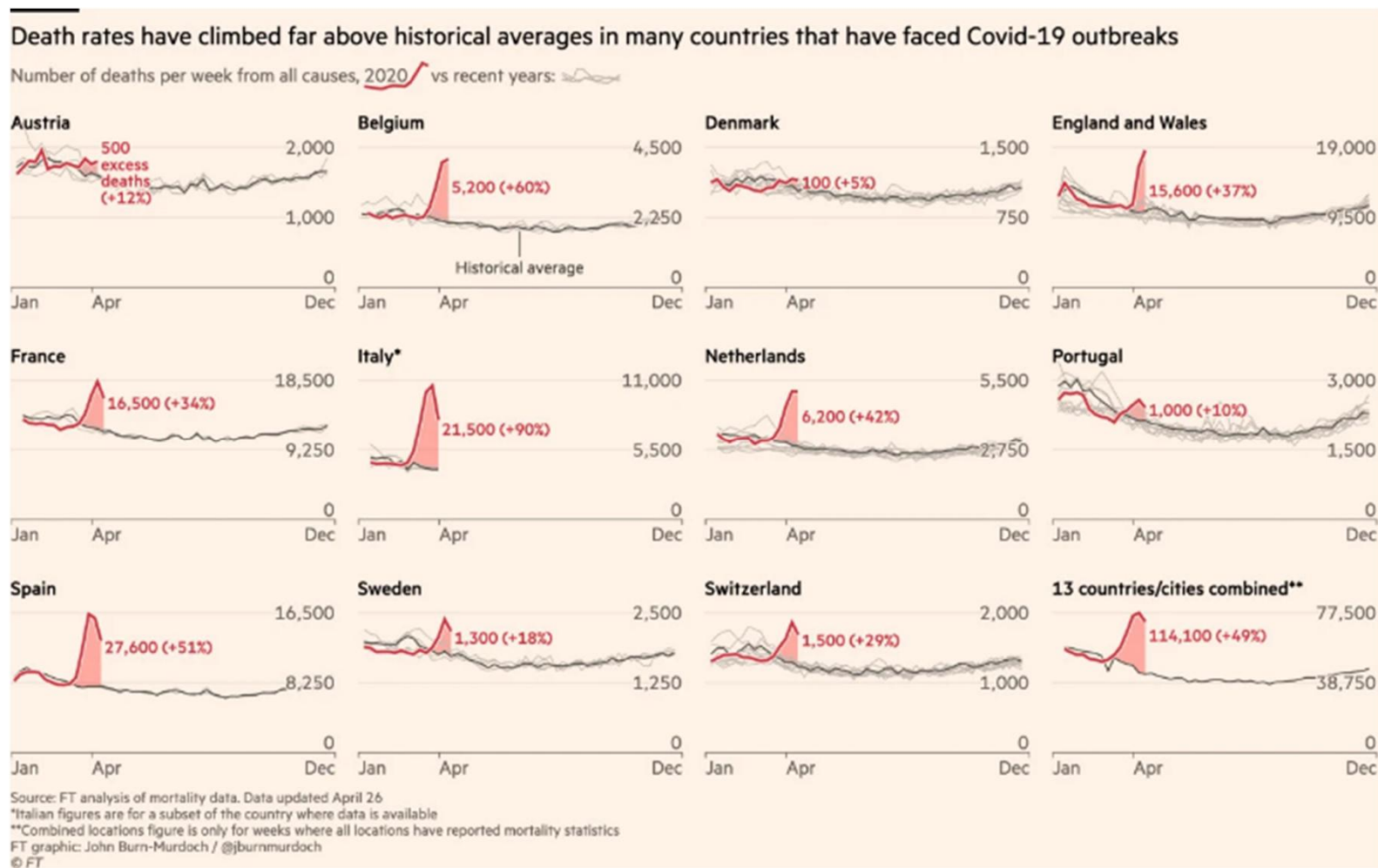# НЕКОТОРЫЕ АКТУАЛЬНЫЕ НАУЧНО-ПРАКТИЧЕСКИЕ ПРОБЛЕМЫ COVID-19
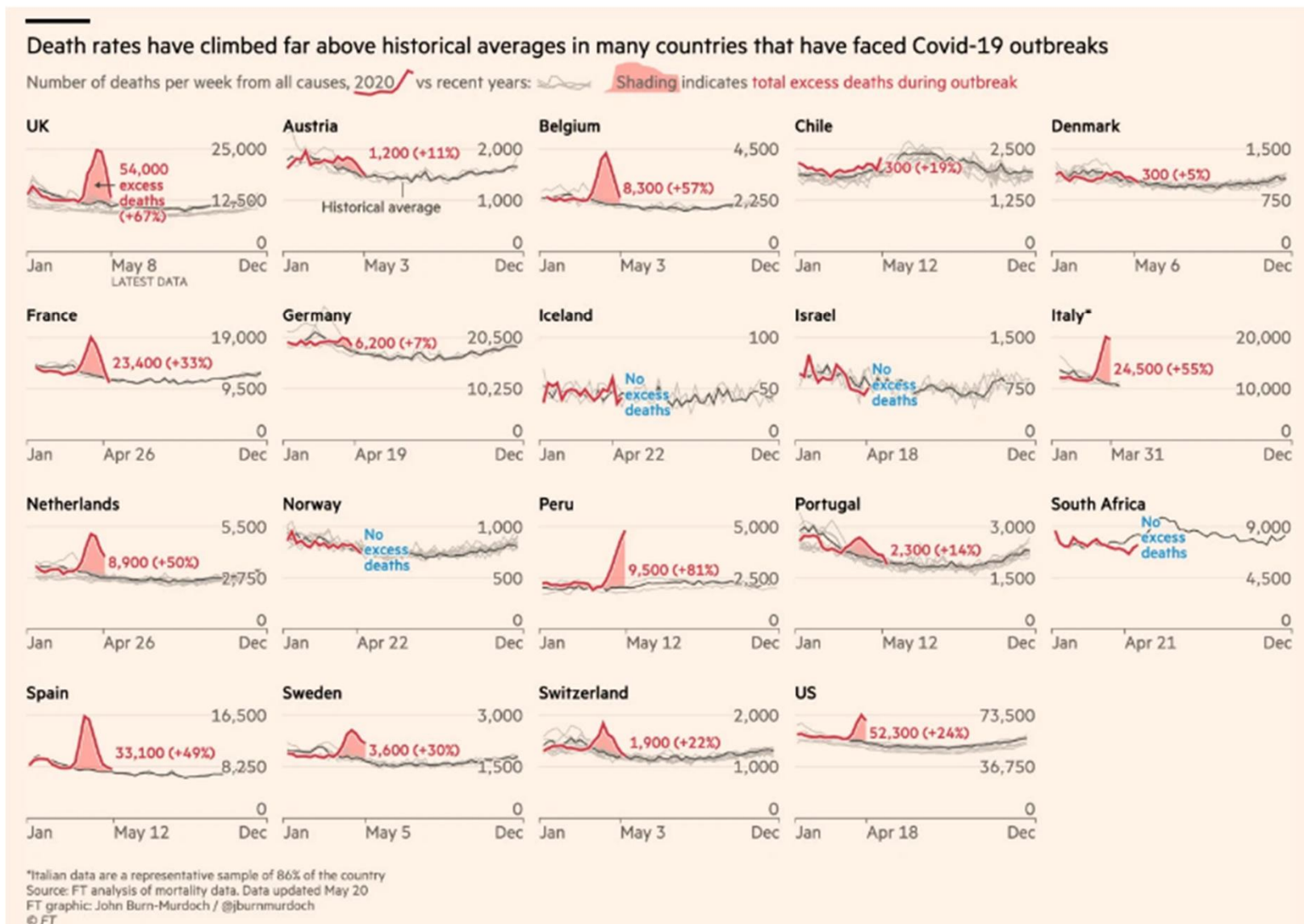
Воевода М.И.

