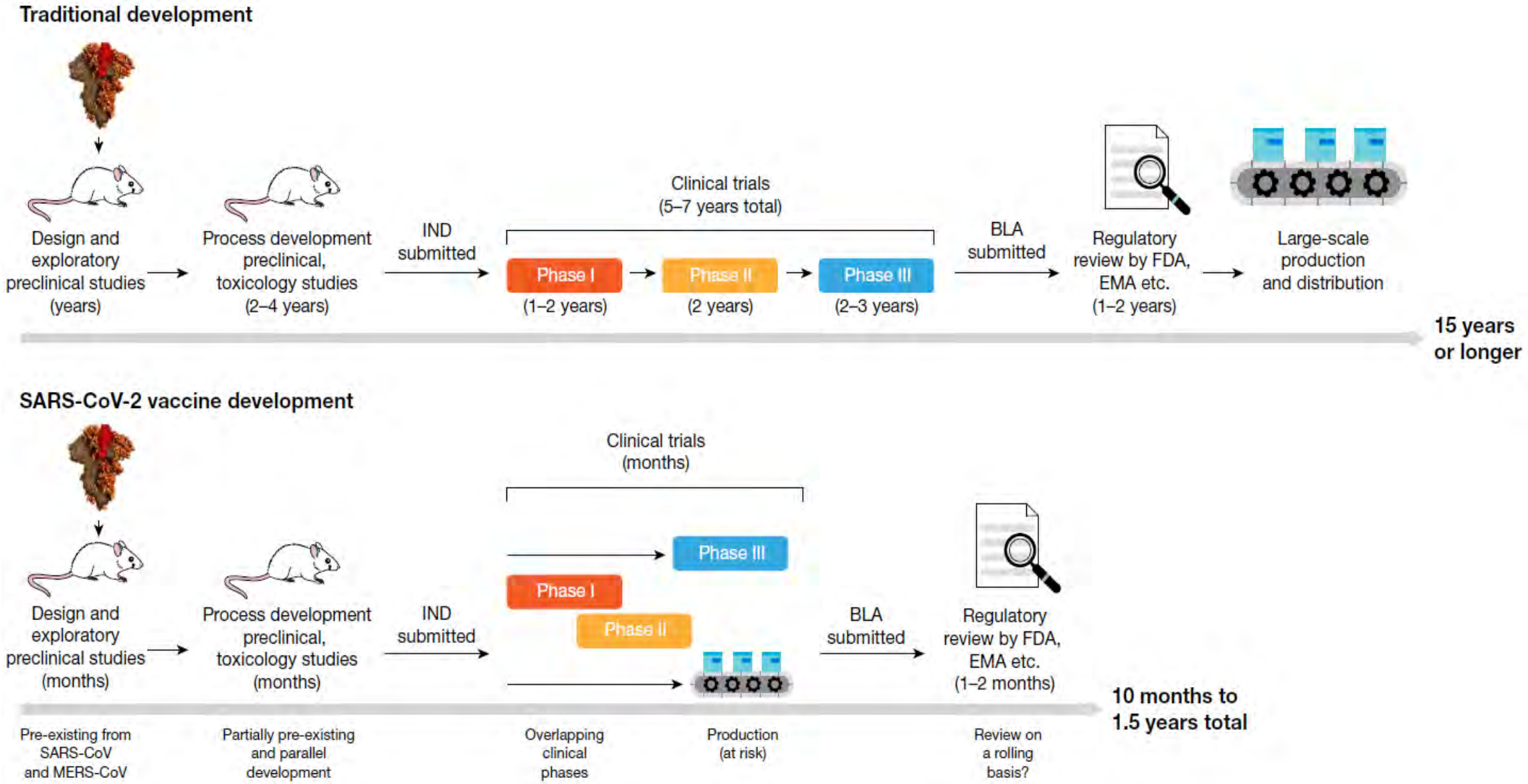
COVID-19 Vaccines

Vaccine Development



- Normal vaccine development occurs in 4-5 years
- Fast-tracking of various steps in pandemic
- EUA, Combine phases, Parallel studies, use of established platforms

Vaccine Development Timeline



Adapted from: Krammer F. SARS-CoV-2 Vaccines in development. Nature 2020; 586 : 516-27

Frontrunner Vaccines

	Platform	Efficacy %	Reference	Temp °C
ChAdoX1 Oxford	Chimpanzee Adenovirus vectored recombinant	70.4	Lancet online Dec 8, 2020	2-8
Moderna	mRNA	94.1	NEJM, Dec 30, 2020	2-8
COVAXIN-Bharat	Inactivated whole virion vaccine	78	Press release	2-8
BioNTech/Pfizer	mRNA	95	NEJM Dec 10, 2020	2-8 (5 days)
Johnson & Johnson	Human adenovirus 26 vectored recombinant	66.3	MMWR; March 5, 2021/70(9);329–332	2-8
Gamaleya (Sputnik V)	Human adenovirus 5 & 26 vectored	91.4	Press release	-18
Novavax	Protein subunit vaccine	96.4	BMJ 2021; 372 doi: https://doi.org/10.1136/bmj.n296	2-8
ZyCoV-D (Cadila)	DNA vaccine	NA	-	NA

Vaccines Authorized for Emergency Use

	ICMR- BBIL COVAXIN	**Serum Institute COVISHIELD**	**Dr Reddy's SPUTNIK**
Type	Inactivated whole virion vaccine	Chimpanzee adenovirus vectored recombinant	Human adenovirus 5 & 26 vectored recombinant
Inventor	BBIL & ICMR	Jenner Institute, Oxford University	Gamaleya Research Institute
Licensing	ICMR-BBIL	AstraZeneca; SII	Gamaleya, Russia

ICMR: COVID-19 Vaccine

BHARAT BIOTECH

- Provided virus strain
- Characterized vaccine strain
- Provided all SoP
- Conducted preclinical studies in hamsters & monkeys
- Technical & Lab support for phase 1 & 2 trials.
- Technical & lab and financial support for phase 3 trials

