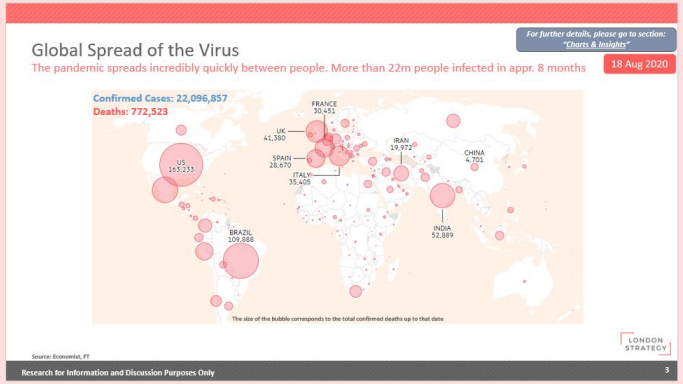
Aug 2020

COVID-19 Series

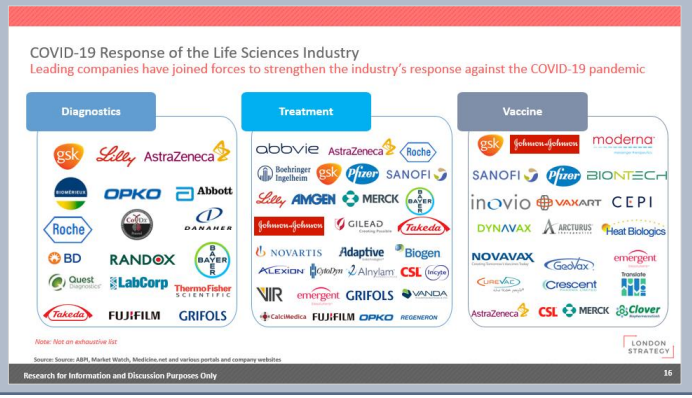
LONDON STRATEGY

COVID-19 Series - Index

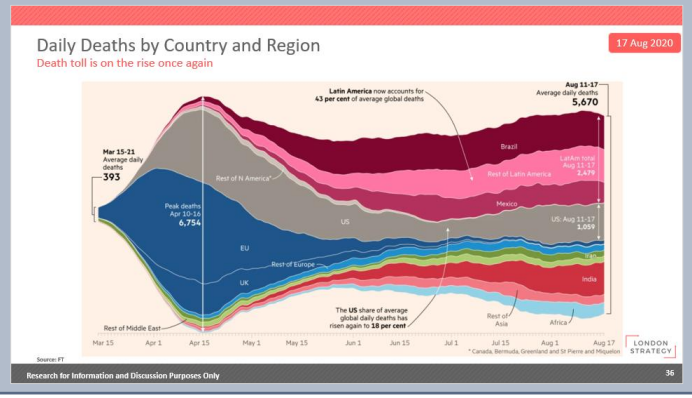
Impact on Life Sciences Sector: 3-13



Response of the Life Sciences Industry:15-33



Charts & Insights: 35-55



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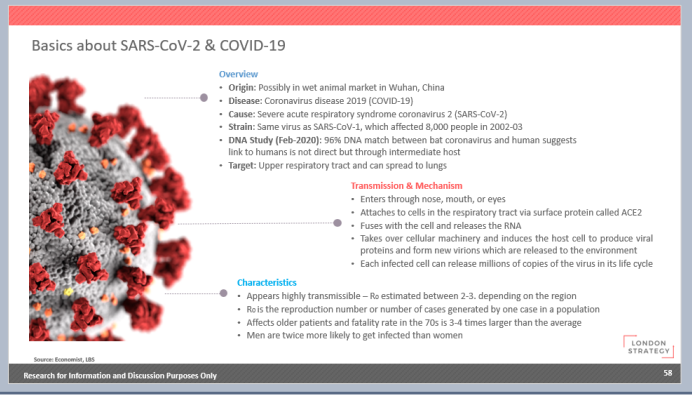

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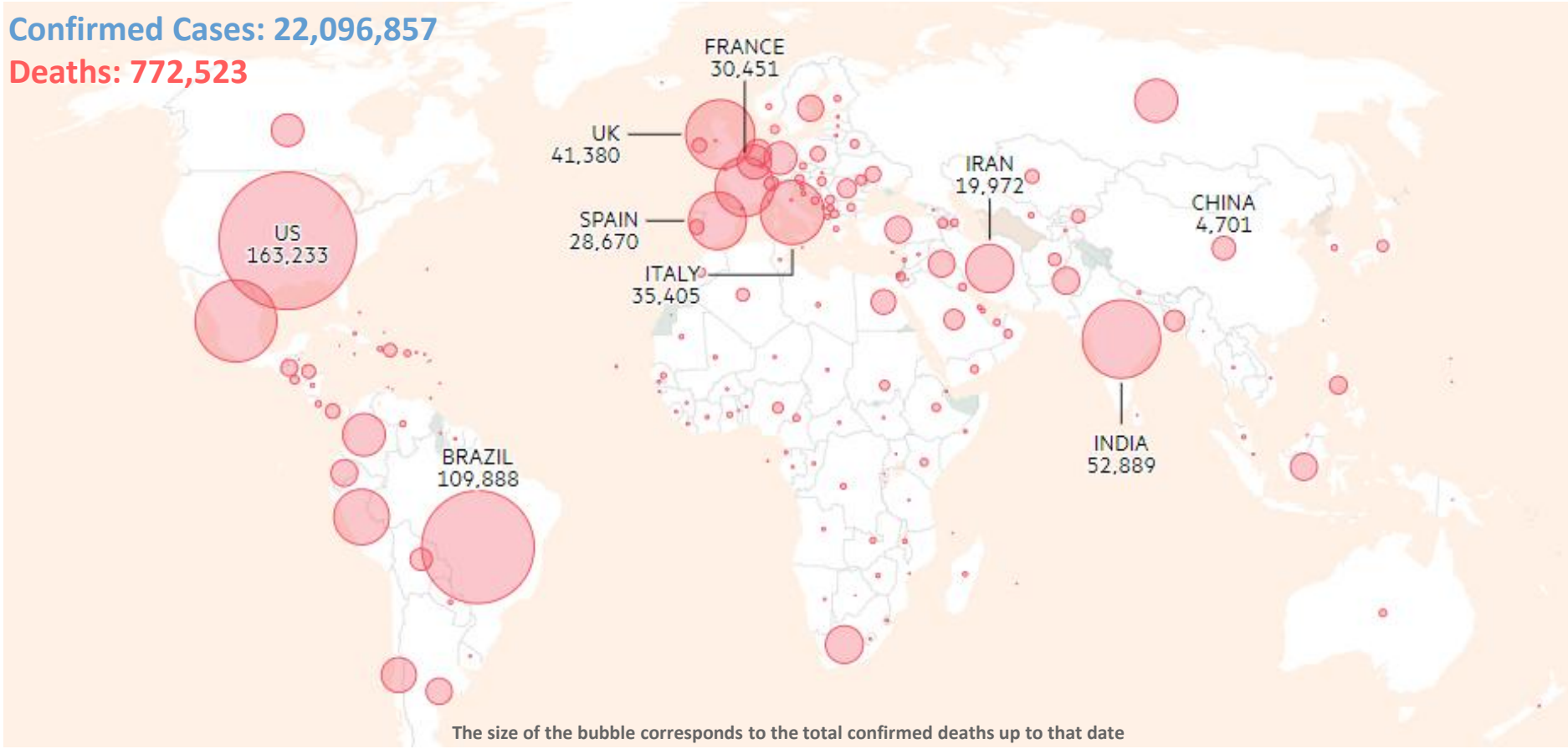
For further details, please go to section: "Charts & Insights"

Global Spread of the Virus

18 Aug 2020

The pandemic spreads incredibly quickly between people. More than 22m people infected in appr. 8 months



Source: Economist, FT

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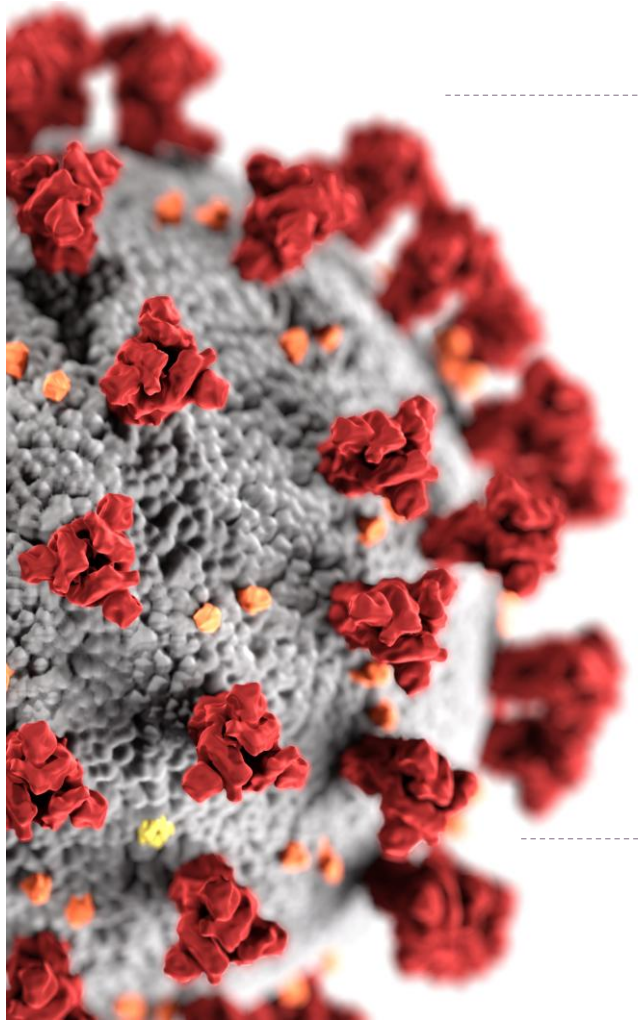
Basics about SARS-CoV-2 & COVID-19

For further details, please go to section: "Details of the Virus"



Overview

- **Origin**: Possibly in wet animal market in Wuhan, China
- **Disease**: Coronavirus disease 2019 (COVID-19)
- **Cause**: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- **Strain**: Same virus as SARS-CoV-1, which affected 8,000 people in 2002-03
- **DNA Study (Feb-2020)**: 96% DNA match between bat coronavirus and human suggests link to humans is not direct but through intermediate host
- **Target**: Upper respiratory tract and can spread to lungs

Transmission & Mechanism

- Enters through nose, mouth, or eyes
- Attaches to cells in the respiratory tract producing a protein called ACE2
- It fuses with the cell and releases the RNA
- The hijacked infected cell will produce proteins based on the "instructions" from the virus' RNA
- Each infected cell can release millions of copies of the virus before dying

Characteristics

- Virus appears highly transmissible - Average patient infects 1.6 to 2.4 other people
- Affects older patients and fatality rate in the 70s is 3-4 times larger than the average
- Men are twice more likely to get infected than women

Source: Economist, LBS

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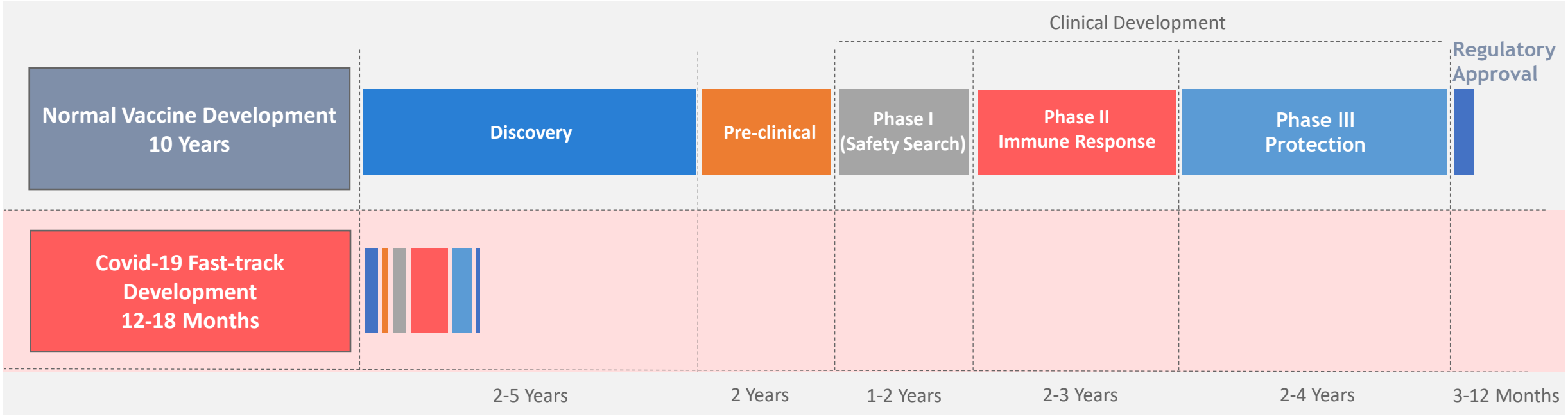
Aug 2020

The Development Timeline of Vaccines vs Covid-19 Vaccine Development Timeline



Source: LSC, FT

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For further details, please go to section: "Response of the Life Sciences"

COVID-19 Response of the Life Sciences Industry

Leading companies have joined forces to strengthen the industry's response against the COVID-19 pandemic

Diagnostics

gsk, Lilly, AstraZeneca, BIOMÉRIEUX, OPKO, Abbott, Roche, CoDx, DANAHER, BD, RANDOX, BAYER, Quest Diagnostics, LabCorp, ThermoFisher SCIENTIFIC, Takeda, FUJIFILM, GRIFOLS

Treatment

abbvie, AstraZeneca, Roche, Boehringer Ingelheim, gsk, Pfizer, SANOFI, Lilly, AMGEN, MERCK, BAYER, Johnson & Johnson, GILEAD Creating Possible, Takeda, NOVARTIS, Adaptive biotechnologies, Biogen, ALEXION, CytoDyn, Alnylam PHARMACEUTICALS, CSL, Incyte, VIR, emergent biosolutions, GRIFOLS, VANDA PHARMACEUTICALS INC., CalciMedica, FUJIFILM, OPKO, REGENERON

Vaccine

gsk, Johnson & Johnson, moderna messenger therapeutics, SANOFI, Pfizer, BIONTECH, inovio, VAXART, CEPI, DYNAVAX, ARCTURUS therapeutics, Heat Biologics, NOVAVAX Creating Tomorrow's Vaccines Today, GeoVax, emergent biosolutions, UREVAC the RNA people, Crescent PHARMA LIMITED, Translate, AstraZeneca, CSL, MERCK, Clover Biopharmaceuticals

Note: Not an exhaustive list

Source: ABPI, Market Watch, Medicine.net and various portals and company websites.

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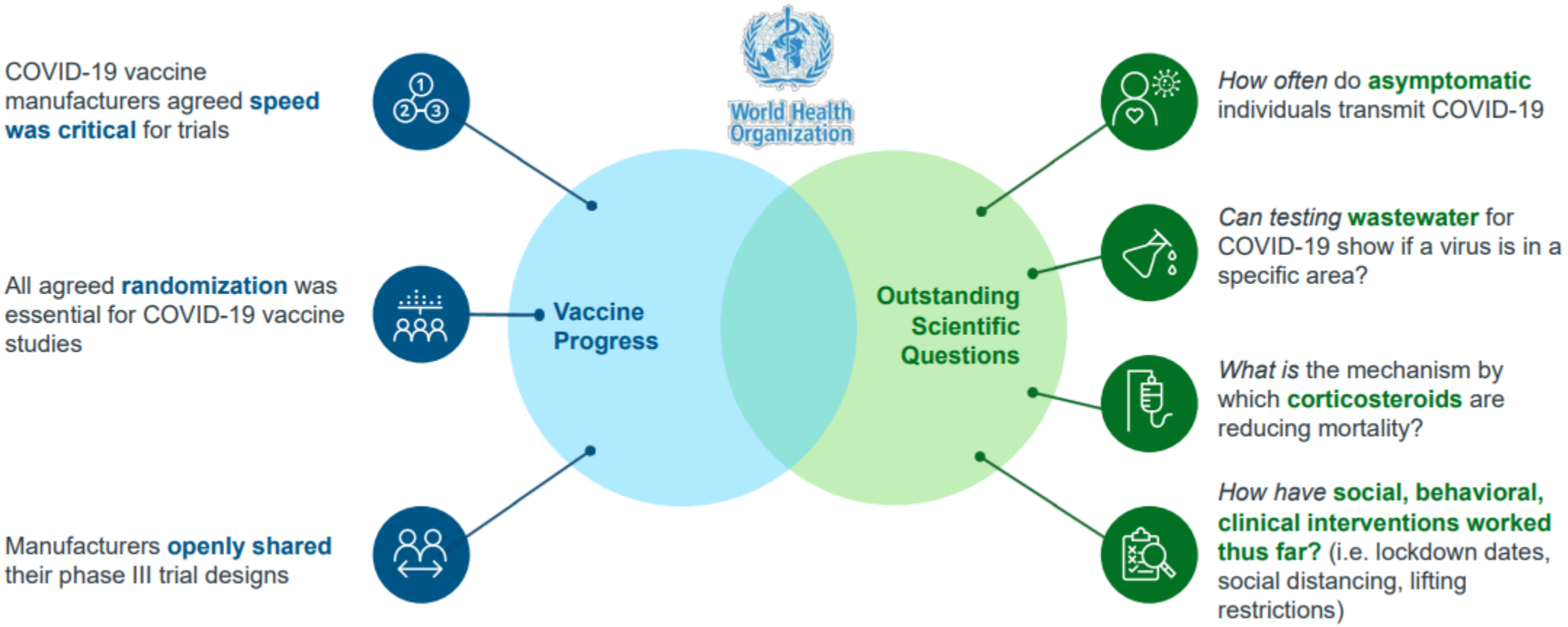
Track Progress on COVID-19 R&D

3 Jul 2020

WHO held its 2nd R&D COVID-19 press forum to share gained knowledge and discuss continuing knowledge gaps



Source: IQVIA

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COVID-19 Industry Impact Heatmap

Aug 2020

COVID-19 INDUSTRY HEATMAP													
INDUSTRY GROUP	GDP W. AVRG.	INDUSTRY	NA		EMEA				APAC			GDP W. AVRG.
			USA	CAN	DEU	UK	ITA	ESP	CHN	JPN	AUS	
Life Sciences & Healthcare	2.9	Bio Pharma & Generics	3	2	4	2	4	2	4	3	4	3.3
		MedTech	2	1	4	2	4	2	4	2	2	2.7
		Health Care Providers, Health Plans & Payers	2	1	4	2	2	2	4	2	3	2.7
Consumer	2.3	Drug & Pharmacy	4	4	4	4	4	4	3	4	3	3.7
		Grocery & Convenience Stores	4	4	4	4	2	4	3	4	4	3.7
		Personal & Household Goods	3	4	4	2	3	2	3	4	3	3.1
		Food & Beverage	3	4	4	3	2	4	3	3	3	3.1
		Mass & Discount Stores	4	1	4	1	1	2	3	2	1	3.0
		Agribusiness	2	2	3	2	2	3	3	3	4	2.5
		Wholesale & Distribution	2	2	2	1	2	2	3	3	2	2.2
		Shipping & Ports	2	2	2	1	1	2	3	2	N/A	2.1
		Specialty Stores & Luxury Goods (Non-essentials)	1	2	2	1	1	1	2	1	1	1.5
		Apparel & footwear	1	1	2	2	1	1	3	1	2	1.5
		Hotels, Restaurants, Health & Wellness	1	1	2	1	1	1	2	2	N/A	1.3
		Cruise Lines	2	1	1	1	1	1	1	1	N/A	1.3
		Automotive	1	1	1	2	1	1	2	1	1	1.2
		Airlines	1	1	1	1	1	1	2	1	N/A	1.2
Financial Services	2.2	Payments	2	N/A	3	3	N/A	2	4	3	N/A	2.8
		Public Institutions (Central Bank, etc.)	2	N/A	2	3	N/A	N/A	3	3	N/A	2.5
		Banking	2	2	2	3	2	3	3	2	3	2.4
		Property & Casualty	2	2	2	3	2	3	3	2	2	2.3
		Reinsurance & London Markets	2	N/A	2	3	N/A	N/A	3	N/A	N/A	2.4
		Life, Health & Savings	2	2	2	3	2	2	3	2	N/A	2.2
		Private / Sovereign Wealth Funds	2	2	3	3	1	1	2	2	2	2.1
		Capital Markets	2	1	2	3	2	2	3	3	N/A	2.0
		Developers & Homebuilders	2	1	3	3	2	1	3	1	N/A	1.9
		Real Estate Services & Brokers	2	1	3	3	1	1	3	1	2	1.9
		Asset Management	2	1	4	4	2	1	2	2	1	1.9
		REITs / Owners – Operators / Private Equity Real Estate	2	1	2	2	2	2	3	1	1	1.8
Technology Media & Telecom	2.2	Telecom	2	3	3	2	3	3	3	3	4	2.7
		Digital Entertainment, Info Services & Publishing	2	2	2	1	2	2	4	2	2	2.5
		Technology	2	2	2	3	3	3	2	2	2	2.1
		Sports & Live Entertainment	1	1	1	1	2	2	2	1	1	1.3
Energy, Resources & Industrials	2.1	Power & Utilities	3	3	3	3	3	3	3	3	3	3.0
		Renewable Energy	3	2	4	3	3	3	3	3	3	2.8
		Mining & Metals	3	2	N/A	3	2	2	3	2	2	2.5
		Engineering & Construction	3	2	2	2	2	2	2	3	N/A	2.4
		Industrial Products	2	2	2	3	2	2	2	2	N/A	2.0
		Chemicals & Specialty Materials	1	2	2	1	2	3	2	3	2	1.8
		Aerospace & Defense	2	1	1	1	2	2	2	1	4	1.6
		Construction & Base Materials	N/A	1	N/A	1	2	1	2	2	2	1.5
		Oil & Gas	1	1	1	1	2	2	2	2	2	1.3
Average	2.2	Average	2.1	1.8	2.5	2.2	2.0	2.1	2.7	2.2	2.4	2.2

LEGEND	
1	High impact on businesses trading & cash flows
2	Significant disruption, likely financial impact loss
3	Neutral or low impact / loss
4	Positive Outlook

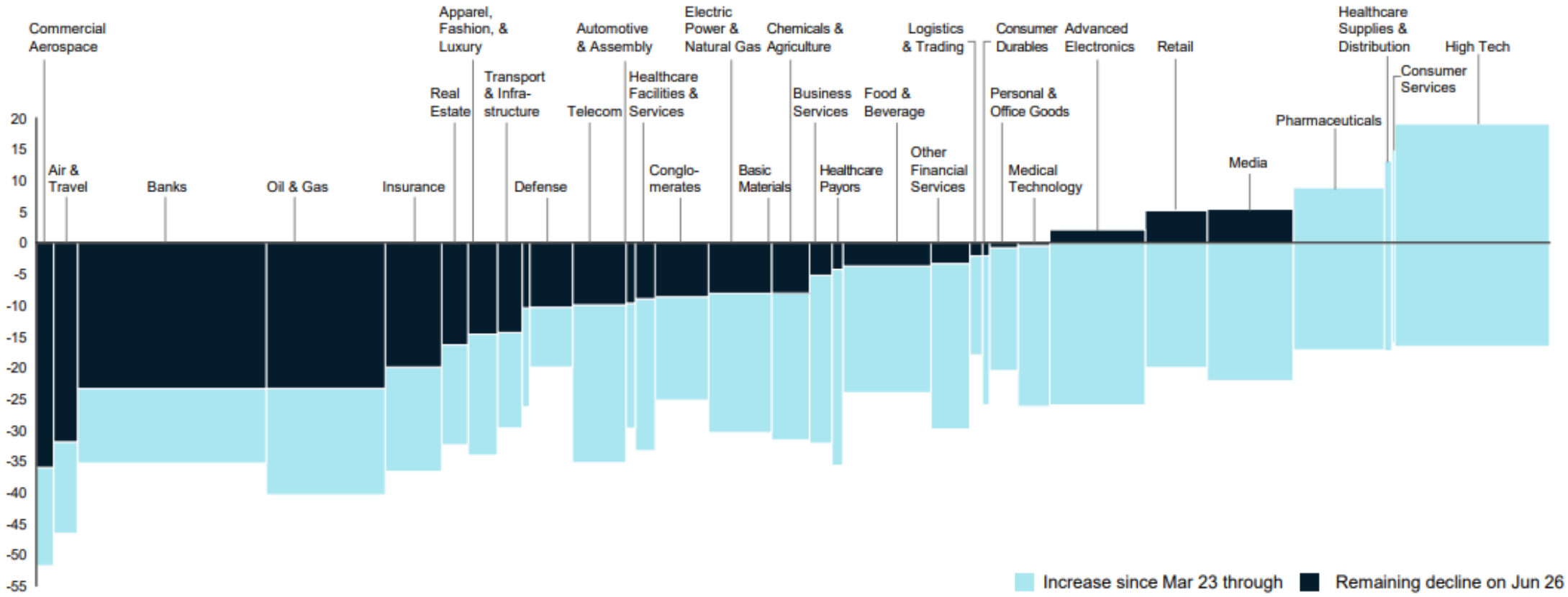
Data Source: Deloitte
Chart: London Strategy