ФИЦ ФТМ

Повышенные уровни общей смертности связывают с Covid-19. 26 апреля

Повышенные уровни общей смертности связывают с Covid-19. 20 мая

Death rates have climbed far above historical averages in many countries that have faced Covid-19 outbreaks

Number of deaths per week from all causes, 2020 vs recent years: Shading indicates total excess deaths during outbreak

*Italian data are a representative sample of 86% of the country
Source: FT analysis of mortality data. Data updated May 20
FT graphic: John Burn-Murdoch / @jburnmurdoch
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America's True Covid Toll Already Exceeds 100,000

The reported numbers leave out thousands of deaths clearly resulting from the pandemic.

By Nicholas Kristof
Opinion Columnist

May 13, 2020

853

Analysis of C.D.C. estimates of deaths from March 8 to April 25 shows that many more people died during those six weeks than died in the corresponding period in years past. In many cases, these "excess deaths" are much higher than the death toll from Covid-19 reported on April 25.


Legend
State
Excess

6,000 deaths

0

March 8   April 25

New York City reported 16,100 deaths from Covid-19, but our estimates show deaths up to 20,900

Excess deaths
Reported deaths

Some states had negative "excess deaths" because fewer died than expected.

| State	Excess
Alaska	-100
Wash.	500
Mont.	0
N.D.	-100
S.D.	0
Minn.	200
Wis.	400
Mich.	5,200
Mass.	3,900
N.H.	100
Maine	0
Vt.	200
R.I.	-100
Ore.	-200
Idaho	0
Wyo.	100
Neb.	-100
Iowa	-127
Ill.	2,900
Ind.	1,000
Ohio	900
N.Y. excluding N.Y.C.	9,000
N.Y.C. only	20,900
Nev.	0
Utah	200
Colo.	1,000
Kan.	-100
Mo.	400
Ky.	-100
W.Va.	300
D.C.	200
Del.	200
N.J.	10,500
Calif.	2,100
Ariz.	700
N.M.	100
Okla.	0
Ark.	-100
Tenn.	200
Va.	1,100
Md.	1,500
Texas	2,200
La.	2,100
Miss.	600
Ala.	300
Ga.	1,100
S.C.	800
Hawaii	-100
Fla.	1,800

В Москве значительно возросло число смертей. В апреле в городе зарегистрировали на 20 процентов больше летальных исходов, чем в среднем за прошлые десять лет, отмечает The Moscow Times со ссылкой на портал открытых данных [правительства столицы](#).

По информации [портала](#), в апреле в городе зафиксировали 11 846 смертей, тогда как среднее число в том же месяце в период с 2010 по 2019 года составляло 9866, то есть на 20 процентов меньше. В том же информационном листе отмечается, что в апреле 2020 года в Москве родились 3959 детей.

