



# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

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## The bad news first

# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

## Tuberculosis is the top infectious killer in the world



IN 2018  
**1.5 MILLION\***  
**PEOPLE DIED FROM TB**

INCLUDING  
251 000 PEOPLE  
WITH HIV

TB is the leading killer of people with HIV and a major cause of deaths related to antimicrobial resistance

\*The 95% uncertainty intervals are 1.4-1.6 million for TB deaths and 223 000 - 281 000 for TB/HIV deaths.



World Health Organization

## More people reached with quality tuberculosis care

IN 2018, AN ESTIMATED

**10 MILLION**  
**PEOPLE FELL ILL WITH TB\***

7 MILLION PEOPLE REPORTED TO HAVE ACCESS TO TB CARE, UP FROM 6.4 MILLION IN 2017

3 MILLION WERE UNDIAGNOSED OR NOT REPORTED

Better reporting, diagnosis and access to care will close this gap

\*The 95% uncertainty interval for TB incidence is 9.0-11.1 million.



World Health Organization

## Drug-resistant tuberculosis remains a public health crisis

IN 2018

**ABOUT 0.5 MILLION**  
**PEOPLE FELL ILL WITH DRUG-RESISTANT TB\***

**ONLY ONE IN THREE**  
**PEOPLE ACCESSED TREATMENT**

Of those treated, Only 56% were treated successfully

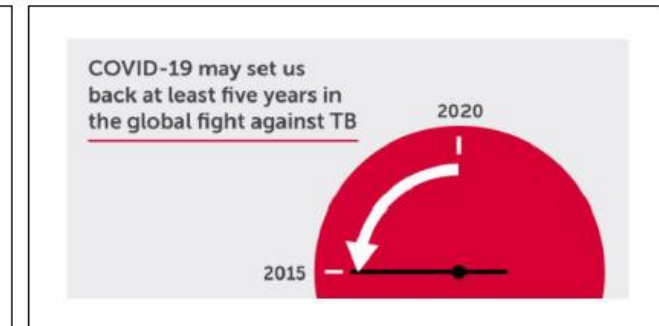
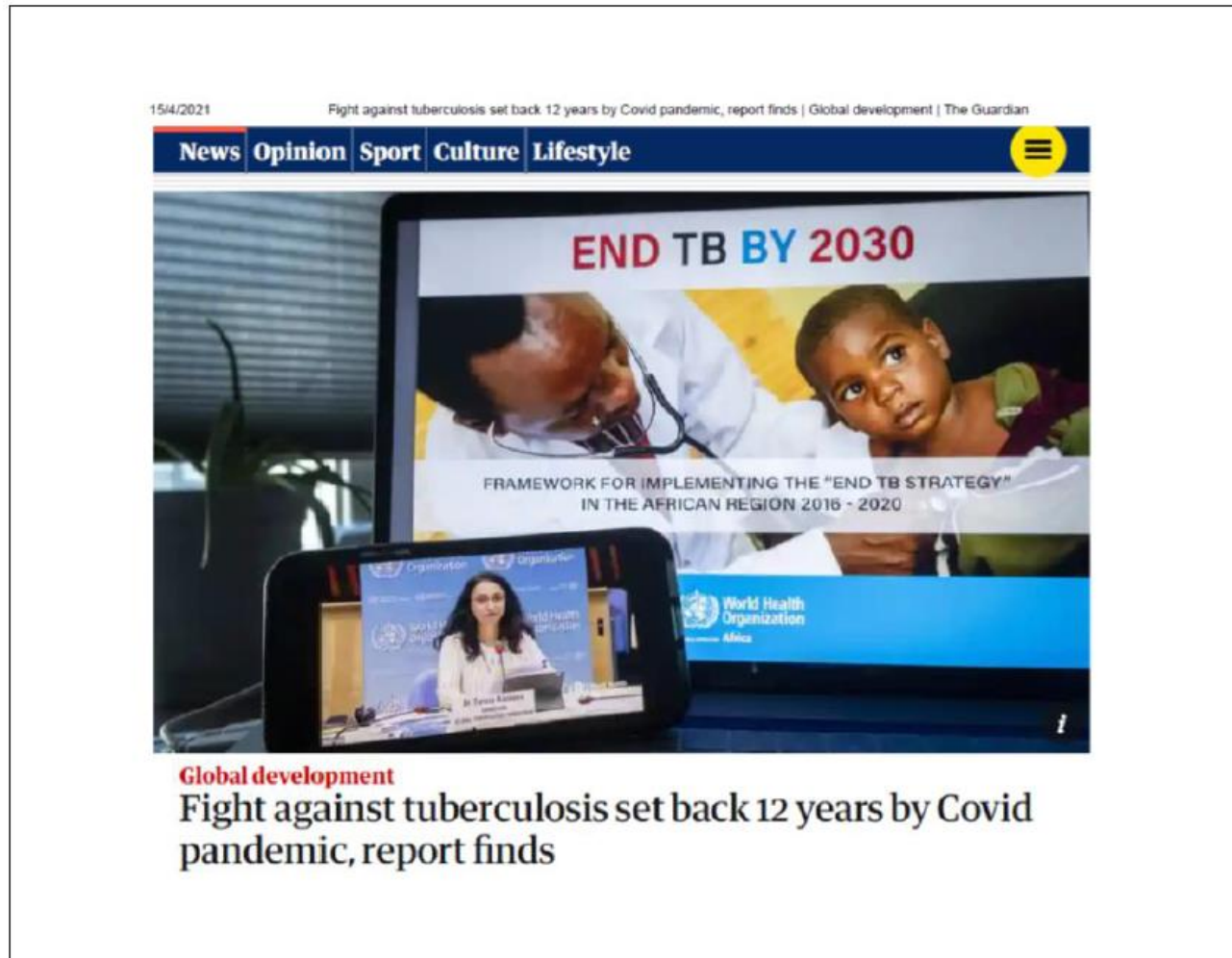
\*The 95% uncertainty interval for the incidence of multidrug-resistant TB is 400 000 - 500 000. About 80% of these cases had multidrug-resistant TB.