LONDON STRATEGY

26 Jun 2020

Covid-19 impact on Share Price

Many industries have recovered most of their share price drop from recent months, some are up YTD



Source: McKinsey&Company

LONDON STRATEGY

Key impacts of the COVID-19 pandemic on Life Sciences Companies

Potential impacts are complex and difficult to quantify

Slowdown of Economic Growth
- Life sciences sector is sensitive to economic growth especially in countries with high out-of-pocket expenses for medicines

Demand Disruption
- Higher demand for symptomatic medicines - analgesics and cough & cold preparations
- Decline in medicines deemed non-critical
- Lower face-to-face interactions with HCP may result in lower demand

Operations Disruption
- Manufacturing delays
- API and generic shortages
- Stockpiling by Wholesalers adding pressure on the supply chain of companies
- Delays in QC testing

Virology Science
- Increased focus of life sciences sector on virology

Clinical Trial Delays
- Postponement of non-urgent trials
- Patient enrolment may be challenging

Impact on Regulatory Function
- FDA and EMA are giving expediated and extended approvals
- Agencies may be less responsive on non-critical approvals and inspections
- Site inspections delays & exemptions

Increase in Costs
- Inc. in API costs due to shortages
- CMOs and CROs may increase costs
- Inc. in warehousing and freight costs

Product Launch Delays
- Companies will prioritise responses to COVID-19 & delay other product launches
- Limited resources could cause delays in regulatory approvals & formulary listings

Source: London Strategy™

Short Term Action Plan for Life Sciences Companies

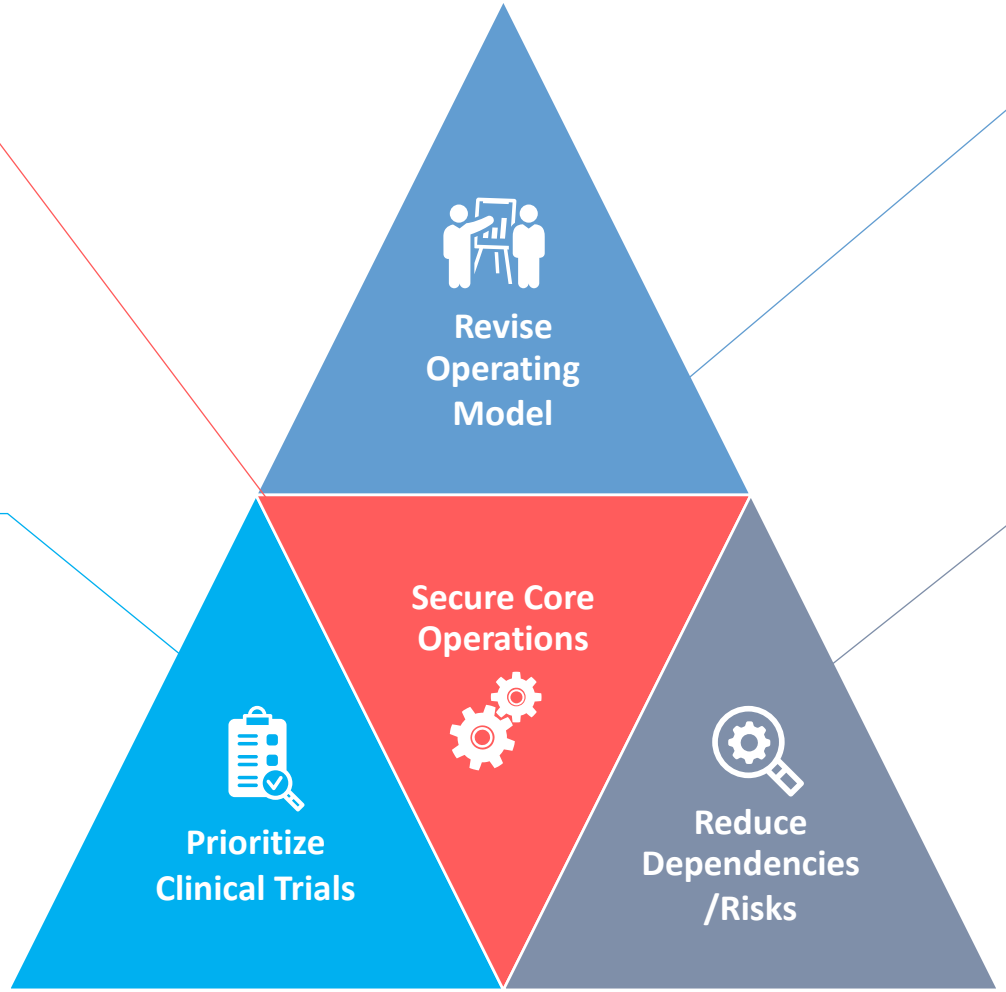
In the short term, it is imperative to stabilise existing operations

Secure Core Operations

- Identify and resolve situations and that may limit patient access to drugs
- Be pro-active to protect the supply of critical products
- Ensure safety of all employees

Prioritize Clinical Trials

- Seek guidance from medical agencies to manage on-going trials
- Address risks and challenges impacting on-going essential trials
- Delay trials as patient enrolment may be challenging



Revise Operating Model

- Assist employees to work remotely
- Use digital platforms to maintain interactions with internal and external stakeholders

Reduce Dependencies/Risks

- Dependence on a single supplier
- Portfolio largely comprises of medicines deemed non-essential
- High dependence on physician or hospital administered products

Source: London Strategy™

LONDON STRATEGY

Long Term Action Plan for Life Sciences Companies

Re-evaluating business strategy can help companies revive business post COVID-19 pandemic crisis

Revise Operating Model

- Make operating model sustainable to function remotely
- Implement supply chain agility

Enterprise Risk Management

- Assess new risks affecting the business
- Devise mitigation plans

Re-evaluate Strategy Plans

- Re-evaluate plans and forecasts
- Undertake cost optimisation
- Revise Capex & Opex plans

Acquisitions & Divestments

- More acquisition opportunities in the market due to lower valuations
- Raise funds by divesting non-primary assets

Ensure Business Continuity

- Revise supply chain network
- Dual sourcing for APIs & excipients

Boost Commercial Activities

- Launch delayed products
- Expedite new launches
- Restart sales efforts

Resume R&D Activities

- Prioritize portfolio
- Resume clinical trials

Source: London Strategy™

LONDON STRATEGY

How can London Strategy help?

Delivering better value for patients by Designing and Driving strategic projects within Life Sciences companies.

Revise Operating Model

- Business & Functional Strategy
- Business Case preparation
- Strategic Agility
- Supply Chain Agility

Enterprise Risk Management

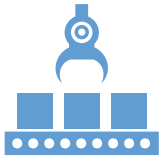
- ERM process establishment
- Scenario planning: Identify, assess and mitigate risks
- Compliance projects

Re-evaluate Strategy Plans

- Business & financial plan preparation
- Strategic Scenario planning
- Cost Optimisation

Acquisitions & Divestments

- M&A program management
- Target due-diligence
- M&A integration
- Divestments
- Out/In-Licensing



Ensure Business Continuity

- BCP Assessment
- Supply network review
- Regulatory driven cross-functional projects
- Programme management

Boost Commercial Activities

- Geographic expansion
- New Product launches
- Distributor Management
- Contracts Review

Operational Improvement

- Process Improvement
- ERP Implementation
- P2P Operational Support
- Change management

Source: London Strategy™

COVID-19 Series - Index

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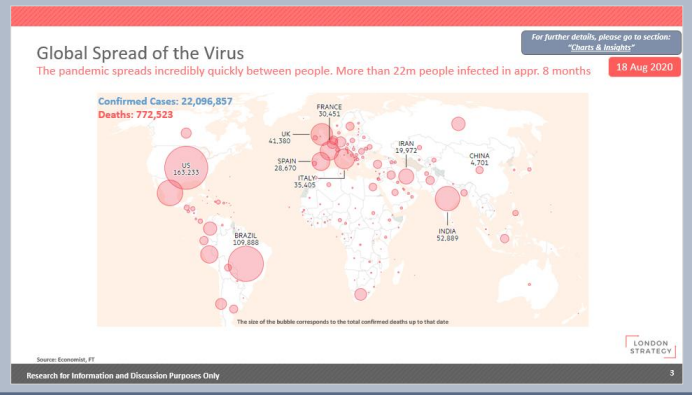

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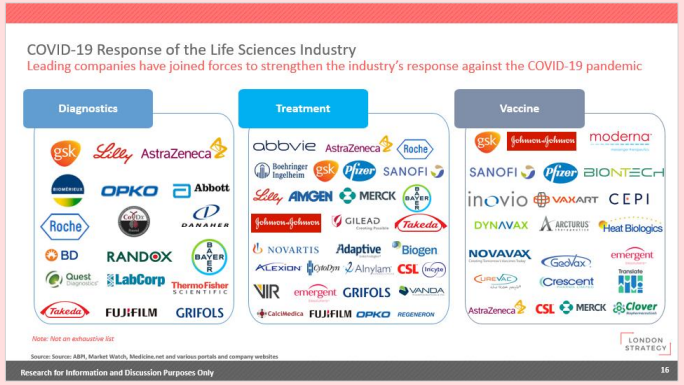

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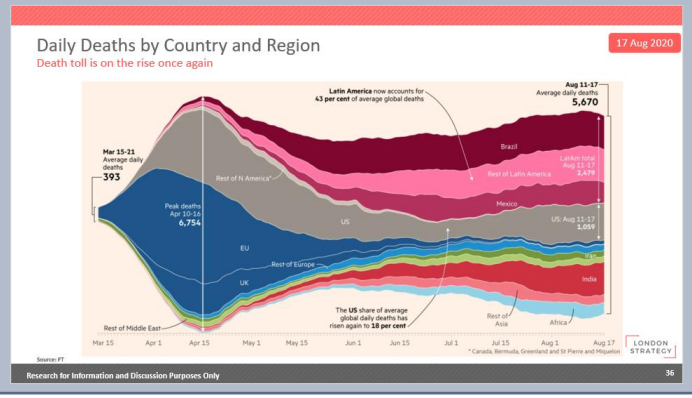

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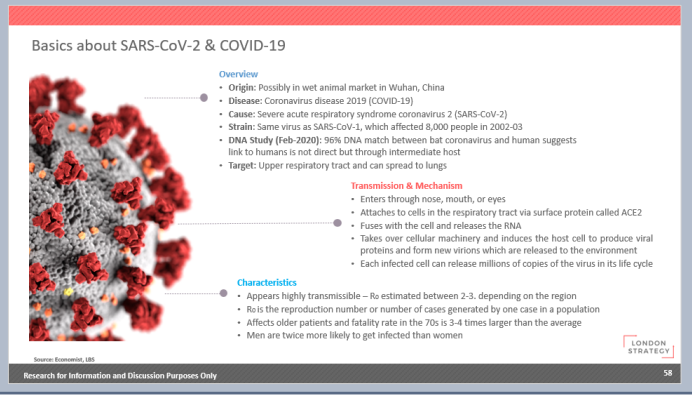

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July 2020

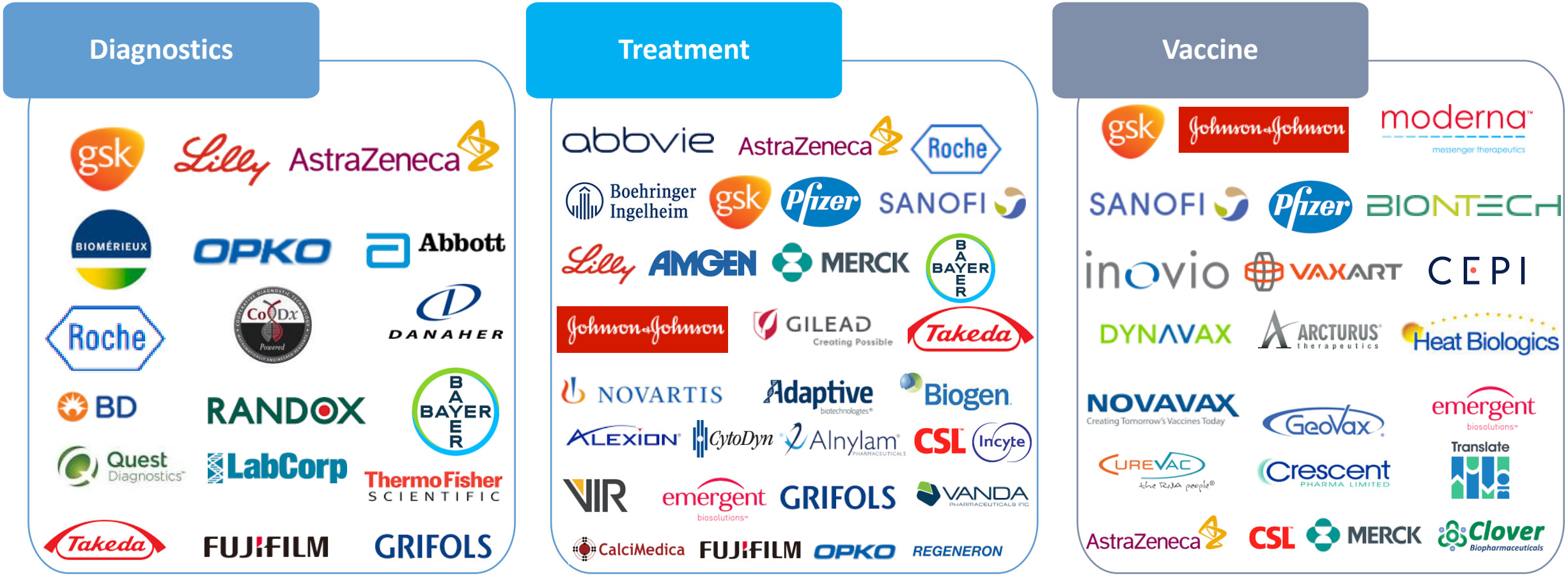
COVID-19 Series

Response of the Life Sciences Industry

LONDON STRATEGY

COVID-19 Response of the Life Sciences Industry

Leading companies have joined forces to strengthen the industry's response against the COVID-19 pandemic



Note: Not an exhaustive list

Source: Source: ABPI, Market Watch, Medicine.net and various portals and company websites

COVID-19 Series

Response of the Life Sciences Industry

1 Treatments

LONDON STRATEGY

Treatment Development

Pharma companies and biotechs are racing to develop an effective treatment for the COVID-19

Treatment

Recent News

- On 1 July 2020, Fujifilm announced a Tripartite Licensing Agreement with Dr. Reddy's, and Global Response Aid for the overseas sales of COVID-19 treatment Drug Avigan
- On 3 July 2020, Gilead announced that the European Commission had granted conditional marketing authorisation for Veklury® (remdesivir)
- On 6 July 2020, Regeneron announced the initiation of late-stage clinical trials evaluating REGN-COV2
- On 7 July 2020, Regeneron announced that, as part of Operation Warp Speed, it had been awarded a $450 million contract to manufacture and supply REGN-COV2
- On 8 July 2020, Mount Sinai Health System, Emergent BioSolutions & ImmunoTek Bio Centers announced collaboration to evaluate COVID-HIG for COVID-19 treatment
- On 3 August 2020, members of the COVID R&D Alliance (AbbVie, Amgen and Takeda) announced the first patients enrolled in the I-SPY COVID Trial
- On 3 August 2020, Eli Lilly announced the initiation of BLAZE-2, a Phase 3 trial studying LY-CoV555 for the prevention of SARS-CoV-2 infection

LONDON STRATEGY

Source: Source: ABPI, Market Watch, Medicine.net and various portals and company websites

Abbvie

- AbbVie is in collaboration with various institutions to determine the efficacy & safety of KALETRA®/Aluvia against COVID-19
- It is supporting clinical studies & research with lopinavir/ritonavir
- On 5 June 2020, AbbVie, Harbour BioMed, Utrecht University and Erasmus MC announced collaboration to develop antibody 47D11
- On 3 August 2020, members of the COVID R&D Alliance (AbbVie, Amgen and Takeda) announced the first patients enrolled in the I-SPY COVID Trial
    - The I-SPY COVID Trial will evaluate the efficacy of cenicriviroc, Otezla® and Firazyr® in severely ill, hospitalised COVID-19 patients who require high-flow oxygen

AstraZeneca

- On 23 April 2020, AstraZeneca and Saint Luke's Mid America Heart Institute initiated global Phase III trial for Farxiga (dapagliflozin) as a treatment in patients hospitalised with COVID-19
- On 5 June 2020, AstraZeneca's Calquence (acalabrutinib) showed encouraging preliminary data which has informed the initiation of global phase II trials
- On 9 June 2020, the Company licensed coronavirus-neutralising antibodies from Vanderbilt University, US, with plans to advance a pair of these mAbs into clinical development as a potential combination therapy for the prevention and treatment of COVID-19

Roche

- On 19 March 2020, Roche confirmed initiation of Phase III clinical trial in collaboration with BARDA
    - The study, COVACTA, will evaluate the safety and efficacy of intravenous Actemra®/RoActemra® (tocilizumab) in hospitalised adult patients with severe COVID-19 pneumonia
- On 29 July 2020, the Company announced that the phase III COVACTA study of Actemra®/RoActemra® did not meet its primary endpoint of improved clinical status in hospitalised adult patients with severe COVID-19 associated pneumonia

Boehringer Ingelheim

- Boehringer Ingelheim team is currently searching for novel virus-neutralising antibodies
    - The Company is screening its entire molecule library for compounds that could target the virus
- Boehringer Ingelheim actively participating in COVID-19 projects with the Innovative Medicines Initiative (EU) and Bill & Melinda Gates Foundation COVID-19 Therapeutic Accelerator

Source: LSC & Company websites **Note: As of 7th Aug 2020**

GSK

- GSK announced a collaboration with Vir Biotechnology to use Vir's monoclonal antibody platform technology to accelerate existing and identify new antiviral antibodies for COVID-19
- The Company is a member of the COVID-19 Therapeutics Accelerator
  - Aimed at the collaboration of pharmaceutical companies and academic institutions to identify molecules to treat COVID-19
- GSK is evaluating its marketed pharmaceutical products and medicines in development to determine if any could be used to treat COVID-19

Pfizer

- Pfizer confirmed a lead compound and analogues are potent inhibitors of the SARS-CoV-2 3C-like (3CL) protease, based on the results of initial screening assays
- Pfizer researchers will publish a review in Clinical Pharmacology and Therapeutics which assesses published in vitro and clinical data regarding azithromycin as an agent with antiviral properties
  - This open-access review may serve to facilitate the use of azithromycin in future research on COVID-19

Sanofi

- On 16 March 2020, Sanofi and Regeneron announced that they had started a clinical program evaluating Kevzara® (sarilumab) in patients hospitalised with severe COVID-19
- On 27 April 2020, Sanofi announced the preliminary results from the Phase 2 portion of an ongoing Phase 2/3 trial evaluating Kevzara®
- On 2 July 2020, Sanofi and Regeneron announced that the US Phase 3 trial of Kevzara® 400 mg in COVID-19 patients requiring mechanical ventilation did not meet its primary and key secondary endpoints
  - Based on the results, the US-based trial has been stopped

Eli Lilly & Co.

- On 15 June 2020, the Company announced that the first patient had been enrolled in a Phase 3 study to evaluate the efficacy and safety of baricitinib in hospitalised adults with COVID-19
  - Baricitinib, marketed as OLUMIANT®, is an oral JAK1/JAK2 inhibitor licensed from Incyte
- On 3 August 2020, Eli Lilly announced the initiation of BLAZE-2, a Phase 3 trial studying LY-CoV555 for the prevention of SARS-CoV-2 infection
  - LY-CoV555 is the lead antibody from Lilly's collaboration with AbCellera

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Amgen & Adaptive

- On 2 April 2020, Amgen and Adaptive Biotechnologies announced a collaboration to discover and develop fully human neutralising antibodies targeting SARS-CoV-2
- On 4 May 2020, Amgen announced that it would start testing psoriasis therapy drug, Otezla as a potential treatment for COVID-19
- On 3 August 2020, members of the COVID R&D Alliance (AbbVie, Amgen and Takeda) announced the first patients enrolled in the I-SPY COVID Trial
    - The I-SPY COVID Trial will evaluate the efficacy of cenicriviroc, Otezla® and Firazyr® in severely ill, hospitalised COVID-19 patients who require high-flow oxygen

Merck & Co.

- On 27 April 2020, Merck and the Institute for Systems Biology (ISB), announced a new research collaboration to investigate and define the molecular mechanisms of SARS-CoV-2 infection and COVID-19
- They aim to identify targets for medicines and vaccines
- Merck has also entered into an agreement with the Biomedical Advanced Research and Development Authority to provide funding for a research

Bayer AG

- On 21 April 2020, Bayer announced a collaboration with Population Health Research Institute (PHRI) to launch a clinical research program aimed at identifying potential treatments against COVID-19
- An outpatient study will evaluate the combination of chloroquine with azithromycin as a treatment to prevent deterioration leading to hospital admission
- Another study will evaluate the combination of chloroquine with azithromycin, as well as interferon beta-1b, to prevent admission to intensive care, mechanical ventilation and/or death

Johnson & Johnson

- Johnson & Johnson and the Biomedical Advanced Research and Development Authority have expanded their partnership to accelerate Janssen's ongoing work in screening compound libraries
- By testing the antiviral activity of these compounds against SARS-CoV-2, the Company hopes to identify an existing, proven-safe drug that has potential to be turned into a new treatment for the virus

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Gilead

- On 1 May 2020, Remdesivir received FDA's Emergency Use Authorisation for the Treatment of COVID-19
- On 7 May 2020, Gilead announced that the Japanese Ministry had granted regulatory approval to Veklury® (remdesivir)
- On 1 June 2020, the Company announced topline results from the Phase 3 Trial of Remdesivir in Patients With moderate COVID-19
- On 3 July 2020, Gilead announced that the European Commission had granted conditional marketing authorisation for Veklury® (remdesivir)
- On 10 July 2020, the Company announced additional data on remdesivir - adding to the available body of knowledge on treatment outcomes with remdesivir

Takeda

- Takeda has joined forces with CSL Behring, Biotest, BPL, LFB and Octapharma to form the CoVIg-19 Plasma Alliance to develop a potential plasma-derived therapy for treating COVID-19
  - The alliance will begin the development of an investigational Hyperimmune globulin (H-Ig) medicine called CoVIg-19
- On 3 August 2020, members of the COVID R&D Alliance (AbbVie, Amgen and Takeda) announced the first patients enrolled in the I-SPY COVID Trial
  - The I-SPY COVID Trial will evaluate the efficacy of cenicriviroc, Otezla® and Firazyr® in severely ill, hospitalised COVID-19 patients who require high-flow oxygen

Novartis

- On 28 April 2020, Novartis announced plans to initiate Phase III CT to study canakinumab in patients with COVID-19 pneumonia
- On 19 June 2020, the Company announced that it had discontinued its hydroxychloroquine clinical trial due to slow enrolment
- Jakavi® (ruxolitinib), Ilaris® (canakinumab) and Cosentyx® (secukinumab) and more medicines are also under evaluation
- On 16 July 2020, Novartis announced a new initiative to help patients in low-income & lower-middle-income countries access affordable medicines to treat the major symptoms of COVID-19

Vir, Biogen, Alnylam

- Vir Biotechnology and GSK announced a collaboration to use Vir's monoclonal antibody platform technology to accelerate existing and identify new antiviral antibodies for COVID-19
- On 4 May 2020, Vir Biotechnology and Alnylam Pharmaceuticals announced the selection of a development candidate for VIR-2703, an investigational RNAi therapeutic targeting the SARS-CoV-2 genome
- On 29 May 2020, Vir Biotechnology and Biogen announced the finalisation of a process development and manufacturing agreement to enable commercial supply of Vir's SARS-CoV-2 monoclonal antibodies

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Alexion Pharmaeuticals

- On 20 April 2020, Alexion Pharmaceuticals announced plans to initiate a global Phase 3 study to investigate ULTOMIRIS® (ravulizumab-cwvz) in COVID-19 patients
  - Adults hospitalised with severe pneumonia or acute respiratory distress syndrome (ARDS)
- ULTOMIRIS® (ravulizumab-cwvz), a biologic medicine, is the first and only long-acting C5 complement inhibitor
- The study is expected to enrol approximately 270 patients across countries with high numbers of diagnosed cases, beginning in May