Захоронения в гробу в г. Новосибирске

Месяц	2019	2020
Январь	949	834
Февраль	843	697
Март	810	793
Апрель	831	786
Май	885	264
Июнь	791	
Июль	699	
Август	750	
Сентябрь	779	
Октябрь	908	
Ноябрь	797	
Декабрь	783	
Итого	9825	3374
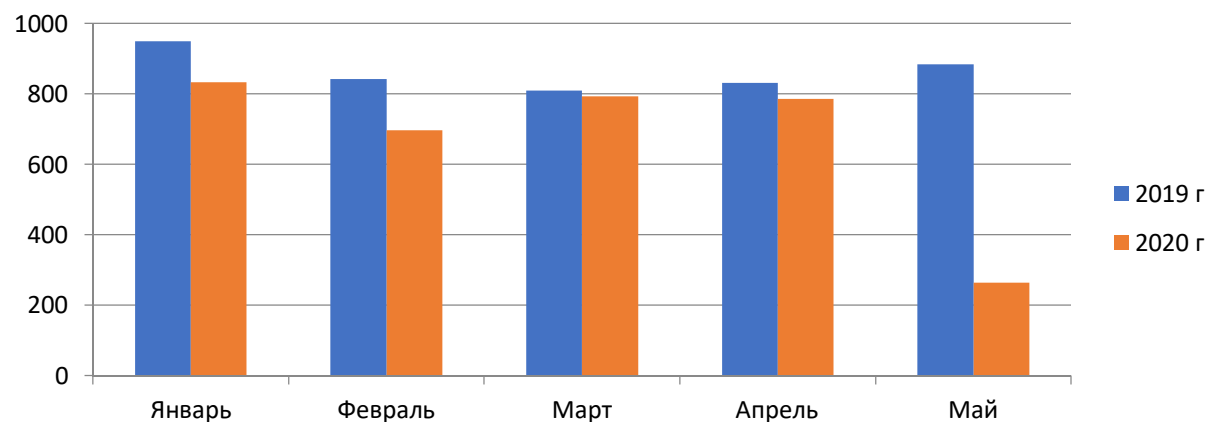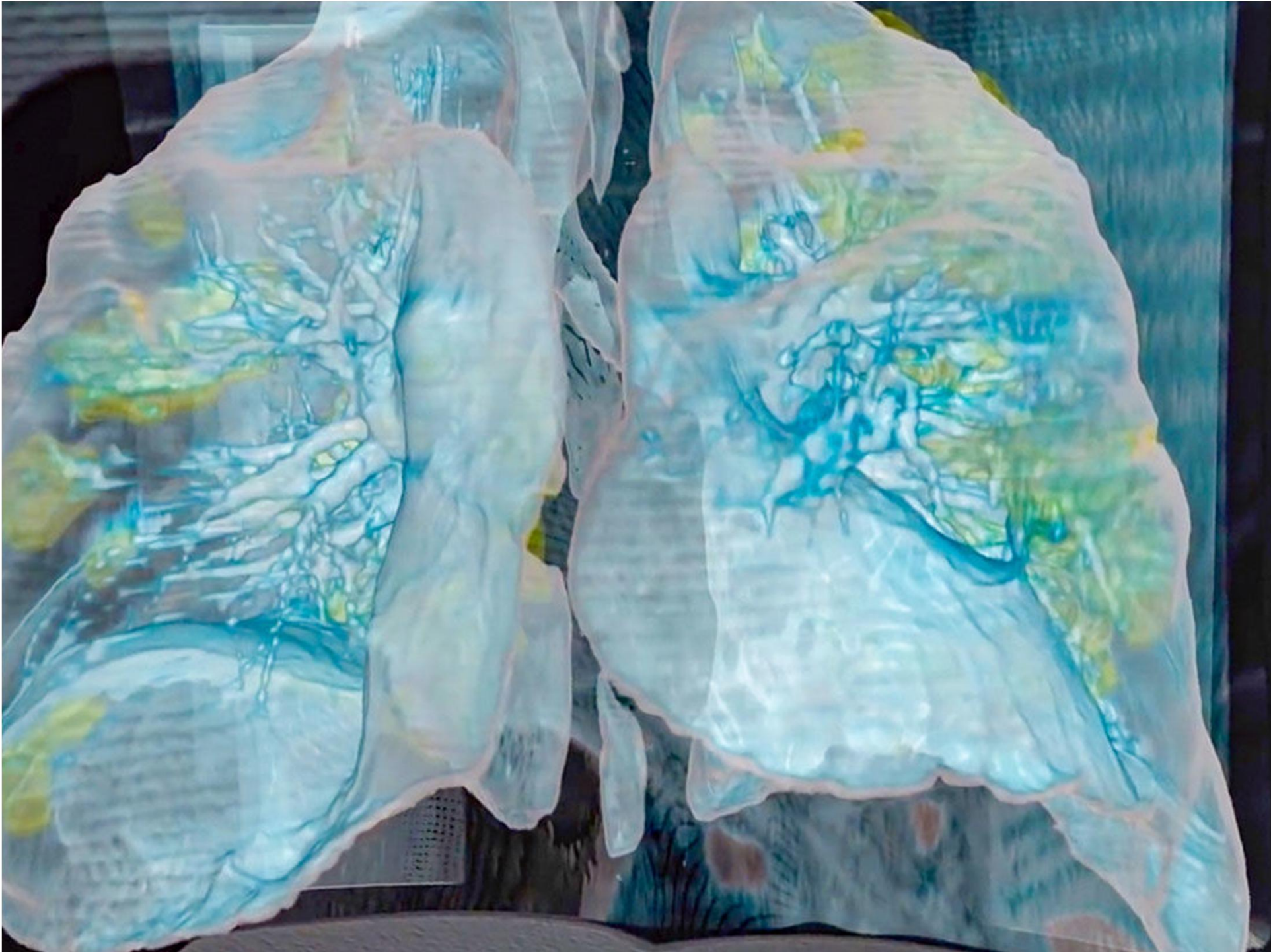
From: Pulmonary Arterial Thrombosis in COVID-19 With Fatal Outcome: Results From a Prospective, Single-Center, Clinicopathologic Case Series
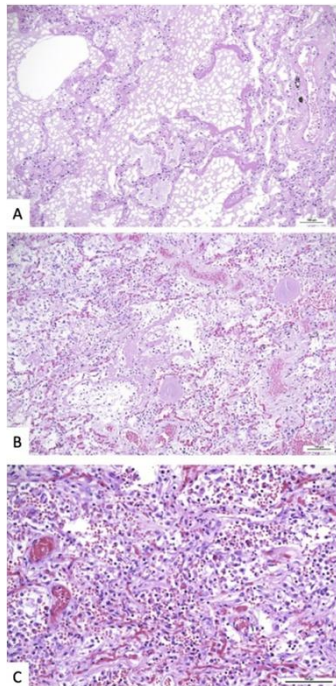
Экспериментальные исследования по заражению приматов также свидетельствуют о первичном поражении легочной ткани

