Guidehouse

COVID-19 – The Virus, Biopharma response to prevention/treatment and the economic impact

What is COVID-19?

Coronaviruses are a family of viruses that can cause illnesses such as:

- Common cold
- SARS – Severe Acute Respiratory Syndrome
- MERS – Middle East Respiratory Syndrome

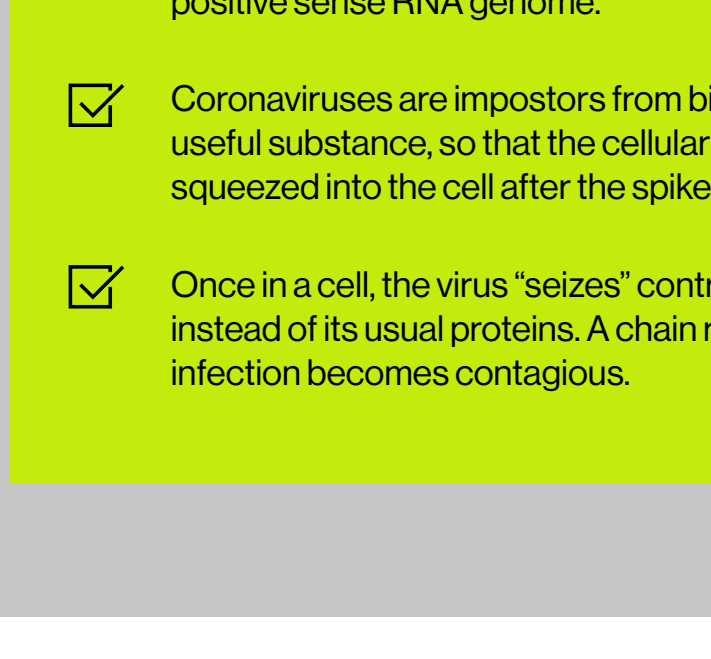
COVID-19 the virus

Virus: an infectious agent of small size and simple composition that can multiply only in living cells of animals, plants, or bacteria. The name is from a Latin word meaning "slimy liquid" or "poison."

Any of a large group of submicroscopic infectious; usually regarded as non-living extremely complex molecules, that typically contain a protein coat surrounding an RNA or DNA core of genetic material but no semipermeable membrane, that are capable of growth and multiplication only in living cells, and that cause various important diseases in humans, animals, and plants.

Size & Content

Diameter: ≈100 nm
Volume: ~10^6 nm^3 = 10^{-3} fL
Mass: ~10^3 MDa ≈ 1 fg



Genome

Nucleotide identity to SARS-CoV-2

bat CoV	pangolin CoV	SARS-CoV-1	MERS	common cold CoV
96%	91%	80%	55%	50%

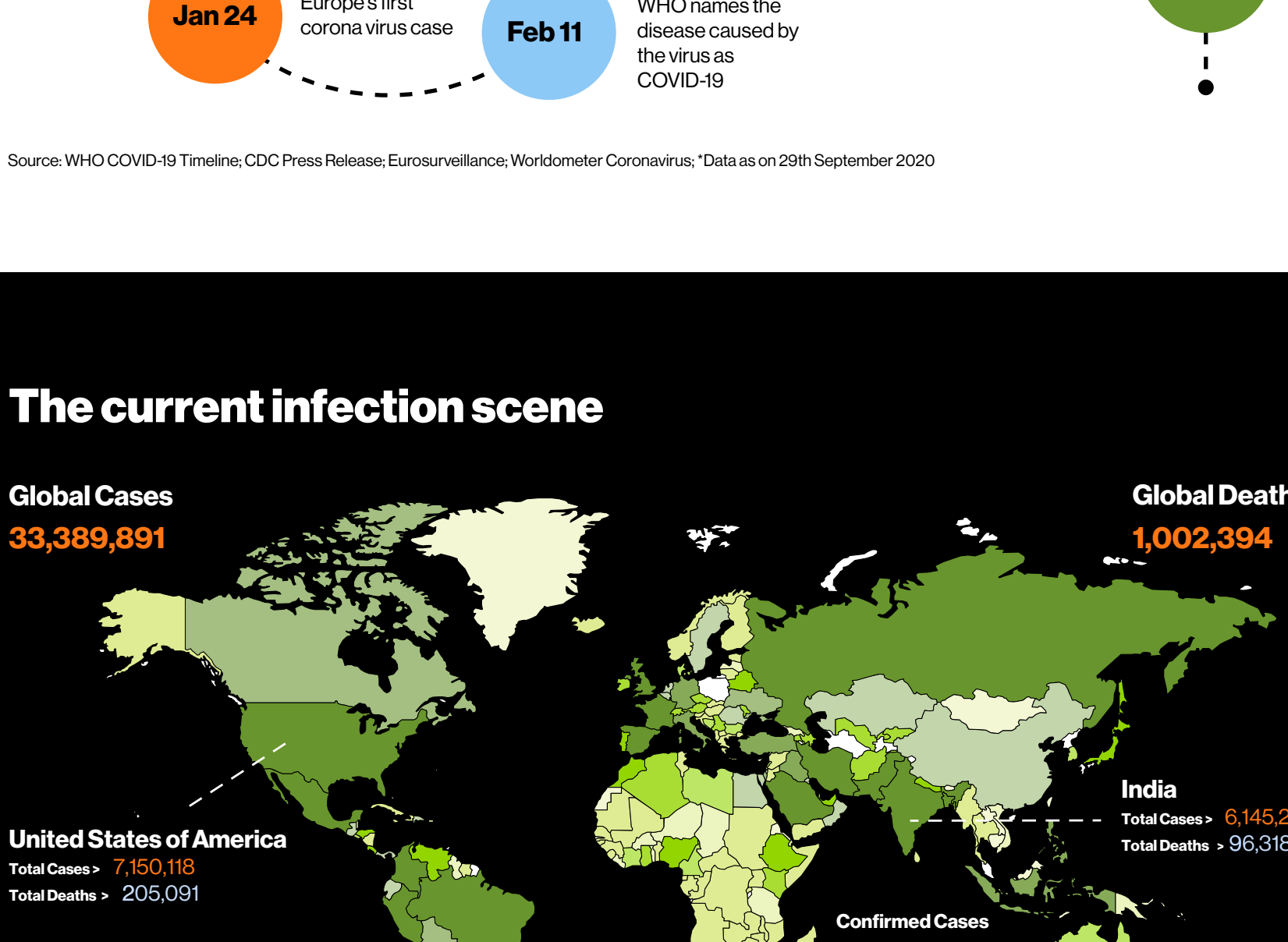
Replication Timescales

in tissue-culture
Virion entry into cell: - 10 min (measured for SARS-cov-1)
Eclipse period: - 10 hrs (time to make intracellular virions)
Burst size: - 103 virions (measured for MHV coronavirus)

A nanometer is one millionth of a millimeter; it is equal to 1 /1,000,000,oooth or one-billionth of a meter. In scientific notation a nanometer is expressed as 1x10-9 m.

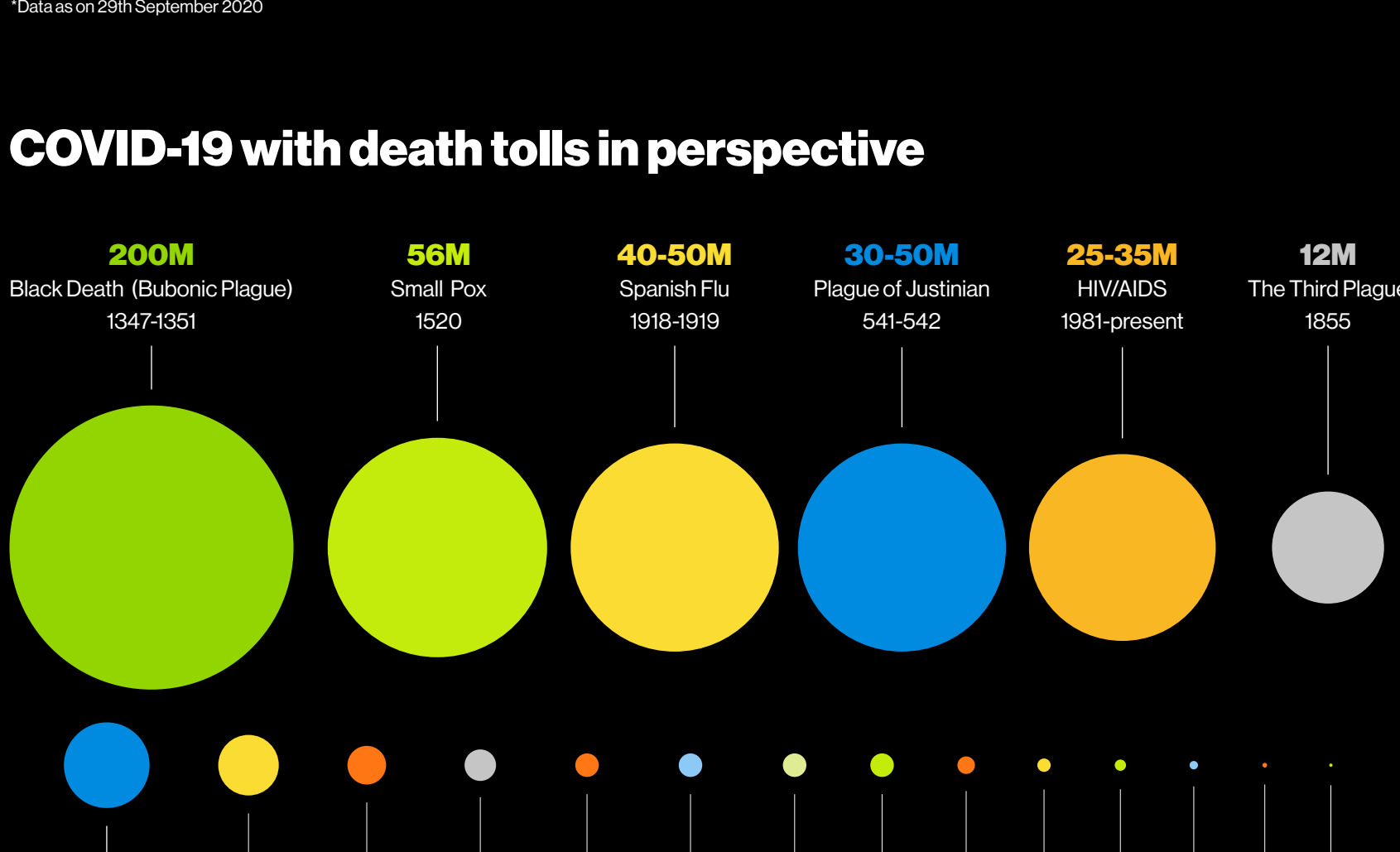
- The coronavirus receives its name from the halo or crown (corona) that is seen when the virus is viewed by an electron microscope. This morphology is actually attributed to the glycoproteins the virus uses to attach to the host cell. Coronaviruses also have an enveloped structure with a positive sense RNA genome.
- Coronaviruses are impostors from biology. The tailpiece of each spike "imitates" the molecule of a useful substance, so that the cellular receptors gladly pull it into themselves, and the whole virus is squeezed into the cell after the spike is in. This is how infection occurs.
- Once in a cell, the virus "seizes" control over it and forces it to endlessly produce its own copies - instead of its usual proteins. A chain reaction begins. As a result, the cell dies, but the carrier of the infection becomes contagious.