World Health Organization

World Tuberculosis Day 2020

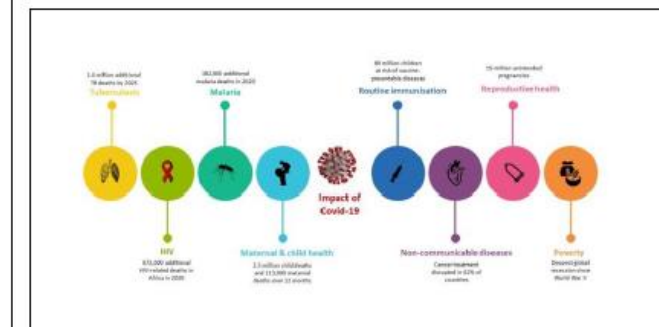
# Impact of COVID-19 on tuberculosis: turn challenges into opportunities



## CORONAVIRUS CRISIS

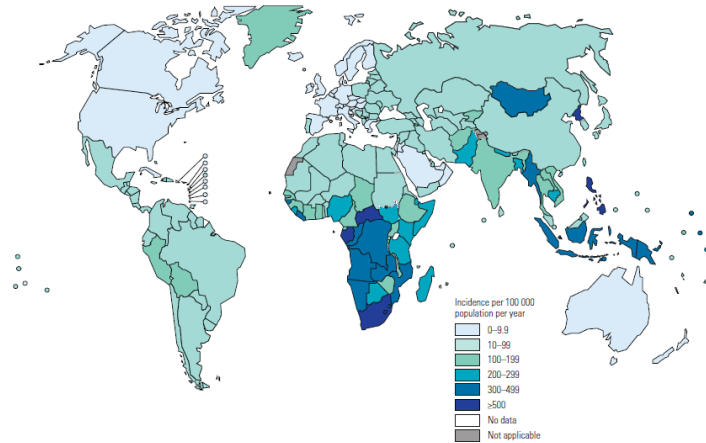
**Many states have reported fewer TB deaths during the lockdown. Here's why this is bad news**

It suggests the system for tracking tuberculosis patients has collapsed.



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FIG. 4.4  
Estimated TB incidence rates, 2019



10 news in September 2019 (4).

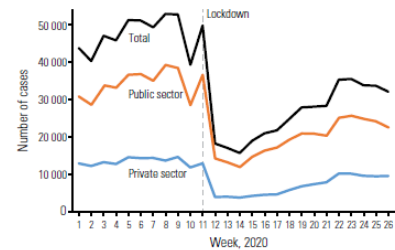
### 3.1 Global annual number of TB deaths in 2020 and beyond

Two modelling analyses have reached similar conclusions about the potential impact of the COVID-19 pandemic on global TB deaths (3, 4). They suggest that the annual number could rise to the levels seen in 2015 or even 2012.

The WHO analysis assessed the additional number of TB deaths that could occur globally in 2020 for different combinations of a decrease in case detection (compared with levels before the pandemic) and the number of months for which this decrease occurs (Fig. 3.1). If the number of people with TB detected and treated were to fall by 25–50% over a period of 3 months – a range considered plausible based on data from several high TB burden countries (Fig 3.2, Fig. 3.3) – there could be between 200 000 and 400 000 excess TB deaths in 2020, bringing the total to about 1.6–1.8 million. An increase of 200 000 would take the world back to 2015 levels and an increase of 400 000 to 2012 levels.<sup>1</sup>