CytoDyn

- CytoDyn is developing Leronlimab, a CCR5 antagonist, as a combination therapy for highly treatment-experienced HIV patients
- On 6 July 2020, the Company signed an exclusive Distribution and Supply Agreement with American Regent for the distribution of leronlimab for the treatment of COVID-19 in the US
- On 21 July 2020, CytoDyn announced positive safety data from the Phase 2 study of leronlimab for the treatment of COVID-19
- On 4 August 2020, the Company received positive recommendation from Data Safety Monitoring Committee for Leronlimab Phase 3 COVID-19 Trial with no cause to modify study

Incyte

- On 17 April 2020, Incyte announced the initiation of RUXCOVID, a Phase 3 clinical trial evaluating the efficacy and safety of ruxolitinib (Jakafi®) plus standard-of-care (SoC) in patients aged ≥12 years with COVID-19 associated cytokine storm
- The collaborative study is sponsored by Incyte in the United States and Novartis outside of the United States

Emergent BioSolutions

- On 2 April 2020, Emergent BioSolutions announced a partnership with the US government to expedite development of a plasma-derived therapy for patients with COVID-19
- Emergent has received $14.5 million from BARDA to support its COVID-HIG program, its hyperimmune development programs
- On 8 July 2020, Mount Sinai Health System, Emergent BioSolutions and ImmunoTek Bio Centers announced collaboration to develop, manufacture, and conduct clinical trials to evaluate COVID-HIG

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Grifols

- On 25 March 2020, Grifols announced its collaboration with BARDA, FDA and other Federal public health agencies to collect plasma from convalescent COVID-19 patients
- The Company will process this specific plasma into a hyperimmune globulin and support the necessary pre-clinical and clinical studies to determine if anti-SARS-CoV-2 hyperimmune globulin therapy can successfully be used to treat COVID-19 disease
- On 28 July 2020, Grifols announced that it had delivered the first manufactured batches of its anti-SARS-CoV-2 hyperimmune globulin for clinical trials

Vanda Pharmaceuticals

- On 8 April 2020, Vanda Pharmaceuticals and the University of Illinois at Chicago announced a research partnership
  - A high-throughput screening assay to identify small molecules that may prevent cathepsin-L cleavage of SARS-CoV-2 glycoproteins that are required for viral processing in host cell
- On 15 April 2020, Vanda and Northwell Health's research arm announced enrolment of the first patient in Vanda's clinical trial, ODYSSEY
  - A Phase III trial investigating the efficacy and safety of Tradipitant, a neurokinin-1 receptor antagonist

CalciMedica

- On 9 April 2020, CalciMedica announced it had received a "Study May Proceed" letter from the FDA to investigate the use of CM4620-IE
- On 28 May 2020, CalciMedica announced positive topline data from an interim analysis of its open-label randomised controlled clinical study of Auxora™ (formerly called CM4620-IE) in patients with severe COVID-19 pneumonia on low-flow oxygen therapy
- On 16 July 2020, the Company announced data showing Auxora substantially improved outcomes in patients with severe COVID-19 pneumonia

Fujifilm

- Fujifilm Life Sciences is advancing treatments and targeting solutions for COVID-19 medical needs
- Fujifilm commenced a phase III clinical trial in Japan to assess the safety and efficacy of Avigan in COVID-19 patients with non-severe pneumonia, alongside a phase II clinical trial in the United States
- On 1 July 2020, Fujifilm announced a Tripartite Licensing Agreement with Dr. Reddy's, and Global Response Aid for the overseas sales of COVID-19 treatment Drug Avigan
  - The agreement gives them exclusive right to develop, manufacture and sell Avigan overseas

Source: LSC & Company websites **Note: As of 7th Aug 2020**

OPKO Health

- On 1 June 2020, OPKO Health announced that the FDA had authorised OPKO to undertake a Phase 2 trial with RAYALDEE® as a treatment for patients with mild-to-moderate COVID-19
  - RAYALDEE is an extended-release oral formulation of calcifediol, a prohormone of calcitriol, the active form of vitamin D3
  - The trial, entitled REsCue is estimated to enrol 166 subjects including many with stage 3 or 4 chronic kidney disease
  - The REsCue trial will have four weeks of treatment with RAYALDEE or placebo and two weeks of follow-up

Regeneron

- On 2 July 2020, Sanofi and Regeneron announced that the US Phase 3 trial of Kevzara® 400 mg in COVID-19 patients requiring mechanical ventilation did not meet its primary and key secondary endpoints
  - Based on the results, the US-based trial has been stopped
- On 6 July 2020, the Company announced the initiation of late-stage clinical trials evaluating REGN-COV2, its investigational double antibody cocktail for the treatment and prevention of COVID-19
- On 7 July 2020, Regeneron announced that, as part of Operation Warp Speed, it had been awarded a $450 million contract to manufacture and supply REGN-COV2

CSL Behring

- CSL Behring is one of the founding members of the CoVIg-19 Plasma Alliance, an industry partnership to develop CoVIg-19
- The Company is developing an anti-SARS-CoV-2 plasma product - COVID-19 Immunoglobulin - for the Australian market
- CSL has also formed a partnership with SAB Biotherapeutics to advance and deliver a novel immunotherapy targeting COVID-19
- On 6 July 2020, the Company announced the enrolled of its first patient in the Phase 2 study of CSL312 - to treat patients suffering from severe respiratory distress, associated with COVID-19 related pneumonia

Source: LSC & Company websites

Note: As of 7th Aug 2020

COVID-19 Series

Response of the Life Sciences Industry

2 Vaccine

LONDON STRATEGY

Vaccine

Life Sciences companies are ratcheting up their efforts with accelerated schedules for creating new vaccines

Vaccine

Recent News

- On 6 July 2020, Emergent BioSolutions announced a manufacturing services agreement with Janssen Pharmaceuticals for investigational SARS-CoV-2 vaccine, Ad26.COV2-S
- On 9 July 2020, Moderna and Laboratorios Farmacéuticos Rovi announced a manufacturing collaboration for mRNA-1273 to supply markets outside of the US
- On 23 July 2020, Novavax and FUJIFILM Diosynth Biotechnologies (FDB) announced an agreement to manufacture bulk drug substance for NVX-CoV2373
- On 27 July 2020, Moderna announced that the Phase 3 study of mRNA-1273
- On 27 July 2020, Pfizer and BioNTech announced the start of a global (excl. China) Phase 2/3 safety & efficacy clinical study to evaluate modRNA candidate from their BNT162 mRNA-based vaccine
- On 6 August 2020, Novavax announced a license agreement with Serum Institute of India for the development and commercialisation of NVX CoV2373 in n low- and middle-income countries and India
- On 7 August 2020, Novavax and Takeda announced a partnership for the development, manufacturing and commercialisation of NVX CoV2373 in Japan

Source: Source: ABPI, Market Watch, Medicine.net and various portals and company websites

LONDON STRATEGY

GSK

- On 7 July 2020, GSK and Medicago announced a collaboration for a COVID-19 vaccine combining Medicago's recombinant CoVLP with GSK's pandemic adjuvant system
- On 29 July 2020, Sanofi and GSK reached an agreement with the UK government to supply 60mn doses of COVID-19 vaccine
    - The vaccine candidate is based on Sanofi's recombinant protein-based technology to produce an influenza vaccine, and GSK's adjuvant technology
- On 31 July 2020, Sanofi and GSK announced a collaborative effort with the US government where they will be provide funding up to $2.1bn for development and delivery of an initial 100mn doses

Johnson & Johnson

- On 10 June 2020, J&J (through Janssen) accelerated the initiation of the Phase 1/2a first-in-human clinical trial of Ad26.COV2.S
- J&J has entered into a collaboration with Emergent BioSolutions to support the manufacturing of the vaccine
- On 30 July 2020, a study published showed that J&J's Ad26.COV2.S elicits a strong immune response that protects against subsequent infection
- On 5 August 2020, J&J announced that Janssen Pharmaceutical had entered into an agreement with the US government for the large scale domestic manufacturing and delivery of 100mn doses of Ad26.COV2.S

Moderna

- On 27 April 2020, Moderna announced submission of an IND application to FDA for its mRNA vaccine candidate (mRNA-1273)
- On 9 July 2020, Moderna and Laboratorios Farmacéuticos Rovi announced a collaboration for large-scale, commercial fill-finish manufacturing of mRNA-1273 to supply markets outside of the US
- On 26 July 2020, the Company announced a modification to its contract with BARDA for an additional commitment of up to $472mn to support late stage clinical development of mRNA-1273
- On 27 July 2020, Moderna announced that the Phase 3 study of mRNA-1273 against COVID-19 had begun dosing participants

Sanofi

- On 29 July 2020, Sanofi and GSK reached an agreement with the UK government to supply 60mn doses of COVID-19 vaccine
    - The vaccine candidate is based on Sanofi's recombinant protein-based technology to produce an influenza vaccine, and GSK's adjuvant technology
- On 31 July 2020, Sanofi and GSK announced a collaborative effort with the US government where they will be provide funding up to $2.1bn for development and delivery of an initial 100mn doses
- Sanofi is also collaborating with Translate Bio to discover, design, and manufacture a vaccine

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Pfizer & BioNTech

- On 13 July 2020, vaccine candidates BNT162b1 and BNT162b2 received Fast Track designation from the FDA
- On 22 July 2020, Pfizer & BioNTech entered into an agreement with the US government to deliver 300mn doses of vaccine in 2021
- On 27 July 2020, Pfizer and BioNTech announced the start of a global (except for China) Phase 2/3 safety and efficacy clinical study to evaluate modRNA candidate from their BNT162 mRNA-based vaccine
- On 31 July 2020, Pfizer and BioNTech announced an agreement with the Japan government to supply 120mn doses of BNT162 vaccine
- On 5 August 2020, Pfizer Canada and BioNTech announced an agreement with the Canada government to supply BNT162 vaccine

INOVIO Pharmaceuticals

- On 6 April 2020, INOVIO announced that FDA had accepted IND application for INO-4800, a vaccine candidate to prevent COVID-19
- CEPI has granted $6.9mn funding to INOVIO to work with KNIH for INO-4800 Phase 1/2 clinical trial in South Korea
- On 23 June 2020, INOVIO received $71mn funding from the US- DoD to support the large-scale manufacture of its proprietary CELLECTRA® 3PSP smart device and the procurement of CELLECTRA® 2000 devices, which are used to deliver INO-4800 directly into the skin
- On 30 July 2020, INOVIO announced that its INO-4800 vaccine targeting SARS-CoV-2 was effective in protecting non-human primates from live virus challenge 13 weeks after the last vaccination

Vaxart

- On 20 May 2020, Vaxart announced that it has selected its lead COVID-19 vaccine candidate and had contracted with KindredBio to manufacture bulk vaccine to complement the manufacturing capacity of partner Emergent BioSolutions
- On 25 June 2020, the Company signed an MoU with AMS for lyophilisation development and large scale manufacturing including tableting & enteric coating for oral COVID-19 vaccine
- On 26 June 2020, Vaxart announced that its oral COVID-19 vaccine has been selected to participate in a non-human primate challenge study, organised and funded by Operation Warp Speed

CEPI

- CEPI has collaborations and funding initiatives with such as CureVac, GSK, Novavax, & University of Oxford, University of HK, Institut Pasteur-led consortium, IVI, INOVIO and KNIH, Clover Bio and Novavax
- On 4 June 2020, CEPI announced partnership with AstraZeneca
- On 5 June 2020, CEPI, CSL The University of Queensland announced an agreement to develop, manufacture & distribute of a COVID-19 vaccine
- On 19 June 2020, CEPI's COVID-19 vaccine programme with Clover Biopharmaceuticals began phase 1 clinical trials in Perth, Australia
- On 8 July 2020, CEPI and Sichuan Clover Biopharmaceuticals announced a $66m partnership for Clover's S-Trimer vaccine candidate

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Dynavax Technologies

- On 8 July 2020, Dynavax and Medicago announced their collaboration to investigate Medicago's Coronavirus Virus-Like Particle (CoVLP) with Dynavax's advanced adjuvant, CpG 1018
- On 14 July 2020, the Company announced that the first participants had been dosed in the Phase 1 CT evaluating Medicago's plant-derived vaccine candidate adjuvanted with CpG 1018
- On 23 July 2020, Dynavax and Medigen Vaccine Biologics announced their collaboration to develop an adjuvanted vaccine candidate
    - The collaboration is evaluating the combination of Medigen's stable prefusion form of the SARS-CoV2 recombinant spike protein with Dynavax's CpG 1018

Arcturus Therapeutics

- On 4 March 2020, Arcturus and Duke-NUS Medical School announced a partnership to develop COVID-19 vaccine for Singapore
- On 4 May 2020, Arcturus and Catalent announced a manufacturing partnership for Arcturus' vaccine candidate (LUNAR-COV19)
- On 21 July 2020, Arcturus and Duke-NUS Medical School announced that the Clinical Trial Application for LUNAR-COV19 had been approved to proceed by the Singapore Health Sciences Authority
- On 23 July 2020, Arcturus announced a binding term sheet with the Israeli Ministry of Health to supply LUNAR-COV19

Heat Biologics

- On 3 March 2020, Heat Biologics announced that the Company had launched a program within its wholly-owned subsidiary, Zolovax, to develop a vaccine using its immune activating gp96 vaccine platform for treating or preventing infection from the SARS-CoV-2
- On 29 July 2020, Heat Biologics announced successful pre-clinical testing of the Company's COVID-19 vaccine
    - demonstrating immunogenicity proof-of-concept

Novavax

- On 7 July 2020, Novavax announced that it had been selected to participate in Operation Wasp Speed and was awarded $1.6bn
- On 23 July 2020, Novavax & FUJIFILM Diosynth Biotech announced an agreement to manufacture bulk drug substance for NVX-CoV2373
- On 4 August 2020, announced positive Phase 1 data for NVX-CoV2373
- On 6 August 2020, Novavax announced a license agreement with Serum Institute of India for the development and commercialisation of NVX-CoV2373 in n low- and middle-income countries and India
- On 7 August 2020, Novavax and Takeda announced a partnership for NVX-CoV2373 in Japan

Source: LSC & Company websites **Note: As of 7th Aug 2020**

GeoVax Labs

- On 27 January 2020, GeoVax Labs and BravoVax, a vaccine developer in Wuhan, China, announced collaboration to jointly develop a vaccine against the SARS-CoV-2
  - Under the collaboration, GeoVax would use its MVA-VLP vaccine platform to design and construct the vaccine candidate
- On 30 April 2020, GeoVax announced that Sino Biological would be its exclusive supplier of SARS-Cov-2 bioreagent research products
  - Sino Biological will provide key bioreagents such as recombinant proteins, antibodies and detection kits

Emergent Biosolutions

- In March 2020, Emergent BioSolutions announced CDMO collaboration to support vaccine candidates of Novavax and Vaxart
- On 23 April 2020, the Company announced CDMO collaboration for Johnson & Johnson lead vaccine candidate
- On 11 June 2020, Emergent BioSolutions announced CDMO collaboration to support AstraZeneca's vaccine candidate AZD1222
- On 6 July 2020, Emergent BioSolutions announced a five-year manufacturing services agreement with Janssen Pharmaceuticals, for large-scale drug substance manufacturing for Johnson & Johnson's investigational SARS-CoV-2 vaccine, Ad26.COV2-S

CureVac

- On 31 January 2020, CureVac AG and CEPI announced a public-private partnership to accelerate development of vaccines against COVID-19
- On 14 May 2020, CureVac announced positive pre-clinical results at a low dose for its lead vaccine candidate against SARS-CoV-2
- On 17 June 2020, CureVac announced that the German Health Authority (PEI) and the Belgian Federal Agency for Medicines and Health Products (FAMHP) had approved the Phase 1 clinical trial for its vaccine program to prevent SARS-CoV-2 infection
  - The trial will be conducted in Germany and Belgium

Crescent

- Crescent Pharma Limited is working to develop a vaccine from chloroquine phosphate, which is being used in 10 COVID-19 trials in China

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Translate Bio

- On 27 March 2020, Translate Bio and Sanofi announced collaboration to develop a novel mRNA vaccine for COVID-19
- The collaboration will leverage an existing agreement from 2018 between the two companies to develop mRNA vaccines for infectious diseases
- Translate Bio has begun to produce multiple mRNA constructs and will use its mRNA platform to discover, design and manufacture SARS-CoV-2 vaccine candidates

AstraZeneca

- On 30 April 2020, AstraZeneca and University of Oxford entered into a development and distribution agreement for AZD1222 vaccine
- On 4 June 2020, the Company entered into an agreement with CEPI & Gavi, and a licensing agreement with Serum Institute of India
- On 11 June 2020, it reached an agreement with Europe's IVA
- On 20 July 2020, interim results from the ongoing Phase I/II COV001 trial showed AZD1222 was tolerated and generated robust immune responses against the SARS-CoV-2
    - A single dose of AZD1222 resulted in a four-fold increase in antibodies to the SARS-CoV-2 virus spike protein in 95% of participants one month after injection

CSL Behring

- CSL Behring is collaborating with the University of Queensland to support the development of a COVID-19 vaccine candidate
    - The Company is providing its vaccine development expertise, proprietary technologies and laboratory facilities

Merck & Co.

- On 26 May 2020, Merck and IAVI announced a new collaboration to develop an investigational vaccine against SARS-CoV-2
- The vaccine candidate will use the recombinant vesicular stomatitis virus (rVSV) technology that is the basis for Merck's Ebola Zaire virus vaccine, ERVEBO® (Ebola Zaire Vaccine, Live), which was the first rVSV vaccine approved for use in humans

Source: LSC & Company websites **Note: As of 7th Aug 2020**

Clover Biopharmaceuticals

- On 24 March 2020, Clover entered into a collaboration with Dynavax for its trimeric Spike-protein ("S-Trimer") subunit vaccine candidate for COVID-19
- On 27 April 2020, CEPI announced US$3.5 million partnering agreement with Clover Australia for COVID-19 vaccine R&D
- On 19 June 2020, Clover Pharmaceuticals & GSK's collaboration to develop an adjuvanted COVID-19 vaccine entered into human CTs
- On 8 July 2020, CEPI & Sichuan Clover Biopharmaceuticals announced $66m partnership for Clover's S-Trimer vaccine candidate

Takeda

- On 7 August 2020, Novavax and Takeda announced a partnership for the development, manufacturing and commercialisation of NVX-CoV2373, Novavax' COVID-19 vaccine candidate, in Japan
  - NVX-CoV2373 is a stable, prefusion protein made using Novavax' recombinant protein nanoparticle technology and includes Novavax' proprietary Matrix-M™ adjuvant
  - Takeda will receive funding from the Government of Japan to support the technology transfer, establish of infrastructure and scale-up of manufacturing
  - Takeda anticipates the capacity to manufacture over 250mn doses of the COVID-19 vaccine per year

Fujifilm

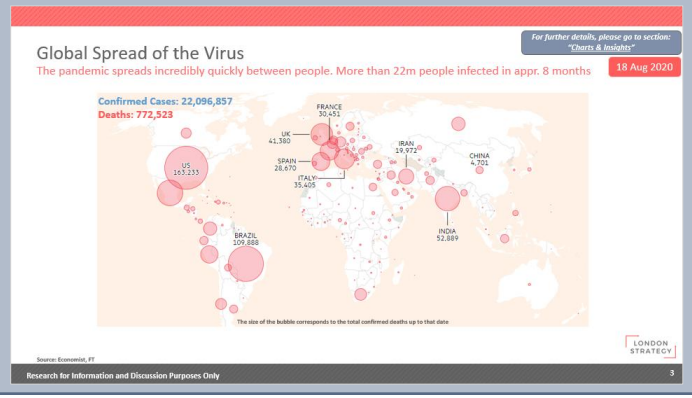
- On 23 July 2020, Novavax and FUJIFILM Diosynth Biotechnologies (FDB) announced an agreement to manufacture bulk drug substance for NVX-CoV2373, Novavax' COVID-19 vaccine candidate
- FDB's site in Morrisville, North Carolina has begun production of the first batch of NVX-CoV2373

Source: LSC & Company websites

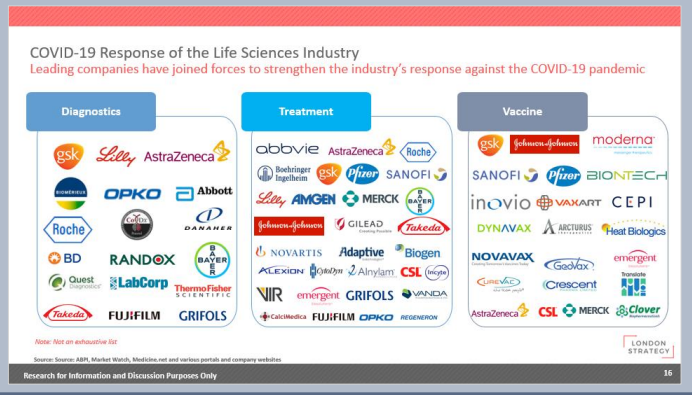
Note: As of 7th Aug 2020

COVID-19 Series - Index

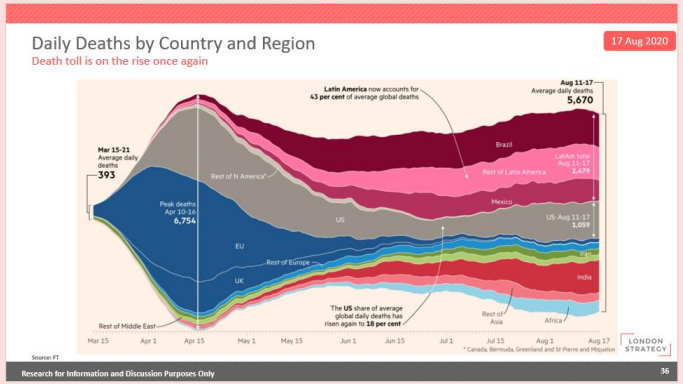
Impact on Life Sciences Sector: 3-13



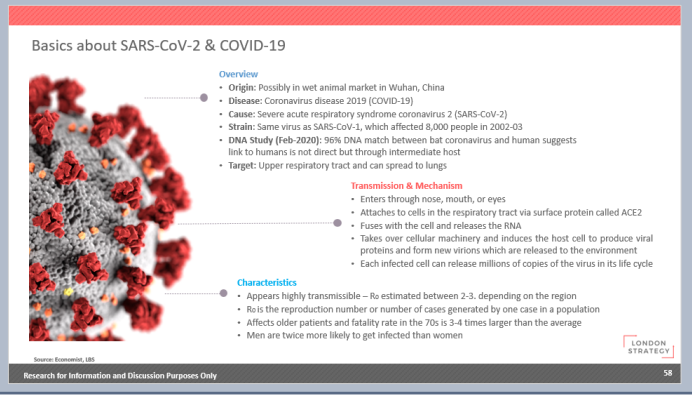
Response of the Life Sciences Industry:15-33