The covid-19 world timeline



Source: WHO COVID-19 Timeline; CDC Press Release; Eurosurveillance; Worldometer Coronavirus; *Data as on 29th September 2020

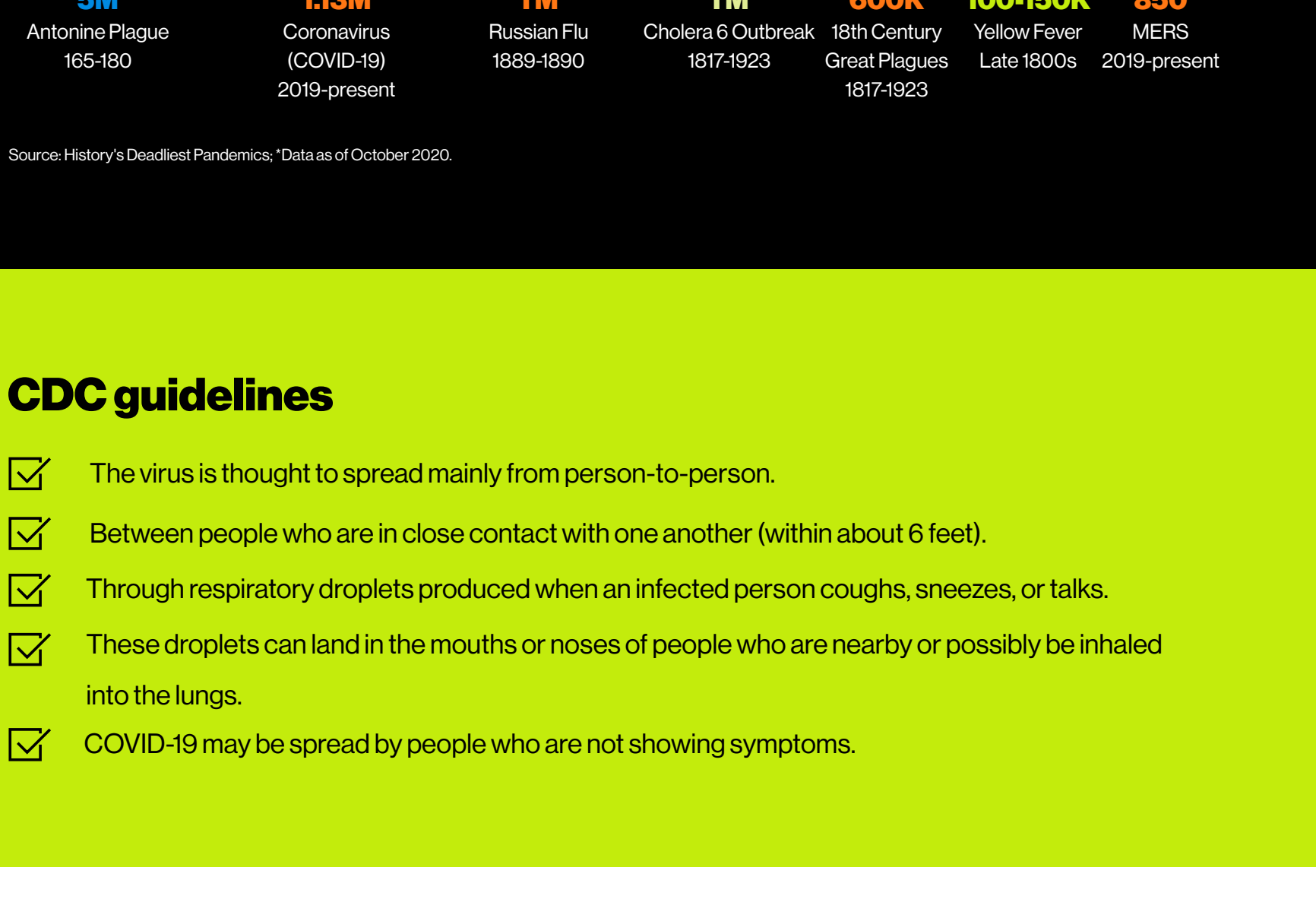
The current infection scene



Source: Johns Hopkins University & Medicine Coronavirus Resource Center*

*Data as on 29th September 2020

COVID-19 with death tolls in perspective



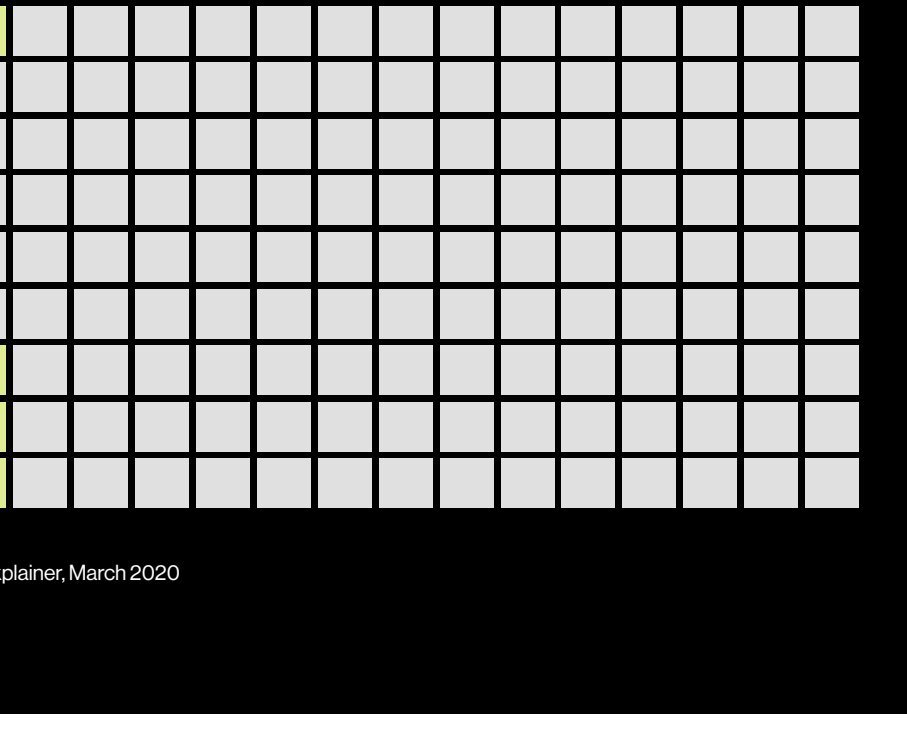
Source: History's Deadliest Pandemics; *Data as of October 2020.

CDC guidelines

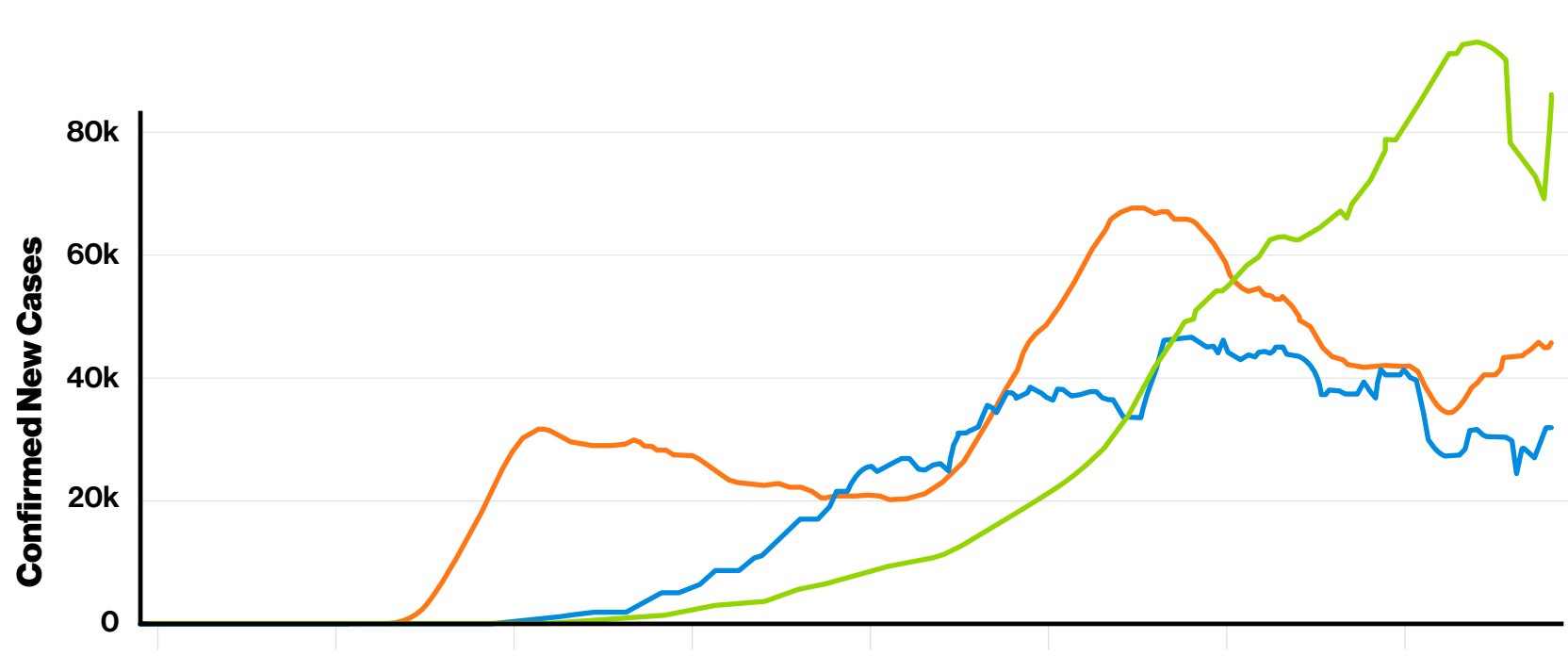
- The virus is thought to spread mainly from person-to-person.
- Between people who are in close contact with one another (within about 6 feet).
- Through respiratory droplets produced when an infected person coughs, sneezes, or talks.
- These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs.
- COVID-19 may be spread by people who are not showing symptoms.