Figure Legend:

Early, with edema and hyaline membranes (original magnification, × 100). B. Intermediate, with proliferation of pneumocytes admixed with lymphocytes and neutrophils, organizing a residual hyaline membrane (original magnification, × 100). C. Late, with proliferation of fibroblasts (original magnification, × 200). Hematoxylin–eosin staining.

From: Pulmonary Arterial Thrombosis in COVID-19 With Fatal Outcome: Results From a Prospective, Single-Center, Clinicopathologic Case Series

Figure Legend:

Thrombosis of a dilated mid-sized pulmonary artery without subsequent infarction. The surrounding lung tissue is in part edematous (original magnification, × 10). B. A small pulmonary artery is obliterated by a thrombus, which is infiltrated by neutrophils (original magnification, × 100). C. Pulmonary artery with thrombosis and infarction and pneumonia of the surrounding lung tissue (original magnification, × 10; corresponding histology to Figure 1, B). D. Microthrombi of small arteries in areas of diffuse alveolar damage (original magnification, × 100). Hematoxylin–eosin staining.

Pathways leading to cytokine release syndrome

Pathways leading to cytokine release syndrome

Coronavirus infection results in monocyte, macrophage, and dendritic cell activation. IL-6 release then instigates an amplification cascade that results in cis signaling with T_H17 differentiation, among other lymphocytic changes, and trans signaling in many cell types, such as endothelial cells. The resulting increased systemic cytokine production contributes to the pathophysiology of severe COVID-19, including hypotension and acute respiratory distress syndrome (ARDS), which might be treated with IL-6 antagonists such as tocilizumab, sarilumab, and siltuximab.
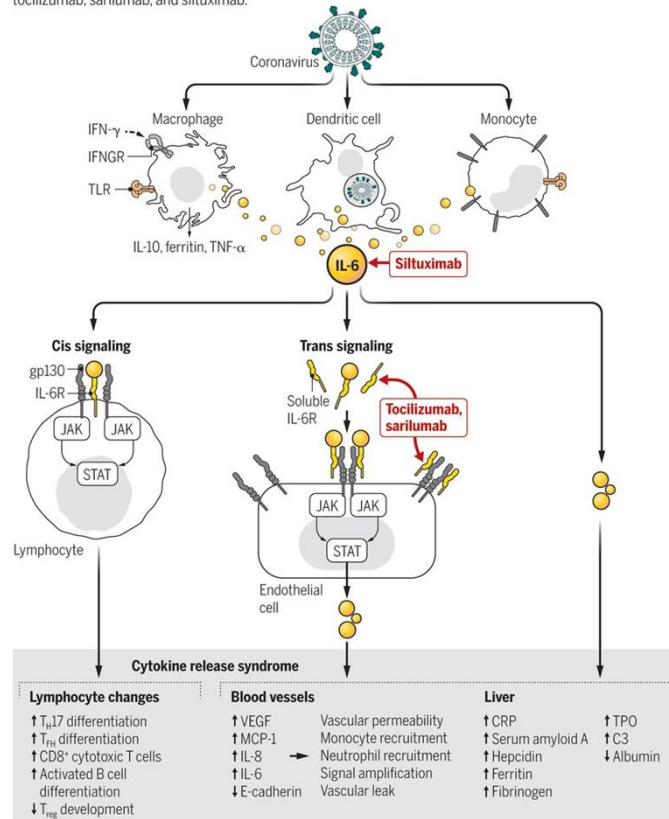
By John B. Moore, and Carl H. June Science 2020;science.abb8925

Не выяснены механизмы определяющие риск развития «цитокинового шторма» – тяжелого осложнения у конкретного индивида

НЕПРЕДСКАЗУЕМОСТЬ:

- развития пневмонии
- развития цитокинового шторма
- развития ОРДС
- развития легочного фиброза
- Развития коагулопатии

Autopsy slowdown hinders quest to determine how coronavirus kills

Strained health-care systems, lockdowns and safety requirements have hampered efforts to collect tissue from patients that is crucial to research.

Heidi Ledford

Global database

Salgado, Leavitt and a team of pathologists are taking up the challenge of creating an international COVID-19 pathology repository. They are working with the World Health Organization, whose International Agency for Research on Cancer maintains a tumour pathology database and has experience juggling legal requirements. And they are putting together guidelines for the safe collection of autopsy samples and a standardized way of recording the results.