Charts & Insights: 35-55



Details of the Virus: 57-67



LONDON STRATEGY

Aug 2020

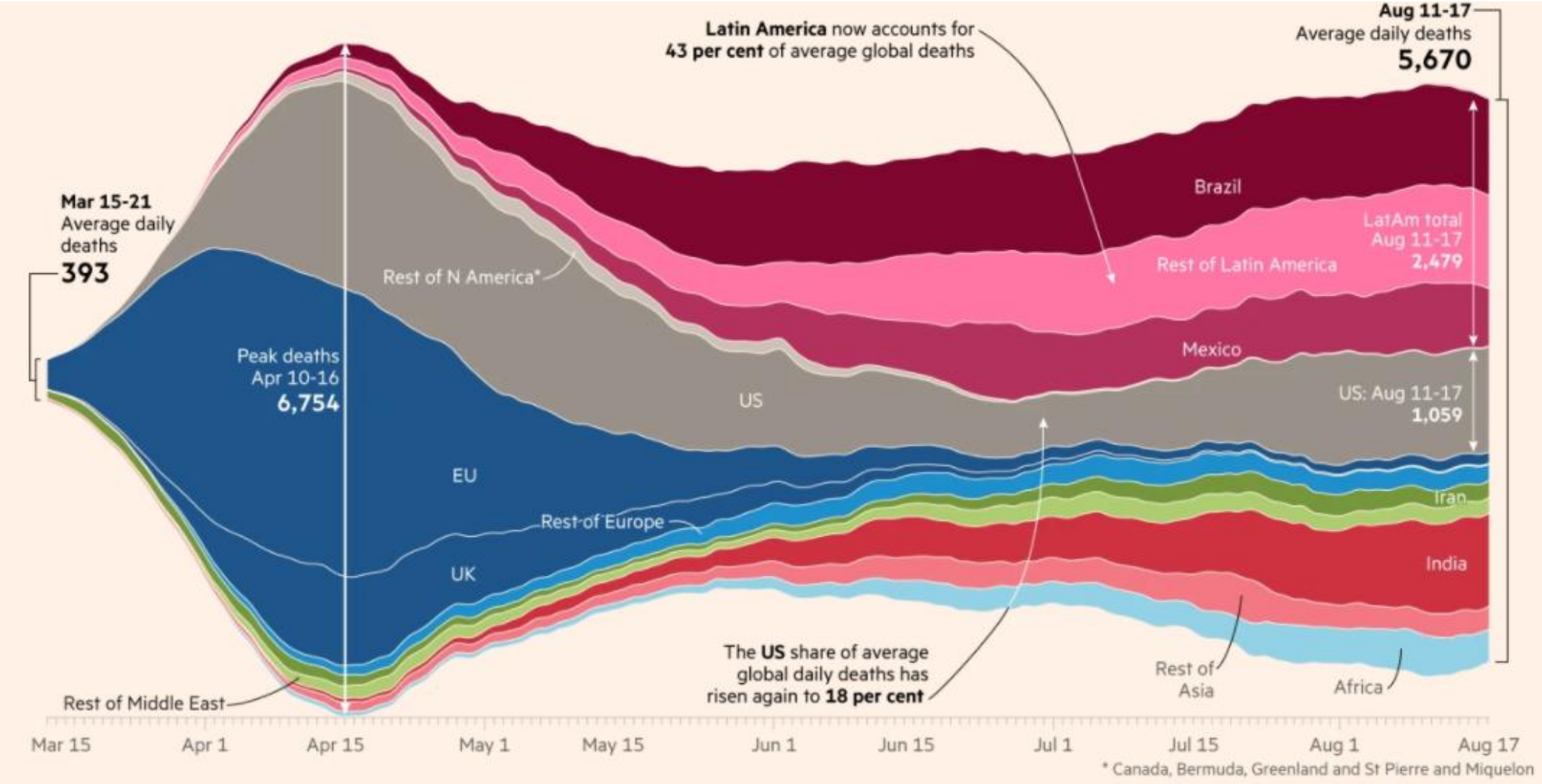
COVID-19
Charts & Insights

LONDON STRATEGY

Daily Deaths by Country and Region

17 Aug 2020

Death toll is on the rise once again



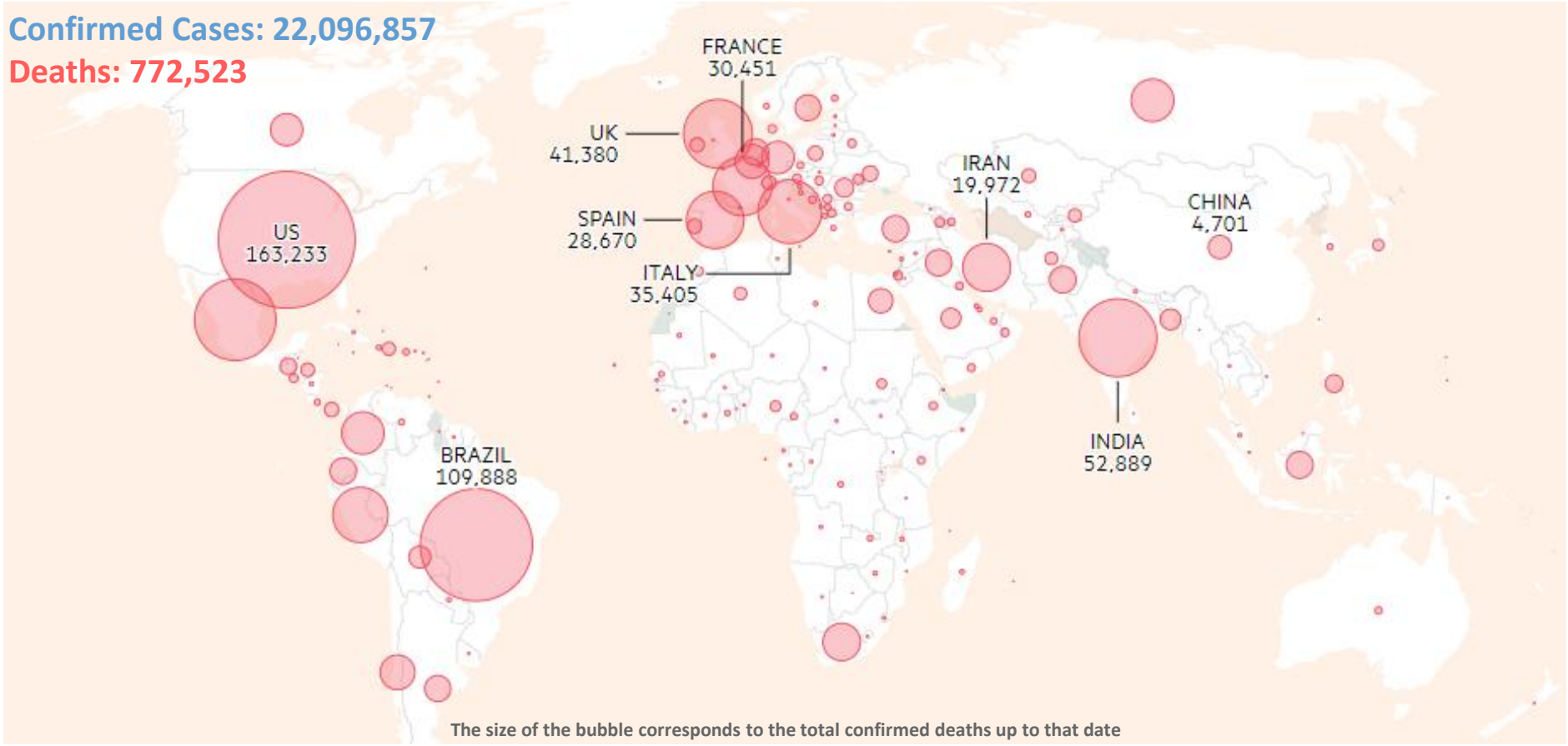
Source: FT

LONDON STRATEGY

19 Aug 2020

Mapping the Covid-19 outbreak

The pandemic spreads incredibly quickly between people. More than 22m people infected in appr. 8 months



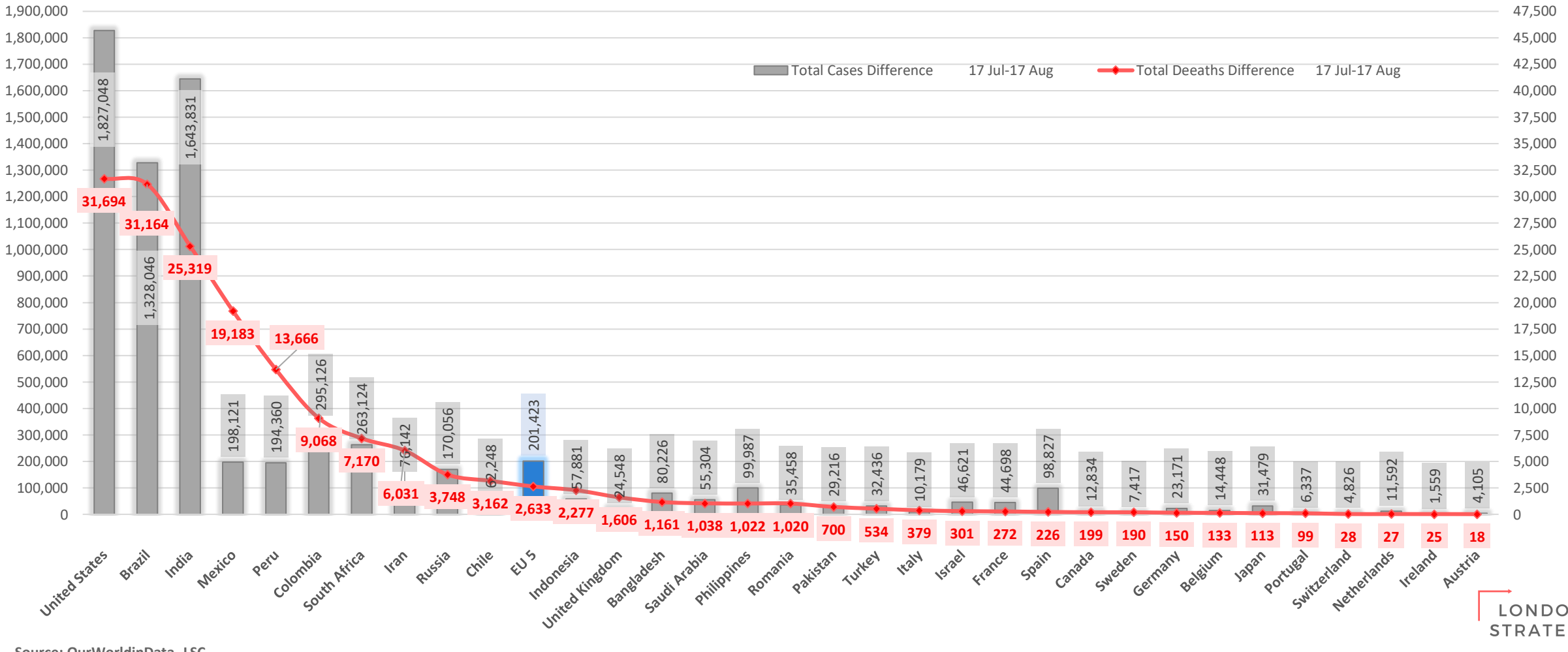
Source: FT

LONDON STRATEGY

The Last Month: Comparison of Total Cases and Death Tolls

18 Aug 2020

We have looked at the change in the last month (The difference between July 17th-August 17th)



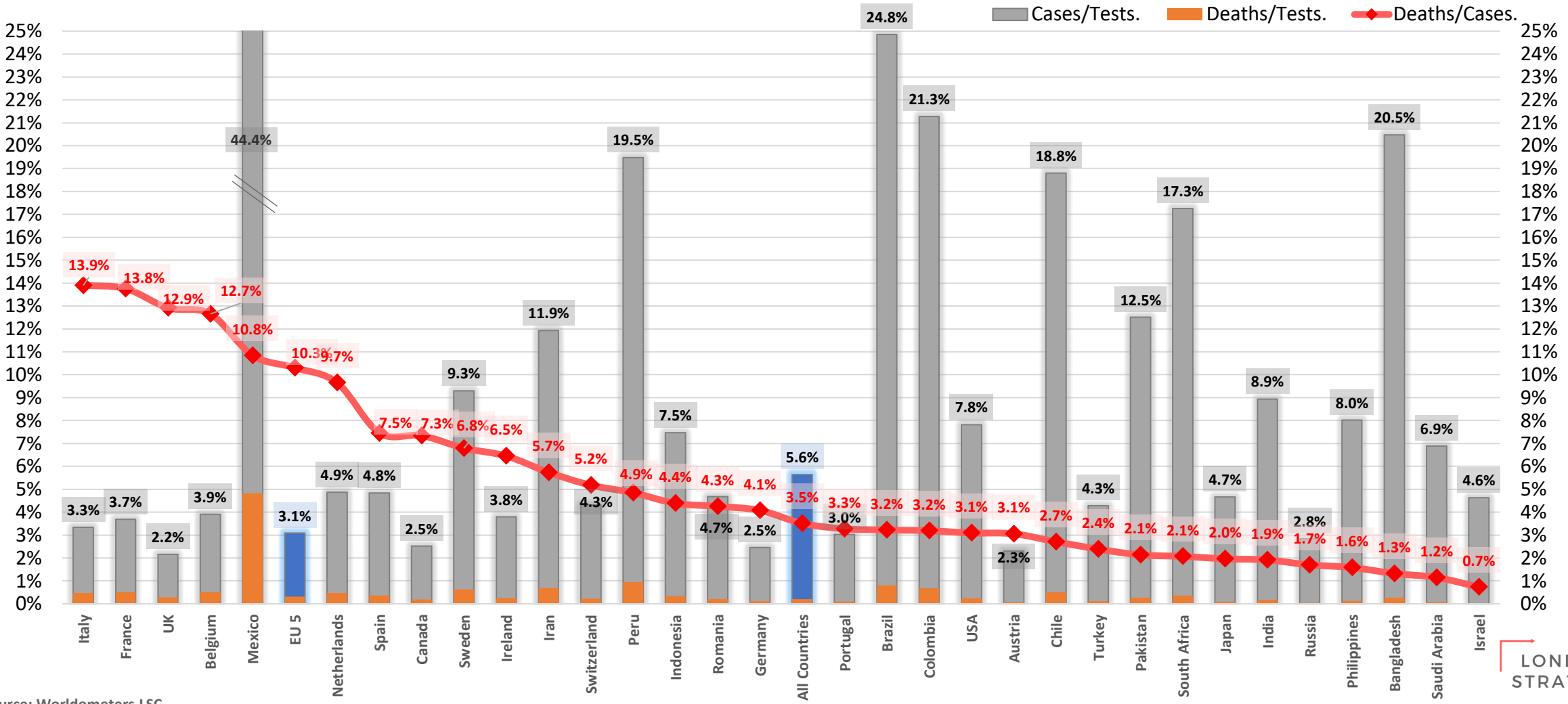
LONDON STRATEGY

Source: OurWorldinData, LSC

Comparison of Tests, Cases and Deaths

18 Aug 2020

Number of cases are not correctly reflected for the countries that are not doing sufficient testing and therefore the calculated death rates are significantly higher



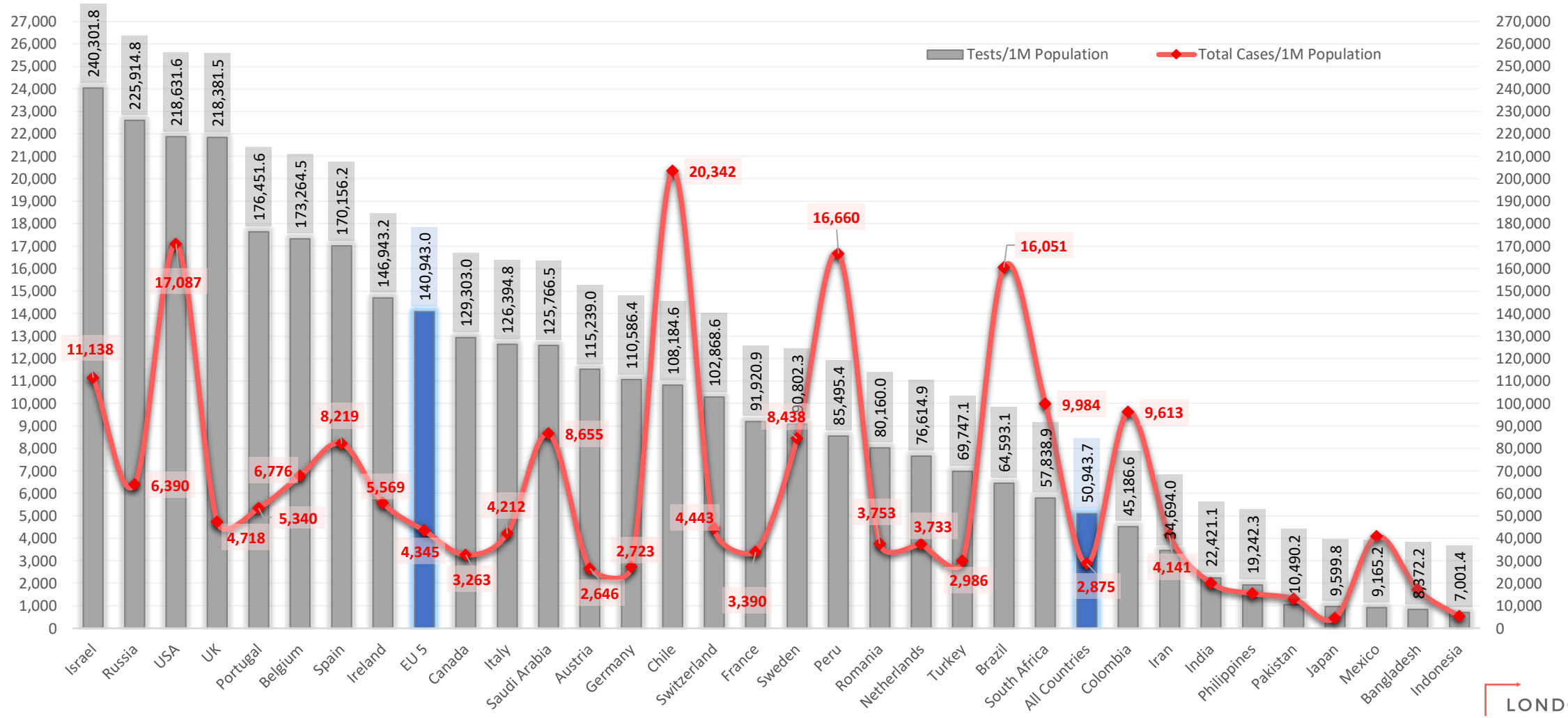
Source: Worldometers,LSC

LONDON STRATEGY

Comparison of Tests vs Cases / 1M Population

18 Aug 2020

There is a clear relationship between test vs cases



Source: Worldometers,LSC

LONDON STRATEGY

Excess Mortality Since Region/Country's First 50 Covid-19 Deaths

11 Aug 2020

In most places, the number of excess deaths is greater than the number of covid-19 fatalities officially recorded by governments in the same period

Excess deaths since country or city's first 50 covid deaths
Last updated on August 11th, 16:57 UTC

COUNTRY / REGION	TIME PERIOD	COVID-19 DEATHS	EXCESS DEATHS	EXCESS DEATHS PER 100K PEOPLE
Mexico City	Apr 6th-Jul 26th	8,674	27,162	305
Peru	Apr 1st-Jul 31st	19,187	55,409	169
Ecuador	Mar 1st-Jul 31st	5,702	28,536	166
Rio de Janeiro	Mar 1st-Jul 31st	8,279	9,798	146
Britain	Mar 14th-Jul 24th	56,063	63,919	96
Spain	Mar 4th-Jul 28th	28,247	43,261	93
Moscow	Apr 1st-Jun 30th	3,796	11,080	88
Italy	Feb 26th-May 26th	32,193	43,945	78
Belgium	Mar 23rd-Jun 7th	9,489	8,210	72
Chile	Apr 8th-Jul 28th	9,196	11,334	64
Netherlands	Mar 16th-Jul 19th	6,116	9,335	54
United States	Mar 8th-Jul 11th	133,253	175,700	54
Portugal	Mar 25th-Jul 28th	1,689	5,368	52
Sweden	Mar 18th-Jul 21st	5,710	5,332	52
France	Mar 11th-Jul 14th	29,996	29,073	45
Jakarta	Mar 1st-May 31st	520	4,465	41

Excess deaths since country or city's first 50 covid deaths
Last updated on July 15th, 17:27 UTC

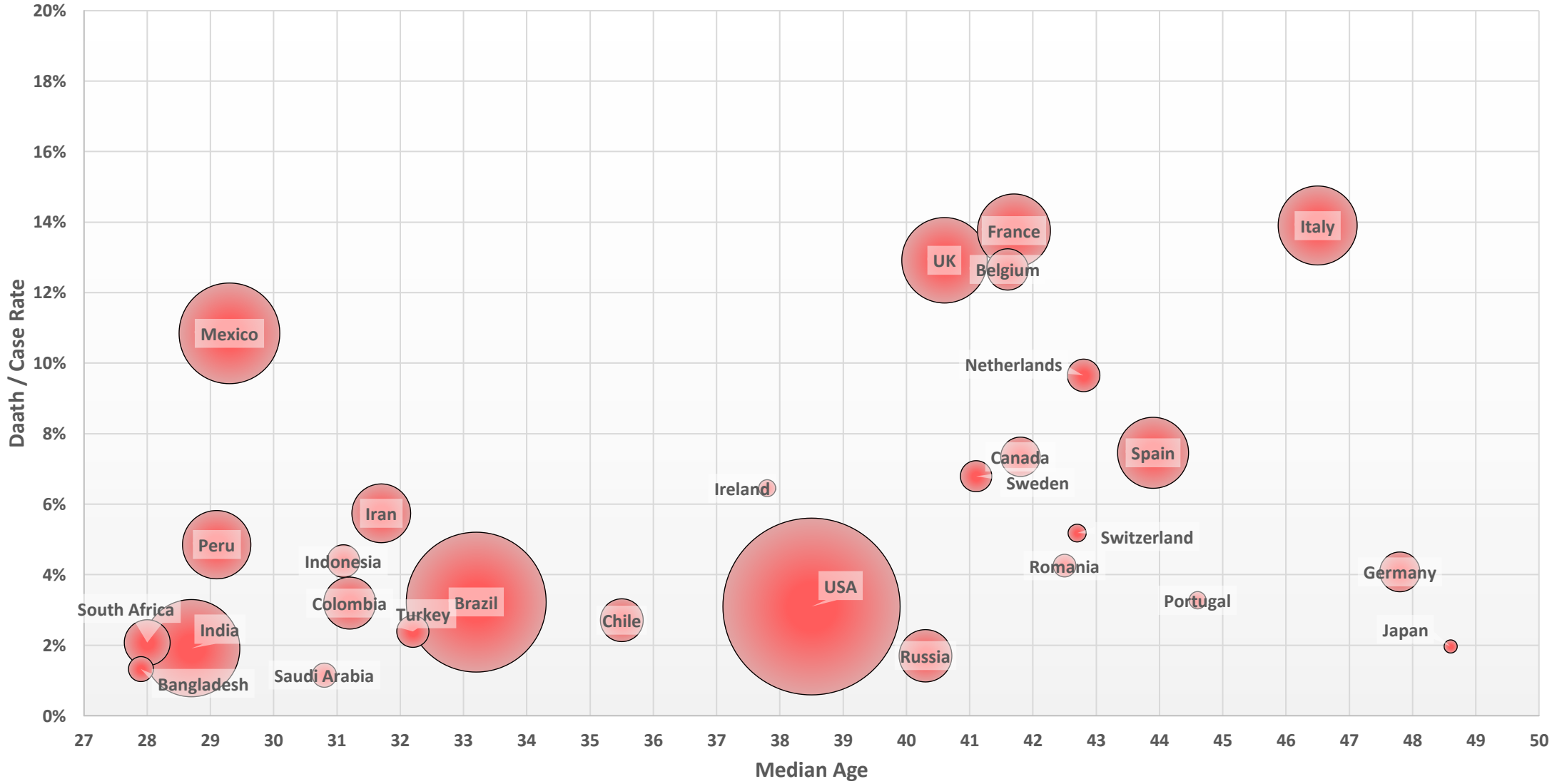
COUNTRY / REGION	TIME PERIOD	COVID-19 DEATHS	EXCESS DEATHS	EXCESS DEATHS PER 100K PEOPLE
Istanbul	Mar 25th-Jul 28th	2,801	4,389	28
South Africa	Apr 15th-Jul 28th	7,230	15,921	27
Austria	Mar 16th-Jul 19th	696	1,502	17
Switzerland	Mar 16th-Jul 26th	1,687	1,444	17
Germany	Mar 18th-Jun 30th	8,972	9,303	11
Denmark	Mar 25th-Jul 21st	579	447	8
Norway	Apr 1st-Jul 21st	227	-291	-5

Source: Economist

LONDON STRATEGY

Comparison of Median Age and Death Rate

18 Aug 2020



Source: Worldometers,LSC

The size of the bubble represents total deaths

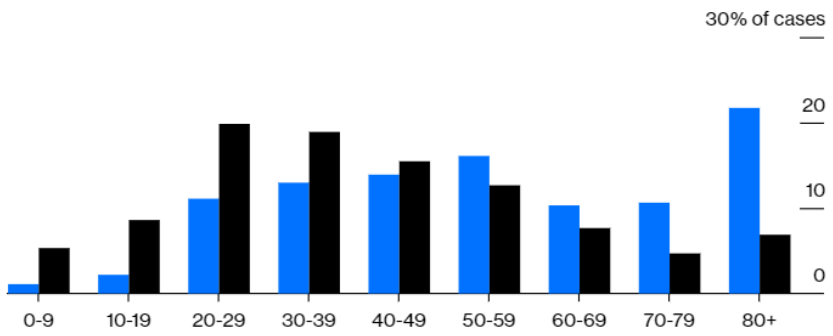
A Demographic shift in Covid-19 cases

13 Aug 2020

With more capacity to test and contact-tracing programs in place, countries are catching milder or asymptomatic cases in younger people that previously went uncounted.

England

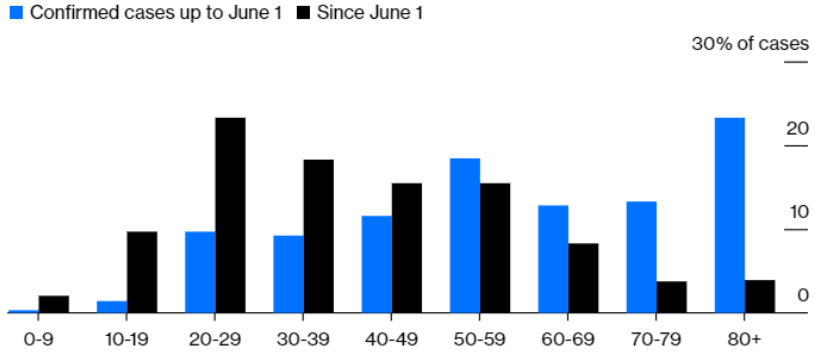
Age distribution of Covid-19 cases in England before and after lockdown eased



Source: Public Health England
Note: Pubs and restaurants opened July 4.