Why social distancing?

Ebola - 3ft
Measles - 6ft
COVID-19 - 6ft

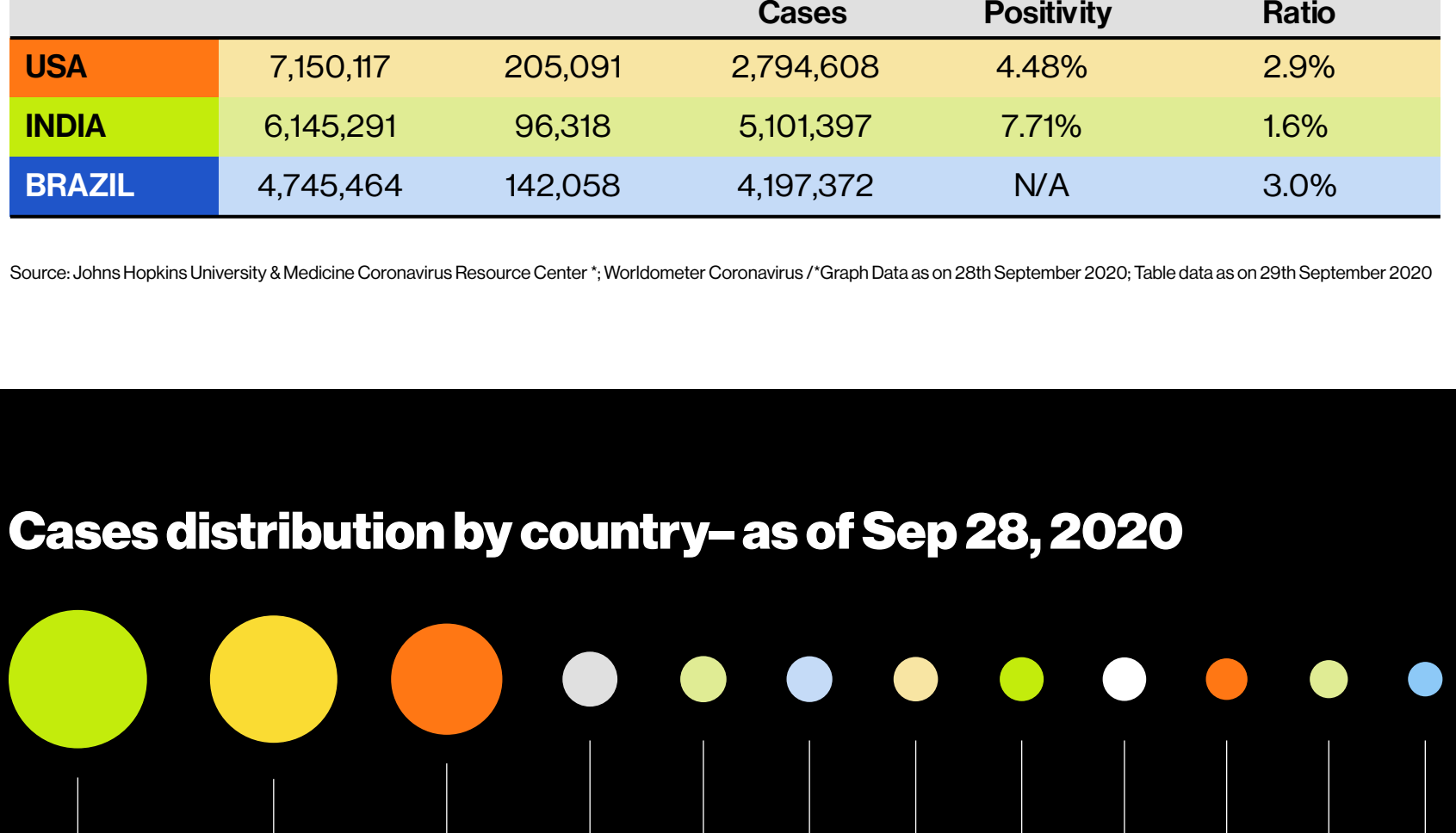


Expected number of people a patient will infect, by disease



Source: How contagious is COVID-19 compared to other viral diseases?, Coronavirus Explainer, March 2020

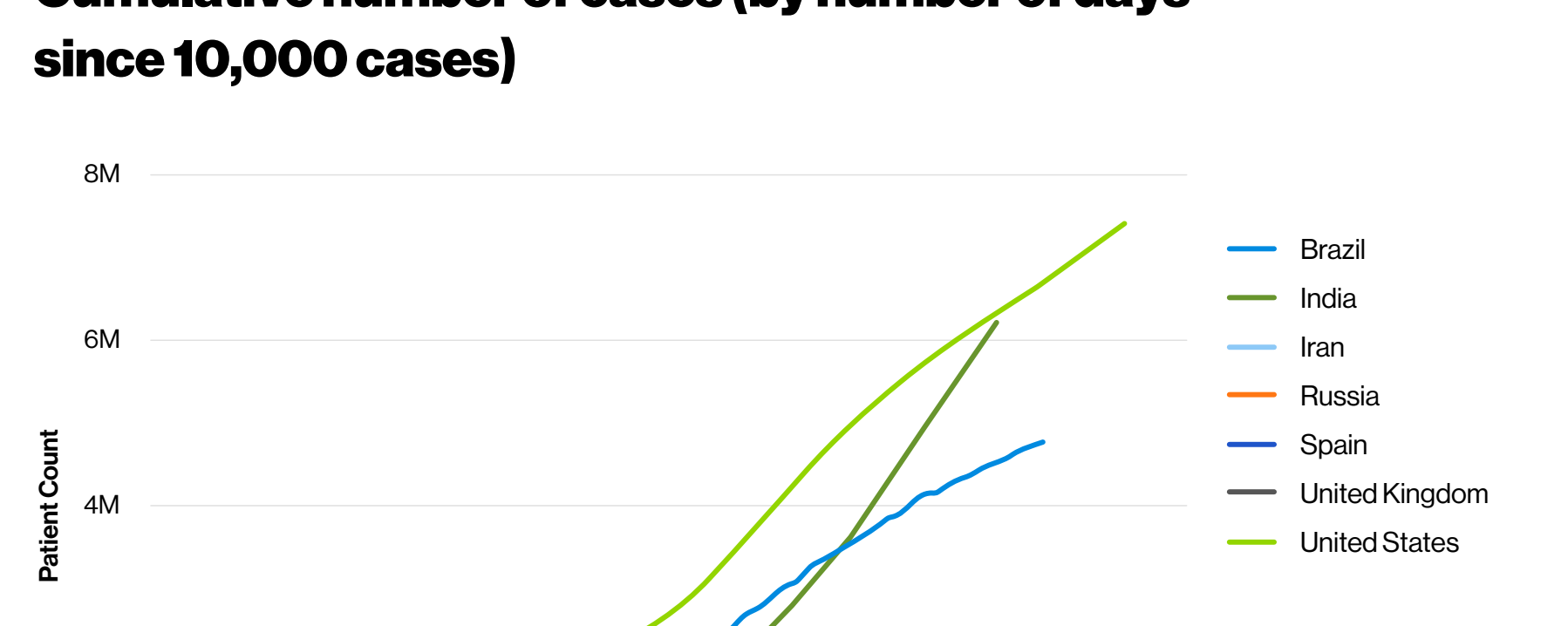
Outbreak evolution for the top 3 most affected countries



Country	Total Cases	Total Deaths	Recovered Cases	Daily Positivity	Case Fatality Ratio
USA	7,150,117	205,091	2,794,608	4.48%	2.9%
INDIA	6,145,291	96,318	5,101,397	7.71%	1.6%
BRAZIL	4,745,464	142,058	4,197,372	N/A	3.0%