So far, researchers from 25 countries have said that they are interested in participating, although such a repository will probably take months to complete, says Amanda Lowe, a managing director at the digital-pathology company Visiopharm in Westminster, Colorado. "Everybody who steps forward and has access to tissue even from one patient is highly valuable."
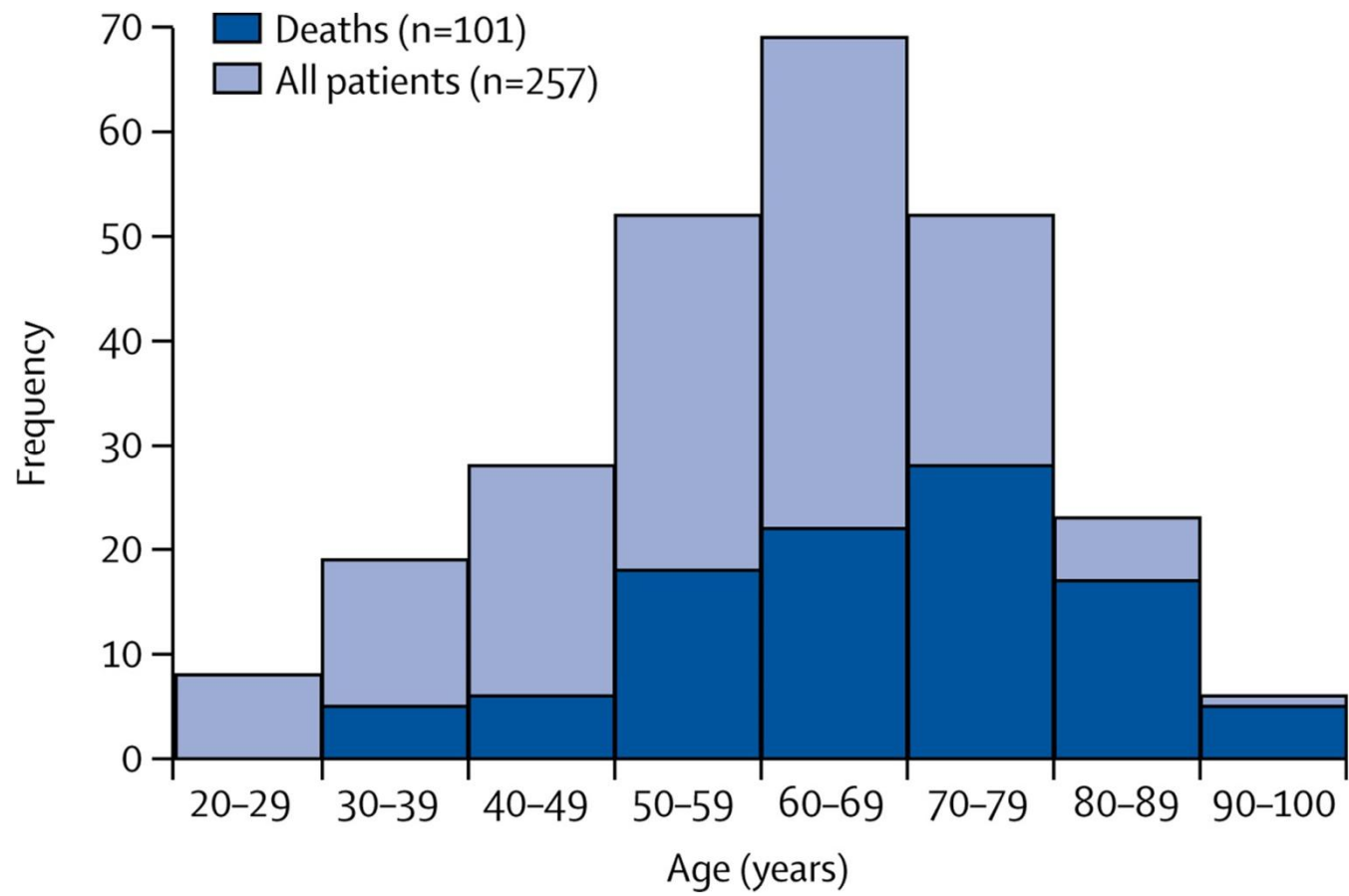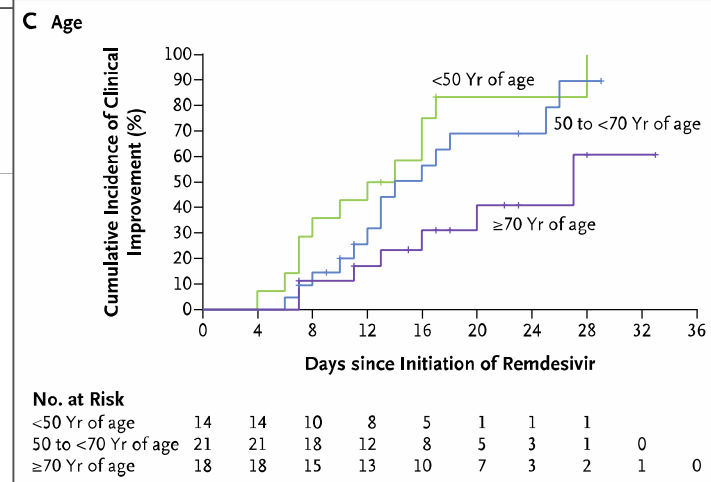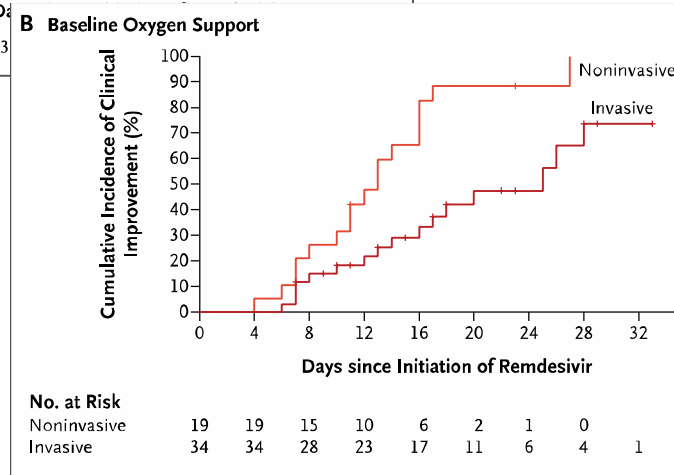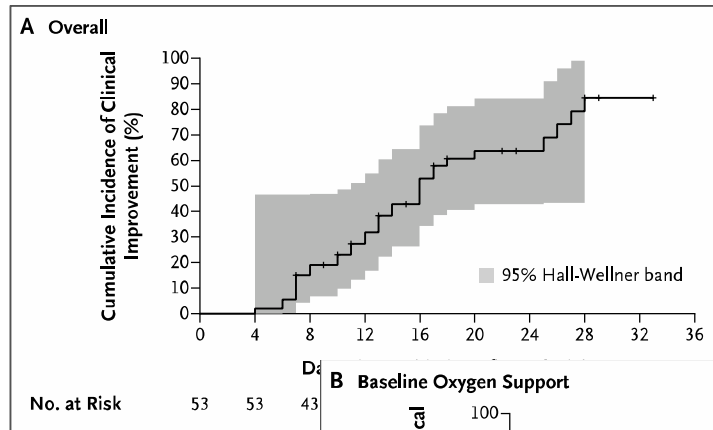
Risk factors for in-hospital mortality

