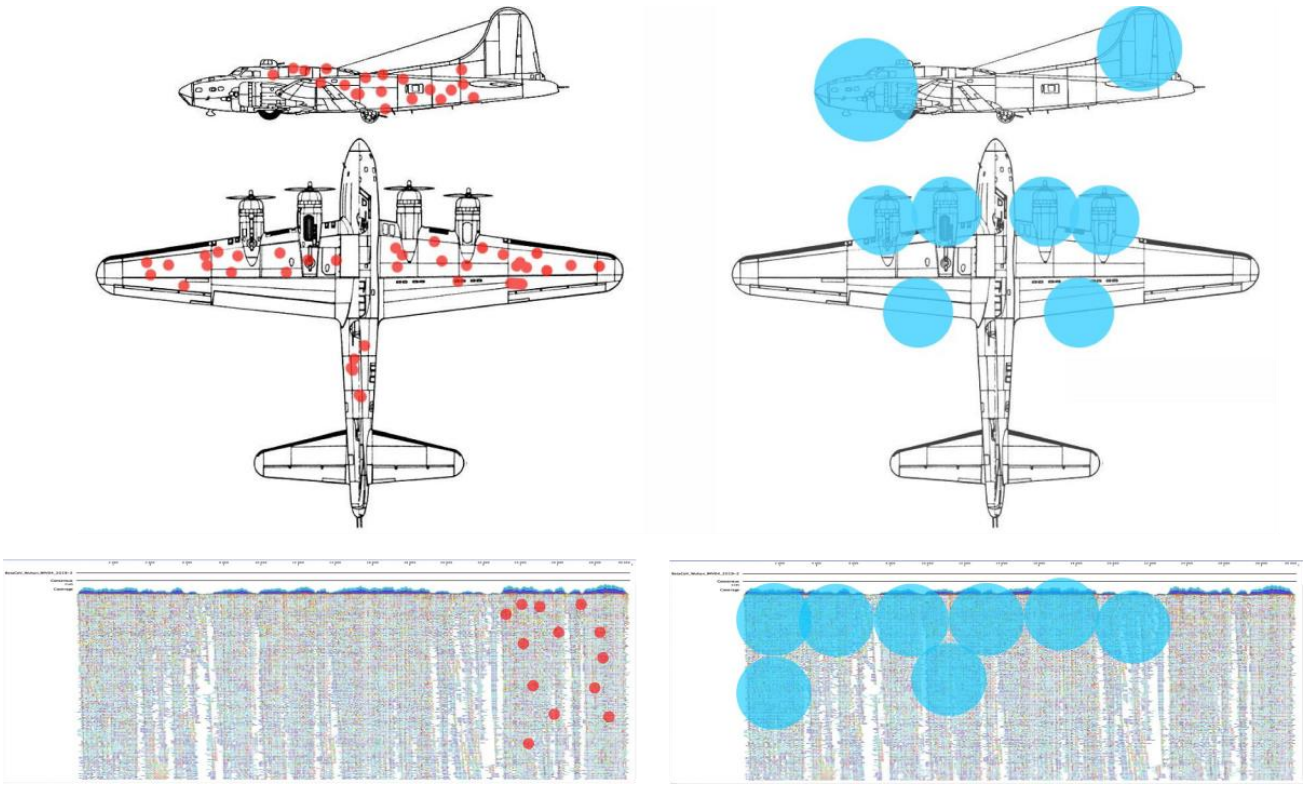

Covid-19: Have we been looking in the wrong place?

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Summary: Covid-19 shares 70% common genetic material with other coronaviruses (Hcov). Genetic information is the basis of immune reactivity. Mild forms of Hcov, common colds, circulate constantly, immunizing layers after layers of people over the years. There is repeated evidence of accrued immunity - T-cells and antibodies - pre-existent to C19. Hence regions infected the most pre-Covid would be naturally the most immune. This explains the astounding differences between Asia and the rest of the world. Countries with denser populations end up with greater immunity. This understanding is a fundamental opportunity to change the paradigm of immunization/vaccine strategies, public health responses seen to date, and accelerate the process out of this crisis.

Most of you have probably read the "**Survival bias**" story about reinforcing WWII bombers. Engineers wanted to protect areas where bullets had hit most these planes who had managed flying back home (see the red circles in the above illustration). As the statistician Abraham Wald pointed out at the time, the armoured plating was required in the areas left untouched (the blue circles). They were the sensitive zones with no coming back when hit: he was highlighting a complete opposite perspective.