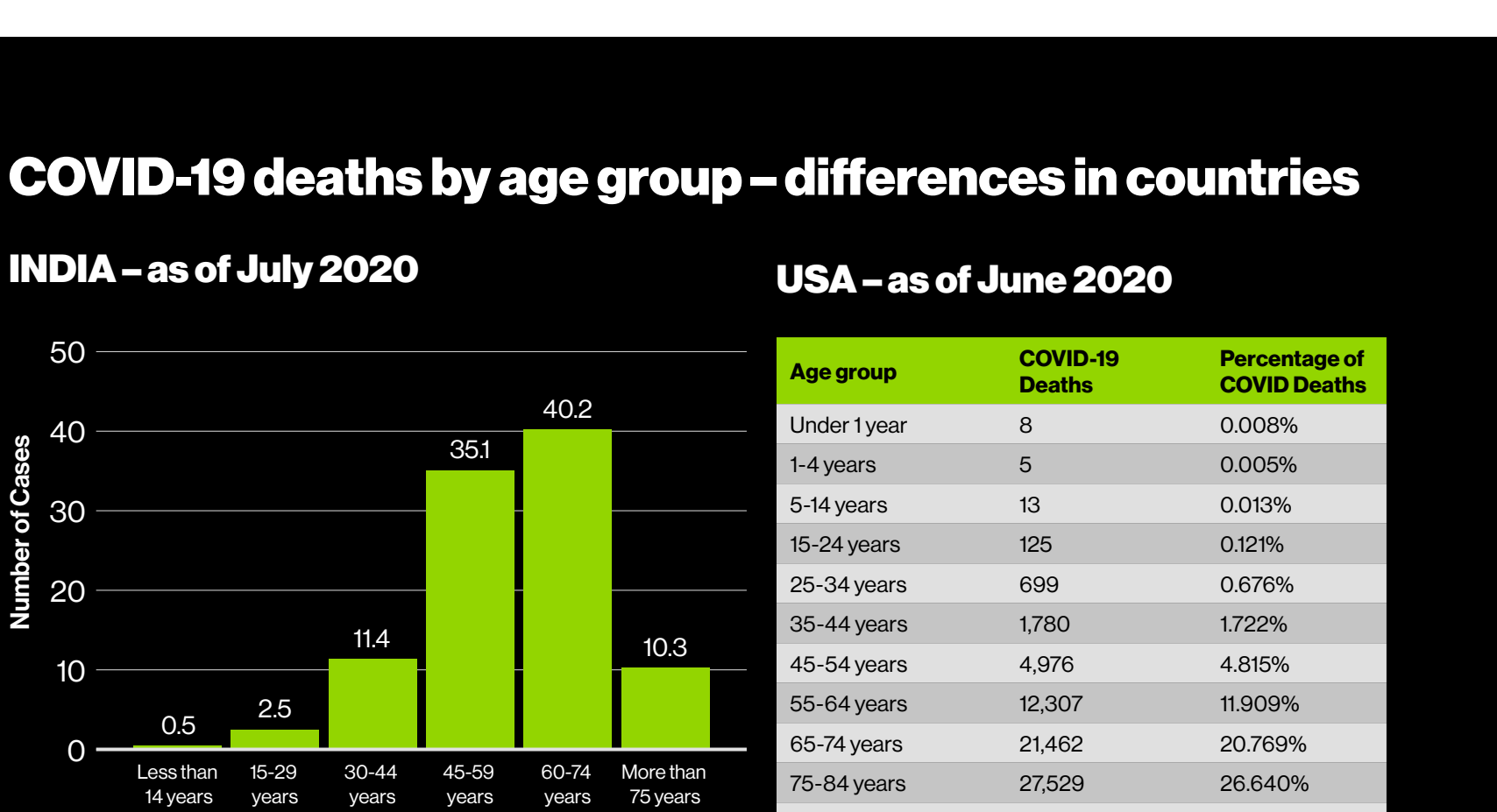
Source: Johns Hopkins University & Medicine Coronavirus Resource Center *; Worldometer Coronavirus /*Graph Data as on 28th September 2020; Table data as on 29th September 2020

Cases distribution by country– as of Sep 28, 2020



Source: Worldometer

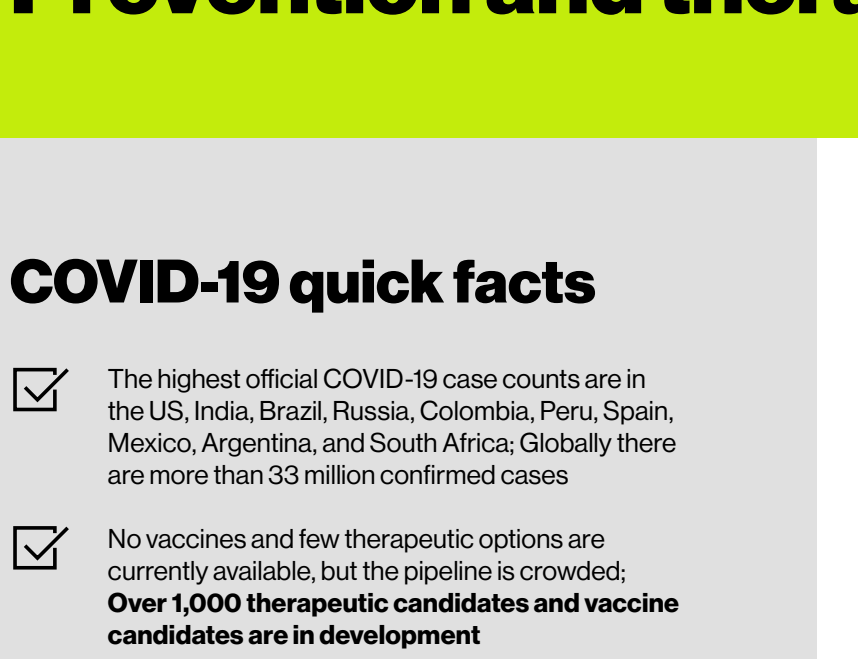
Cumulative number of cases (by number of days since 10,000 cases)



Source: Worldometer

COVID-19 deaths by age group – differences in countries

INDIA – as of July 2020



Source: Statista 2020 (https://www.statista.com/statistics/1110522/india-number-of-coronavirus-cases-by-age-group/).

USA – as of June 2020

Age group	COVID-19 Deaths	Percentage of COVID Deaths
Under 1 year	8	0.008%
1-4 years	5	0.005%
5-14 years	13	0.013%
15-24 years	125	0.121%
25-34 years	699	0.676%
35-44 years	1,780	1.722%
45-54 years	4,976	4.815%
55-64 years	12,307	11.909%
65-74 years	21,462	20.769%
75-84 years	27,529	26.640%
85 years and over	34,435	33.322%
All Ages	1,03,339	100.000%

Source: CDC

Prevention and therapeutic intervention

COVID-19 quick facts

- The highest official COVID-19 case counts are in the US, India, Brazil, Russia, Colombia, Peru, Spain, Mexico, Argentina, and South Africa; Globally there are more than 33 million confirmed cases
- No vaccines and few therapeutic options are currently available, but the pipeline is crowded; **Over 1,000 therapeutic candidates and vaccine candidates are in development**
- Vaccine candidates using classic technology will likely take at least 12-18 months to develop but development timelines for DNA or mRNA vaccines could be shorter.
- Several already-marketed antivirals such as remdesivir, favipiravir and immunomodulatory drugs are pursued as COVID-19 treatment since they have already demonstrated safety and tolerability for other indications

Industry experts estimate that the first COVID-19 vaccine will be approved and available within this year

Sources: 1. CDC US Count 2. Global Data as of September 29, 2020 3. FDA news

Vaccines

Developers from around the world are using different platforms to build vaccines to protect people against COVID-19 disease

mRNA Vaccines

These vaccines function by introducing an mRNA sequence coded for a disease specific antigen. Once produced within the body the antigen is recognized and immune response is mounted

DNA Vaccines

DNA vaccines are made up of circular pieces of bacterial DNA called plasmids. Once injected, using the DNA proteins are synthesized by the body which further elicit an immune response

Protein-based Vaccines

Protein vaccines are composed of purified or recombinant proteinaceous antigens from a pathogen, such as a bacterium or a virus. These antigens are subsequently recognized by the body and protective response is elicited

Inactivated/ Attenuated Vaccines

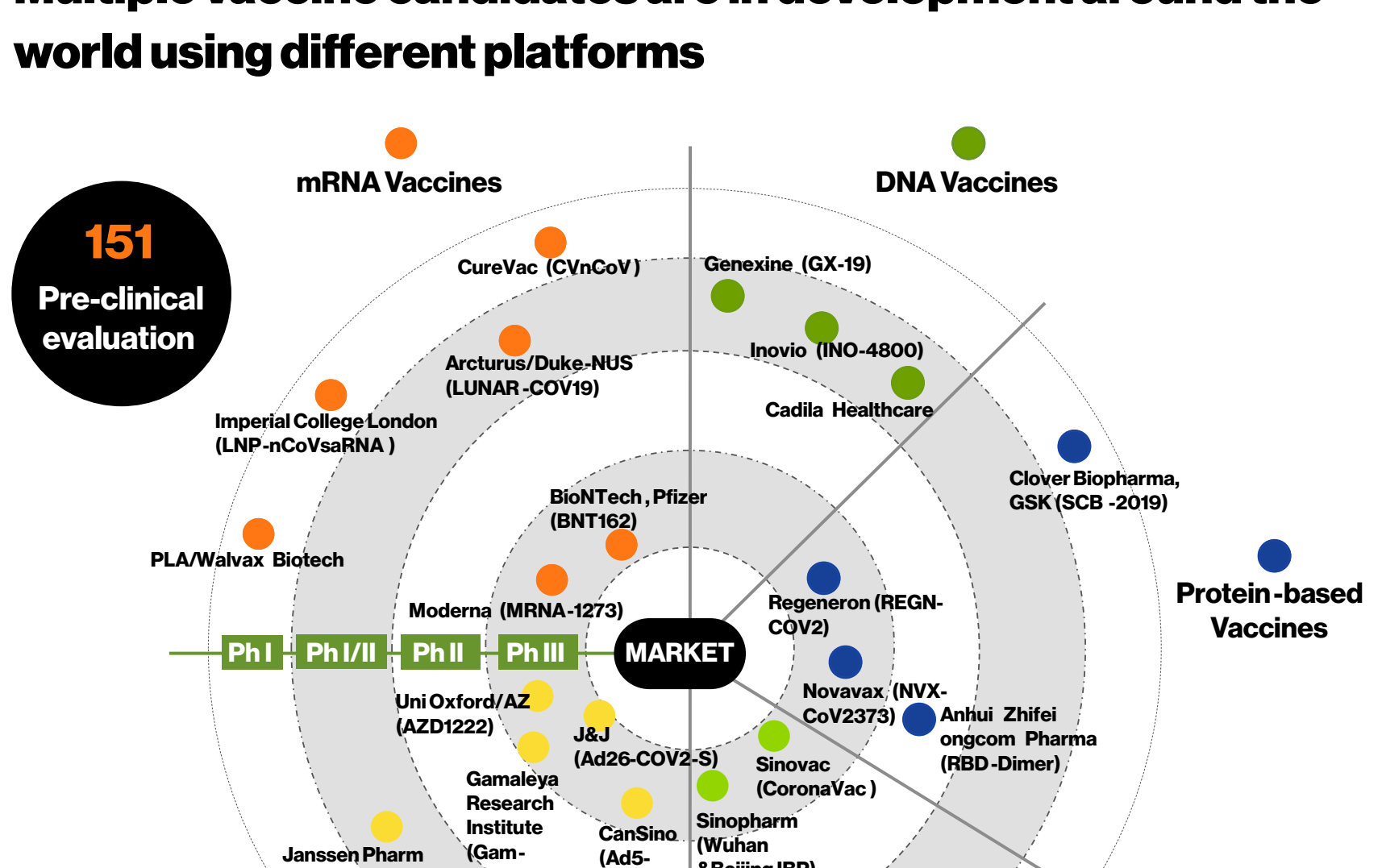
An attenuated vaccine is developed by reducing the virulence of the virus because of which it is unable to replicate sufficiently to cause disease, but will still induce an immune response in the body