The Netherlands

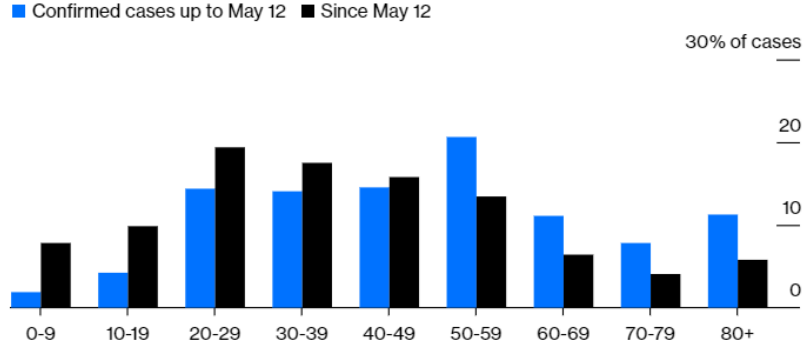
Age distribution of Covid-19 cases in the Netherlands before and after lockdown eased



Source: Center for Epidemiology and Surveillance of Infectious Diseases
Note: Bars and restaurants opened June 1.

Germany

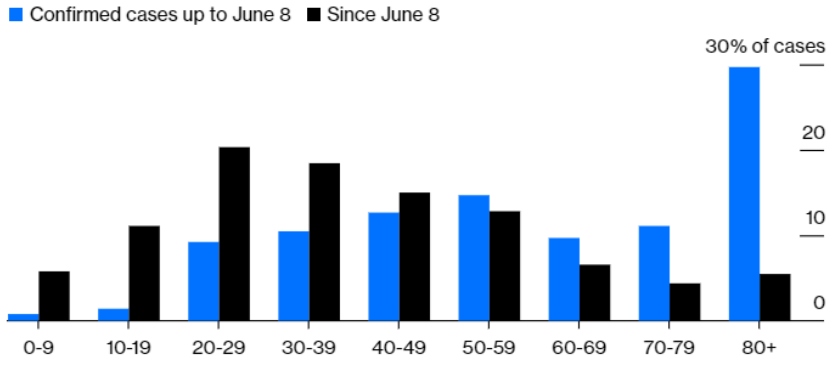
Age distribution of Covid-19 cases in Germany before and after lockdown eased



Source: Robert Koch Institut
Note: The first pubs in Germany opened May 11

Belgium

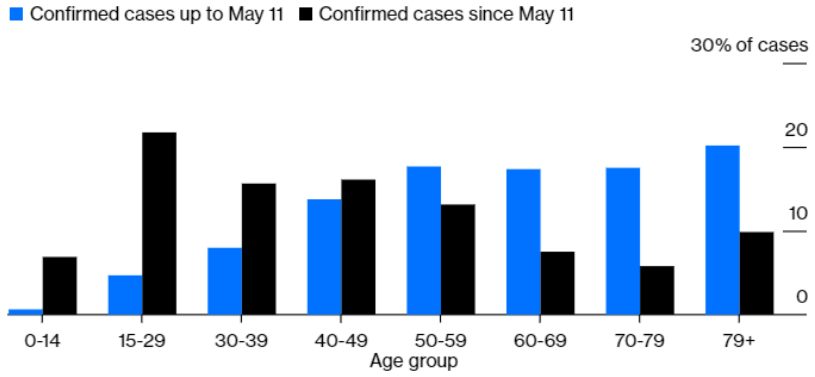
Age distribution of Covid-19 cases in Belgium before and after lockdown eased



Source: Epistat, Sciensano
Note: Cafes and bars opened June 8.

Spain

Age distribution of Covid-19 cases in Spain before and after lockdown eased



Source: National Center of Epidemiology

Source: Bloomberg

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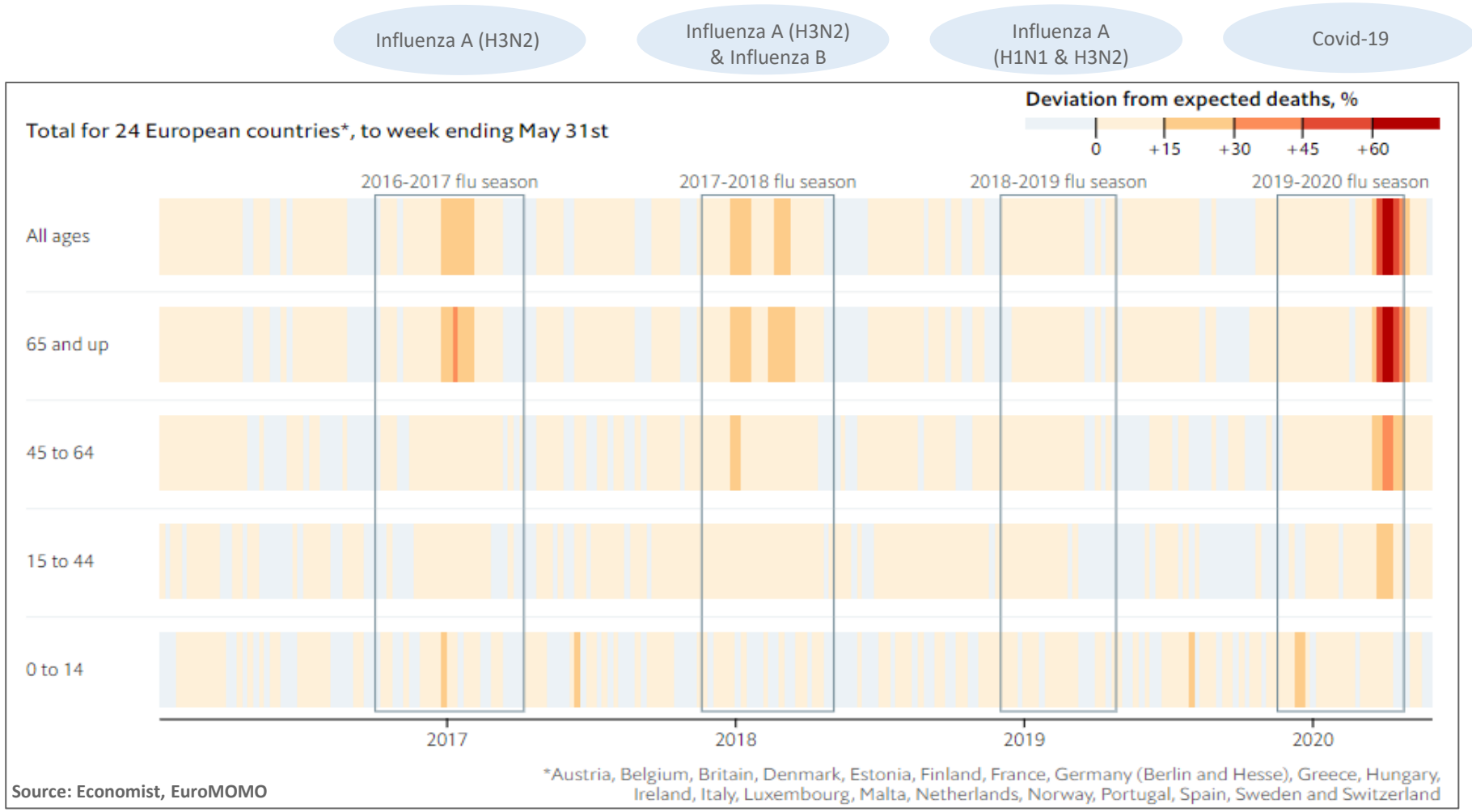
Weekly Estimated Excess Deaths by Age Group

1 Jun 2020

Most of victims have been older than 65, the number of deaths among Europeans aged 45-64 was 40% higher than usual in early April.



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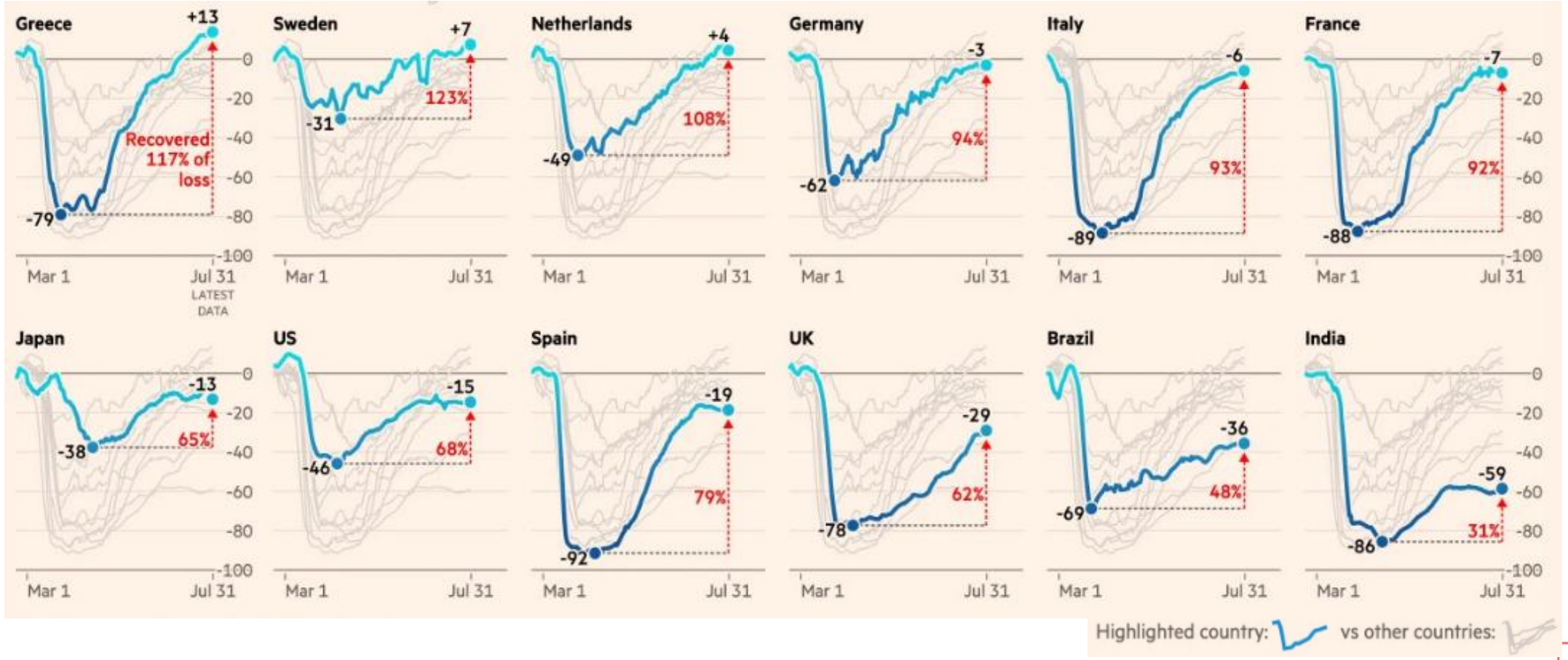
Covid-19 Impact on Consumer Habits

31 Jul 2020

Visits to entertainment and restaurant hubs have recovered in many countries

% change in visits to cafés, restaurants & entertainment venues, compared to baseline
Baseline=average for same day of week, Jan 3- Feb 6, 2020



Source: FT

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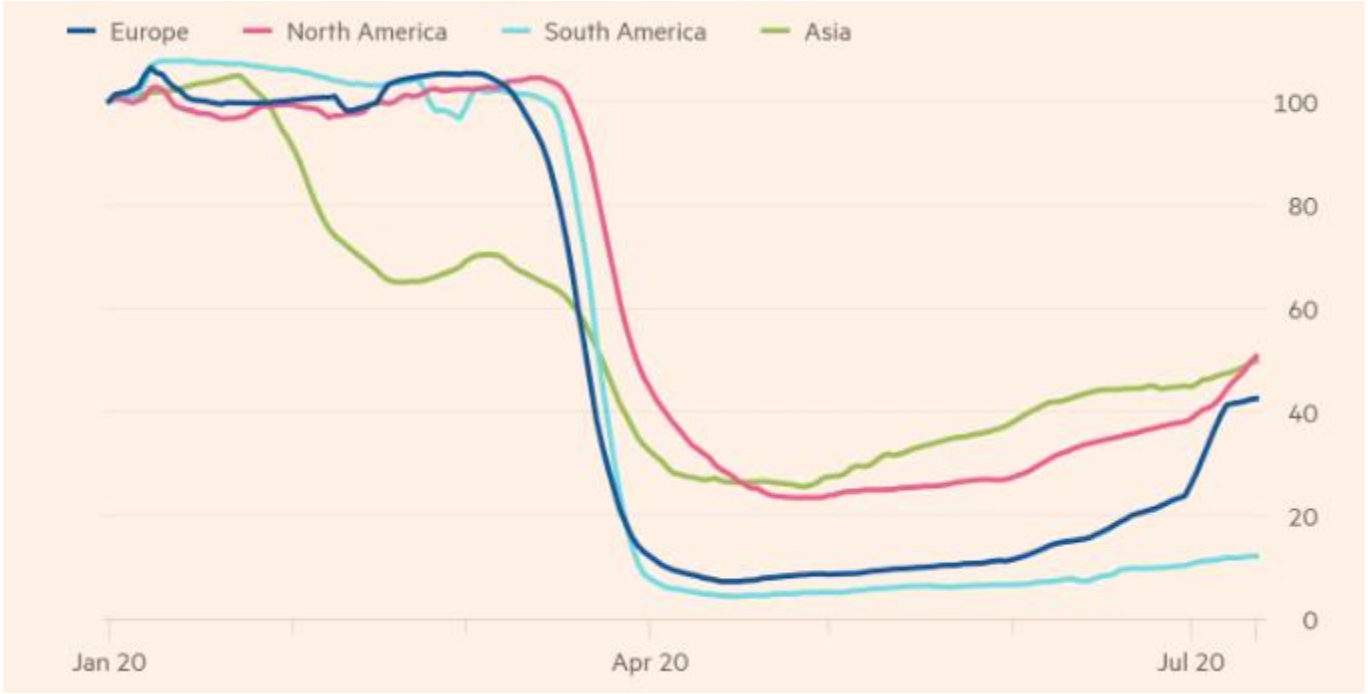
Covid-19 Impact on Travel & Tourism

21 Jul 2020

Numbers of international tourists in Europe are recovering and hotels are welcoming more guests

Year-on-year % change in number of non-residents present in each country

Room occupancy rate (%, open hotels only)



Source: FT

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Covid-19 Impact on Employment

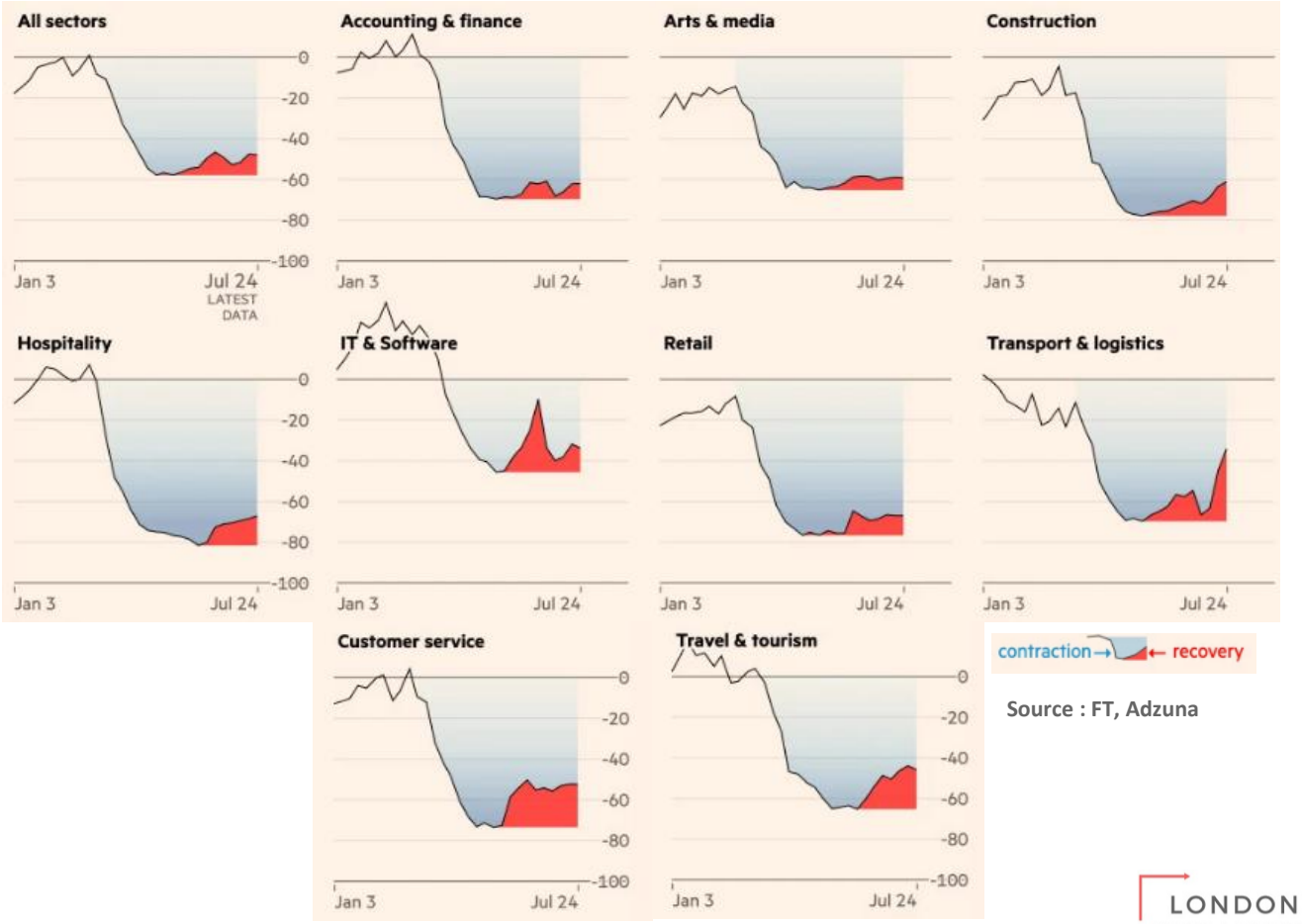
24 Jul 2020

Vacancies are below usual levels.
Job vacancies collapsed in most sectors, but are beginning to recover in UK

Job postings, 2020 vs 2019, gap in trend (%)

Source : FT, Indeed

Year-on-year % change in online UK Job ads by sector



Source : FT, Adzuna

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3 Aug 2020

COVID-19 Cases and Pharma Sales Evolution by Channel

						
COVID-19 Reported Numbers** *As of 11th Aug*	***Total Cases***	251,237	219,540	326,612	226,313	311,641
	7-day New Cases	2,818	6,712	23,798	10,120	5,348
	Total Deaths	35,215	9,208	28,581	30,201	46,526
Pharma Retail: Sell out Units Growth (Rx + CH)	*YTD[1]*	-2.8%	-4.4%	-1.3%	-2.9%	NA
	Latest Week[1]	-3.1%	+0.9%	+2.2%	+6.3%	NA
CH Market Units Growth	*YTD[1]*	+0.1%	-5.2%	-0.1%	+2.1%	+2.0%[3]
	Latest Week[1]	+2.3%	+0.1%	+1.0%	+8.0%	-1.4%[3]
Rx Retail Units Growth	*YTD[1]*	-4.8%	-3.9%	-1.9%	-4.6%	+0.1%[2]
	Latest Week[1]	-6.6%	+1.4%	+2.8%	+5.7%	-0.6%[2]

Note: Retail pharmacy sales/Rx data has been used across countries. Any cross-country analysis needs to account for differences in healthcare systems.
1: Weekly sell out data – Italy – W/S 27th July, Germany, Spain, France, UK (Rx) – W/S 3rd August 2020
2: Since UK weekly data was unavailable for 2019, the growth has been calculated over baseline of Rx Jan 2020
3: UK CH market calculations are based on weekly sell in data; UK (CH) – W/S 3rd August 2020
W/S refers to week start
** Source: Center for System Science and Engineering (CSSE) at John Hopkins University (JHU)

Source: IQVIA

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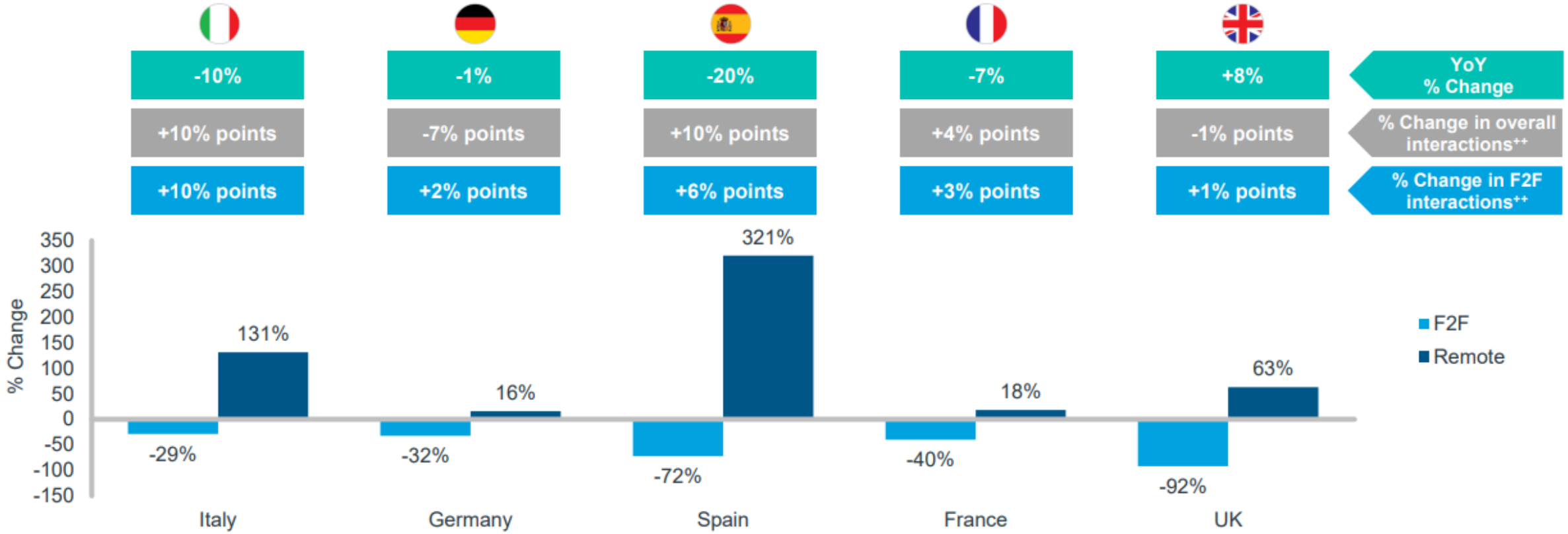
Medication interactions in EU5

F2F interactions have started to pick up in Italy, Germany, Spain and France

August* 2020 vs August* 2019 – % Change in absolute recorded HCP interaction volume