SERUM INSTITUTE OF INDIA
Cyrus Poonawalla Group

- Phase 2/3 studies of COVISHIELD (AstraZeneca)
- Phase 2/3 studies of COVOVAX (Novavax)
- Preclinical Hamster studies: indigenous candidates

Zydus Cadila
Healthcare Limited

Preclinical studies in monkeys at ICMR-NIV, Pune

Studies in pipeline

- Preclinical studies in Monkeys of Biological Evans vaccine candidate.
- Preclinical studies in rats and hamsters of vaccine candidates of Reliance Industries

COVISHIELD: UK Studies

- **Animal studies:** prevents SARS-CoV-2 pneumonia in monkeys & elicits good immunogenicity in mice

Nature | Vol586 | 22October2020

- **Clinical trials:**
  - Phase 1/2 in 1077 participants showed an acceptable safety profile, and homologous boosting increased antibody responses

Lancet 2020; 396: 467–78

  - Phase 2/3 in prime-boost regimen in 560 participants better tolerated in older adults than in younger adults and has similar immunogenicity across all age groups after a boost dose.

Lancet 2020; 396: 1979–93

  - Phase 3 in 11,636 participants from UK and Brazil):
    - Two standard doses ($5X10^{10}$ viral particles), vaccine efficacy was **62·1%**.
    - Low dose ($2.2X10^{10}$ viral particles) followed by a standard dose, efficacy was **90·0%**.
    - **Overall vaccine efficacy was 70·4%**

The Lancet: Published online December 8, 2020

COVISHIELD: India Phase 2/3 Study

Number of Participants: 1600

Age group: ≥ 18 years

Randomization: 3:1 (COVISHIELD-900; Placebo-300)

Immunogenicity cohort: 400 (COVISHIELD-300; Oxford/AZ ChAdOx1 Vaccine - 100)

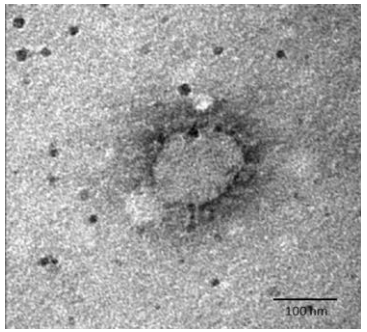
Interim analysis: COVISHIELD is safe and immunogenic

Results: NONINFERIOR to UK product

COVAXIN: Public Private Partnership

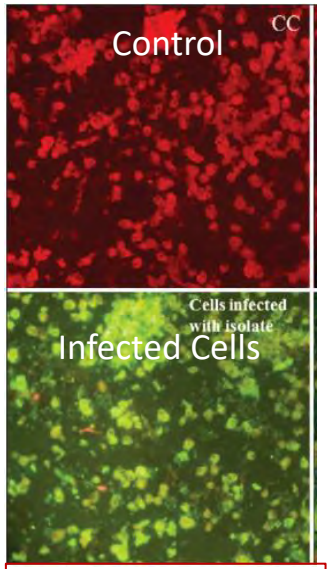
- SARS-CoV-2 strain isolated and characterized by ICMR-NIV, Pune
- Strain and SoPs transferred to Bharat Biotech International Ltd (BBIL)
- Inactivated whole virion vaccine candidate (BBV152 or COVAXIN) developed by BBIL
- Candidate vaccine characterized at ICMR-NIV, Pune
- Preclinical studies completed (Small and Large animals including NHP)
- Phase I, II and III clinical trials completed: 375, 380 and 25,600 participants
- Other sub-studies panned/ initiated

Isolation & Characterization of SARS-CoV-2



EM Imaging SARS-CoV-2

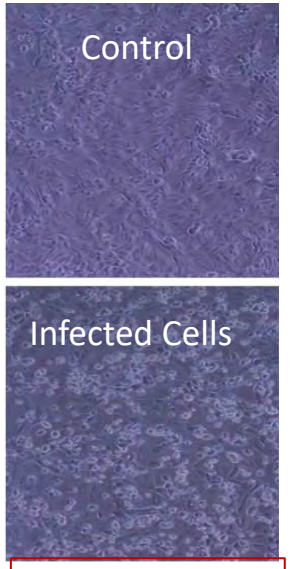
Indian J Med Res.
2020 ;151(2 & 3):241-243



B.1 G clade
Standard Strain

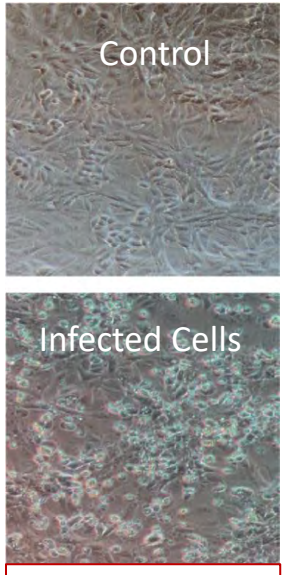
March 2020: 5th Country in the world to isolate