Viral Vector (Replicating/ Non-Replicating)

Viral vector vaccines carry DNA into a host cell for production of antigenic proteins. They usually contain a live attenuated virus that is genetically engineered to carry DNA encoding protein antigens from an unrelated organism

Source: BiopharmaDive

Multiple vaccine candidates are in development around the world using different platforms



Source: WHO Draft landscape of COVID-19 Vaccines; https://www.biopharmadive.com/news/coronavirus-vaccine-pipeline-types/579122/; https://covid-19tracker.milkeninstitute.org/#vaccines_intro; McKinsey & Company COVID-19 Briefing Materials

Planned capacity puts leading programs on track to vaccinate ~3 Billion patients in 2021

Source: Company data, Credit Suisse estimates

Key factors impacting vaccine success

Safety & Efficacy

In a historical move, vaccine frontrunners AstraZeneca, Johnson & Johnson, BioNTech, GSK, Pfizer, Merck, Moderna, Sanofi, and Novavax have pledged to apply for regulatory approval ONLY after ensuring the safety and efficacy of the vaccines through all the 3 phases of clinical study, upholding scientific and ethical standards.

Distribution Challenges

In addition to strict temperature requirements for efficacious vaccines and the need for a proper immunization program, supply chain complexity will be on the top of the many distribution pain points, which include product quality issues, constrained transportation capacity, as well as complex customs and regulatory requirements across the globe.

Re-Infection & Virus Mutations

Although mutations and/or re-infections do not imply that the vaccine will not work, they do reinforce the need for booster doses and vaccination strategies need to be designed to account for these.

Manufacturing Capacity

With companies aiming to manufacture more than a billion doses per year, local drug makers are being tapped to meet this requirement. Furthermore, production of syringes, vials, and cold storage containers are being ramped up to meet this demand.

Who Gets It First?

As governments jockey to secure supplies, reserving millions of doses, what remains to be established is who gets the first supply of vaccines-1st responders? The elderly? People with comorbidities? Children?

Pricing Pressure

Gavi's COVAX Advanced Market Commitment made to 92 low-and middle-income countries aims at pricing the vaccines at US$3 per dose. The question is, with the growing dip in global economies, will these countries be able to afford even this low cost of the vaccine?

Antiviral Drugs

Clinical investigations for therapeutics and vaccines for COVID-19

Robust research of novel and existing drugs leading to exponential increase in trials

Countries with >90 COVID trials	Trials (n)
United States	605
China	435
Iran	333
India	328
Spain	152
Brazil	116
France	100
Italy	99
UK	91

Source: Clinicaltrial.gov

- Currently there are 3,310 clinical trials for COVID-19, and around 1,005 companies and institutions driving prophylactic and curative innovation
- US and India have shown increase in number of trials in respective geographies compared to other countries, with US surpassing China and India to surpass Iran soon in total number of COVID-19 trials
- Promising clinical data are continuing to emerge for COVID-19 vaccines and experts believe that mRNA vaccines are the most promising technology

Clinical investigations of novel and existing drugs continue to grow

Treatment of COVID-19

590+ Drug development programs in planning stages

310+ Trials reviewed by FDA (safe to proceed INDs)

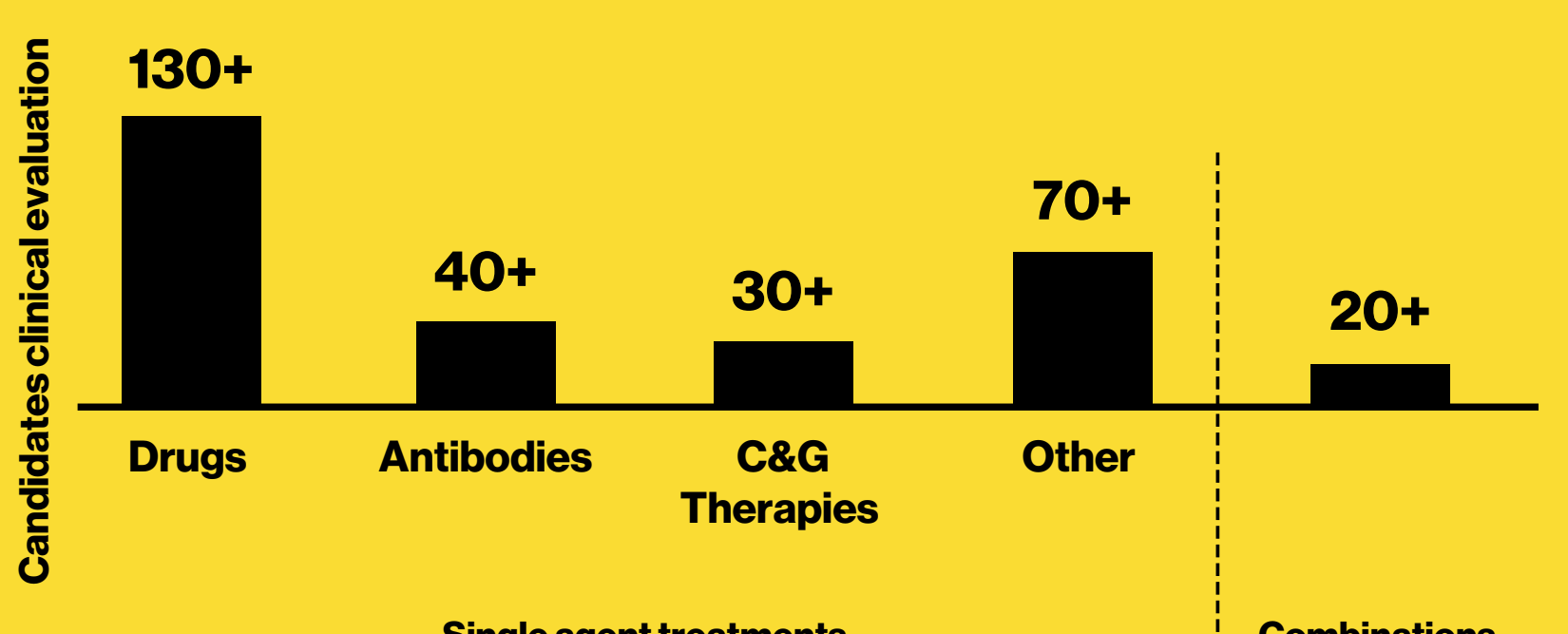
5 Treatments with Emergency Use Authorization*

0 Treatments approved by FDA for COVID-19

70+ Pre-clinical and early-stage trials (0, 1, 1/2, 2)

240+ Late/end-stage trials (2/3, 3, 4)

*This number includes authorization for both medical devices and investigational drugs/therapies for emergency use



Source: Coronavirus Treatment Acceleration Program-FDA; Milken Institute's COVID-19 Tracker / Data as on 31st August 2020

Frontline therapeutic candidates

Drugs

- Antivirals and Immunomodulators already approved for other diseases like HIV and Ebola.
- Antiviral treatments stop viruses from making more of themselves by blocking one or more steps in the process.
- Immunomodulators are aimed at tamping down the body's own immune reaction to the virus, in cases where the body's reaction basically goes overboard and starts attacking the patient's own organs.

Antibodies

- Antibodies obtained from plasma of recovered patients, or from animal sources, or bio-engineered from previous viruses.
- Attach to the foreign intruders and target them for destruction.
- Also created to attach to different molecules in the body (not foreign intruders); can treat disease by turning down immune response to stop it from overreacting and causing damage to the body (a phenomenon known as "cytokine storm").