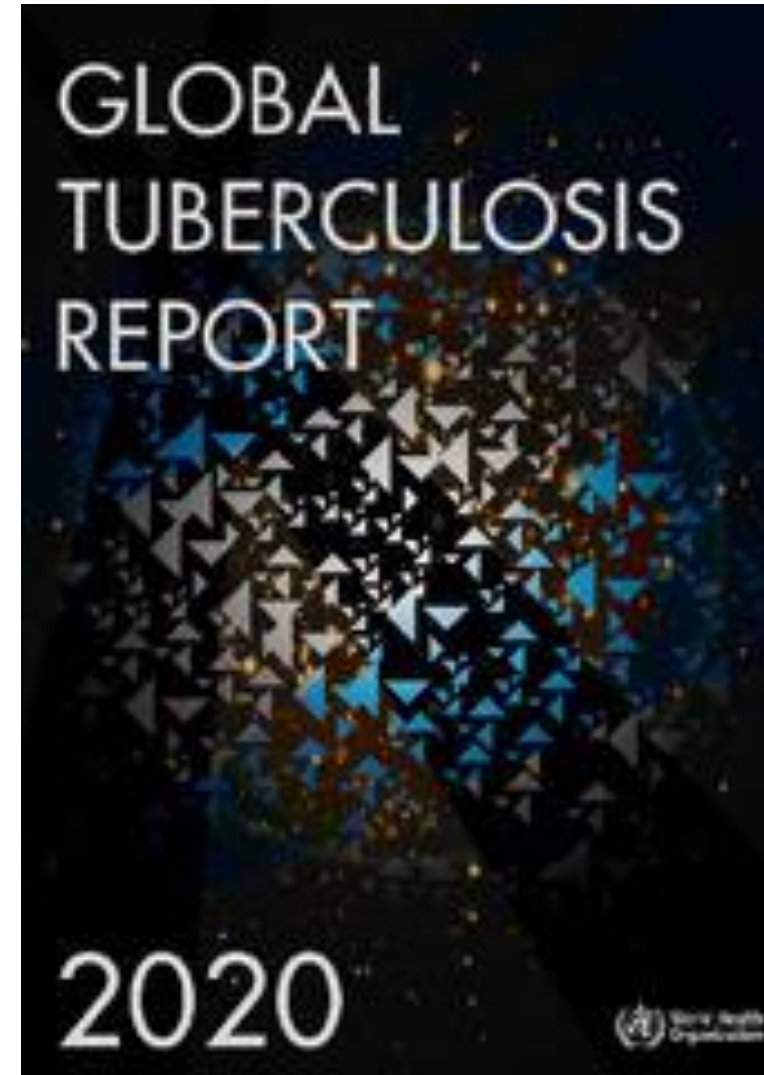
<sup>1</sup> It is also possible that TB could worsen outcomes in people with COVID-19.

FIG. 3.2  
Trends in weekly TB case notifications in India in 2020, before and after lockdown



Source: <https://reports.nikshay.in/Reports/TBNotification>, accessed 31 July 2020

► GLOBAL TUBERCULOSIS REPORT 2020 15



10 opportunities to take into consideration



# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

Life goes on...

Epidemiological and technological changes

- Ageing, comorbidities
  - Changes in **migration routes**: socio-economical conditions, globalization conflict, climate change and availability of resources
  - Influence of **non communicable diseases**
  - **HAART** (*highly active antiretroviral therapy*) effects
  - Wide use of biologic response modifiers (**anti-TNF** and more)
  - Emerging pathogens, antimicrobial resistance: **one health perspective**
- 
- Advances in **diagnostic methods**: Next generation sequencing, mass spectrometry
  - Advances in **radiology** and Interventional pulmonology
  - Advances in big data management
  - Social media

Own Slide from  
3 years ago

## Opportunity 1:

Social awareness

Transmissible infectious diseases exist

Respiratory diseases exist

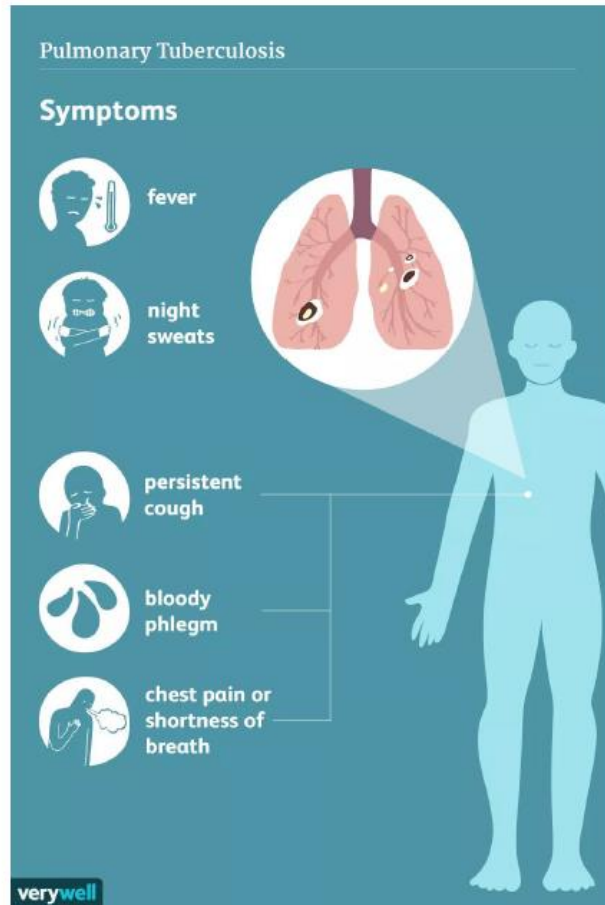


# Impact of COVID-19 on tuberculosis: turn challenges into opportunities



# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

## The importance of clinical suspicion



## COVID-19

Disease caused by the SARS-CoV-2 virus

### Novel coronavirus

Coronaviruses are viruses that circulate among animals but some of them are also known to affect humans.