Indian J Med Res 2020; 151: 244-250



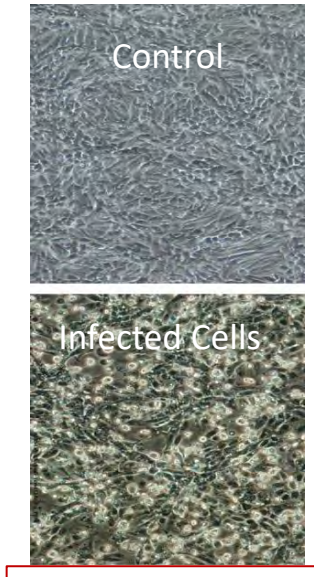
B.1.1.7
UK VoC

Jan. 2021: 1st country in the world



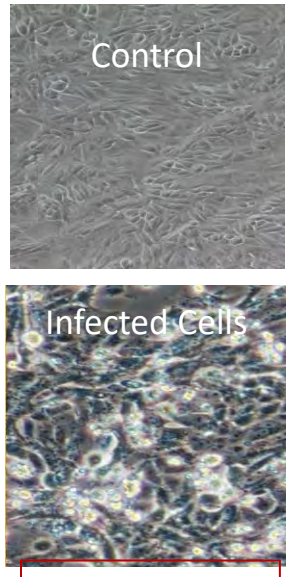
B.1.1.28
Brazil VoC

Feb 2021



B.1.351
South Africa VoC

March 2021



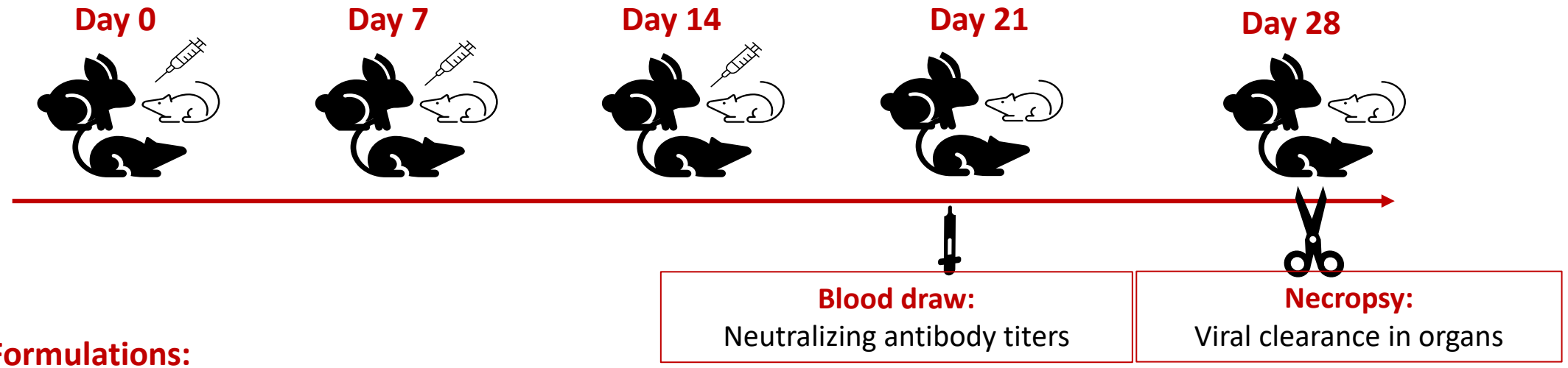
B.1.617

April 2021

Journal of Travel Medicine,
2021, 1–3

COVAXIN - Preclinical

Small animals: Mice, Rats, & Rabbits



Vaccine Formulations:

Adjuvants: A (Algel); B (Algel + IMDG [TLR7/8 Agonist]); **Antigen dose:** 3 µg; 6 µg; 9 µg

Safety analysis (BALB/c Mice, Winstar Rats & New Zealand Rabbits):

(i) Repeat dose toxicity studies; (ii) Mutagenicity assays; (iii) Maximum tolerated dose

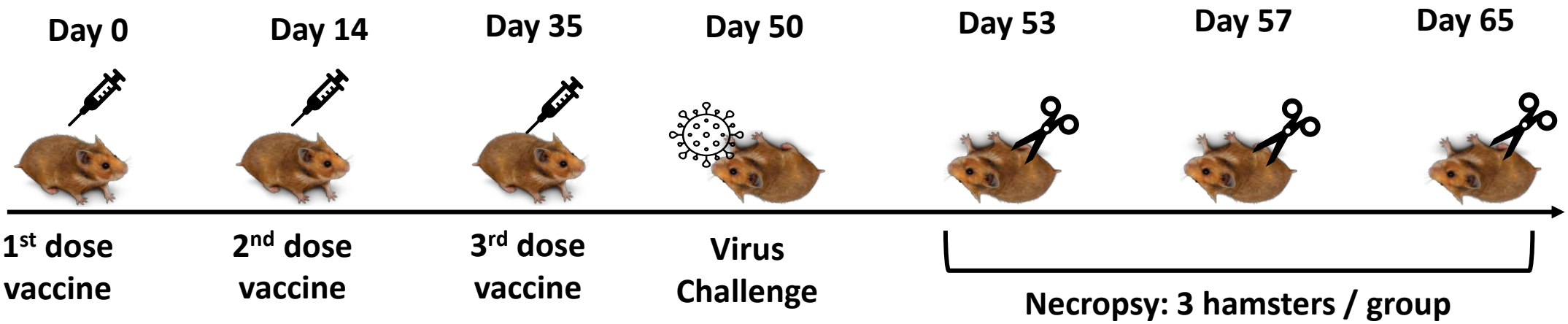
Results:

- High safety profile in all three species
- High neutralizing antibody titres, at 3µg and 6µg concentrations.
- BBV152 formulations with TLR7/8 agonist adjuvant-induced Th1 biased antibody responses

iScience; Cell Press; https://doi.org/10.1016/j.isci.2021.102298

COVAXIN – Preclinical

Hamster Challenge



Samples collected at different time points: blood, throat swabs, nasal wash and tissues.