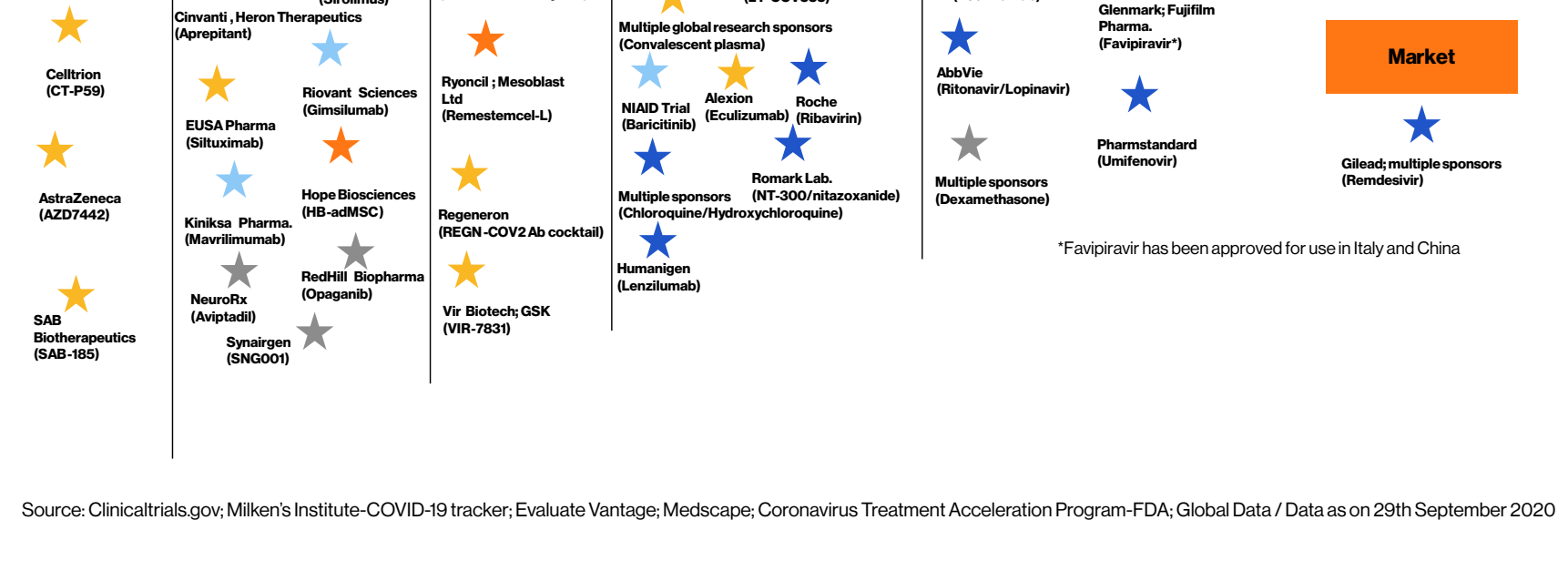
Cell & Gene Therapies

- Cellular immunotherapies using autologous and allogeneic cells, like stem cells and related products or modifying/manipulating the expression of a gene to alter the biological properties of a cell.
- Different cell types from different sources can be used (e.g. stem cells from fat tissue or bone marrow, cells from placenta, T-cells, natural killer [NK] cells).
- Help the patient's immune system work better (and not overreact) by releasing signals to other cells in the body to coordinate a proper reaction to the infection and help healing.

FDA Emergency Use Authorization

Drug	Company	Approval details
Convalescent Plasma	—	Distribution of COVID-19 Convalescent Plasma in the U.S. and its administration by health care providers, as appropriate, to treat suspected or laboratory confirmed COVID-19 in hospitalized patients with the disease.
REGIOCIT replacement solution	Baxter Healthcare	REGIOCIT to be used as a replacement solution only in adult patients treated with continuous renal replacement therapy (CRRT), and for whom regional citrate anticoagulation is appropriate, in a critical care setting.
Remdesivir	Gilead Sciences	Now under the brand name Veklury, has been approved by the FDA as a prescription medicine to treat COVID-19 in adults and children at least 12 years old and weighing at least 88 pounds requiring hospitalization.
Fresenius Propoven 2% Emulsion	Fresenius Kabi	Fresenius Propoven 2% Emulsion is approved to maintain sedation via continuous infusion in patients greater than 16 years old who require mechanical ventilation in an ICU setting.
Continuous renal replacement therapy	Fresenius Kabi	Continuous renal replacement therapy (CRRT) to treat patients in an acute care environment during the COVID-19 pandemic.

Pipeline of therapeutic candidates for COVID-19



Source: Clinicaltrials.gov; Milken's Institute-COVID-19 tracker; Evaluate Vantage; Medscape; Coronavirus Treatment Acceleration Program-FDA; Global Data / Data as on 29th September 2020

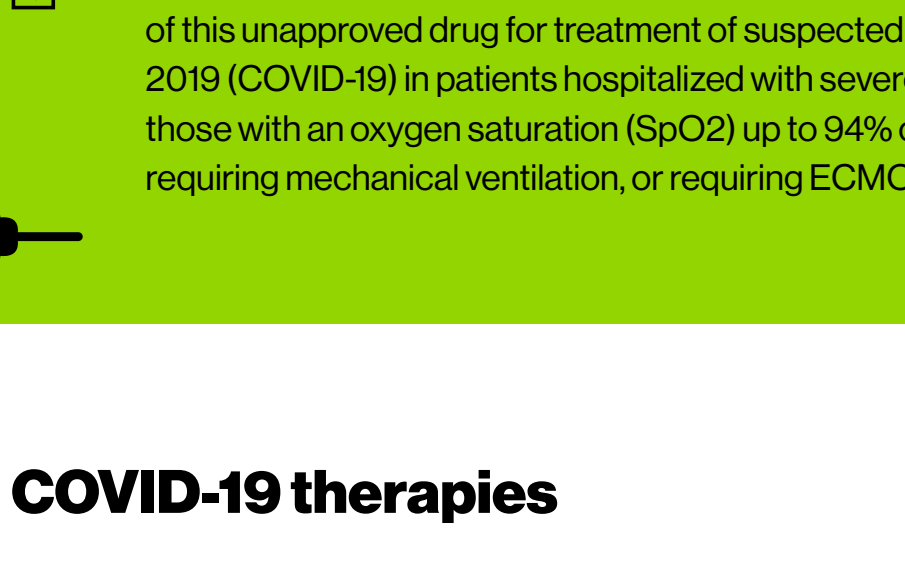
What is remdesivir?

- Remdesivir is an experimental medicine being studied for use in treating conditions caused by coronaviruses. It is not yet known if remdesivir is a safe and effective treatment for any condition.
- Remdesivir has not been approved to treat coronavirus or COVID-19. However, the US Food and Drug Administration (FDA) has authorized emergency use of remdesivir in adults and children who are hospitalized with COVID-19.
- Remdesivir is one medication that is currently being trialled to treat patients with complications from COVID-19.
- Remdesivir stops the virus from making copies of itself by stopping the RdRp from doing its job properly. This stops the virus numbers from increasing and stops the infection getting worse.
- Remdesivir is not currently approved by FDA and is in the clinical trial stage of development and also available under the "expanded access" program.
- In May 2020, the US FDA issued an emergency use authorization (EUA) to allow the emergency use of this unapproved drug for treatment of suspected or laboratory confirmed coronavirus disease 2019 (COVID-19) in patients hospitalized with severe disease; patients with severe disease include those with an oxygen saturation (SpO2) up to 94% on room air, requiring supplemental oxygen, requiring mechanical ventilation, or requiring ECMO.

COVID-19 therapies

Trials are investigating novel agents as well as repurposed drugs

Investigational Drugs in COVID-19 Trials



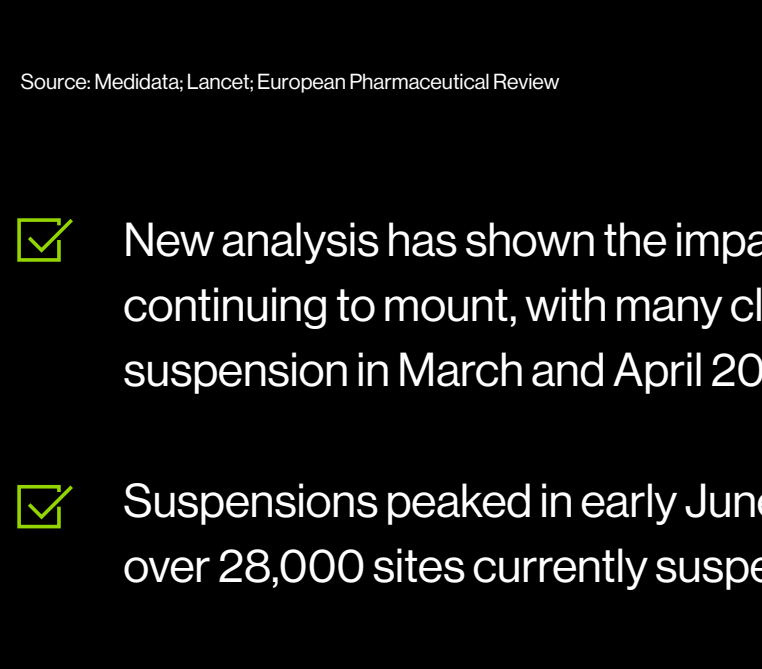
Source: Clinicaltrials.gov

- ~268 trials are investigating vaccines. While >80% of vaccine candidates are still in discovery or preclinical development
- Most trials are conducted for drugs Chloroquine or Hydroxychloroquine (anti malarial) followed by others such as Lopinavir/Ritonavir (HIV protease inhibitors), Toclizumab (Monoclonal antibody), Remdesivir (RNA polymerase Inhibitor: Antiviral-Ebola drug) etc.,
- Trials are testing various combinations and regimens of antiviral therapies
- Biologicals and investigational drugs are also been tested as potential treatments

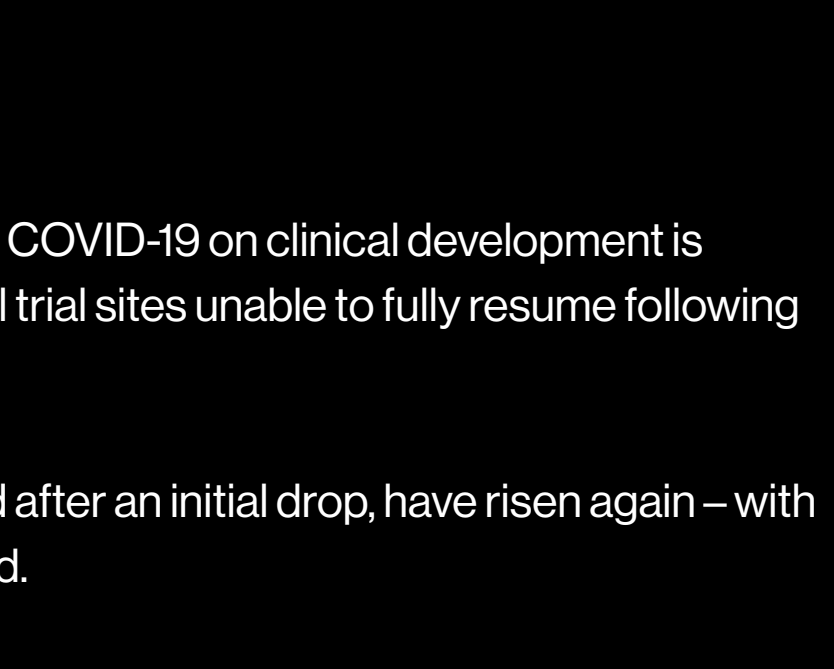
The global impact of COVID-19 on clinical trials

- There was a 65% worldwide average decrease in new patient enrollment year-over-year during March.
- The impact of COVID-19 is not uniform across therapeutic areas – some are more affected than others.