	Univariable HR (95% CI)	Multivariable HR (95% CI)
Age (per 10-year increase)	1·49 (1·29–1·73)	1·31 (1·09–1·57)
Male sex	0·85 (0·57–1·27)	1·13 (0·71–1·81)
Symptom duration before hospital presentation (per day)	0·98 (0·93–1·02)	1·01 (0·96–1·05)
Hypertension	2·24 (1·40–3·59)	1·58 (0·89–2·81)
Chronic cardiac disease*	2·21 (1·44–3·39)	1·76 (1·08–2·86)
Chronic obstructive pulmonary disease or interstitial lung disease	3·15 (1·84–5·39)	2·94 (1·48–5·84)
Chronic kidney disease	1·50 (0·92–2·45)	..
Diabetes	1·65 (1·11–2·44)	1·31 (0·81–2·10)
Body-mass index ≥40	0·76 (0·40–1·47)	..
Interleukin-6 (per decile increase)	1·12 (1·04–1·21)	1·11 (1·02–1·20)
D-dimer (per decile increase	1·18 (1·10–1·27)	1·10 (1·01–1·19)

- Противовирусные препараты

- Иммуномодуляторы

- Препараты для лечения ОРДС и «цитокинового шторма»

- Иммунотерапевтические препараты

- Терапевтические антитела

- Вакцины

- *Блокада РАС и COVID-19*

- *Диабет и COVID-19*

- *Использование антикоагулянтов и тромболитиков*

Ремдесивир

A Overall

Cumulative Incidence of Clinical Improvement (%)

95% Hall-Wellner band

No. at Risk   53   53   43

B Baseline Oxygen Support

Cumulative Incidence of Clinical Improvement (%)

Noninvasive

Invasive

Days since Initiation of Remdesivir

No. at Risk

Noninvasive	19	19	15	10	6	2	1	0	1
Invasive	34	34	28	23	17	11	6	4	1

C Age

Cumulative Incidence of Clinical Improvement (%)

<50 Yr of age

50 to <70 Yr of age

≥70 Yr of age

Days since Initiation of Remdesivir

No. at Risk

<50 Yr of age	14	14	10	8	5	1	1	1	
50 to <70 Yr of age	21	21	18	12	8	5	3	1	0
≥70 Yr of age	18	18	15	13	10	7	3	2	1	0

Hopes rise for coronavirus drug remdesivir

Despite conflicting studies, results from largest trial yet show th
up recovery, putting it on track to become a standard of care in th

Heidi Ledford

Coronavirus causes severe respiratory illness in some people.   Credit: Zhang Yazi/China News

Генная инженерия может сделать вакцину COVID-19 за месяцы, а не годы – Scientific American