The 2019 novel coronavirus was identified in China at the end of 2019 and is a new strain that has not previously been seen in humans.

### Symptoms

- FEVER
- COUGH
- DIFFICULTY BREATHING
- MUSCLE PAIN
- TIREDFNESS

### Prevention

#### When visiting affected areas

Avoid contact with sick people

Wash your hands with soap and water

If you develop cough, use a medical face mask

Wherever you travel apply general hygiene rules

### Transmission

VIA RESPIRATORY DROPLETS

**2-14** days  
estimated incubation period

[ecdc.europa.eu/en/novel-coronavirus-china](https://ecdc.europa.eu/en/novel-coronavirus-china)



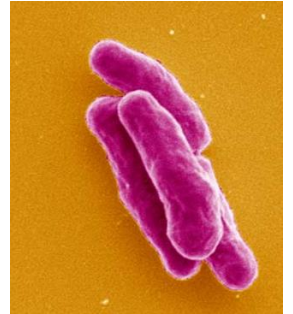
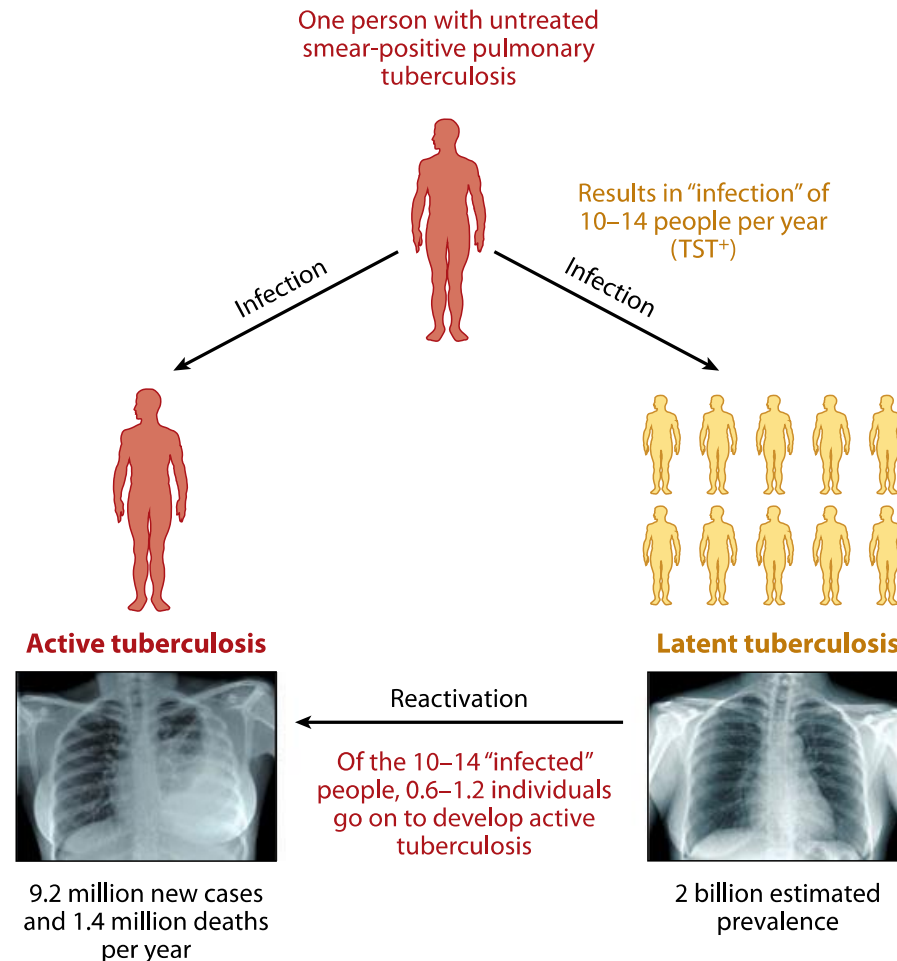
## Opportunity 2:

The value of rapid and accurate diagnostics

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**Objectives for tuberculosis control: to prevent transmission, to prevent progression from infection to disease**

- Early **diagnosis** of active tuberculosis cases
- Early **diagnosis** of latent tuberculosis cases
- **Adequate treatment**