% decrease in avg patient enrollment yr-over-yr in major markets



% decrease in avg patient enrollment across different therapeutic areas



Source: Medidata; Lancet; European Pharmaceutical Review

- New analysis has shown the impact of COVID-19 on clinical development is continuing to mount, with many clinical trial sites unable to fully resume following suspension in March and April 2020.
- Suspensions peaked in early June and after an initial drop, have risen again – with over 28,000 sites currently suspended.
- Around 80% of non-COVID-19 trials have been stopped or interrupted.

In addition to drugs and vaccines as potential COVID-19 therapies, some medical devices are also playing a crucial role in treating the disease

These potential treatments include blood purification devices that filter patients' blood to remove excess proteins (for example cytokines causing the "cytokine storm") or toxins that are causing problems that can lead to respiratory or organ failure in patients.

Device	Company/Developer	FDA EUA Status
Hemolung Respiratory Assist System	Alung Technologies	✔
Impella RP Heart Pump	Abiomed	✔
Oxiris Blood Purification Filter	Baxter	✔
Cytosorb (Blood Purification Device, Extracorporeal Cytokine Adsorber)	Cytosorbents Corporation	✔
Seraph100microbindaffinity Blood Filter (Seraphy 100), Approved In The Eu For Pathogen Reduction	Ex thera Medical	✔
Multifiltrate Pro System And Multibic/ Multiplus Solutions, Continuous Renal Replacement Therapy (Crrt)	Fresenius Medical	✔
Extracorporeal Blood Purification (Ebp) Devices	Terumo Bct Inc / Marker Therapeutics Ag	✔
Gammacore Sapphire Cv, Vagus Nerve Stimulation Device	Electrocore	✔

Source: Clinicaltrials.gov; Milken's Institute-COVID-19 tracker/ Data as on 29th September 2020

Risk factors and uncertainty associated with COVID-19

Risk Factors

Several countries worldwide are reporting a higher death rate in males than in females

Older adults (> 65 years of age) appear to be at a high risk for COVID-19

The risk of developing dangerous symptoms of COVID-19 is considerably high in people of any other age with serious health problems and weakened immune systems

- Chronic Respiratory Disorders; Tuberculosis
- Cardiovascular Disease; Hypertension
- Diabetes
- Malaria

Uncertainty about...

- Continuing spread of virus
- True morbidity and mortality rates
- The development of herd immunity
- When treatment/ vaccination for virus will come into existence
- Extent of damage to the economy the longer the pandemic persists

Economic impact of COVID-19

The Big Picture

To put this quarter's 9.5% drop into perspective, it helps to look back in history. Since record keeping began in 1947, quarterly GDP had never exceeded even a 3% drop (non-annualized). Here are just a few of the problems currently plaguing the economy:

Employment

Well over 50 million people are still out of the workforce as businesses shutter permanently and restrictions continue in many parts of the country. New unemployment claims have now exceeded 1 million for 19 consecutive weeks.

Consumer Spending

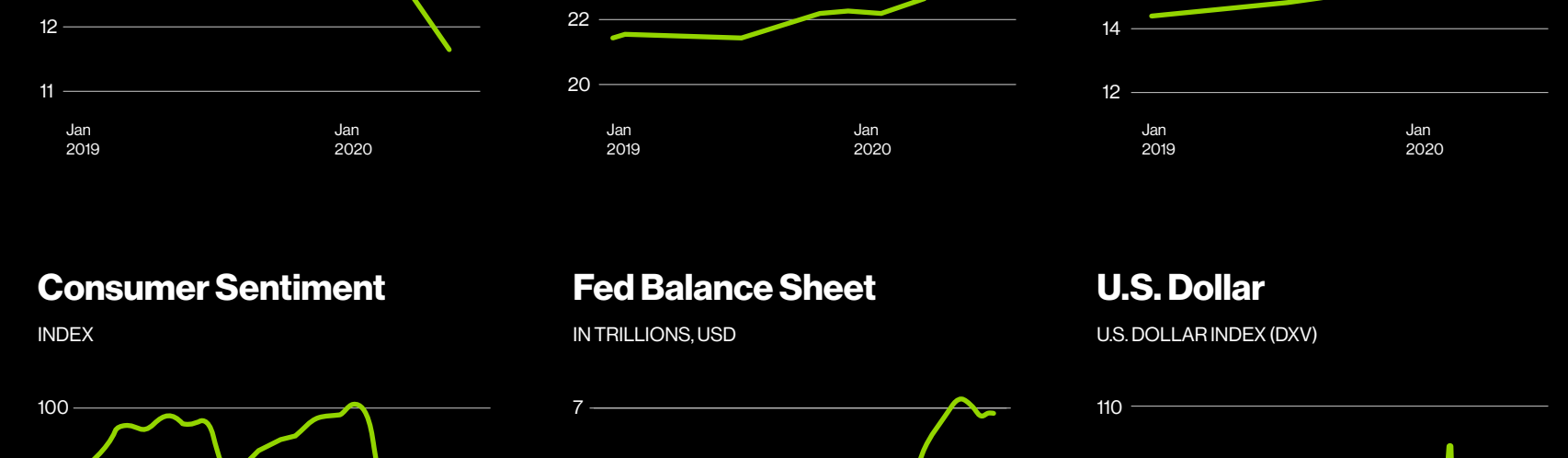
This makes up more than two-thirds of the U.S. economy, and it sank by the sharpest rate in April—declining by 12.6%. The weekly payments of $600 provided through the CARES Act helped bolster household income, partially offsetting steeper losses. However, the payments expired July 31, and may not be renewed as an initiative.

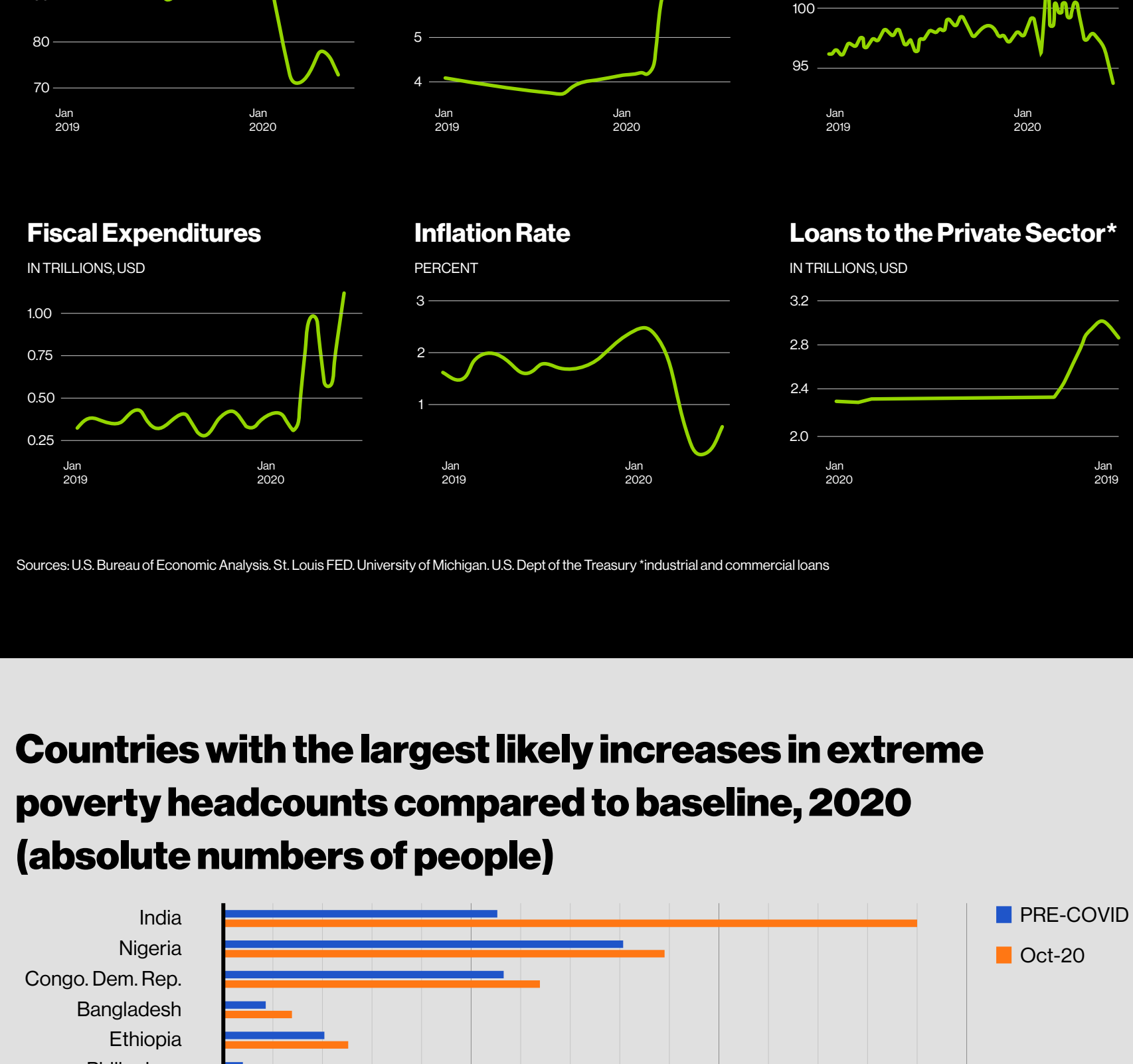
Monetary Policy

Trillions of dollars have been borrowed to counter the crisis, money supply (M2) has rapidly risen, and central bank balance sheets are shattering records. Despite the injection of money into the system, inflation has dropped to almost zero–well below the Fed's ideal 2% rate–signalling deflationary pressure on the economy.