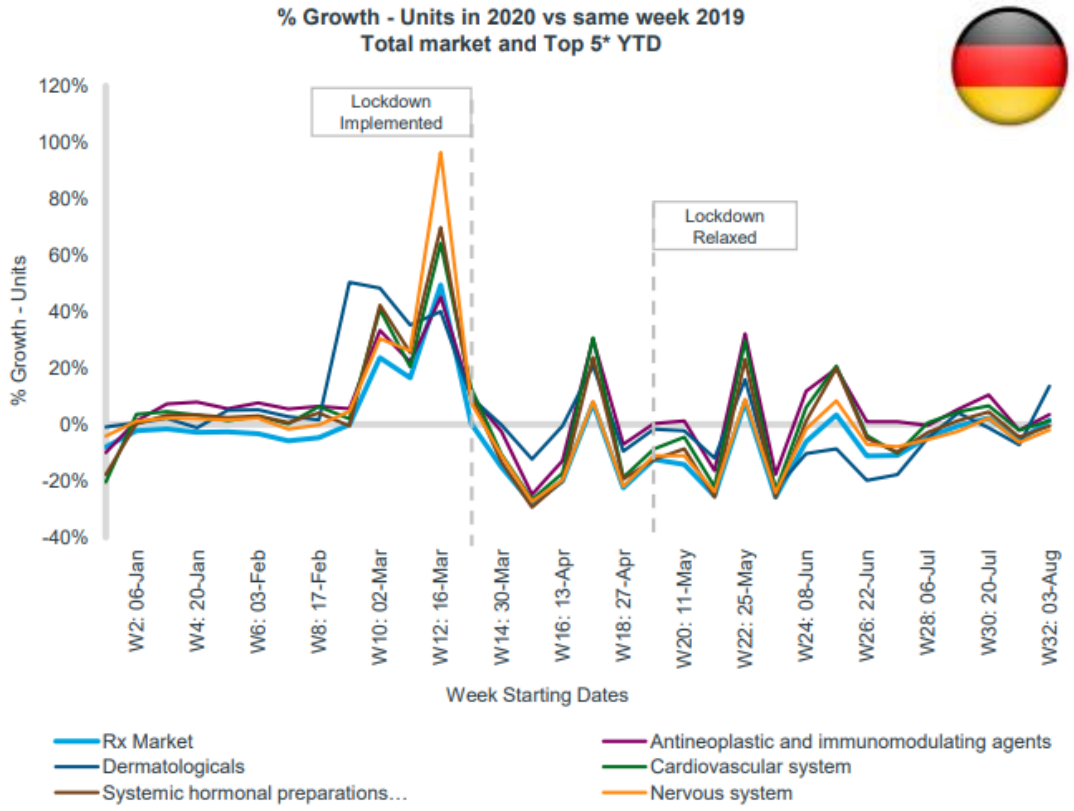


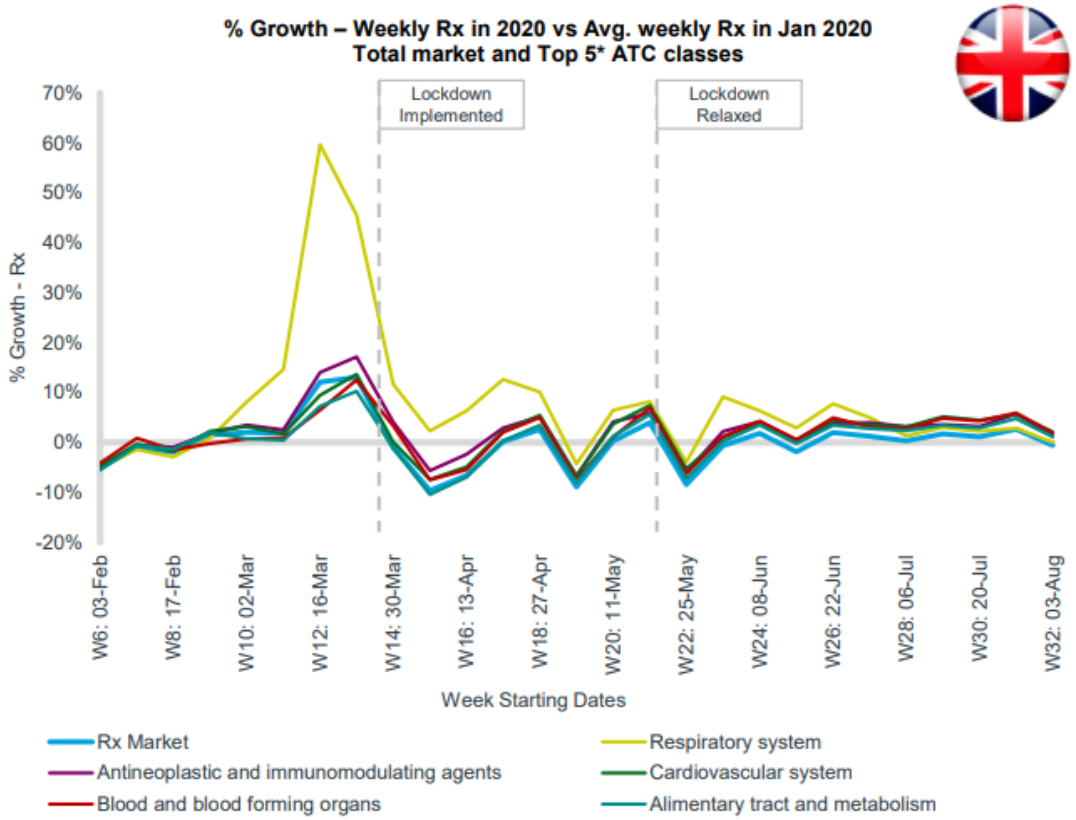
Note: UK and Germany already had sizeable remote interactions (>60%)
*30 day period to 09/08
++ Change over previous release (30 day period to 26/07)
Source: IQVIA European Thought Leadership; ChannelDynamics 09/08/2020; F2F includes detailing and meetings, Remote includes phone detailing, e-detailing (live+automated), postal & e-mailings, e-meetings (live+automated)

Source: IQVIA

EU5 Prescription Market (Sales) Scorecards - 1/3

3 Aug 2020





Source: IQVIA

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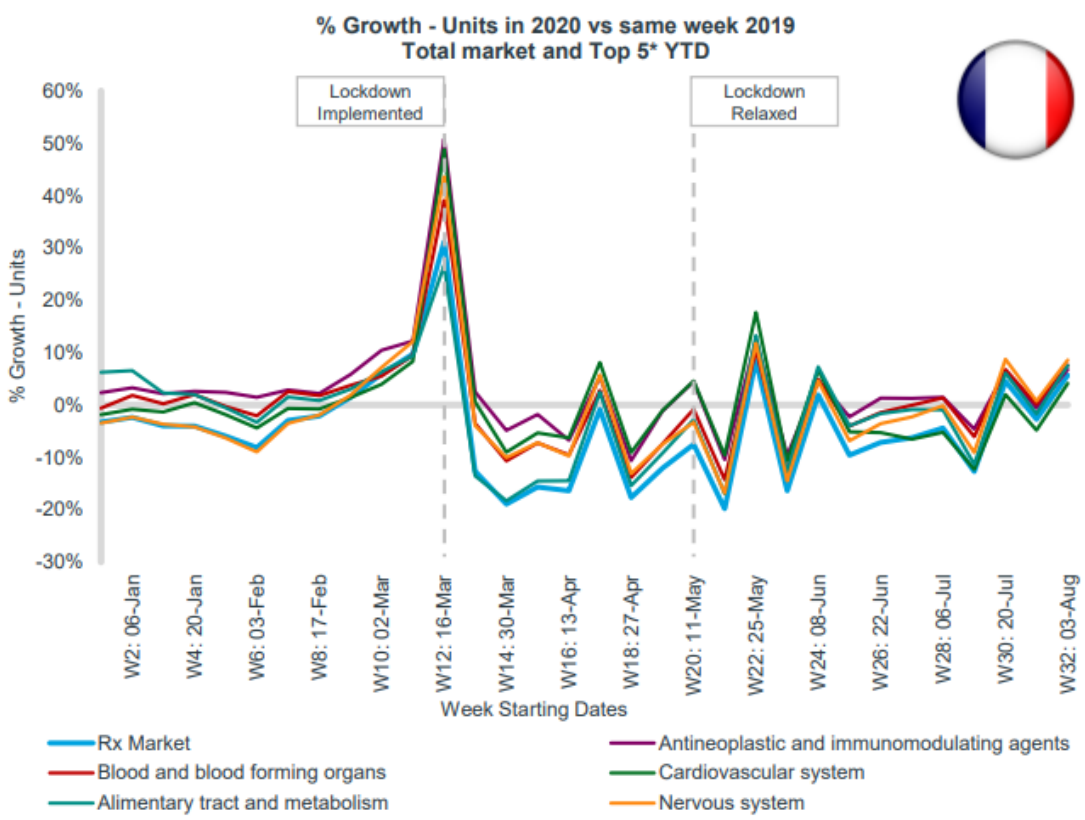
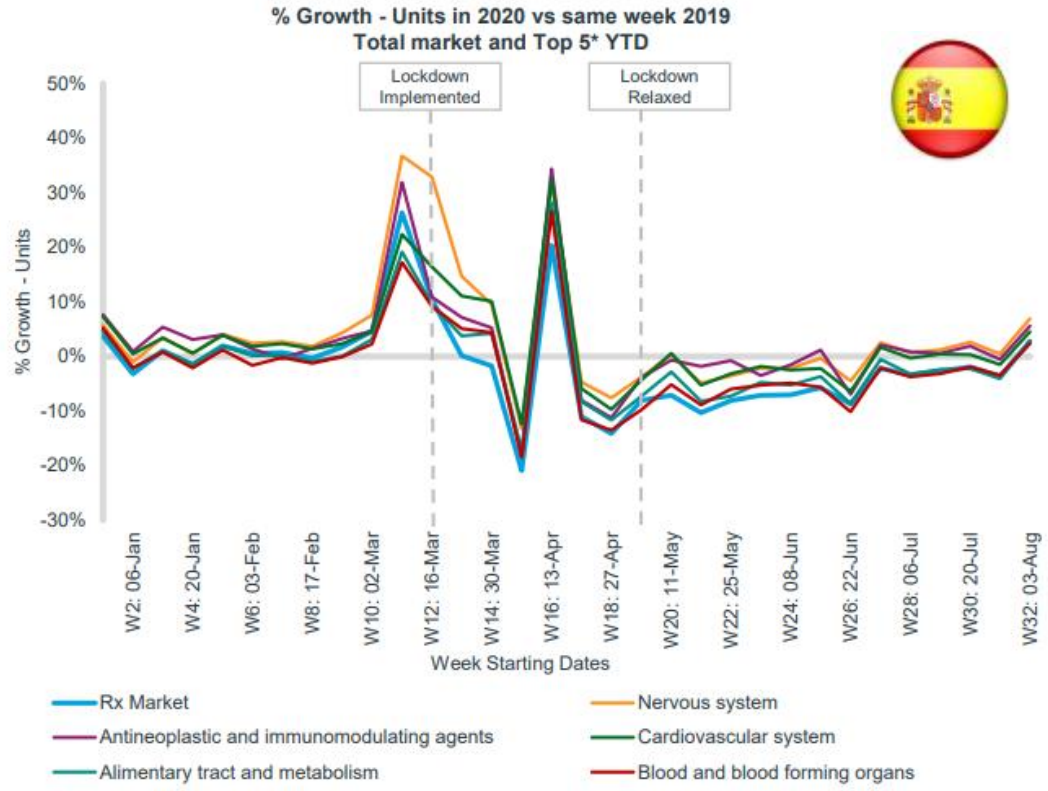
EU5 Prescription Market (Sales) Scorecards - 2/3

3 Aug 2020

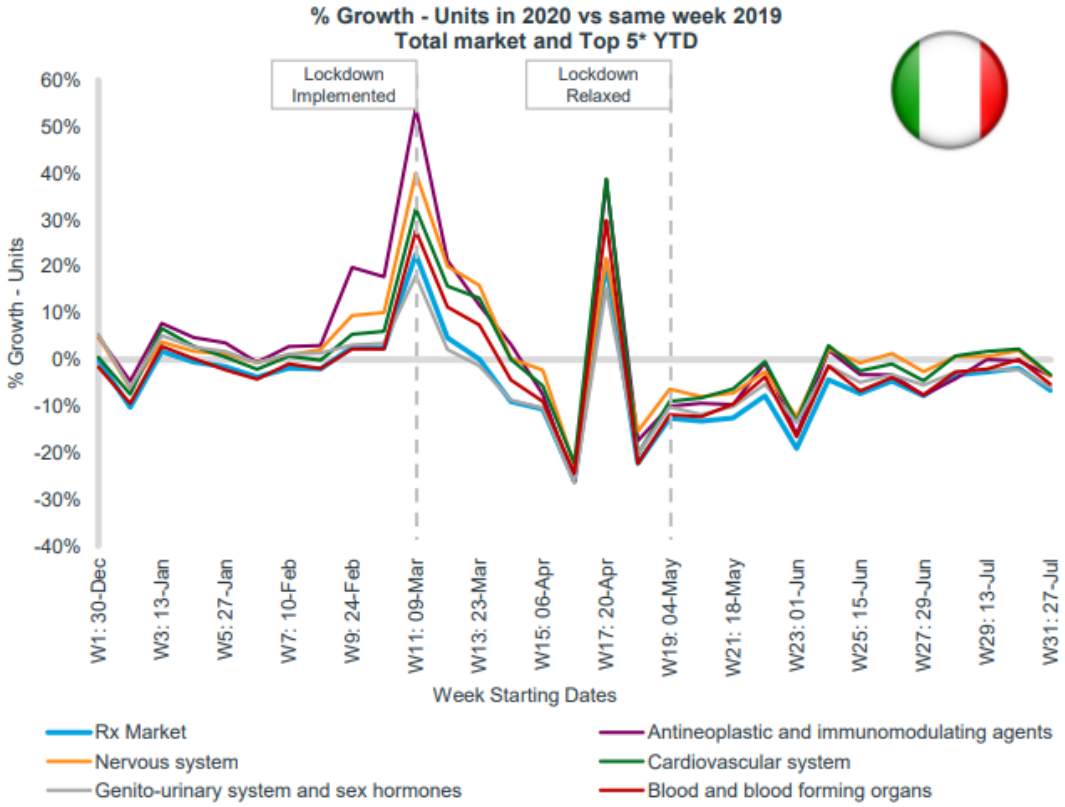




Source: IQVIA

EU5 Prescription Market (Sales) Scorecards - 3/3

3 Aug 2020



Source: IQVIA

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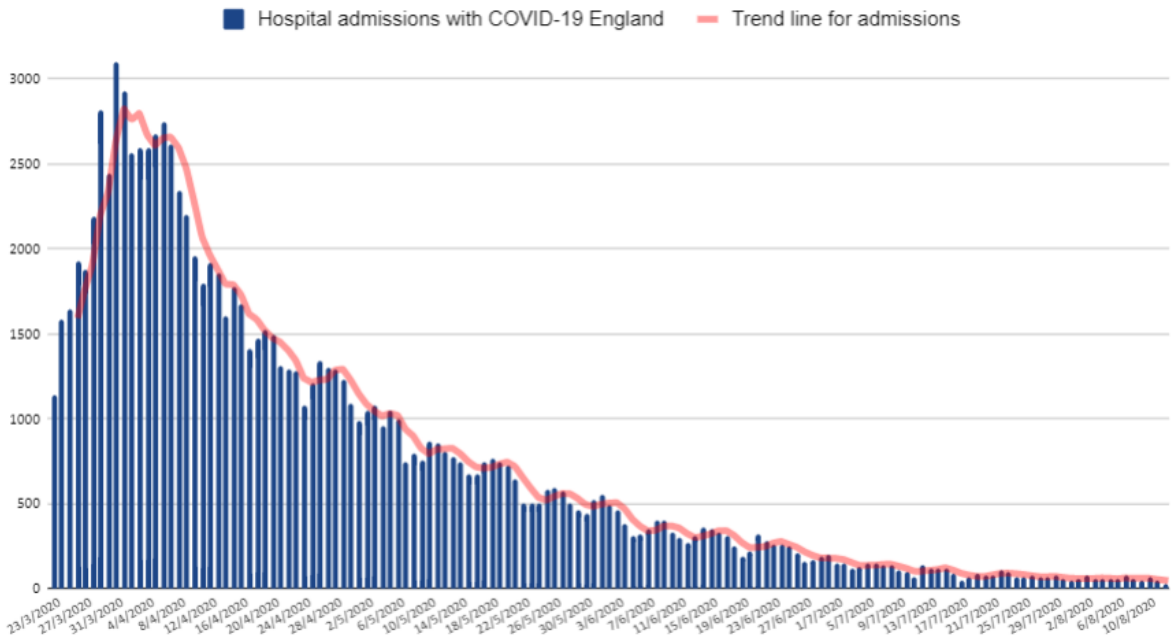
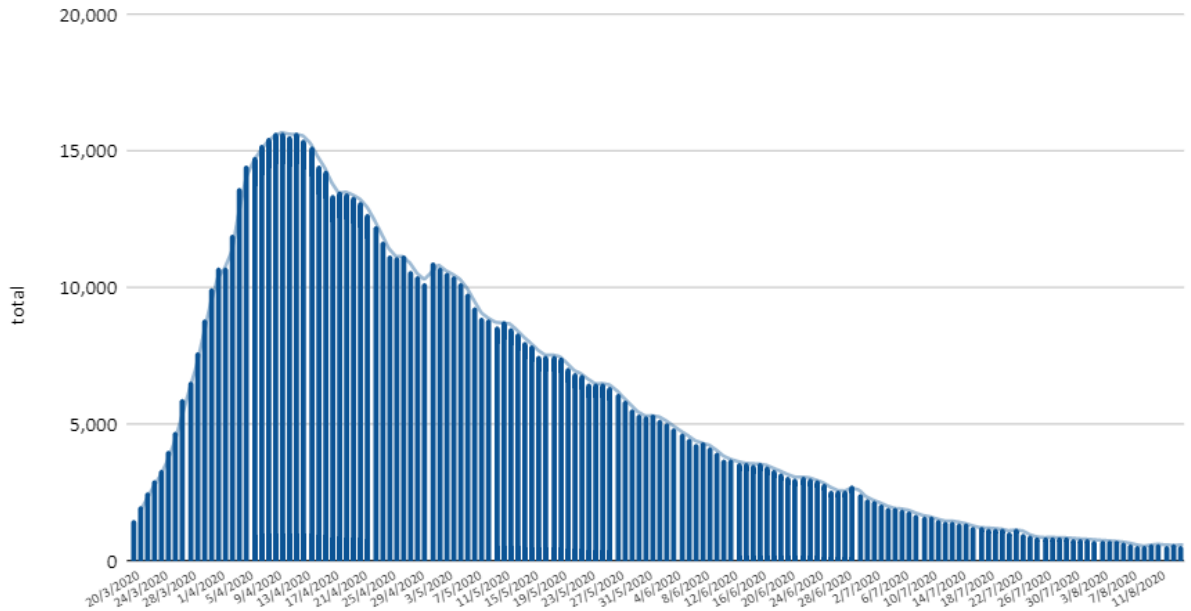
11 Aug 2020

Hospitalized people due to Covid-19 in UK

Daily Covid-19 Hospital Admissions



Total Covid-19 Hospital Admissions



Source: CEBM The Centre for Evidence-Based Medicine

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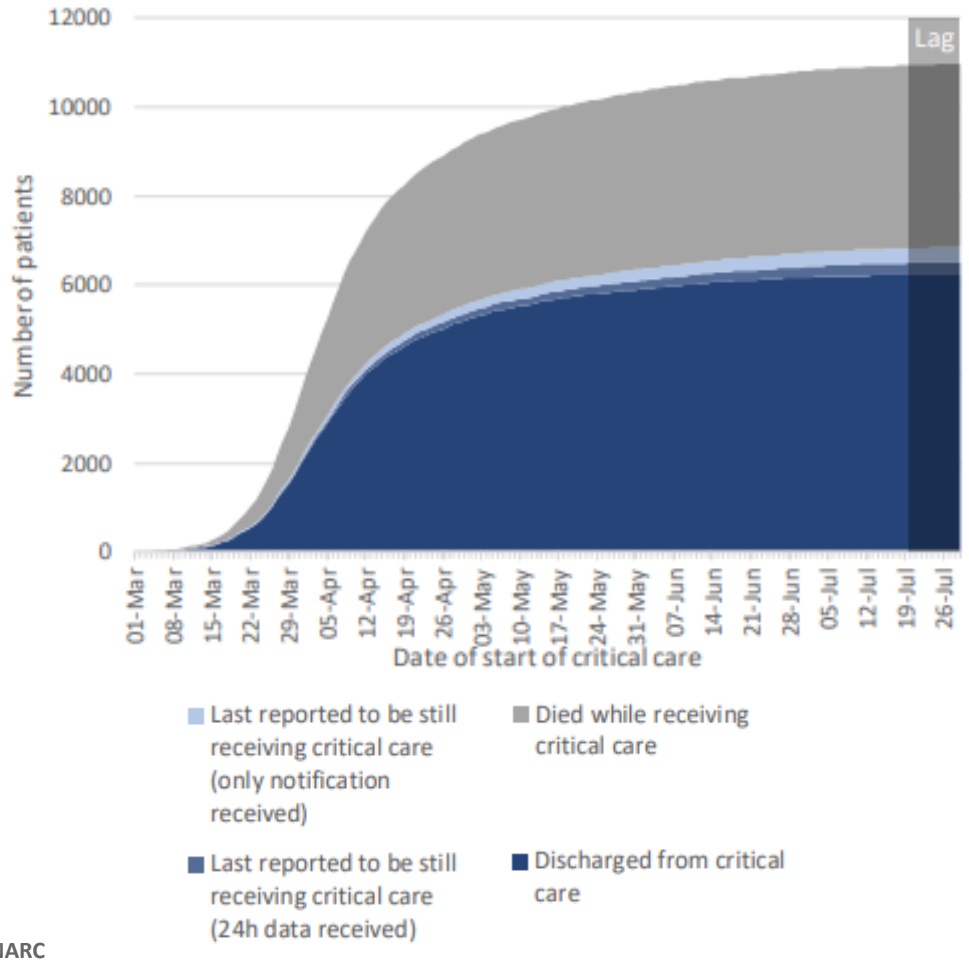
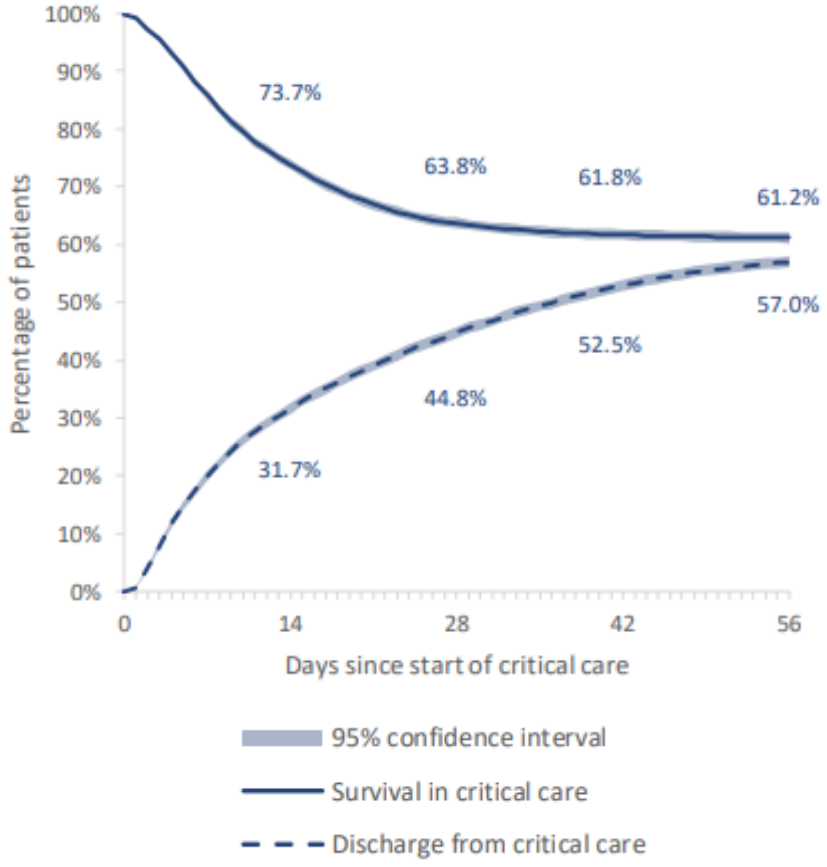
Critical care and acute hospital outcomes in UK

Cumulative outcomes by date of start of critical care



Survival and discharge among patients with at least 24h data received



Source: ICNARC

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Chart Data Sources

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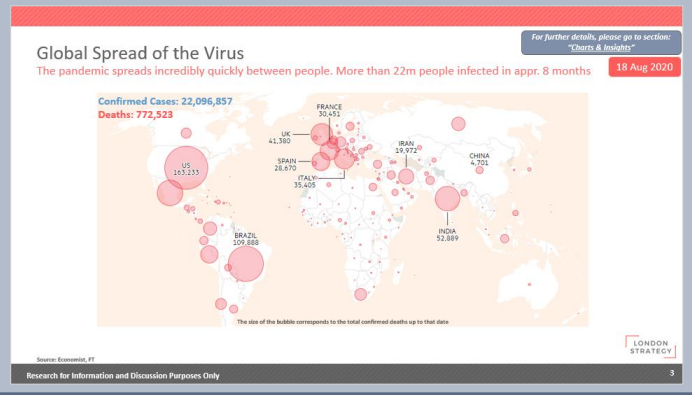
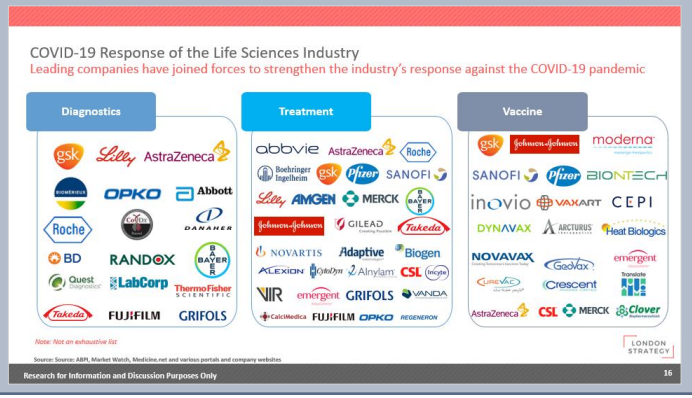
COVID-19 Series - Index