Annu. Rev. Immunol. 2013. 31:475–527



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Three branches of medicine  
“Diagnosis, diagnosis &  
diagnosis”

William Osler

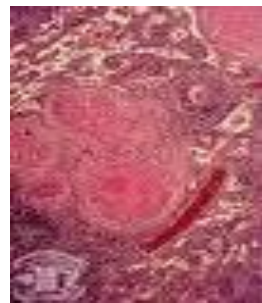
Interdisciplinary communication

**clinical-radiology-microbiology-pathology-epidemiology-farmacology**

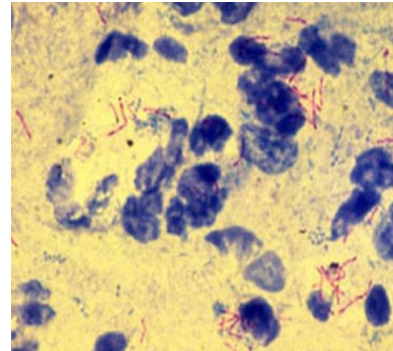
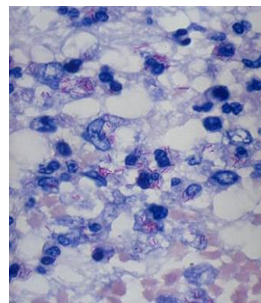
**... And basic and traslational research**



Clinical suspicion



Histology



Microbiology



**Clinical Microbiology:**  
**diagnostic of infectious diseases**

**Direct diagnosis:** detection of  
the microorganism or its  
components

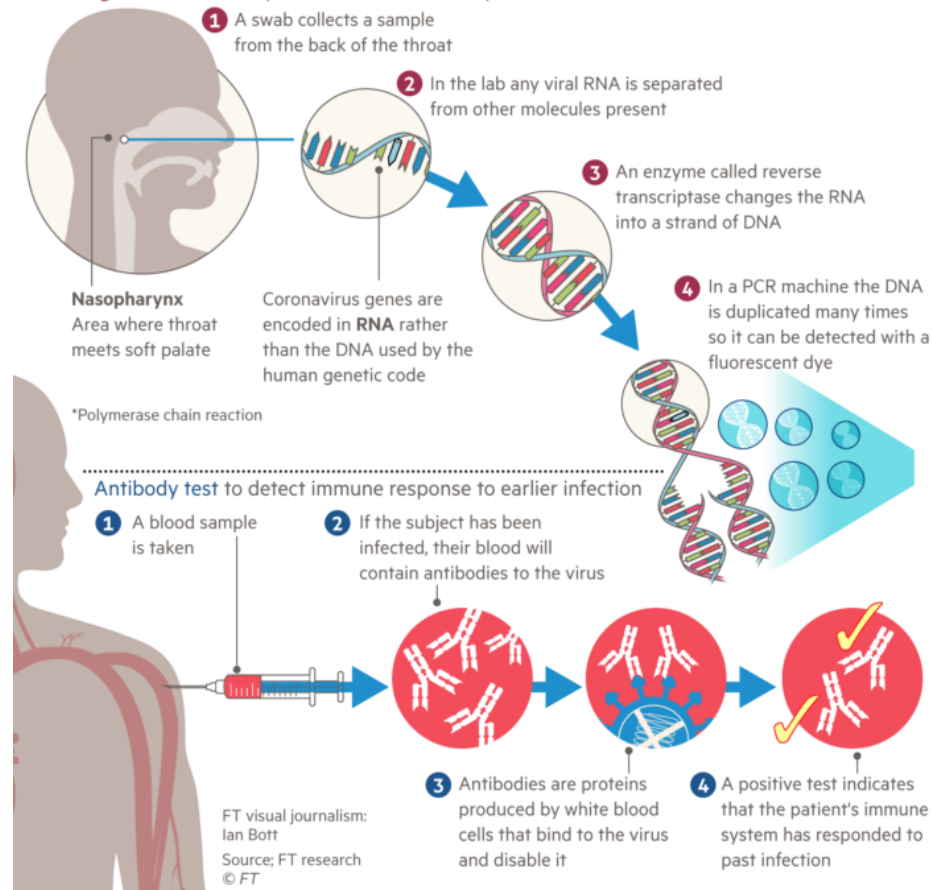
**Indirect diagnosis:** detection of  
the immune response

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## Unprecedented development of diagnostic tests