Source: Visual Capitalist, July 31, 2020

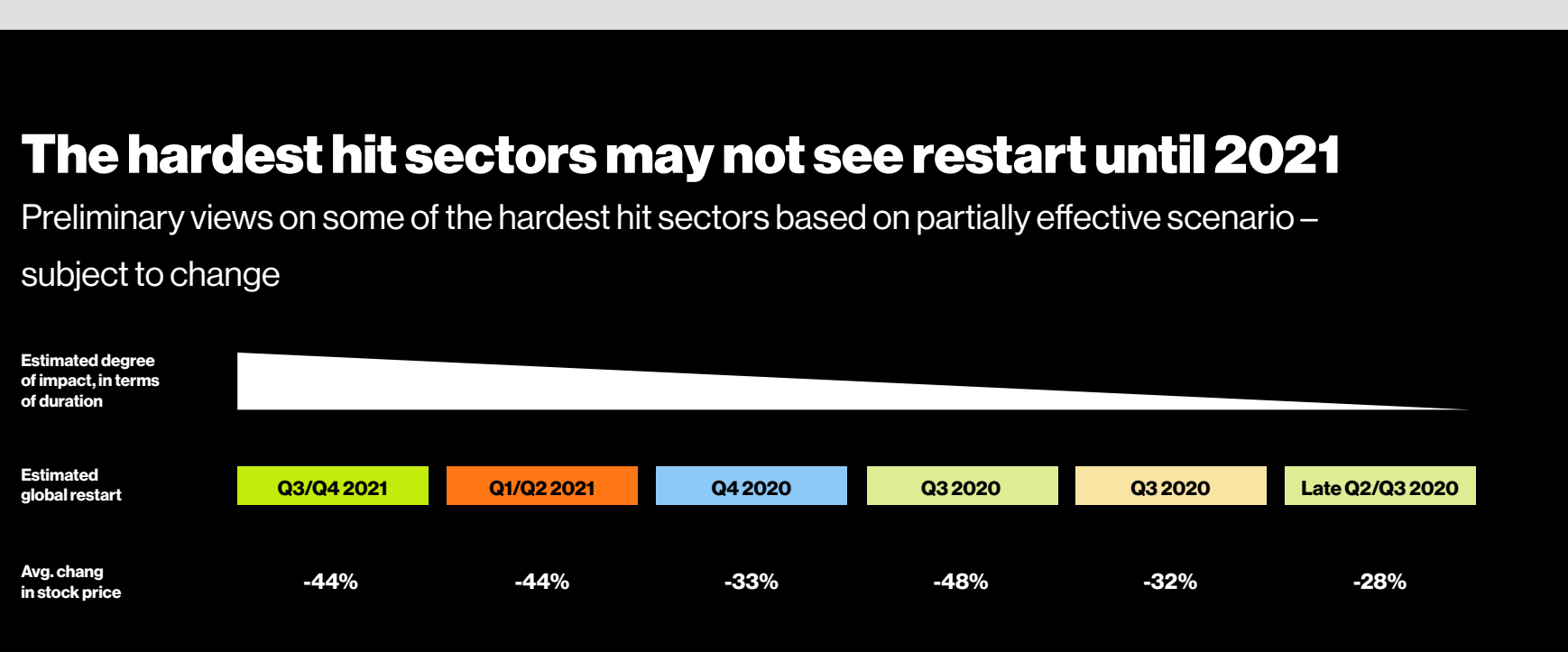
Q2 2020: The economic impact of COVID-19





Sources: U.S. Bureau of Economic Analysis. St. Louis FED. University of Michigan. U.S. Dept of the Treasury *industrial and commercial loans

Countries with the largest likely increases in extreme poverty headcounts compared to baseline, 2020 (absolute numbers of people)



Source: Author's calculations based on IMF World Economic Outlook October 2020 and World Bank Povcal data

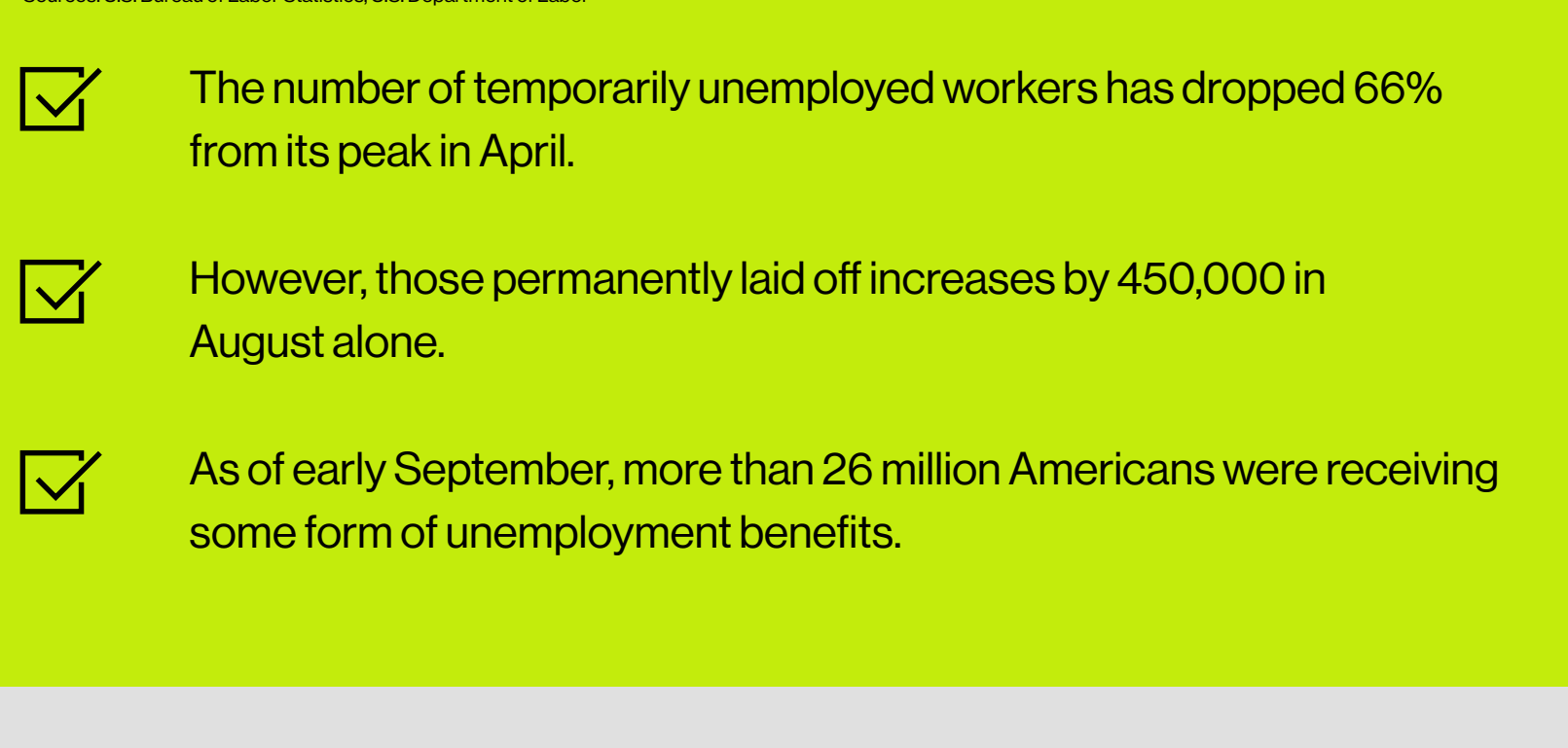
The hardest hit sectors may not see restart until 2021

Preliminary views on some of the hardest hit sectors based on partially effective scenario – subject to change

Estimated degree of impact, in terms of duration						
Estimated global restart	Q3/Q4 2021	Q1/Q2 2021	Q4 2020	Q3 2020	Q3 2020	Late Q2/Q3 2020
Avg. chang in stock price	-44%	-44%	-33%	-48%	-32%	-28%

Source: Remembering eDiscovery Defensibility in a Crisis July 7, 2020/in ACEDS Blog, Data and Technology, Security

Temporary vs. Permanent job losses due to COVID-19 (000s)



Sources: U.S. Bureau of Labor Statistics, U.S. Department of Labor

- The number of temporarily unemployed workers has dropped 66% from its peak in April.
- However, those permanently laid off increases by 450,000 in August alone.
- As of early September, more than 26 million Americans were receiving some form of unemployment benefits.

Financial sacrifices to keep up with rent payments

Since the start of the COVID-19 pandemic, which of the following are true?

Source: Apartment list survey data, Sept. 2020

- About 36% of renters surveyed reported using savings for rent payments.
- One in 3 renters started September owing back rent.
- One-in-four have borrowed from friends or family: about the same number have started to accumulate credit card debt.

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