By early April almost 80 companies and institutes in 19 countries were working on vaccines, most gene-based instead of using traditional approaches, such as those that have been employed in influenza vaccines for more than 70 years. The labs predicted that a commercial vaccine could be available for emergency or compassionate use by early 2021—incredibly fast, given that vaccines to brand-new pathogens have taken a decade to be perfected and deployed. Even the Ebola vaccine, which was fast-tracked, took five years to reach widespread trials. If Barouch and his counterparts can offer a safe, effective concoction in a year, "it will be the fastest vaccine development in history," he says.
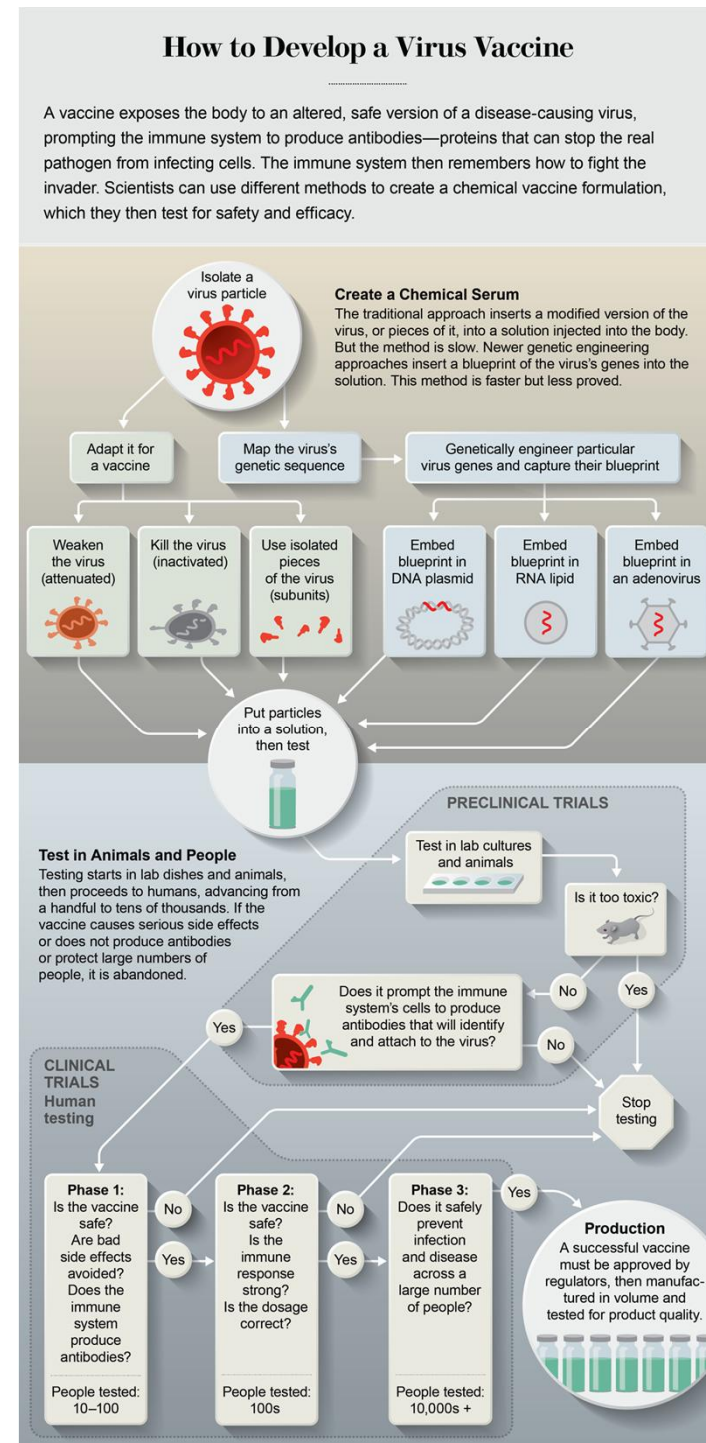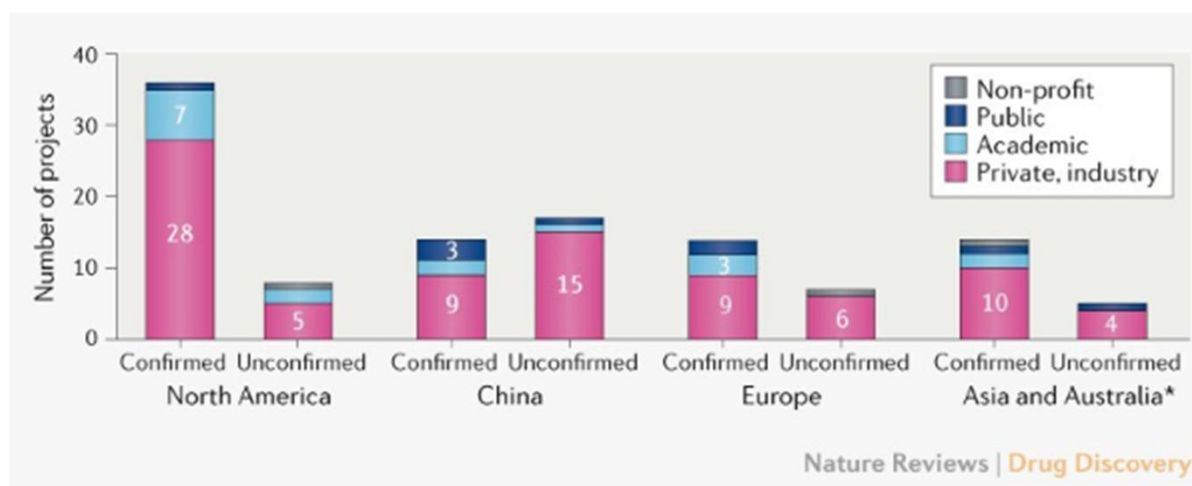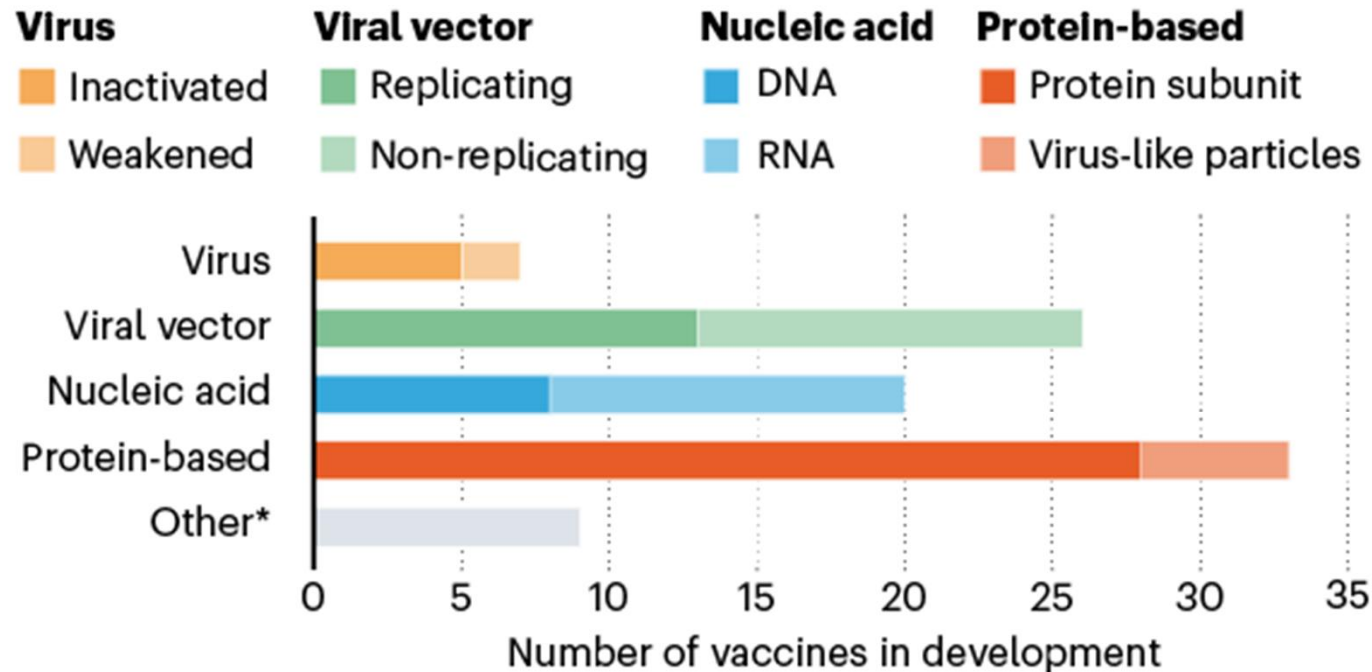
Разработчики вакцины
по типу и местоположению