### Coronavirus testing methods

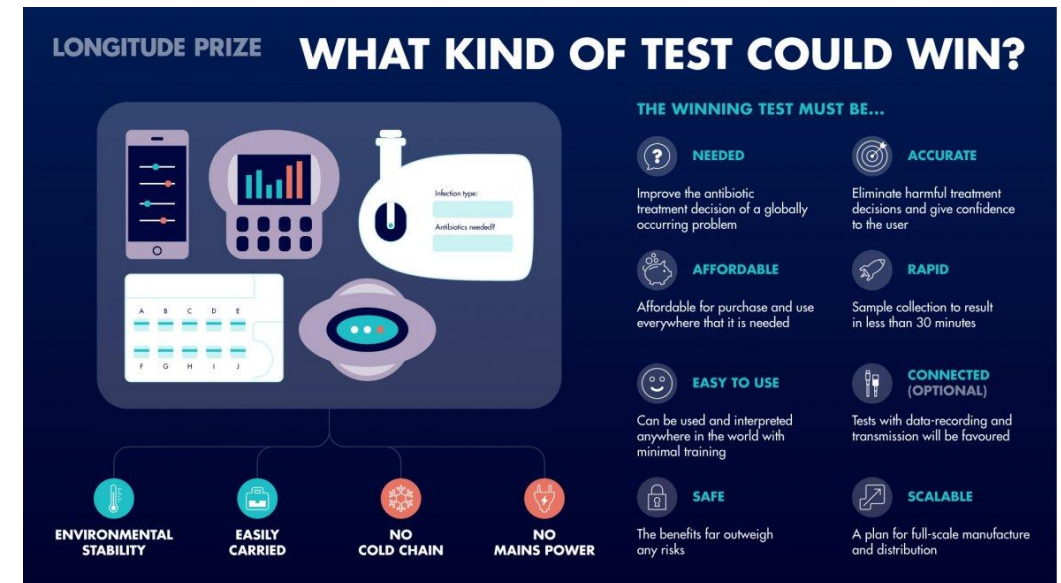
PCR\* antigen test to detect presence of virus in body



Because diagnosis matters

FIND. Foundation for Innovative New diagnostics  
To check for diagnostic tests in the pipeline

<https://www.finddx.org/dx-pipeline-status/>

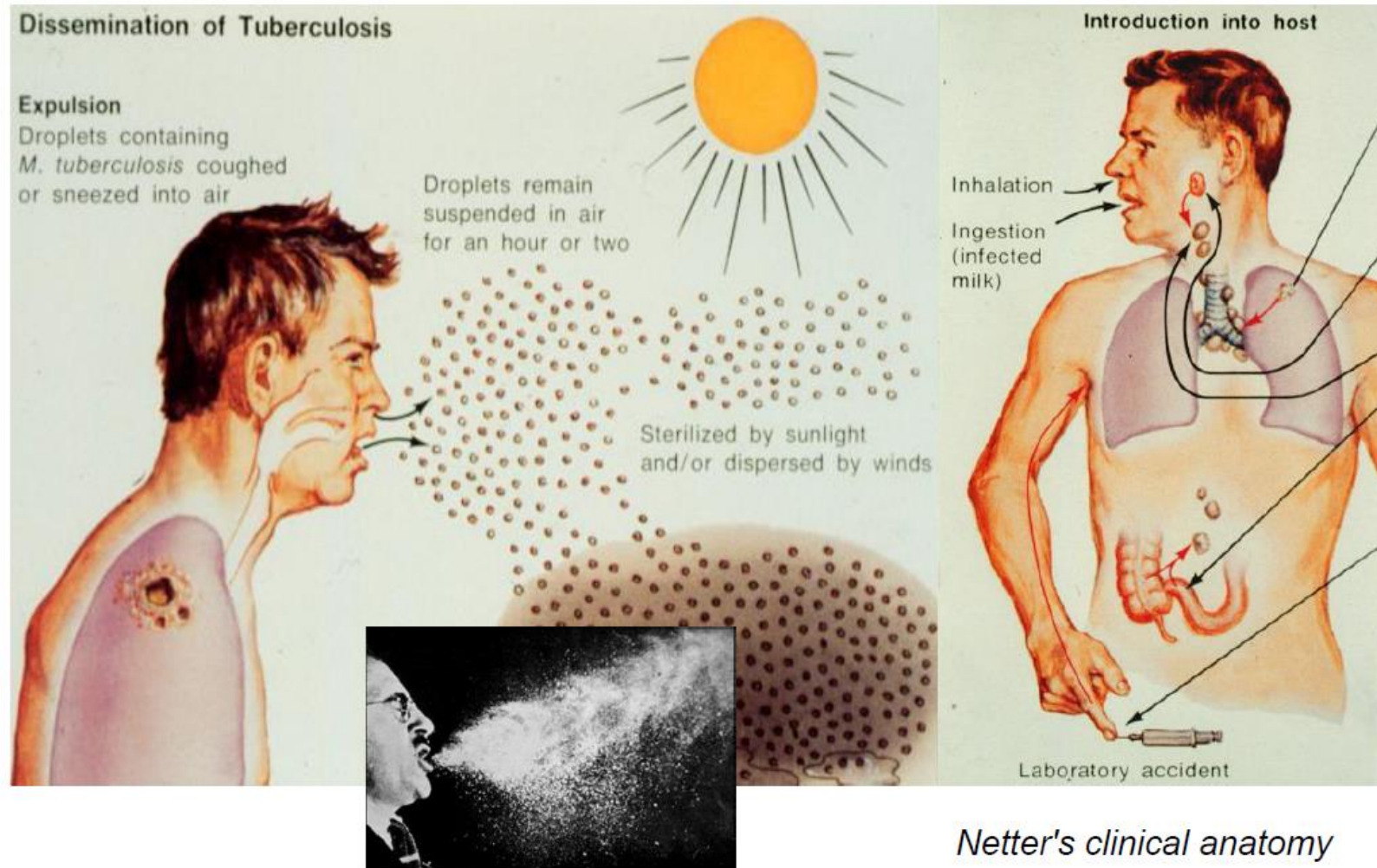


## Opportunity 3:

Getting familiar with contact tracing:  
clinical epidemiology and molecular epidemiology