What's that got to do with Covid? Well, collectively, I believe, we are doing the same mistake on Covid-19 as these well-intended smart American engineers did nearly 80 years ago. We are essentially focusing on the wrong information .

In January 2020, the genome of SARS-Cov2 was rapidly sequenced (see illustration), and immediately the research community started investigating its novelty. How was Covid-19 unique? and different from SARS-Cov1? What was its mode of action?...Naturally, the research started focusing on the now famous **Spike protein**, the basis for the upcoming RNA vaccines.

But overall, everyone was oblivious of the elephant in the room: **Covid-19 shares 65-82% genome with other Coronaviruses**.

Why is this so critical? Roughly 21,000 nucleotides are shared between SARS-Cov2 and other HCovs. And mild forms of coronaviruses, common colds, are permanently circulating the planet and have been infecting people for centuries: millions - if not billions - of people have had to gain immunity against the most immunogenic parts of this long string of common RNA. **Past infections have had to act as "vaccination campaigns"**, only with a universal stable material: immunizing against COVID-19 even before it ever existed.

Working in biotech, I am a big believer in biotechnology and the future of RNA/DNA vaccines. I am also utterly convinced of their efficacy, safety and applicability, notably for cancer. And **if one believes in RNA vaccines for Covid; one necessarily needs to believe that past coronaviruses have already immunized a big part of the population**. And vice versa. They are based on the same immunological processes. Saying otherwise contradicts the very laws these biotech startups are hacking successfully: it would be like astronomers negating gravity.

If you believe in RNA vaccines, you believe in acquired immunity from past viral coronavirus infections.

If you believe in natural immunization, you believe in RNA vaccines.

There are now ample signs, **proofs** and demonstrations of this pre-existing immunity throughout the world:

- The most prominent evidence is **the wide pervasiveness of *asymptomatics*** in the population witnessed throughout the globe, notably in very dense urban areas such as New York (see **previous article**).

- This summer, **a study** by Tübingen University Hospital proved that 81% of pre-Covid blood samples had T-cells capable of killing C19 infected cells in Germany.
- **Another** in Singapore found 50%. Depending on the geographic zone, these levels may vary significantly up and down.
- A **recent study** published in *Science* demonstrates that a range of **preexisting memory T-cells** were targeting SARS-CoV-2 as well as other common cold coronaviruses.
- **Another one** recently even showed cross-reactive antibodies.

This is not anecdotal evidence, this is scientific proof applicable and generalizable, and it's been **proven repeatedly**.

And, as a general law, this is not specific to coronaviruses: after the H1N1 epidemic, the *La Jolla Institute for Allergy and Immunology* already **demonstrated** large pre-existing cell immunity against H1N1 from past influenza infections.

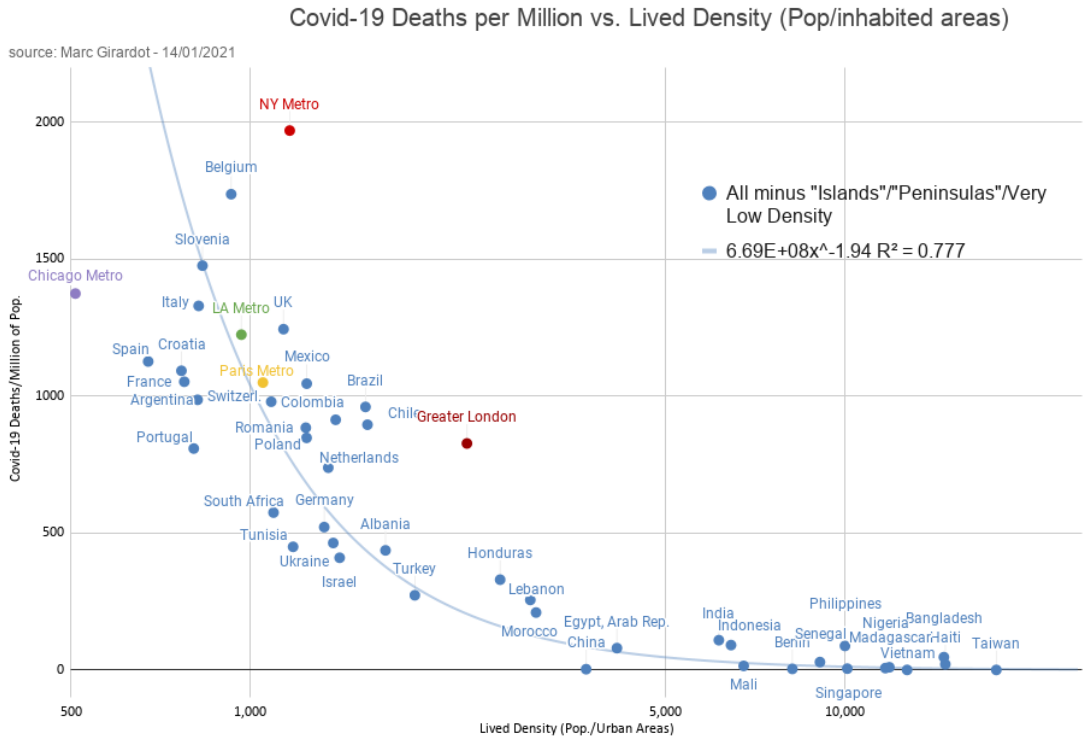
You are probably thinking ... So what? (if you've come this far, thanks :-))

