Twitter Thread by Suraj

Suraj @surajbrf



and @BharatBiotech recently released new Covid-19 vaccine prices. Enrolment for 18+ begins today.

Are they profiteering?

This thread covers their production effort, scaling and some other factors. Starting with SII:

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Serum Institute of India							
Date	Size (million)	Dose cost (Rs)	Order cost	Stated capability	Scaling Goal	Funding	Notes
Jan 11 2021	11	210	Rs.231 cr	50m doses/mth		Health Min	Health Min
Feb 3 2021	10	210	Rs.210 cr	50m doses/mth		Health Min	Health Min
Mar 17 2021	100	157.5	Rs.1575 cr	60m doses/mth	100m by April/May	PM CARES	Bulk order; support Mar/Apr ramp up + 100m/mth rate
April 20 2021	75	400	Rs.3000 cr	100m doses/mth	>100m by June	PM CARES + Health Min	Prepaid bulk order, support scaling above 100m/mth

SII started out with 50-60 million doses/mth capacity. Apr 1 it announced efforts to scale up to 100m by May using internal resources, and requested Rs.3000cr funding to scale up. The bulk order came thru mid April, enabling further scale up and deliveries through May/June.

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A common mistake made is to extrapolate latest prices to all future orders. Prices are tied to capital costs of scaling up and order size. Early SII orders were Rs.200/dose + GST. The higher initial price Is due to setup and initial investment SII made, described later.

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The March order was cheaper per dose but 10x larger. Govt ordered 120 million doses, 100m from SII, 20m from BB, for same 150/dose. This was a tradeoff they agreed to - very large bulk order but low margin. Enough for SII to invest for 100m/month production, but no more.

One can either pay intermittently higher per dose costs while demanding more volume, or can pay expansion costs upfront. The US did the latter during Op Warp Speed - \$18 billion invested in vaccine research and infrastructure upfront:

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Operation Warp Speed Vaccine Investments

Companies	Amount Invested	Phase
Moderna	\$2.5b	3
Sanofi with GSK	\$2b	1/2
Pfizer with BioNTech	\$1.95b	3
Novavax	\$1.6b	1/2 (US) 3 (UK)
Johnson & Johnson	\$1.5b	3
AstraZeneca	\$1.2b	3

Data: U.S. Department of Health and Human Services

India already has a massive vaccine supply chain infrastructure. In recent years SII alone accounts for over 90% of the savings in vaccine-avertable healthcare costs in the developing world: https://t.co/5vQVP2ac5u.

Table 4.Estimates of SII vaccines impact on various parameters between 2001 and 2020

Pathogen		Mortalit	DALYs averted (millions)	Averted costs of illness		
	Deaths (thousands)	Cases (millions)	Long-term disability (thousands)	Acute disease hospitalizations (millions)		Total (billions of US\$)
Measles	5 100	210	350	21	310	142
NmA	470	3.1	380	1.4	23	8.6
Rubella	280	0.9	270	0.5	26	5.1
Total	5.85 million	214	1 million	22.9 million	359 million	155.7 billions of US\$
Estimated SII total	5.27 million	192.6 million	0.9 million	20.6 million	323 million	140.13 billions of US\$

While SII are not an R&D setup and don't have high overheads, they are restricted by licensing deals. E.g. they cannot subsidize Indian sales by high prices elsewhere. Medecins Sans Frontiers states: https://t.co/wrHQdYa8E5

7/

While AstraZeneca has signed licensing agreements facilitating technology transfer on COVISHIELD – one of the first vaccine candidates to reach phase III – with manufacturers in Argentina, Brazil, China, India, and Indonesia, these agreements are shrouded in secrecy. The limited details that have been released reveal worrying terms. For example, while India has multiple manufacturers of vaccines, the license is restricted to the Serum Institute of India (SII). Further, SII is barred from supplying upper-middle-income and high-income countries, the most profitable markets for AstraZeneca. The corporation's deal with Brazilian public research body Fundação Oswaldo Cruz (Fiocruz) gives AstraZeneca the power to declare the pandemic over as soon as July 2021. This implies that, after July 2021, AstraZeneca can charge governments and other purchasers higher prices for a vaccine that was funded by public research and investments.