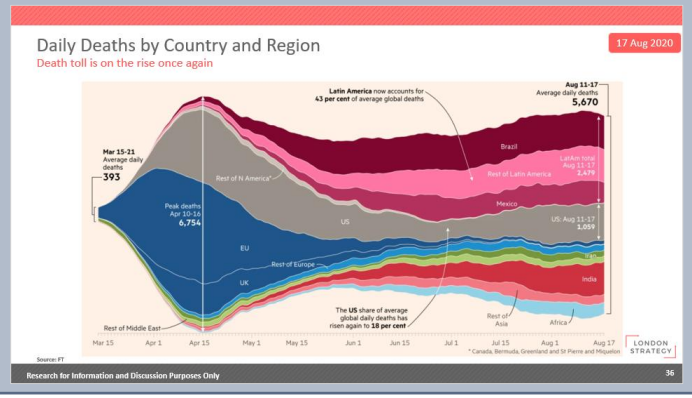
Impact on Life Sciences Sector: 3-13



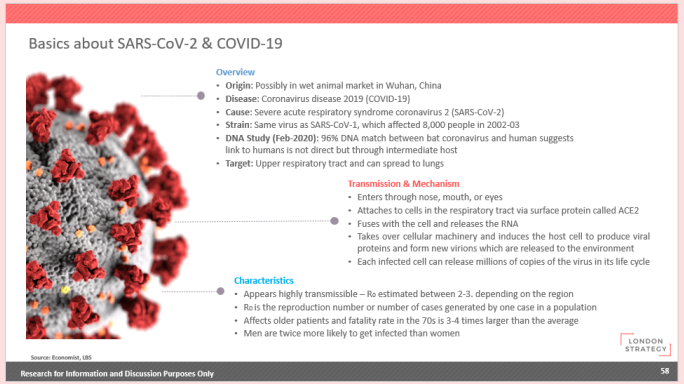
Response of the Life Sciences Industry:15-33



Charts & Insights: 35-55



Details of the Virus: 57-67



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COVID-19
Details of the Virus

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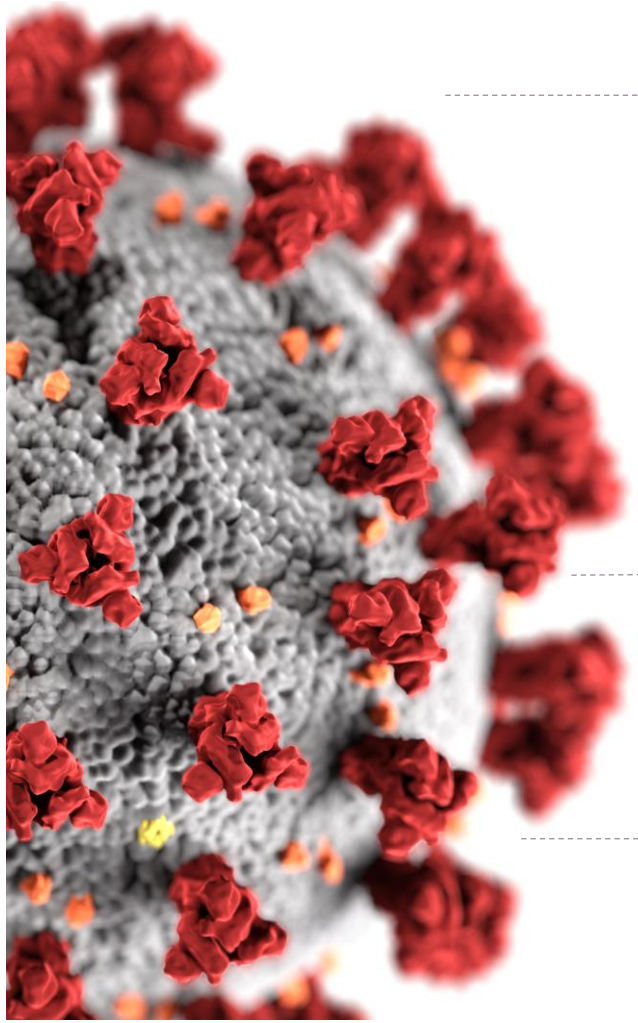
Basics about SARS-CoV-2 & COVID-19



Overview

- **Origin**: Possibly in wet animal market in Wuhan, China
- **Disease**: Coronavirus disease 2019 (COVID-19)
- **Cause**: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- **Strain**: Same virus as SARS-CoV-1, which affected 8,000 people in 2002-03
- **DNA Study (Feb-2020)**: 96% DNA match between bat coronavirus and human suggests link to humans is not direct but through intermediate host
- **Target**: Upper respiratory tract and can spread to lungs

Transmission & Mechanism

- Enters through nose, mouth, or eyes
- Attaches to cells in the respiratory tract via surface protein called ACE2
- Fuses with the cell and releases the RNA
- Takes over cellular machinery and induces the host cell to produce viral proteins and form new virions which are released to the environment
- Each infected cell can release millions of copies of the virus in its life cycle

Characteristics

- Appears highly transmissible – R_0 estimated between 2-3. depending on the region
- R_0 is the reproduction number or number of cases generated by one case in a population
- Affects older patients and fatality rate in the 70s is 3-4 times larger than the average
- Men are twice more likely to get infected than women

Source: Economist, LBS

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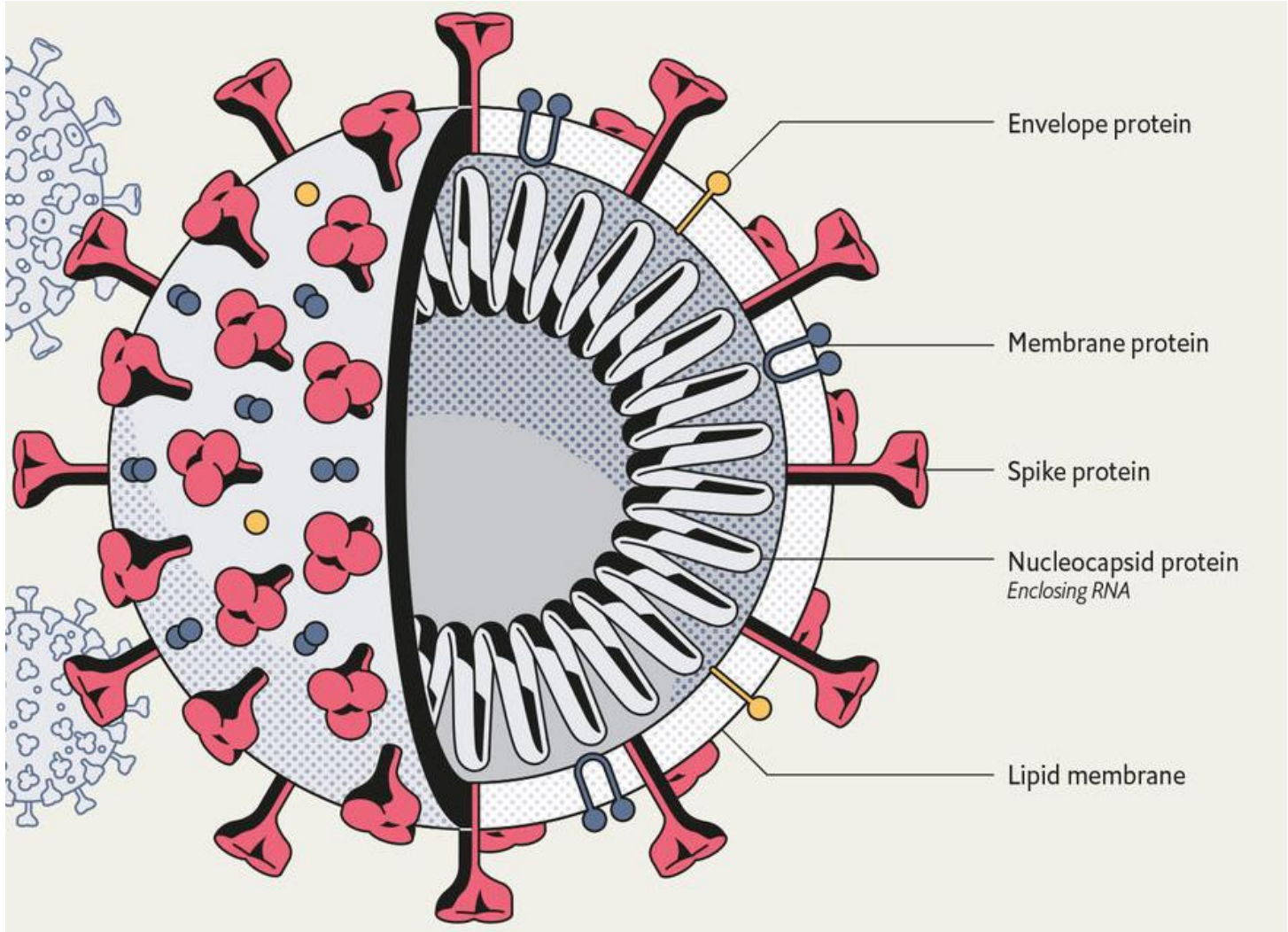
Anatomy of the Virus: SARS-CoV-2



Size & Morphology

- SARS-CoV-2 has a diameter of approximately 60–140nm.
- It has a round or elliptic shape like most viruses.
- Club-shaped protrusions give a crown-like appearance under an electron-microscope.

Structure

- It is composed of 4 structural proteins; the spike glycoproteins, which are present on the surface of the envelope, that surround lipid membrane, which encapsulates the RNA-containing nucleocapsid protein.
- These surface proteins are responsible for mediating antibody neutralization and host receptor-binding.

Genomic Characteristics

- Single-stranded positive RNA molecule with a 5’-cap structure and 3’-poly-A tail
- Coronaviruses (CoVs) possess the largest genomes (26.4–31.7 kb) among all known RNA viruses

Source: Economist, NCBI

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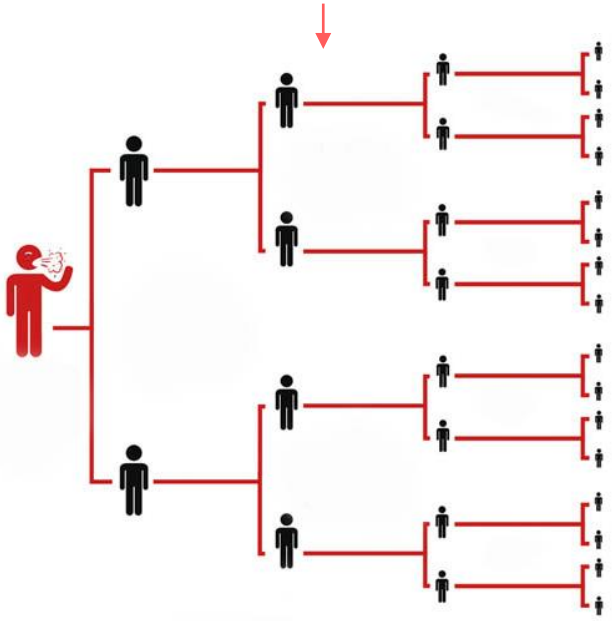
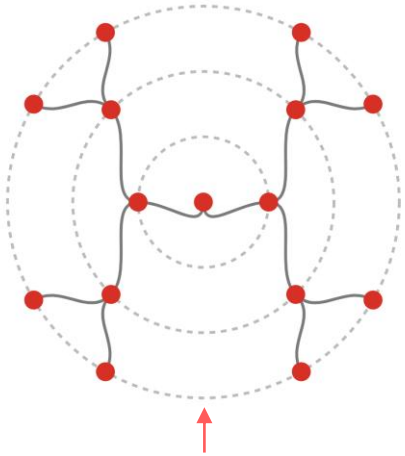
Covid-19 Transmission & R0 Reproductive Number

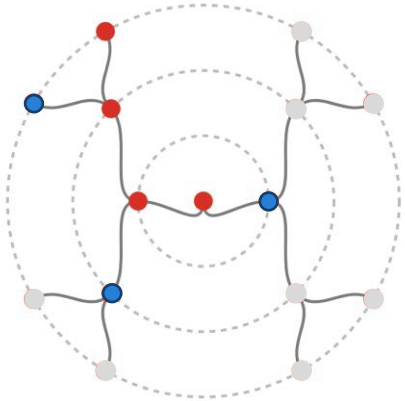
What is R0? - Basic Reproduction Number
The expected number of cases directly generated by one case in a population where all individuals are susceptible to infection.

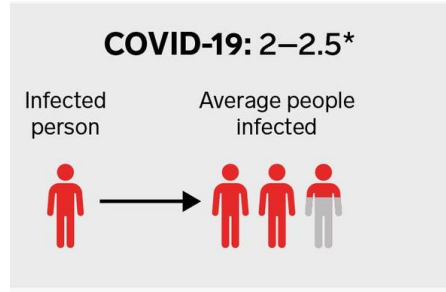
- Pictured below is an example of a disease spread with a reproduction number (R0) equal to 2.
- As illustrated, the individual carrying the disease infects on average two additional individuals.

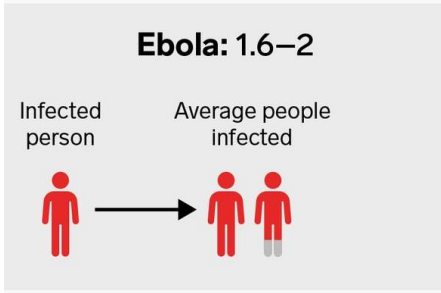


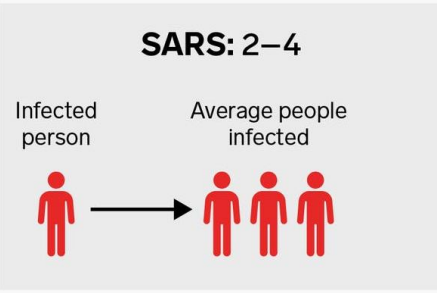


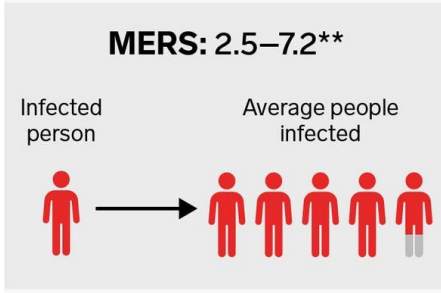
- Pictured above is a different illustration of a disease spread with a reproduction number (R0) equal to 2.
- Pictured below illustrates the impact (decrease in transmission) of a self-isolating 50% of infectees (●).

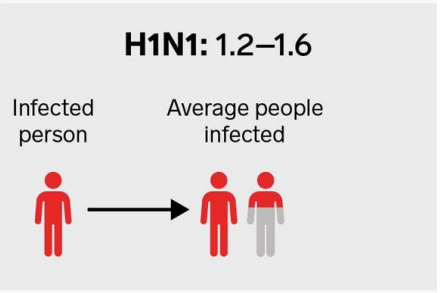












Estimated values of R0 of Covid-19 and other infectious diseases.

* Based on early case WHO reports in Wuhan (February 2020)
** Calculated solely on 2015 outbreak in South Korea

Source: McFall-Johnson et Bendix (2020) Business Insider – How Contagious is Coronavirus?
Eisenberg (2020) University of Michigan - How Scientists Quantify the Intensity of an Outbreak Like COVID-19

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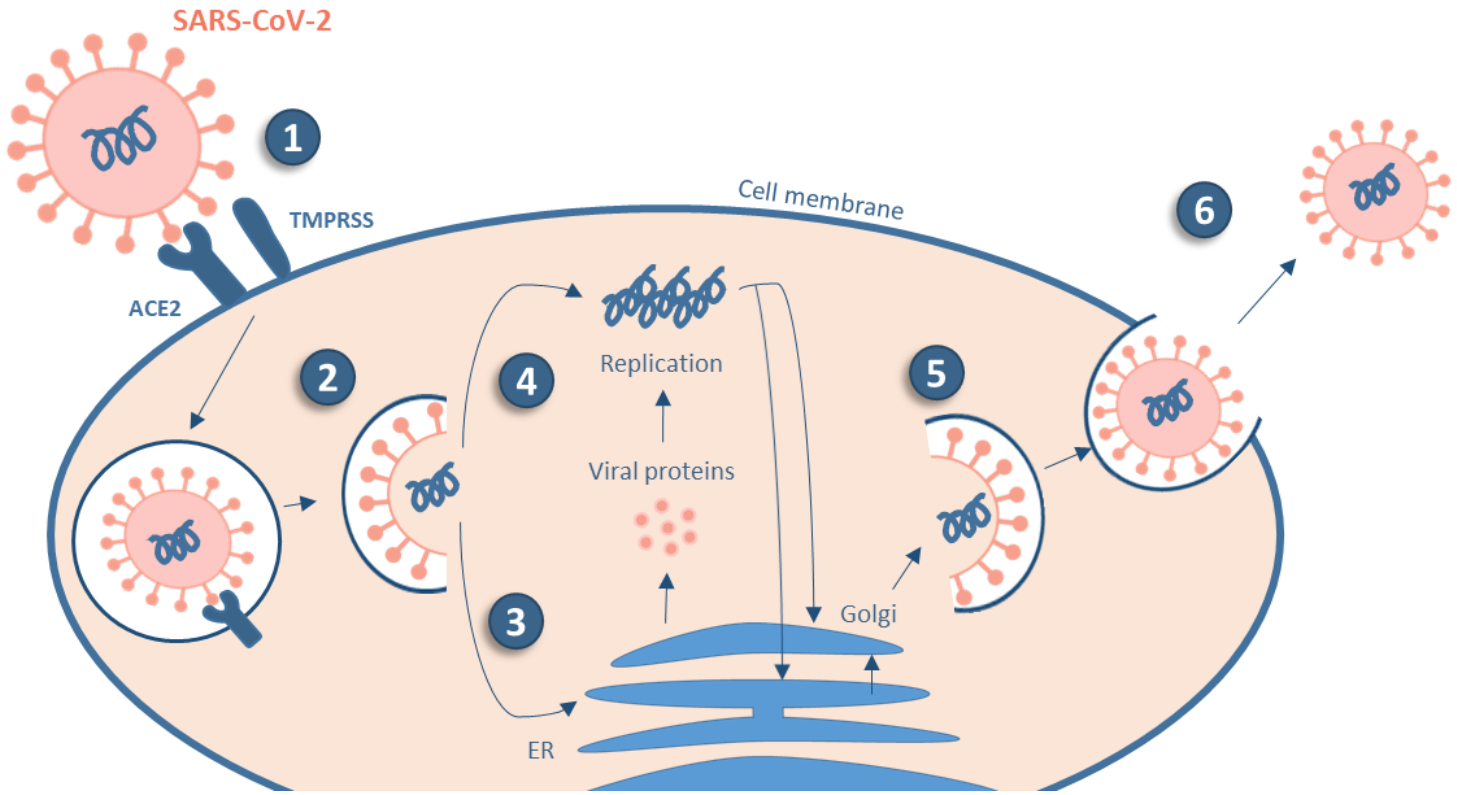
Cellular Pathogenesis of the Virus: SARS-CoV-2

Replication Cycle of SARS-CoV-2

1. **Adsorption & Endocytosis:** SARS-CoV-2 binds to ACE2, a host surface receptor protein via its spike protein. Another cell-surface protein, TMPRSS, assists this internalisation process
2. **Unfolding:** The genetic material, containing non-structural proteins essential for intracellular replication of the virus, are released into the cell.
3. **Translation:** The viral RNA mounts the cellular machinery to translate its genetic material into new viral proteins
4. **Synthesis:** These proteins form a replication complex which allows more viral genetic material to be transcribed and translated via the ERGIC apparatus.
5. **Virion Assembly:** The viral RNA and proteins are assembled into a new virion
6. **Exocytosis:** The fully-assembled virion is then released via exocytosis into the environment to infect other cells



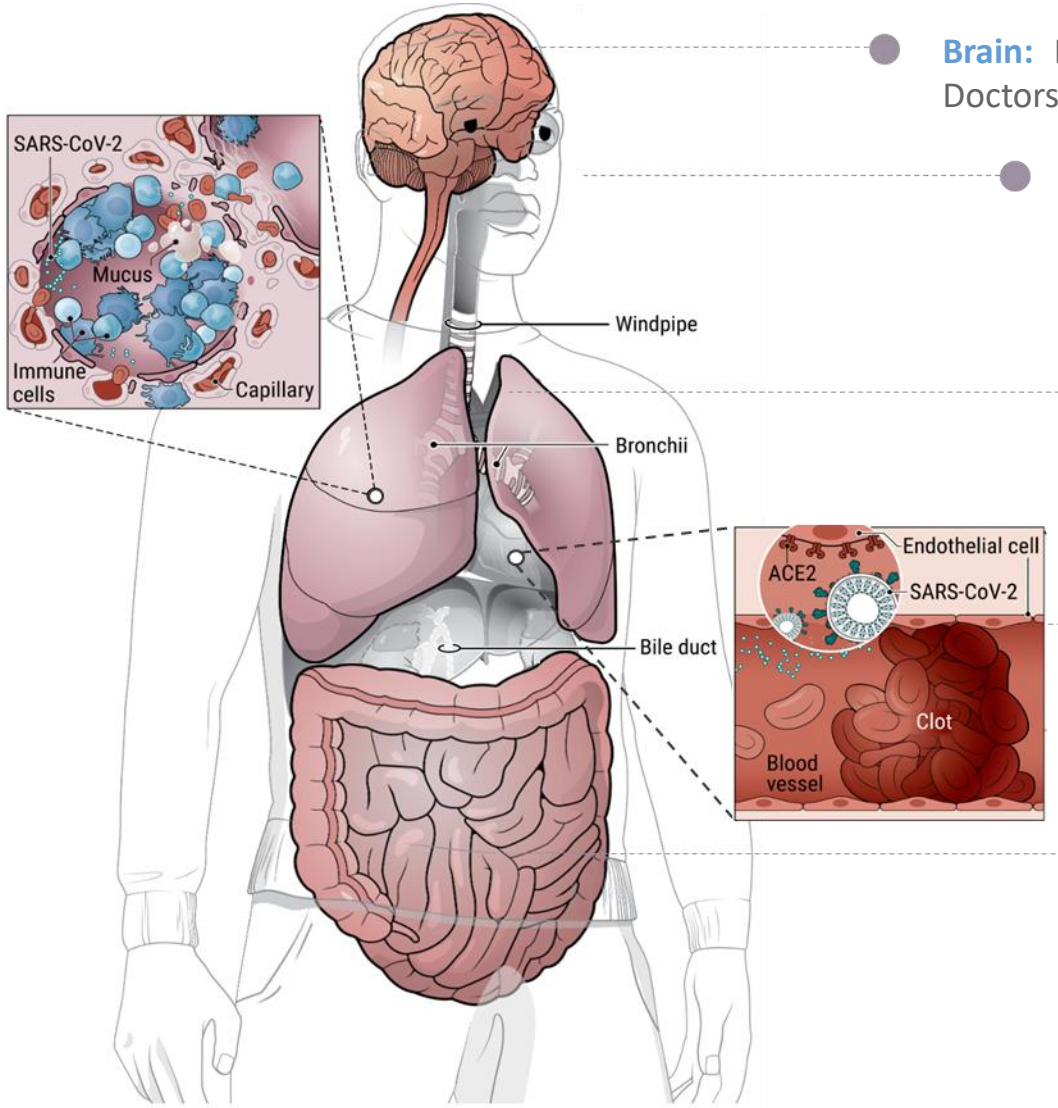
Adapted from Faculty of Pharmaceutical Medicine

Hypothesis for Pathogenesis of SARS-CoV-2

- The virus enters the respiratory system and causes infection as ACE2 receptors are highly expressed in the lower respiratory tract of humans.
- This triggers the overproduction of pro-inflammatory cytokines, leading to the development of an acute viral pneumonia.
- Some cases develop into respiratory failure and uncontrolled systemic inflammatory response, leading to further organ complications.
- This mechanism of pathogenesis of SARS-CoV-2 in humans merits further investigation.

Source: FPM,Thelancet

Covid-19 Disease Progression and Multi-Organ Injuries



Adapted from V.Altounian/Science Interactive

Brain: Patients have suffered from strokes, seizures, confusion, and brain inflammation. Doctors are trying to understand which are directly caused by the virus.

Nose: There have been reports of a loss of the sense of smell. Scientists speculate this may be caused by the virus moving up the nerve endings of the nose and damaging these cells.

Lungs: The primary site of infection. The cross section shows immune cells crowding an inflamed alveolus that fills with fluid and/or whose walls break down during attack by the virus, diminishing oxygen uptake. Patients cough, fevers rise, and breathing becomes laboured as pneumonia develops in the body.