36 Golden Syrian Hamsters experimented in 4 groups of 9 each:

Gp 1: Placebo; **Gp 2:** 6µg + Adjuvant A

Gp 3: 3µg + Adjuvant B; **Gp 4:** 6µg + Adjuvant B

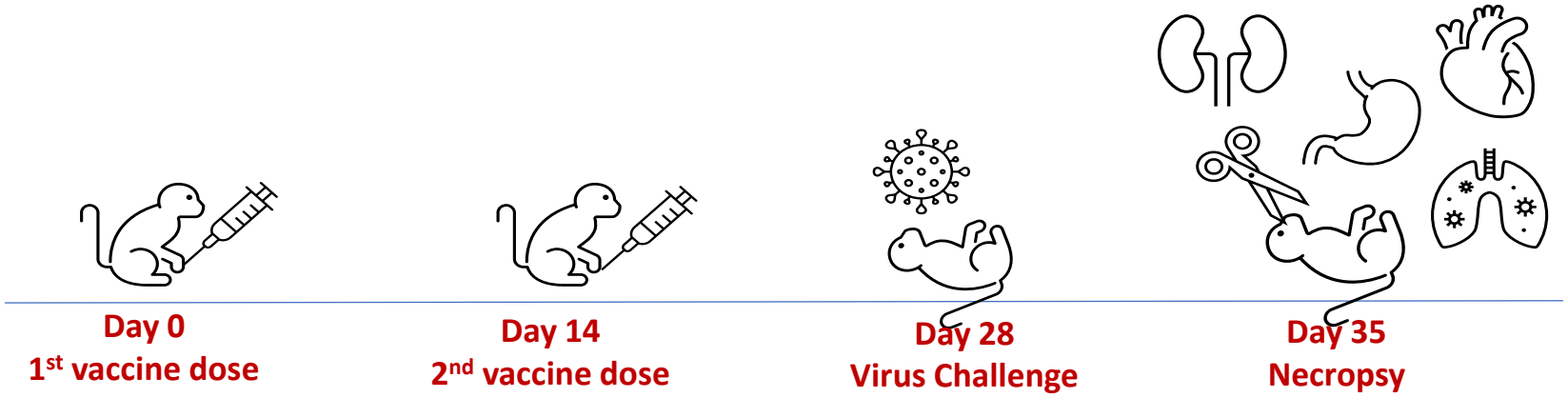
Results:

- Robust humoral immune response in Gp 3 & 4
- Th1 biased immune response in Gp 3 & 4
- Rapid viral clearance from upper and lower respiratory tract in Gp 3 &4

https://www.sciencedirect.com/science/journal/25890042/24/2

COVAXIN – Preclinical

Monkeys Challenge



Samples collected at different time points: Blood, Nasal, throat and rectal swabs, BAL, urine, stool and all organs on day 35

20 Rhesus Macaques experimented in 4 groups of 5 each:

Gp 1: Placebo; **Gp 2:** 6µg + Adjuvant A

Gp 3: 3µg + Adjuvant B; **Gp 4:** 6µg + Adjuvant B

Results:

- High neutralizing antibody response in Gp 3 & 4
- Helper T cell response in Gp 3 & 4
- Complete viral clearance from body fluids and organs on day 35 in Gp 3 &4

Nature Communications; doi: 10.1038/s41467-021-21639-w.

COVAXIN

Phase 1 & 2 Clinical Trials

Phase 1:

- 2 doses at day 0 and 14 (imi)
- 375 participants
- 4 arms (3 vaccine formulations & placebo)

Results:

- Safety of 3µg and 6µg Algel-IMDG same as placebo arm.
- Nab immune response detected in 3µg and 6µg+Algel-IMDG arms for homo/heterologous virus strains.
- Nab titres comparable to convalescent plasma .
- Binding ab titres for S1, RBD & N domains
- Th1 biased T-cell responses

Lancet Infectious Diseases:
DOI:https://doi.org/10.1016/S1473-3099(20)30942-7

Phase 2:

- 2 doses at day 0 & 28 (imi)
- 380 participants
- 2 arms (3µg & 6µg with Algel-IMDG)

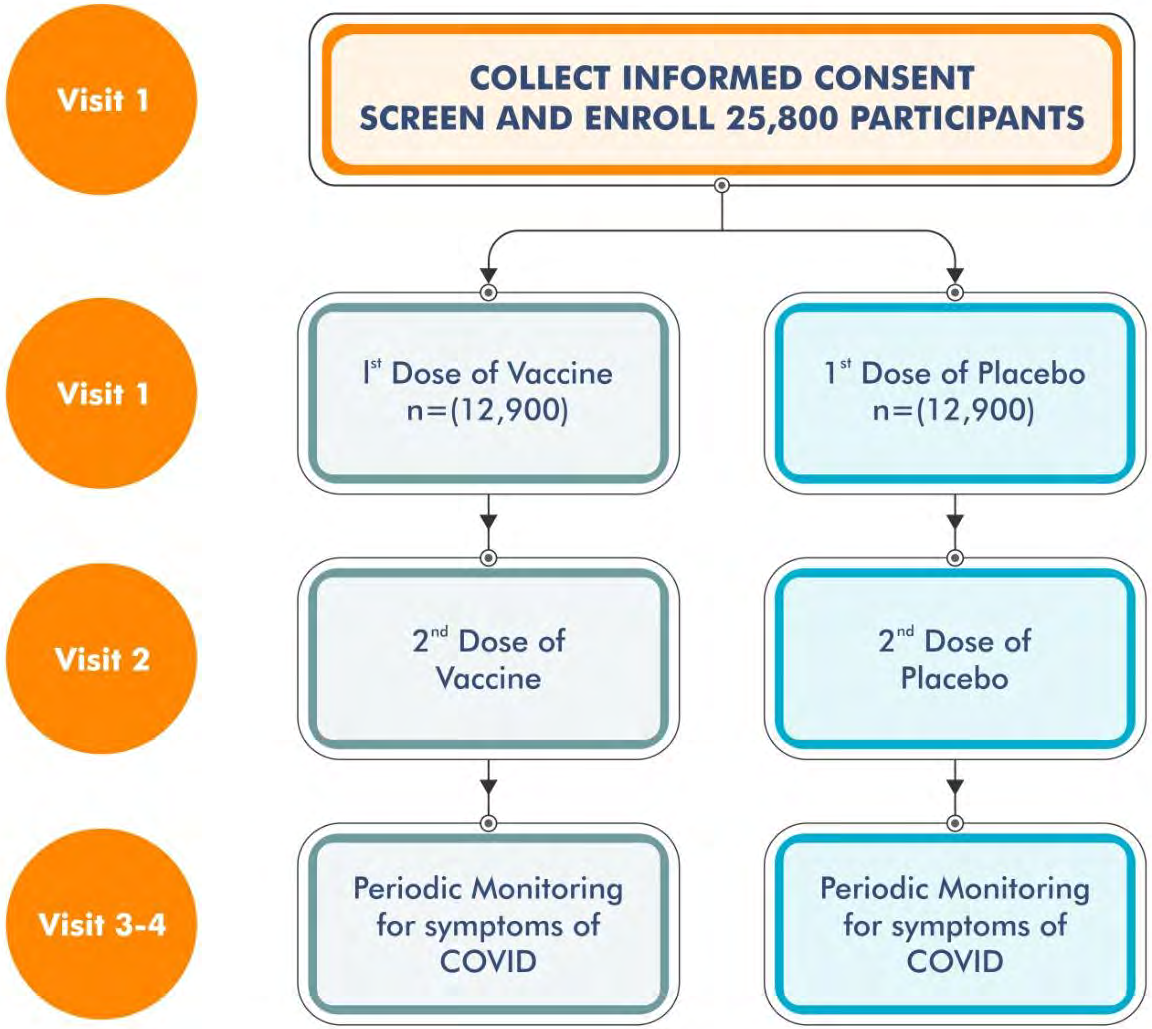
Results:

- Neutralizing antibodies in vaccinees to homo/ heterologous SARS-CoV-2
- Nab titres at day 56 were >98% in the 6µg+Algel-IMDG arm (included in phase 3).
- Binding ab titres also seen for S1, RBD & N domains
- Th1 biased T-cell responses
- Tolerable safety outcomes. No SAEs.

Lancet Infectious Diseases:
DOI:https://doi.org/10.1016/S1473-3099(21)00070-0

COVAXIN

Phase 3 Clinical Trials



- Efficacy endpoint is 130 COVID-19 laboratory confirmed symptomatic cases
- Healthy adults (>=18 yrs) and 21% at-risk participants ≥ 60 years or < 60 years with co-morbid conditions, and health care workers recruited

Parameter	Cases		Vaccine Efficacy (98.8%CI)
	Vaccine (n=12,219)	Placebo (n=12,198)	
Symptomatic	23 (0.18)	104 (0.85)	78% (60.8-88.4)
Severe	0	9	100% (60.5-100)

COVAXIN

Scientific Publications

	PRECLINICAL STUDIES	CLINICAL TRIALS	
	MOUSE, RABBITS & RATS **Link:** https://doi.org/10.1016/j.isci.2021.102298	PHASE 1: 375 VOLUNTEERS **Link:** DOI:https://doi.org/10.1016/S1473-3099(20)30942-7	THE LANCET Infectious Diseases
nature COMMUNICATIONS	MONKEYS **Link:** doi: 10.1038/s41467-021-21639-w.	PHASE 2: 380 VOLUNTEERS **Link:** DOI:https://doi.org/10.1016/S1473-3099(21)00070-0	THE LANCET Infectious Diseases
	HAMSTERS **Link:** https://www.sciencedirect.com/science/journal/25890042/24/2	PHASE 3: 25800 VOLUNTEERS Recruitment complete	
	COMPARATIVE IMMUNOGENECITY & PROTECTIVE EFFICACY OF 18 GLOBAL VACCINE CANDIDATES IN MONKEYS: **COVAXIN IN TOP 6** **Link:** DOI: 10.4103/ijmr.IJMR_4431_20		

COVAXIN And VoCs

	B.1 G Clade (standard strain)	++
	B.1.1.7 (Alpha)	++ *Journal of Travel Medicine, 2021, 1–3*
	P.1 (Beta)	+ *MS under review*
	B.1.1.248 (Gamma)	+ *MS under review*
	B.1.617 (Delta)	+ *Clinical Infectious Diseases, 2021 (In press)*

Virus Sharing

Patents

Data Sharing

Partnerships

Virus Sharing: ICMR

Company/Institute	Antigen form	Inactivated Antigen (ml)	Purpose
Karwa Enterprises Pvt Ltd, New Delhi	Gamma Inactivated	12074	ELISA
Meril diagnostics, Vapi		2868	
J.Mitra & Co. Pvt. Ltd, New Delhi		5670	
Trivitron Healthcare Pvt. Ltd., Chennai		5612	
Cadila, Ahmedabad		3980	
Voxtur Bio Ltd., Palghar		50	
Avecon, Haryana		50	
Biological E Ltd, Hyderabad		10638	Antisera in horse
Vins Bioproducts Ltd, Hyderabad		18030	
Central Research Institute, Kasauli	Formalin Inactivated	500	
Bharat Biotech Pvt Ltd, Hyderabad	SARS-COV-2 strain 770	10	Vaccine Development
	Gamma Inactivated	10	
	Brazil P2 strain	10	
Zydus Cadila	SARS-COV-2 strain 77	10	
CCMB, Hyderabad	Gamma Inactivated	0.5	R& D
ICMR NIIH	Gamma & Formalin Inactivated	10	R& D
CSIR IGIB, New Delhi	Gamma Inactivated	0.5	R& D