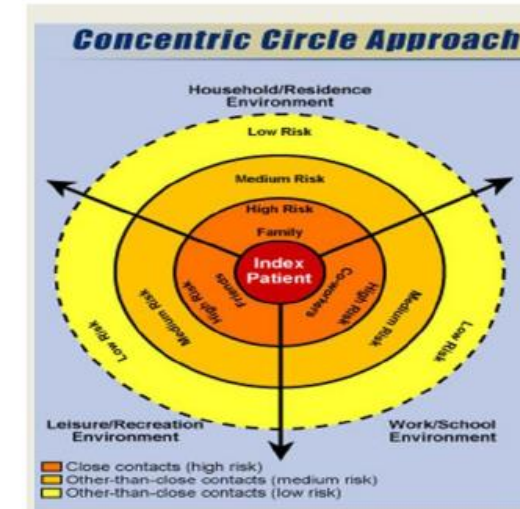
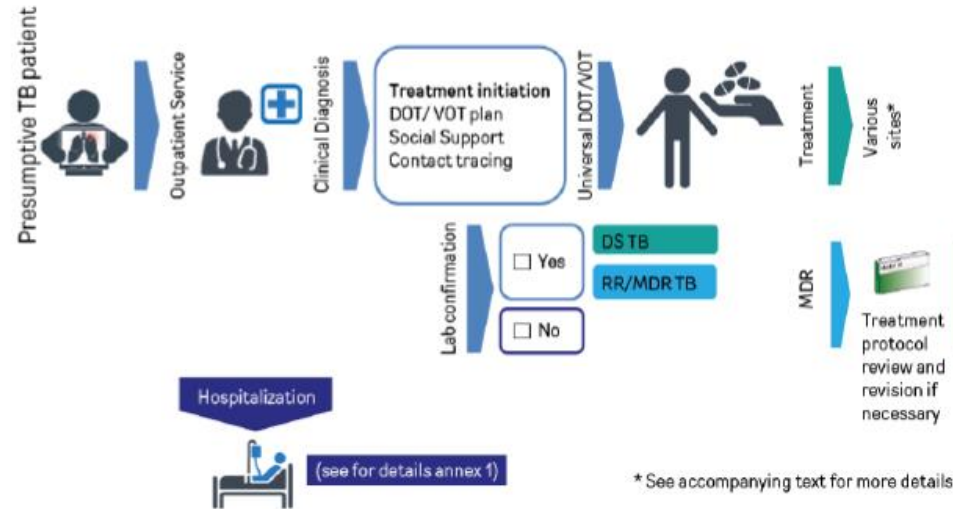
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*Netter's clinical anatomy*

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Fig. 2. Graphical illustration of a possible patient pathway



## People-Centered Model of TB Care: Blueprint for EECA Countries

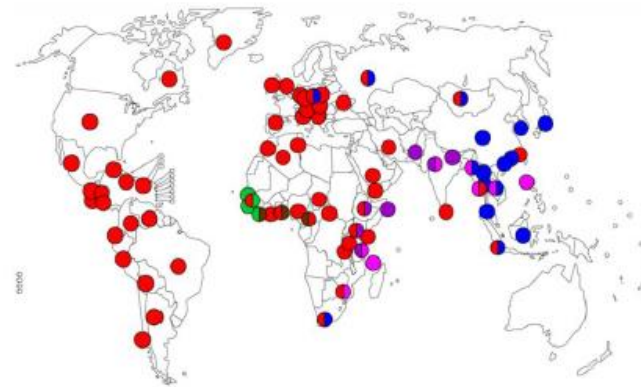


Figure 2. Global distribution of the six main lineages of human MTBC. Each dot represents the most frequent lineage(s) circulating in a country. Colour correspond to the lineages defined in Figure 3 (adapted from [20]). doi:10.1371/journal.ppat.1000600.g002