However, SII made an enormous gamble on Covid vaccines, that may have bankrupted them if it didn't work out: https://t.co/cb3YvmpvVf

Adar Poonawalla, 40, told NPR last June that he decided to invest tens of millions of dollars in glass vials alone and produce four different coronavirus vaccines, including the Oxford-AstraZeneca one. And that was before clinical trials proved any of them would work.

If these vaccines did prove effective, Serum would already have hundreds of millions of doses stockpiled, to start shipping out.

If they didn't, Serum would end up with useless vaccines — and hundreds of millions of dollars in losses.

They delivered volume on demand, and need to scale. They invested up front and risked their company to produce vaccines ahead of time. But for their initiative, India would have far fewer vaccine doses. Instead, it will hit 150 million doses today - 90% Covishield.

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What's more, they deferred COVAX/Gavi supplies to prioritize India mid wave, and are facing legal trouble:

https://t.co/gFC8FLe4AW

https://t.co/WbRAdLD9aM

10/

<u>@BharatBiotech</u> is its own different story. Covaxin is Indian IP. It was developed from a Covid strain isolated at NIV Indore, India's most advanced biosafety level 4 lab and one of only the 10 located in Asia: https://t.co/bT3wyRYfz6

11/

As developer, BB had to spend on R&D and is also responsible for preclinical and clinical trials, SII does not have such overhead, AZ is responsible for it. Thus BB started out priced higher (Rs.295). They also require more to scale.

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Bharat Biotech							
Date	Size (million)	Dose cost (Rs)	Order cost	Stated capability	Scaling Goal	Funding	Notes
Jan 11 2021	5.5	295	Rs.115 cr	5m doses/mth		Health Min	First order, 1.65m doses donated free
Jan 19 2021	4.5	295	Rs.135 cr	5m doses/mth		Health Min	Monthly Order
Feb 9 2021	4.5	295	Rs.135 cr	5m doses/mth		Health Min	Monthly Order
Mar 17 2021	20	150	Rs.510 cr	6m doses/mth	10-12m by April	PM CARES	Bulk order; support May ramp to 20m/mth
April 20 2021	100	150	Rs.1500 cr	10m doses/mth	60-70m by August	PM CARE + HealthMin	Prepaid bulk order, plus 130cr to BB+Haffkine
Totals 134.5		Avg 190	Rs.2395 cr + facilities				Facilities: BB Hyderabad (expanded) + BB Bangalore + BIBCOL + IIL + Panacea Biotec + Haffkine

Covaxin requires the Covid virus culture to be grown in a biosafety level 3 facility, and it is then killed before being sent through manufacturing process. Currently BB and Panacea Biotech are the only BSL-3 private facilities in India.

13/

Some argue why didn't we invest in building all these facilities last year. This was done. It must also be remembered that vaccine development isn't easy. Major entities like Glaxo, Merck all failed, but BB didn't. Probability of success: https://t.co/2nrGYB2aQI

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	Preclinical	Phase 1	Phase 2	Study period start (year)	Study period end (year)
Struck (1996) ¹³	57%	72%	79%	1983	1994
Wilson (2010) ¹⁶	40%	33%	33%	Expert based (phase 1 and 2 together)	Expert based (phase 1 and 2 together)
Davis et al (2010) ¹²	48%	74%	58%	1995	2011
Pronker (2013) ⁶	41%	81%	31%	1998	2009
Chit et al (2014) ¹⁵	N/A	40%	74%	2000	2013
BIO (2015) ¹⁴	N/A	70%	43%	2006	2015
WHO (2016; simple) ³	41%	68%	46%	Data from Di Masi (2003) ¹⁷	Data from Di Masi (2003) ¹⁷
WHO (2016; complex) ³	41%	50%	22%	Data from Di Masi (2003) ¹⁷	Data from Di Masi (2003) ¹⁷
Wong et al (2018; all indications)18	N/A	77%	58%	2000	2015
Wong et al (2018; orphan vaccines)18	N/A	90%	54%	2000	2015
Lowest PoS reported in literature	41%	50%	22%	N/A	N/A
Highest PoS reported in literature	57%	90%	79%	N/A	N/A
N/A=not applicable.					