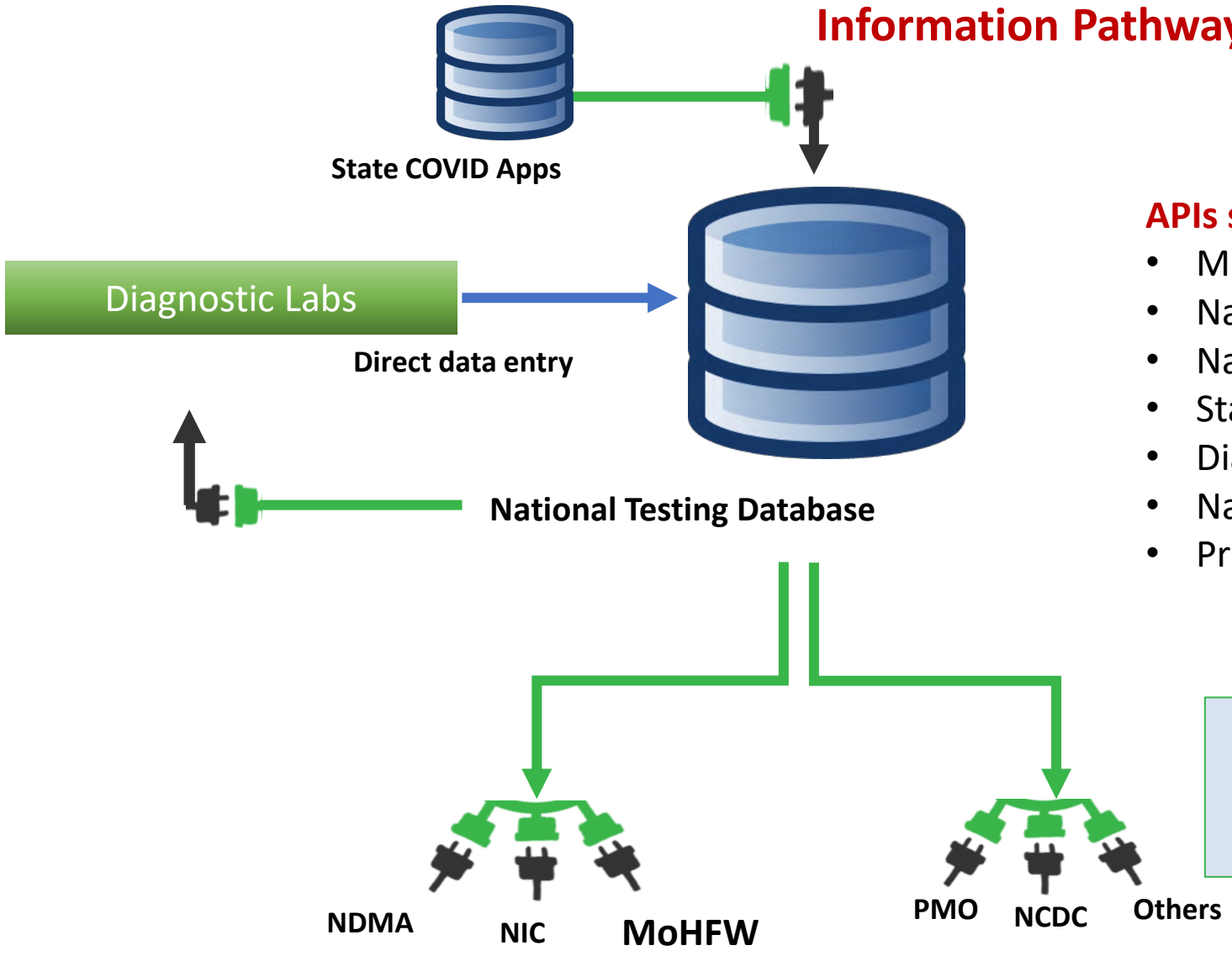
ICMR Patents: COVID-19

Title	Institute
RT-LAMP Assay for detection of Human β –Actin housekeeping gene IPA Number: 202111012867 Year: 2021	NIV Mumbai Field Unit
RAPID Assay targetting SARS CoV-2 IPA: 202011023573 Year: 2021	NIV Mumbai Field Unit
Development of TaqMan SARS CoV-2 multiplex RT PCR assay for screening human respiratory samples IPA Number: 202111015708 Year: 2021	NIV Pune
Human monoclonal antibodies against COVID-19 IPA Number: 202111002004 Year: 2021	• DBT-ICGEB, Delhi • ICMR-NIMR, Delhi • Emory Vaccine Centre, USA

ICMR COVID-19 Data Sharing

- ICMR hosts the data entry portal of COVID-19 testing only
- MoHFW captures hospital capacity, clinical or mortality related information
- All ICMR testing data is accessible to NIC, MoH&FW, NCDC, NDMA, PMO, State Govts
- ICMR data are linked with limited personal identifiers of patients
- In the interest of patient confidentiality, anonymized data access is used
- Request for data sharing is reviewed through a systematic process

Data Entry Portal of ICMR GOI



APIs shared with:

- Ministry of Health
- National Centre for Disease Control
- National Information Center
- State Governments
- Diagnostic laboratory chains
- National Disaster Management Authority
- Prime Minister Office

Disease trends; Policy making; Resource planning, Clinical decision making etc.

ICMR Data Sharing

Principles and Practices

Context -PANDEMIC

- Responsible data sharing
- Associated Safety and Security Concerns
- Misinterpretation of data and potential damage

Partnerships

जैवप्रौद्योगिकी विभाग
DEPARTMENT OF
BIOTECHNOLOGY

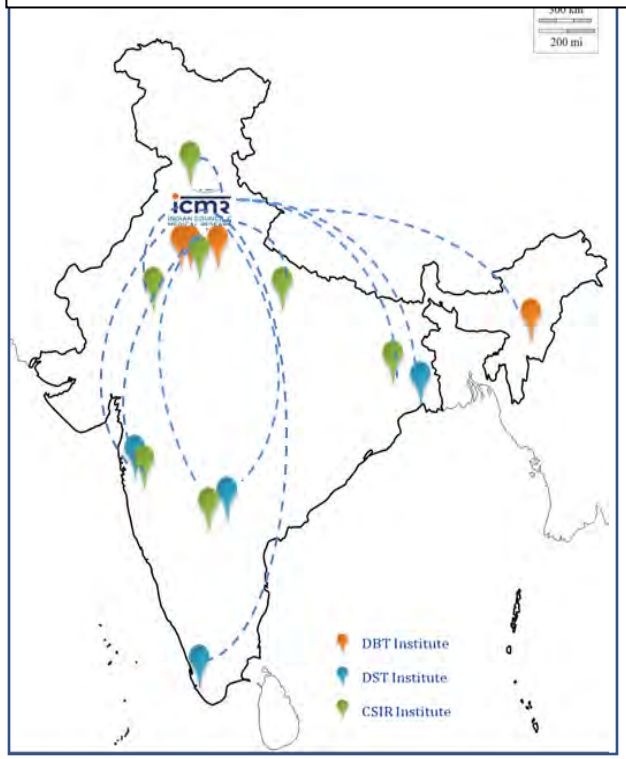
CSIR
Council of Scientific & Industrial Research