Fig. 2 | **Profile of COVID-19 vaccine developers by type and geographic location.** For partnerships, the location is that of the lead developer. *Excluding China.

Типы вакцин

AN ARRAY OF VACCINES

Virus
- Inactivated
- Weakened

Viral vector
- Replicating
- Non-replicating

Nucleic acid
- DNA
- RNA

Protein-based
- Protein subunit
- Virus-like particles

Number of vaccines in development

* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

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Вирусные вакцины:
ослабленный и деактивированный вирус

ФИЦ ФТМ

Получение изолятов вируса
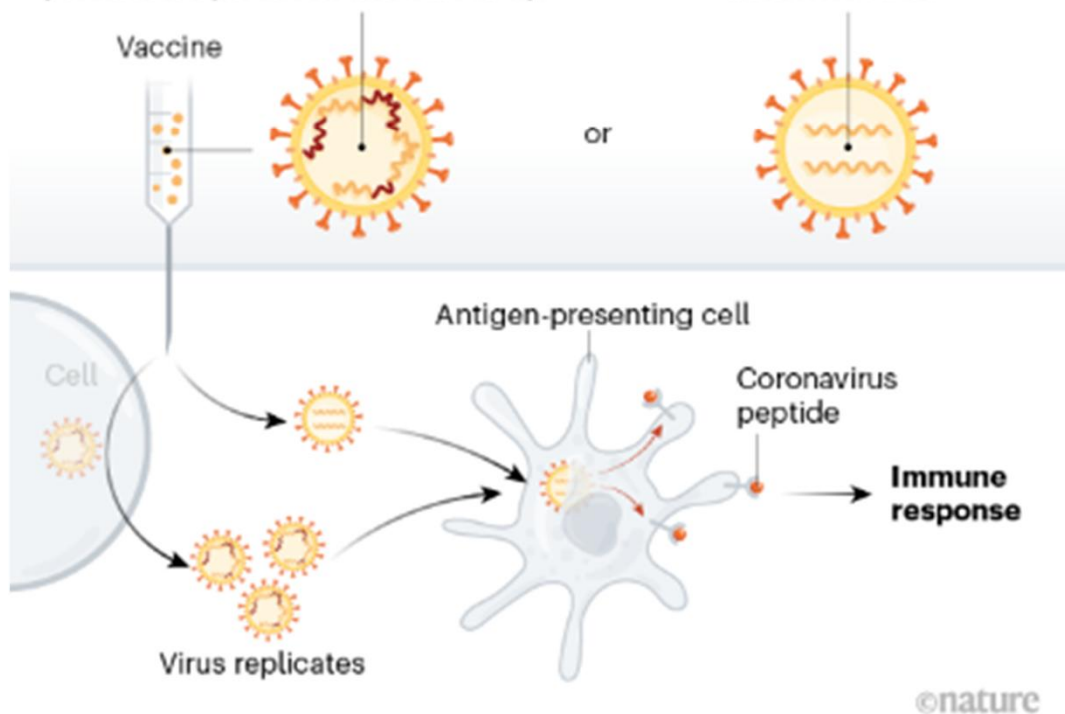SARS-Cov-2

д.м.н. А.М. Шестопалов
д.м.н. А.А. Чепурнов

VIRUS VACCINES

Weakened virus
A virus is conventionally weakened for a vaccine by being passed through animal or human cells until it picks up mutations that make it less able to cause disease. Codagenix in Farmingdale, New York, is working with the Serum Institute of India, a vaccine manufacturer in Pune, to weaken SARS-CoV-2 by altering its genetic code so that viral proteins are produced less efficiently.

Inactivated virus
In these vaccines, the virus is rendered uninfectious using chemicals, such as formaldehyde, or heat. Making them, however, requires starting with large quantities of infectious virus.

Vaccine

or

Cell

Virus replicates

Antigen-presenting cell

Coronavirus peptide

Immune response

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