In addition to high risk of failure, the cost of vaccine development is not cheap. BB received support from ICMR funds. Even US spent \$10 billion across 6 companies but could get only 2 candidates to production by end 2020. India had one bet and BB succeeded.

Table 1: Published estimates of probability of success for vaccine research and development

	Number of preclinical candidates (high PoS/ high cost to low PoS/ low cost scenario)		Number of phase 1 candidates (high PoS/high cost to low PoS/low cost scenario): number of available candidates	Number of phase 2 candidates (high PoS/high cost to low PoS/low cost scenario): number of available candidates	Expected US\$ cost, preclinical through phase 2a (95% CI)		
	Number of available of new candidates needed				Low PoS/low cost scenario	High PoS-high cost scenario	
Chikungunya	0-3		2–5	2	155 million (66–289 million)	112 million (34–252 million)	
Zika			4-8	1	149 million (54-299 million)	158 million (45-357 million)	
Rift Valley fever	5-13			2	224 million (100-409 million)	244 million (61–570 million)	
MERS	3-12		4		244 million (108-439 million)	245 million (71-543 million)	
Marburg	7–16		2		274 million (119-495 million)	358 million (86-792 million)	
Lassa	11-21			••	319 million (137-590 million)	469 million (99-1100 million)	
CCHF	6	3-12	1		289 million (125-531 million)	414 million (94-911 million)	
Nipah	11-13	0-8			319 million (137-590 million)	469 million (99-1100 million)	
SARS	6	5-15			319 million (137–590 million)	469 million (99–1100 million)	
SFTS	1	10-20			319 million (137-590 million)	469 million (99-1100 million)	
Total	50-91	18-55	13-20	5	2800 million (1200–5000 million)	3700 million (900–8400 million)	

To scale up Covaxin production, Govt granted BB Rs.65 crore to expand Hyderabad facility and invest in a new one near Bengaluru. They brokered a deal between BB and Panacea for the latter to make Covaxin.

Table 5: Minimum R&D portfolios and costs for progressing at least one vaccine candidate through end of phase 2a, per epidemic infectious disease

16/

Late last year Govt invested Rs.75cr in Indian Immunologicals PSU to prepare, including BSL-3 capability:

https://t.co/11jllfgb2k

They will start production by August :

https://t.co/LxyyS5tIKW



With its expertise in rabies vaccine production using the vero cell

platform, public sector vaccine-maker Indian Immunologicals Ltd (IIL), an arm of the National Dairy Development Board (NDDB), is confident of starting Covaxin production by July/August as this vaccine uses the same technology, a top company official said.

In addition, Govt invested in BIBCOL and Haffkine to also produce Covaxin: https://t.co/35o53XEh7b

18/

Speaking to *Businessline*, SK Lal, Company Secretary, BIBCOL informed that the company has the capabilities to manufacture Covid-19 vaccine as per the government directives. "We won't need major changes to our existing infrastructure. The plant is operational and makes oral polio vaccine. As a standard practice, we have some machineries and other materials in stand-by. Currently, we are having orders for 250 million doses of polio vaccine as against the installed capacity of 600 million doses per year. So, there is sufficient spare capacity to manufacture Covid-19 vaccine comfortably."

The combination of all these - brokering agreements between BB and multiple private and PSUs, is intended to dramatically scale up Covaxin from 10m/month now to 70m by August. Ocugen, a US licensee, may get EUA to produce Covaxin there:

https://t.co/cOco64uizu

19/

As of today, total Indian-made vaccine consumption is over 250 million doses. 150m jabs, ~70m exports, few % wasted and rest in pipeline or at mfg. This fits very closely with prior estimates made I made: production to March = consumption to April.

20/ https://t.co/mWVXQHQV9O

This thread discusses \u201cvaccine shortage\u201d. Data from news reports over last 6 months.