Heart: The virus enters endothelial cells of the heart by binding to ACE2 receptors on the cell surface. This infection can promote blood clots, cardiac inflammation and a subsequent heart attack.

Intestine: Patient reports and biopsy data suggest the virus can infect the lower gastrointestinal tract, which is rich in ACE2 receptors. Around 20% or more of patients reported symptoms of diarrhoea.

Source: London Strategy Consulting 2020; Wadman et al. 2020 How does Coronavirus kill? Doi: 10.1126/science.abc3208

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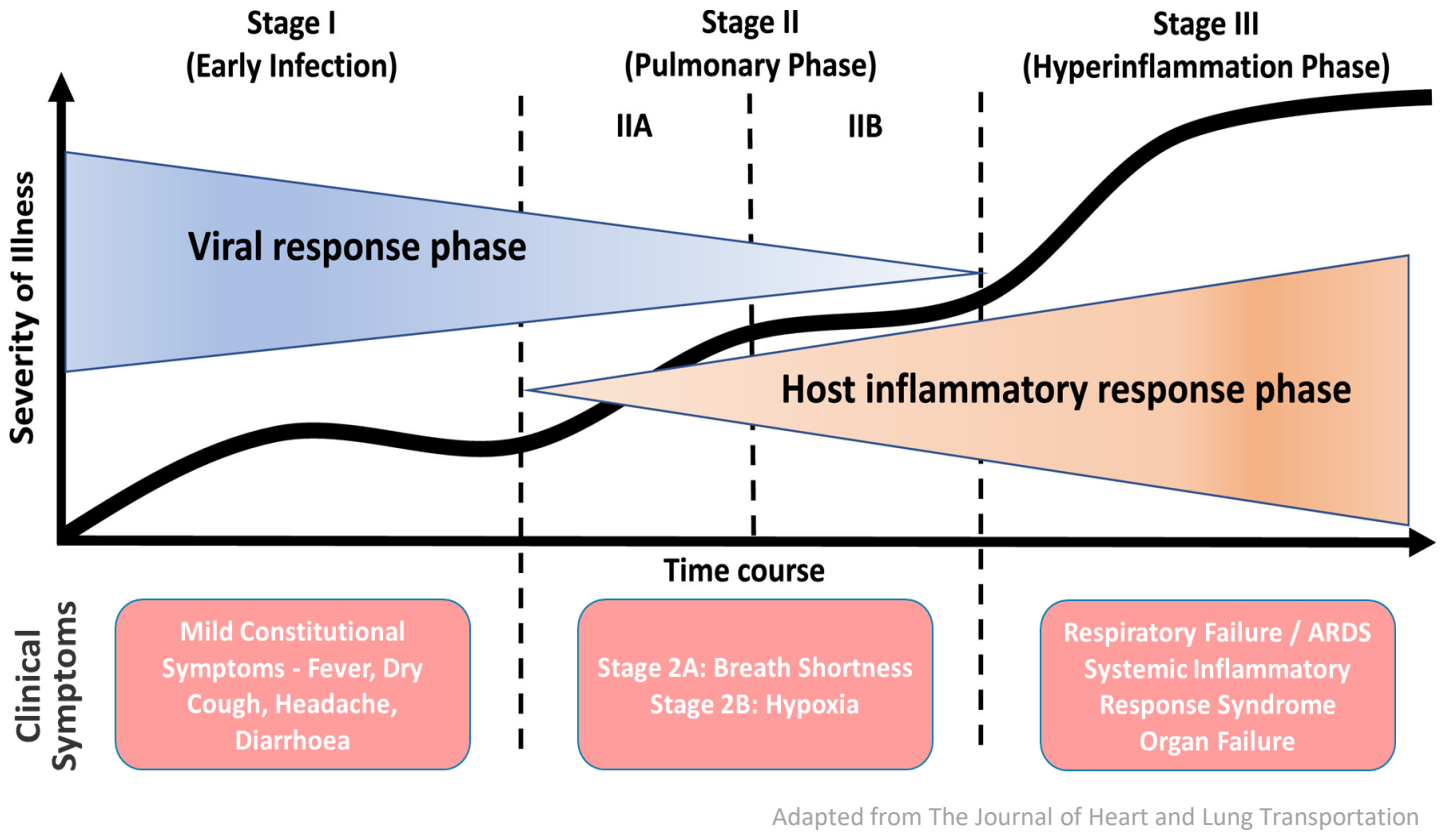
Three Clinical Phases of Covid-19 Infection and Disease Progression



Adapted from The Journal of Heart and Lung Transportation

Clinical Phases of Covid-19 Infection

Stage 1: Viremia / Early Infection Phase

- This stage marks viral contraction and early establishment of disease.
- SARS-CoV-2 multiplies and establishes residence in the host, primarily focusing on the respiratory system
- Patients undergo an incubation period associated with mild and often non-specific symptoms, such as a fever and dry cough.

Stage 2: Acute Pneumonia / Pulmonary Phase

- At this stage, virus multiplication and localized inflammation in the lung is established.
- Patients develop a viral pneumonia, with cough and fever.
- This stage is sub-divided into IIA (without hypoxia) and stage IIB (with hypoxia – deprivation of adequate oxygen supply at the tissue level).
- It is at this stage IIB where mechanical ventilation is required.

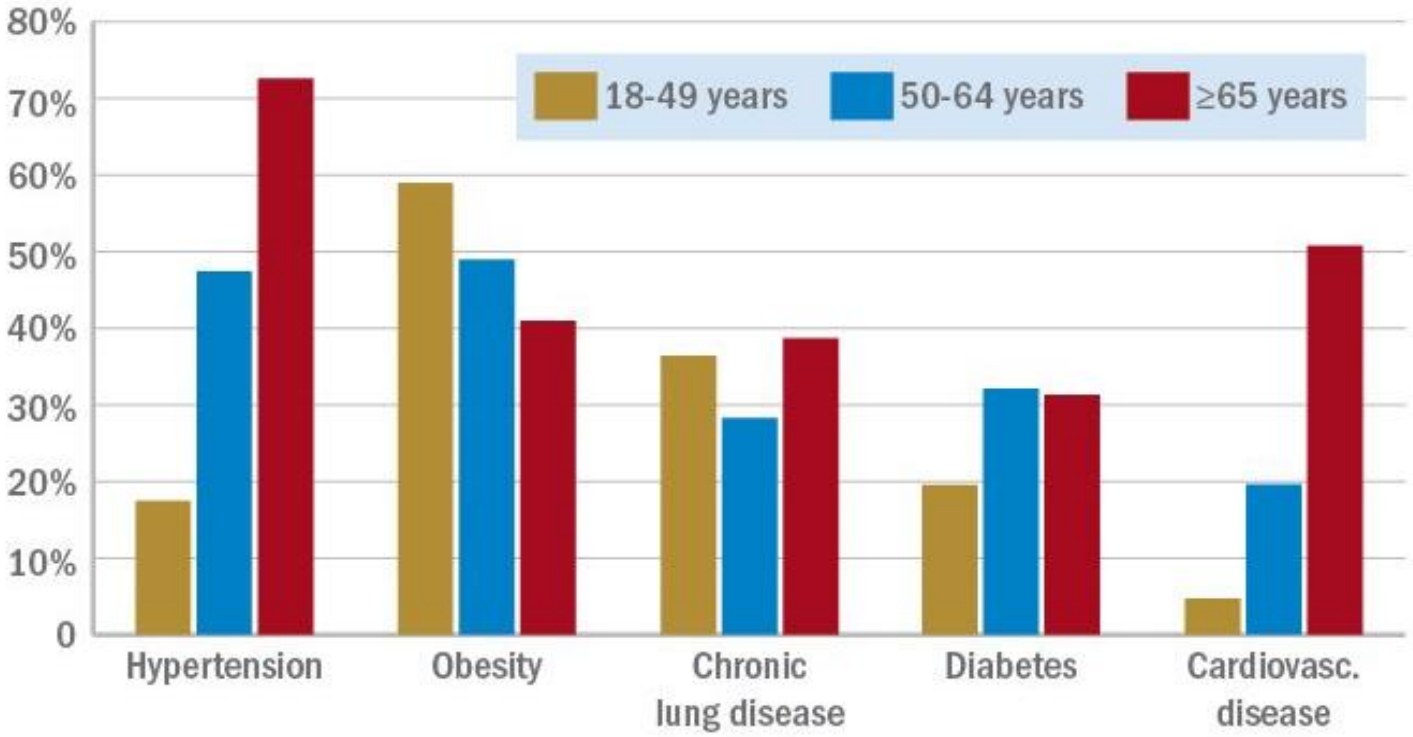
Stage 3: Hyperinflammation / Critical Phase

- A minority of Covid-19 patients will transition into this third and most severe stage of illness, which manifests as an extra-pulmonary systemic hyperinflammation syndrome
- Several markers of systematic inflammation are significantly elevated, and respiratory failure, among other systemic organ failures, are likely.
- The prognosis and recovery from this critical stage is poor.

Source: Jhtlonline,Tandfonline

Almost 90% of Covid-19 Hospital Admissions involve Comorbidities

Underlying Conditions among Adults Hospitalised with Covid-19



Note: This figure is based on data from the Covid-19-Association Hospitalisation Surveillance Network for patients admitted to hospitals in 99 counties in 14 states throughout March 2020

Covid-19 Disease Comorbidity Demographics

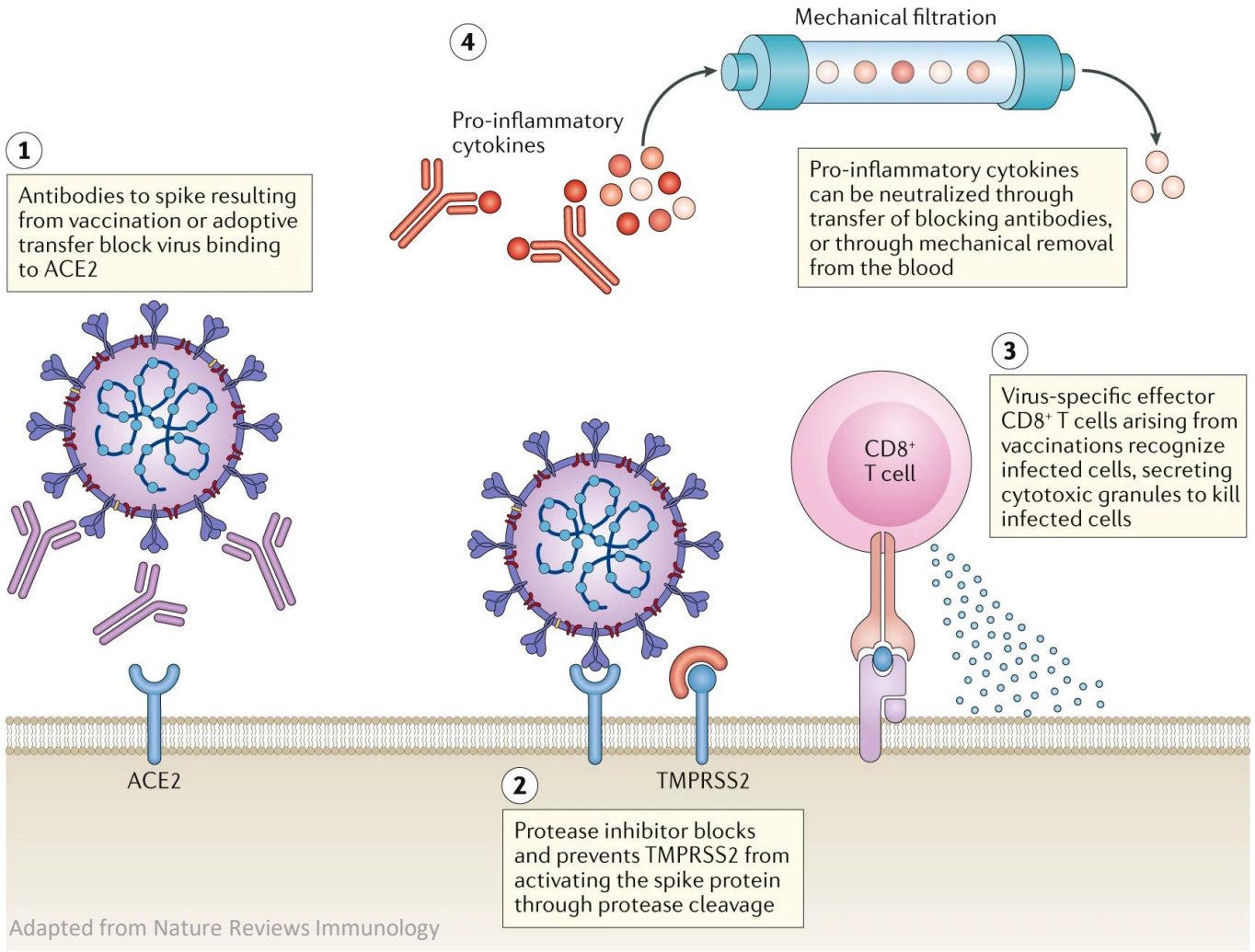
- Almost 90% of patients admitted to hospital for Covid-19 have some underlying health conditions
- Hypertension was the most common co-morbidity amongst patients aged ≥ 65 years.
- Obesity is the most prevalent underlying condition for Covid-19 patients, most specially for the younger age groups.
- Meta-analyses studies have shown that hypertension, respiratory and cardiovascular disease are the most prevalent risk factors for severe patients compared with non-severe patients.

Comorbidities and Covid-19 Pathogenesis

- All underlying health conditions are coupled with an increased risk of Covid-19 disease progression due to the associated pro-inflammatory state and attenuation to immune responses.
- Further analyses is required to determine the direct links of these observations with disease progression.

Source: Medscape, Ijıdonline

Potential Therapeutic Targets for SARS-CoV-2



Source: Nature

There are Four Potential Therapeutic Targets for SARS-CoV-2:

1. **Antibodies targeting spike proteins** to inhibit interaction of the virus with the ACE2 receptor on host cells.

2. **Protease Inhibitors against the cell-surface protein TMPRSS2** to block the receptor from assisting the internalisation process of the virus into the host cell.

3. **Memory CD8+ T-cells specific to SARS-CoV-2** from a previous vaccination or infection are able to differentiate into effector cells, identify infected cells, degranulate and kill these cells before they can produce mature virions.

4. **Blocking-antibodies or mechanical filtration of pro-inflammatory cytokines** in the blood of infected patients, via customized columns designed to trap pro-inflammatory cytokines, thereby alleviating the inflammatory reaction.

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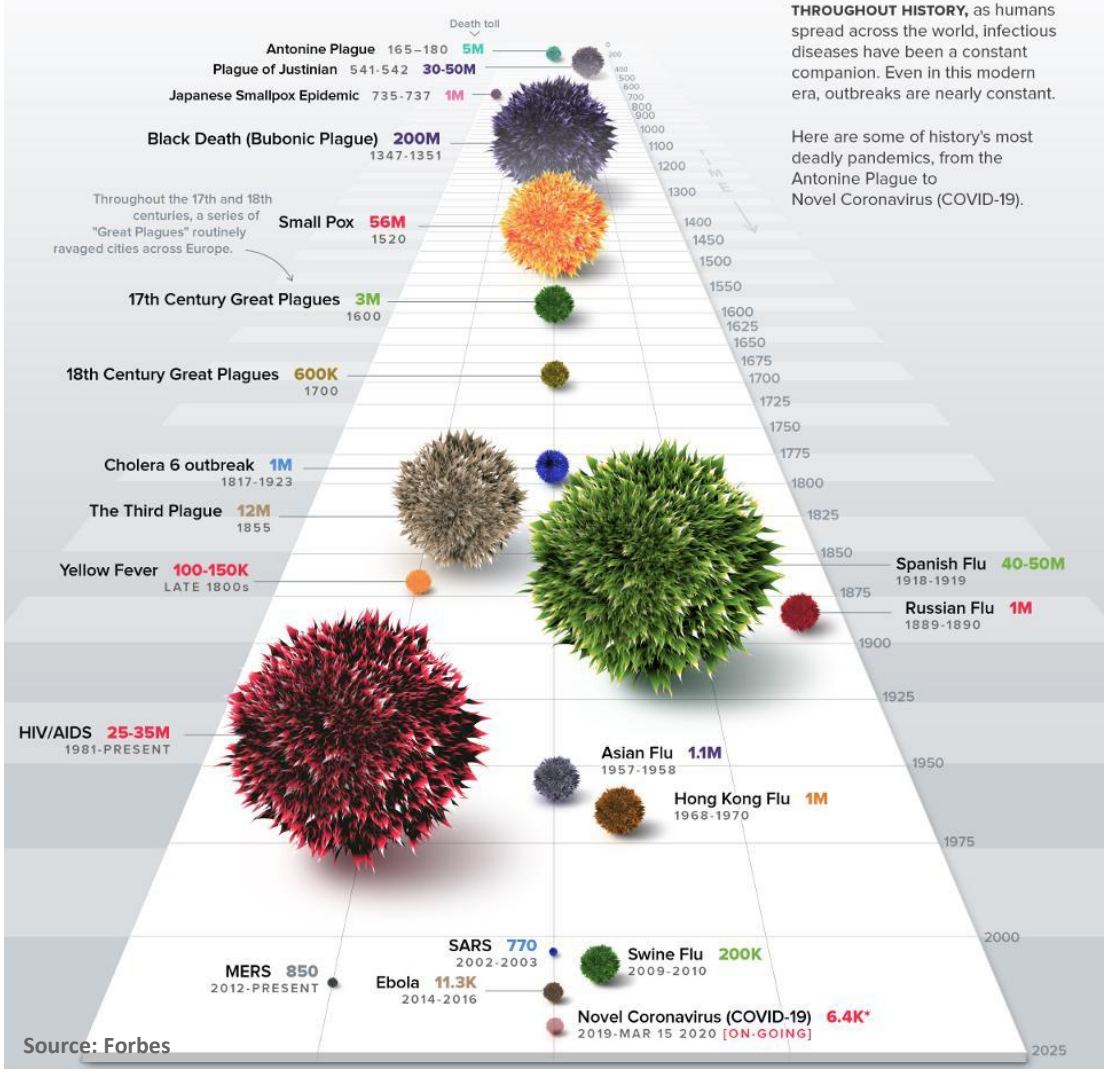
HISTORY OF **PANDEMICS**

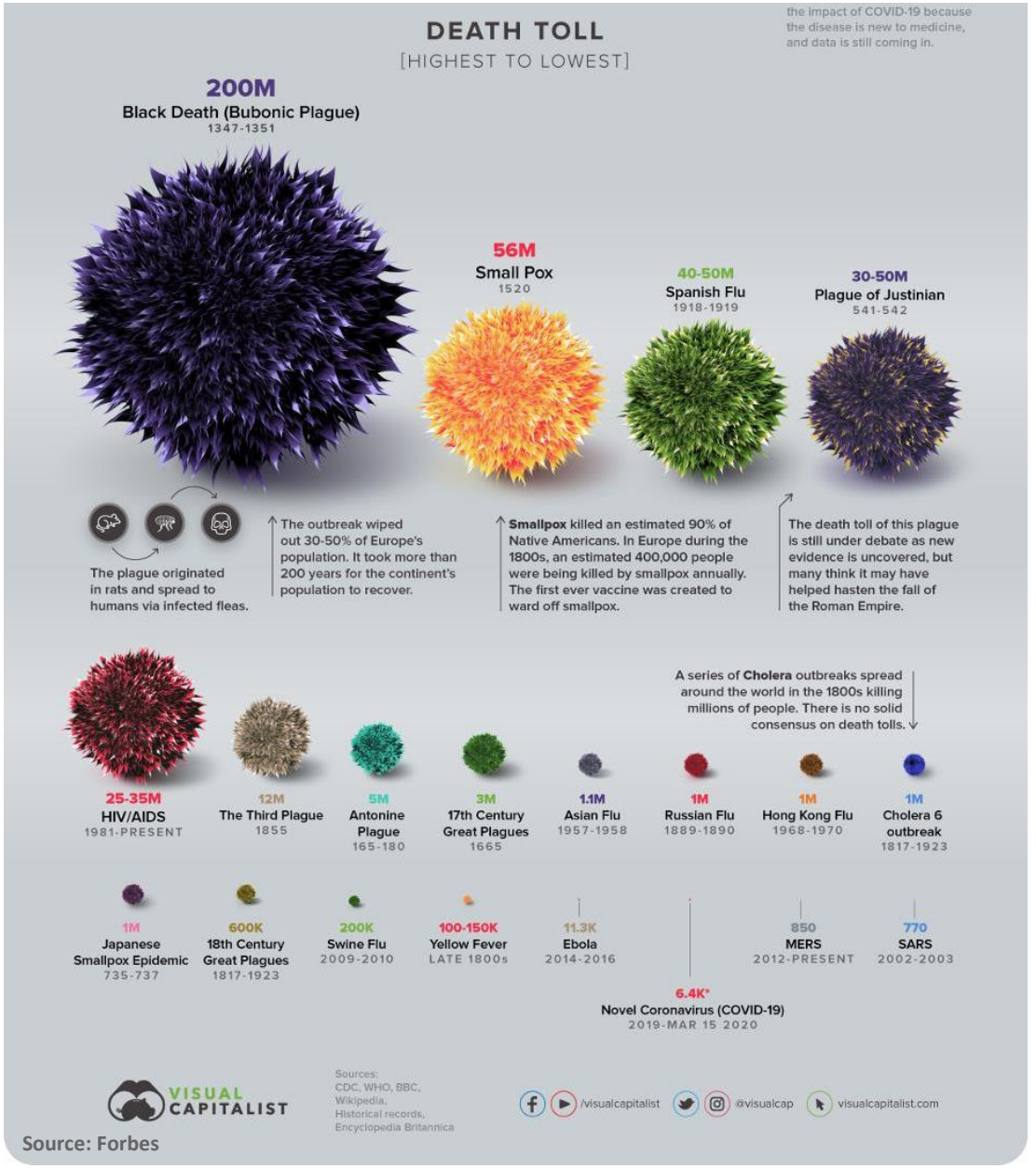
PAN·DEM·IC (of a disease) prevalent over a whole country or the world.

THROUGHOUT HISTORY, as humans spread across the world, infectious diseases have been a constant companion. Even in this modern era, outbreaks are nearly constant.

Here are some of history's most deadly pandemics, from the Antonine Plague to Novel Coronavirus (COVID-19).



Source: Forbes



Source: Forbes

LONDON STRATEGY

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Covid-19: The Mysteries Scientists are Racing to Solve

Why does the virus affect people differently?

- The stark differences in clinical outcome of the disease, that range from asymptomatic patients to sever or fatal pneumonia, remains unclear.
- Scientists looking for human gene variants have found strong genetic links in patients from Italy and Spain with severe COVID-19 symptoms.
- Patients who have developed respiratory failure were more likely to carry one of two genetic variants than people without the disease.
- Research is ongoing to find mutations with a more definitive role in the outcome of the disease, with hope to link extreme susceptibility to a single genetic mutation.

What is the nature of immunity and how long does it last?

- Scientists are working to understand the nature and permanence of SARS-COV-2 immunity.
- The principal focus has been on 'neutralising antibodies', whose levels begin to disappear after some time, and a quicker rate for people with acute infections compared to severely-infected patients.
- The levels of these antibodies needed to fight off re-infection or reduce the symptoms of a second illness is yet to be determined.
- The full picture of immunity is also likely to extend beyond antibodies, with scientists investigating the role of T-cells in long-term immunity.
- The intricacies of immune durability between 'sterilizing immunity' (infection prevention) versus 'protective immunity' (symptom prevention or easing) also remains unresolved.

Has the virus developed any concerning mutations?

- All viruses acquire minute mutations as they infect patients and scientists use these mutations to trace the global spread of the virus.
- Scientists are working to understand if these mutations affect the virus' properties (i.e. fitness, virulence, transmission, response to vaccines etc.)
- Versions of the virus identified in hotspots at the start of the epidemic, may seem to be more fatal. However this association may be spurious, due to the early uncontrolled conditions of the outbreak.
- Studies have hypothesised that prevalent variances, as a result of positive selection, have emerged (i.e. mutation of the virus' spike protein for increased infectivity).
- However whether this is a product of the 'founder effect' or a consequential change to the virus' biology remains inconclusive.

How well will a vaccine work?

- Naturally, an effective vaccine may be the only solution to overcoming this pandemic.
- Initial animal trails show that the leading candidates are able to prevent lung infection and resulting pneumonia, but not avert high viral loads in other body parts (i.e. clinical trial primates' noses), raising the possibility that vaccines may be able to prevent disease, but perhaps not the spread of the virus.
- Human data suggests that vaccines will effectively prompt our body to make potent neutralising antibodies to prevent infection, but whether these levels of are high or stable enough to prevent re-infection remains unclear.

Source: Nature

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