Well **the epidemiologic consequences of this validation are far reaching**. It means:

1. The actual spread of the pandemic was widely underestimated and its lethality widely overestimated. That everybody had a sense of...
2. Many simply don't need vaccination, because they were/are already immune in a big way.
3. Immunity protects, but doesn't necessarily seem to stop transmission of the disease, which possibly puts a dent in the ambition of collective immunity through vaccination: remember the level of pre-existing immunity in NYC was bound to be very high (asymptomatics were approx.80-85% according to some data points).
4. There's a change in vaccine paradigm with **the possibility of designing vaccines that are universal for coronaviruses, or influenza**, have wider targets and are not sensitive to virus mutations, as they would target a permanent genetic scaffold. That's an encouraging possibility though no one - to my knowledge - has taken this route yet.
5. Immunity layers are being built over the years, and **the more a region is susceptible to viral infections, the more its population is actually immune today** (give or take immigration). So, more than measures (which were often taken too late), this likely explains why high density regions like Asia were significantly less hit than Europe and the US.
   Remember **China is 9 times denser than the US** (counting only inhabited

land). And if you add that Chinese grand-parents often live with, or close to, their grandchildren, you end up with a China radically more immune than any other country.

6. Finally, this demonstrates that trying to stop contamination at all cost - if effective - might end up being a very bad strategy long term as more young people will be infectable, and thus the next pandemic might be more brutal.