TI;dr: Situation is not shortage as such. India has stockpile of ~140m doses end March. However there\u2019s a tricky situation with supply vs consumption over short term.

1/ pic.twitter.com/dq9UE56jjy

- Suraj (@surajbrf) April 13, 2021

After much success with vaccine dev, India was desperately unlucky that a huge wave hit just as vaccinations began. As of today though, 150m doses will be done, 125m people with at least one dose, 25m fully vaccinated.

21/

Data from Maharashtra shows reduction in hospitalization and morality due to vaccination. Each vaccinated person - even after one dose - is one less person who will require hospitalization or extensive oxygenation as we have seen recently.

22/

In April, BB scaled up to 10m, SII is scaling up to 100m, and May/June, both scale up higher thanks to new bulk orders. Sputnik deliveries start early May, production at Dr.Reddys Labs end May/early June. Zycov-D may also become available in May/June.

23/

As India learned, not having supply chain at home means others can block you. SII and Covaxin both faced this: https://t.co/Lo4hscWNaj

However BB collaborated with CSIR to indigenize this: https://t.co/hNrcvOGtvv

24/

The west tried to guarantee access by placing huge orders, but slow deliveries hurt them. Entire countries were at the mercy of Pfizer:

https://t.co/ZZxYmEgKT0



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announced the cuts. The country's virus emergency czar at the time, Domenico Arcuri, lashed out, complaining that Pfizer had cut its shipments by almost 30% just as Italy was about to start vaccinating people older than 80 en masse. He warned that Italy could take unspecified action against

the company.

Days after Arcuri aired his grievances, Pfizer began shipping millions of doses to Israel. Within a week, Israel expanded its rollout to include 16- to 18-year-olds.

"Look, we are very angry," Luca Zaia, president of Italy's Veneto region—one of the areas most affected by Covid, with more than 9,800 deaths—told reporters, sitting in front of EU and Italian flags. He'd recently learned that supplies to his region would be cut 53% for that week. "I want to understand what Nobel Prize winner they paid to organize the distribution, or which principle or algorithm they used."

India must recognize how its own domestic technology & industrial base has helped during this crisis. No country with <\$3000 per capita GDP has our ability to do vaccine dev and production.

We are not at the mercy of a Pfizer deciding to send exports elsewhere one week.

26/

The vaccine dev and production concerns must be recognized to understand why they need cash. They're being pushed to scale up and for that, they set a dose price high enough. They have delivered so far, and for that they deserve to be spared name-calling and criticism.

Further, they have kept up near 100% capacity utilization for months on end while urgently scaling up, and also have managed to avoid catastrophic contamination issues such as what J&J faced: https://t.co/comCMiq1b8

28/

The best way to ensure later orders can have lower per dose prices is to give the companies early bulk orders, so they can plan, price in the costs of expansion. When equilibrium is achieved they can lower price because capital investments are paid for by prior orders.

29/

It is extremely poor when celebs like <u>@FarOutAkhtar</u> criticise SII. Due to their influence, they have a role in spreading a positive message. These celebs earned little early on but charge more per film now. Why? Scaling up a business and personal brand costs money, too.

30/

In the middle of a crisis, it is pointless to dumb down the level of conversation to a point where people make angry twitter posts about Rs.600 dose price of life saving medicine from iPhones that cost 100x. Most states are making it free. Govt already offers it free.

31/

Yes prices have doubled over recent orders. One company is trying to double production, the other trying to increase it by 7x. This costs money. States should recognize this. Govt has paid all the over 7000cr so far. Pool money and negotiate a large order w/ SII or BB.

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By late summer with potentially 4 vaccines and over 200m/month production capability, prices will drop as multiple lines can utilize previous sunk investments and price vaccines according to production and operating cost, instead of also adding expansion costs.

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Despite the wave hitting at such a bad time, vaccination still continues at pace - 3.3 million Monday, 2.6 million Tuesday this week. Over next 3 months production capacity will increase a lot.

Our vaccine companies need the support to scale up. Let's give them that.

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