विज्ञान एवं प्रौद्योगिकी विभाग
DEPARTMENT OF
SCIENCE & TECHNOLOGY

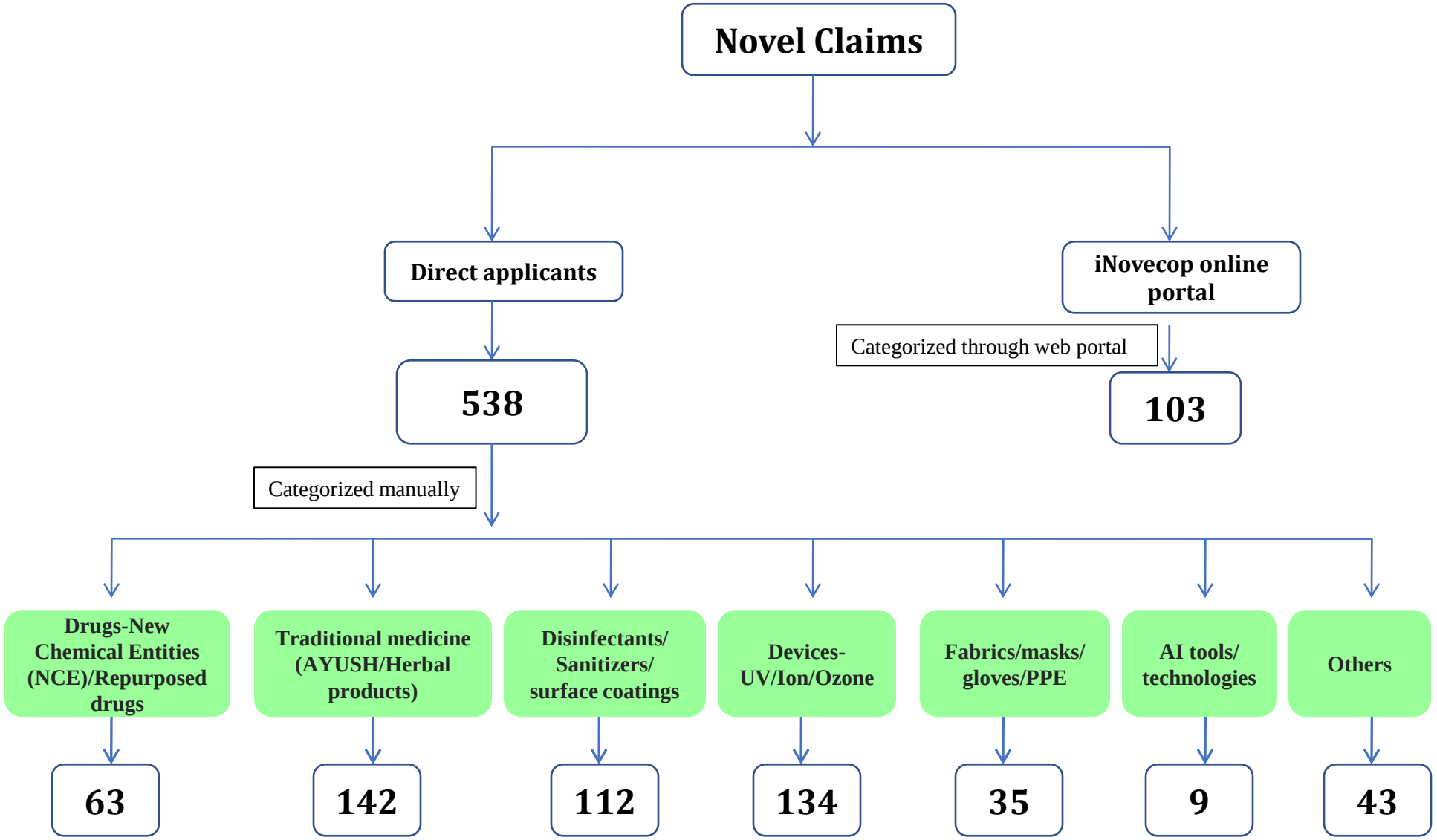
DBT:
- ICGEB
- RCB
- THSTI
- RGCB

CSR:
- IGIB
- CMERI
- CEERI
- NCL
- CCMB
- IMTech
- NBRI

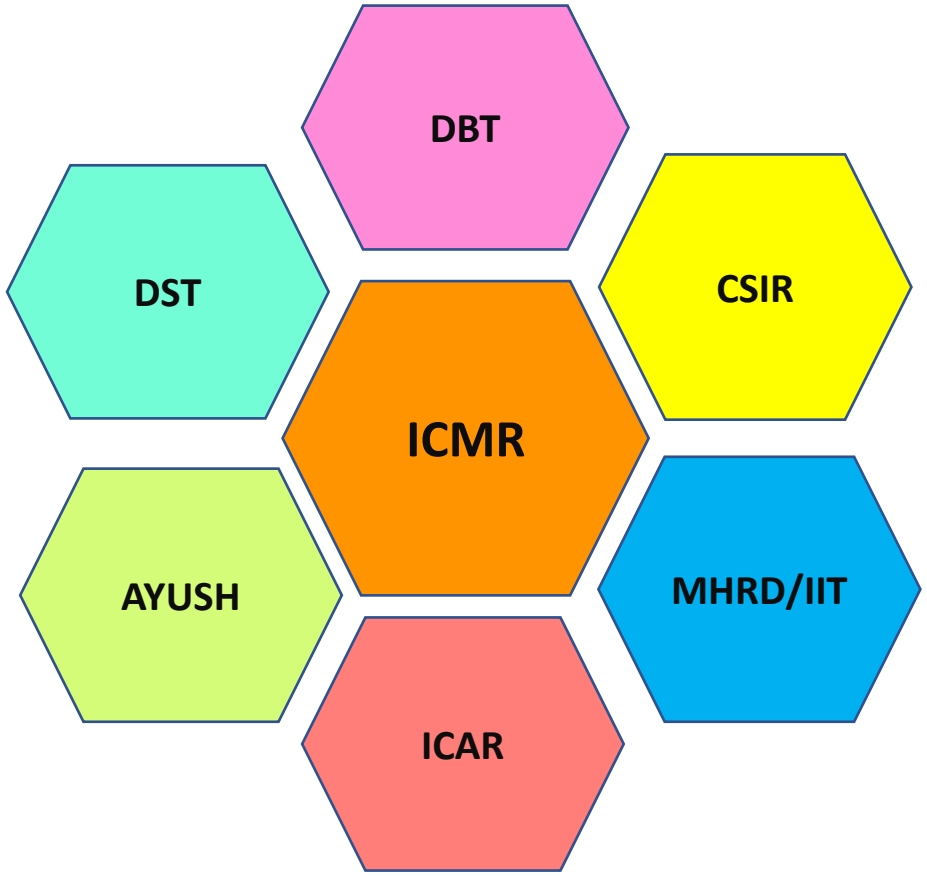
DST:
- IACS
- ARI
- ARCI
- IBSD
- SCTIMST