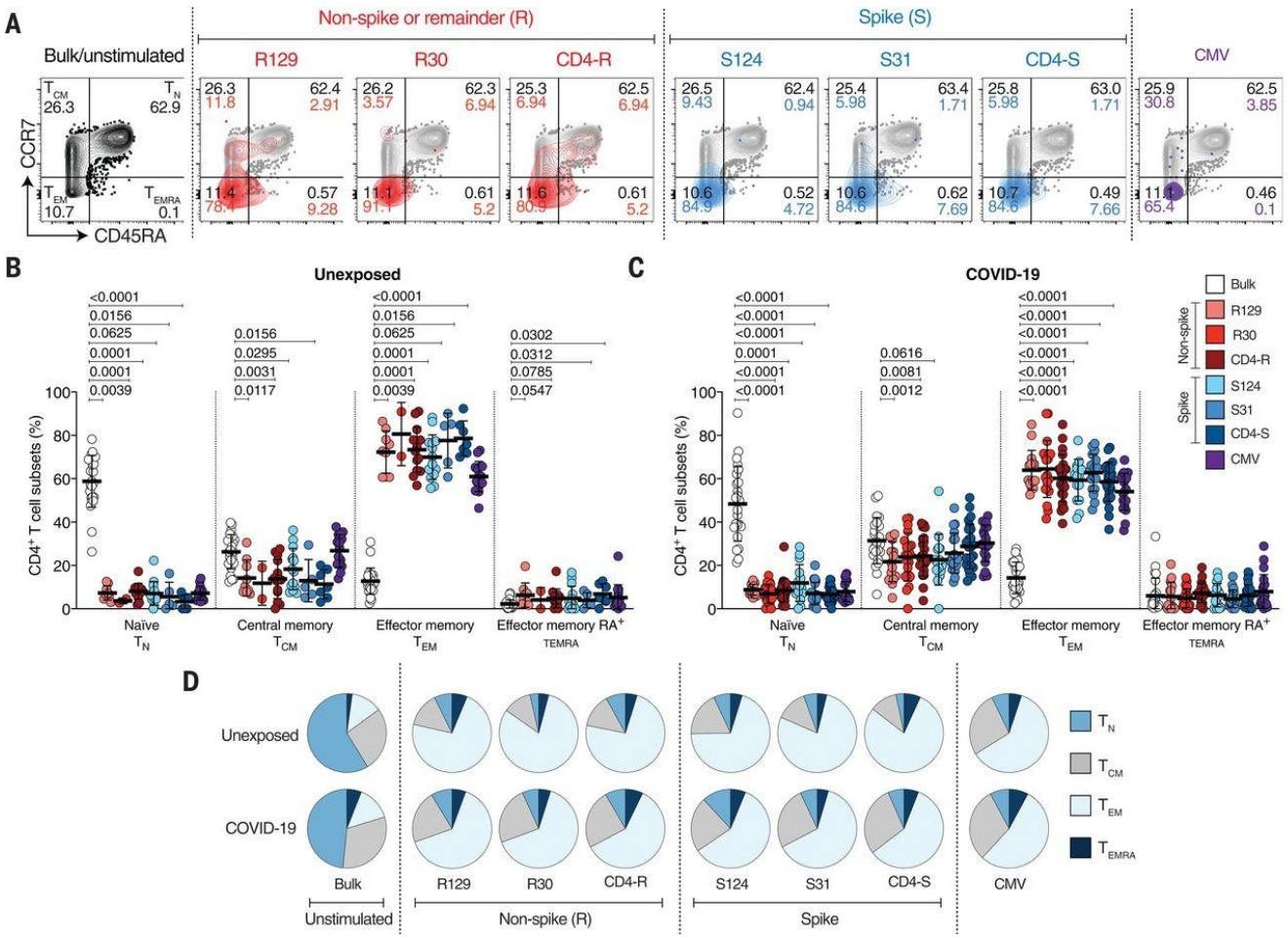
And if one acknowledges that common colds play an immunization role every year, one can estimate the level of immunity of a community, a city or a country based on a few pointers (attack rate in the <10 yrs old) as this is a relatively simple geometric progression q= (1-rate of attack%).

		ESTIMATED ACCRUED IMMUNITY LEVEL					
		PER AGE AND PER LOCATION TYPICAL INFECTION RATE					
		Estimated Attack Rate of Infectables					
		Low		Medium		High	
		5.0%	10.0%	20.0%	30.0%	40.0%	60.0%
Estim.accruded immunity at .. yrs old	10	22%	38%	58%	70%	77%	85%
	20	37%	58%	76%	84%	88%	92%
	30	49%	69%	84%	89%	92%	95%
	40	57%	76%	88%	92%	94%	96%
	50	64%	80%	90%	93%	95%	97%
	60	69%	84%	92%	95%	96%	97%
	70	73%	86%	93%	95%	96%	98%
	Average Immunity	53%	70%	83%	88%	91%	94%
	Exposed	47%	30%	17%	12%	9%	6%
		=1-((1-(1-Infection_Rate)^(Accrued_Age+1))/(Infection_Rate))/(Accrued_Age+1)					

I am sure many will challenge some of the herein hypotheses taken. This is a multi-factor dynamic system and it's next to impossible to predict precisely: more favourable outlier weather conditions can extend - or stop - a seasonal epidemic one year, immigration can change the dynamics, etc. However, the immunological laws cannot vary (at least with a virus that doesn't cripple it), and I have tried to four-wall as much as possible my reasoning with actual data and redundant research evidence. I hope this can contribute somehow to the acceleration of the collective understanding of Covid-19.

Thank you for your time and attention.

Paris, December 6, 2020



Source: Science - "Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans"

Note: This is my personal opinion. My purpose here is to be constructive and highlight some fundamental data and findings extracted from my personal experience and research that are not being put forth. Most of us want this period over. I am trying to open a new perspective. We all love our families and our friends. I am lucky enough to be comfortable in many fields relevant to this

pandemic, most noteworthy immunology from work I have done with an immuno-oncology company. I hope you will bare with me.