ICMR Coordinated Inter-Departmental Network for Examining Novel Claims for COVID-19


Novel Claims
Direct applicants
iNovecop online portal
Categorized through web portal
538
103
Categorized manually
Drugs-New Chemical Entities (NCE)/Repurposed drugs
Traditional medicine (AYUSH/Herbal products)
Disinfectants/ Sanitizers/ surface coatings
Devices- UV/Ion/Ozone
Fabrics/masks/ gloves/PPE
AI tools/ technologies
Others
63
142
112
134
35
9
43

Partnerships



Domains:

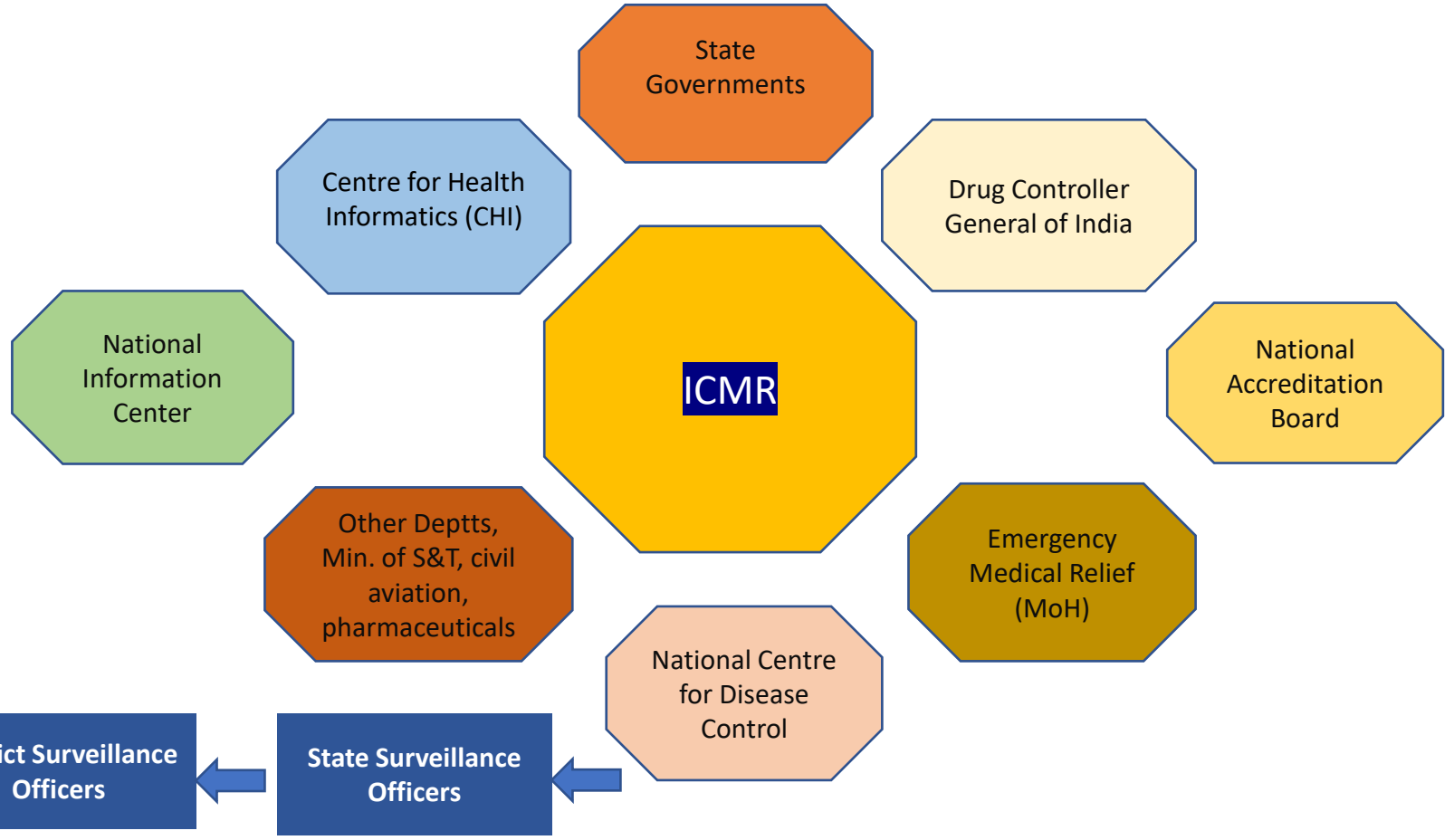
1. Validation of diagnostic kits
2. Antiviral screening of new molecules / re-purposed drugs/ AYUSH regimens
3. Validation of devices, textile products, mobile applications etc.
4. On-boarding COVID-19 testing labs
5. Establishment of Biorepositories
6. Development of indigenous vaccines & diagnostics

Whole of Government

Cabinet Secretary & Empowered Groups, Govt. of India

National Task Force

Ministry of Health & Family Welfare



Remembering Our Colleagues

“Attention is the rarest and purest form of generosity”

- Simone Weil

Thank You For Your Attention!