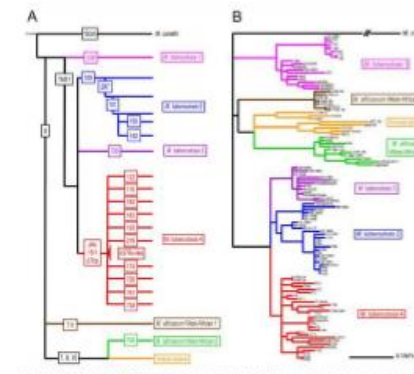
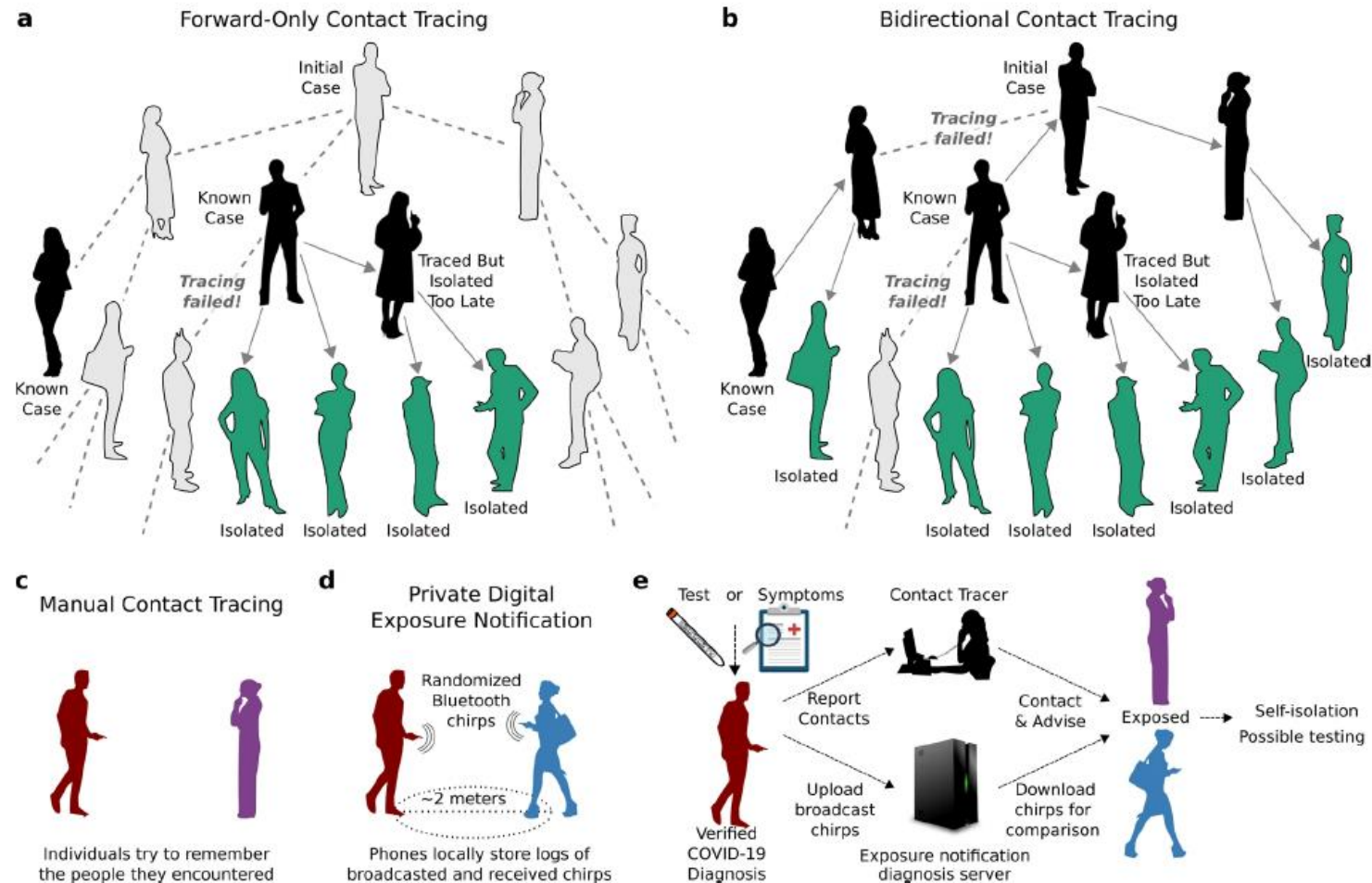


Figure 3. The global phylogeny of Mycobacterium tuberculosis complex (MTBC). The phylogenetic relationships between various human and animal-derived MTBC lineages are shown. The tree is color-coded by lineage: 1 (red), 2 (blue), 3 (green), 4 (purple), 5 (orange), and 6 (pink). The tree shows a clear clustering of lineages into six main groups, corresponding to the six main lineages of human MTBC. doi:10.1371/journal.ppat.1000600.g003

Comas I, Gagneux S. The past and future of tuberculosis research. PLoS Pathog. 2009

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Bradshaw W et al. Bidirectional contact tracing could dramatically improve COVID-19 control. Nat Commun. 2021 Jan 11;12(1):232

## Opportunity 4:

Interdisciplinary technological impulse.

Importance of biobanking



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There are at least two players in the infectious diseases

Host (human)-pathogen interaction → Dynamic phenomenon

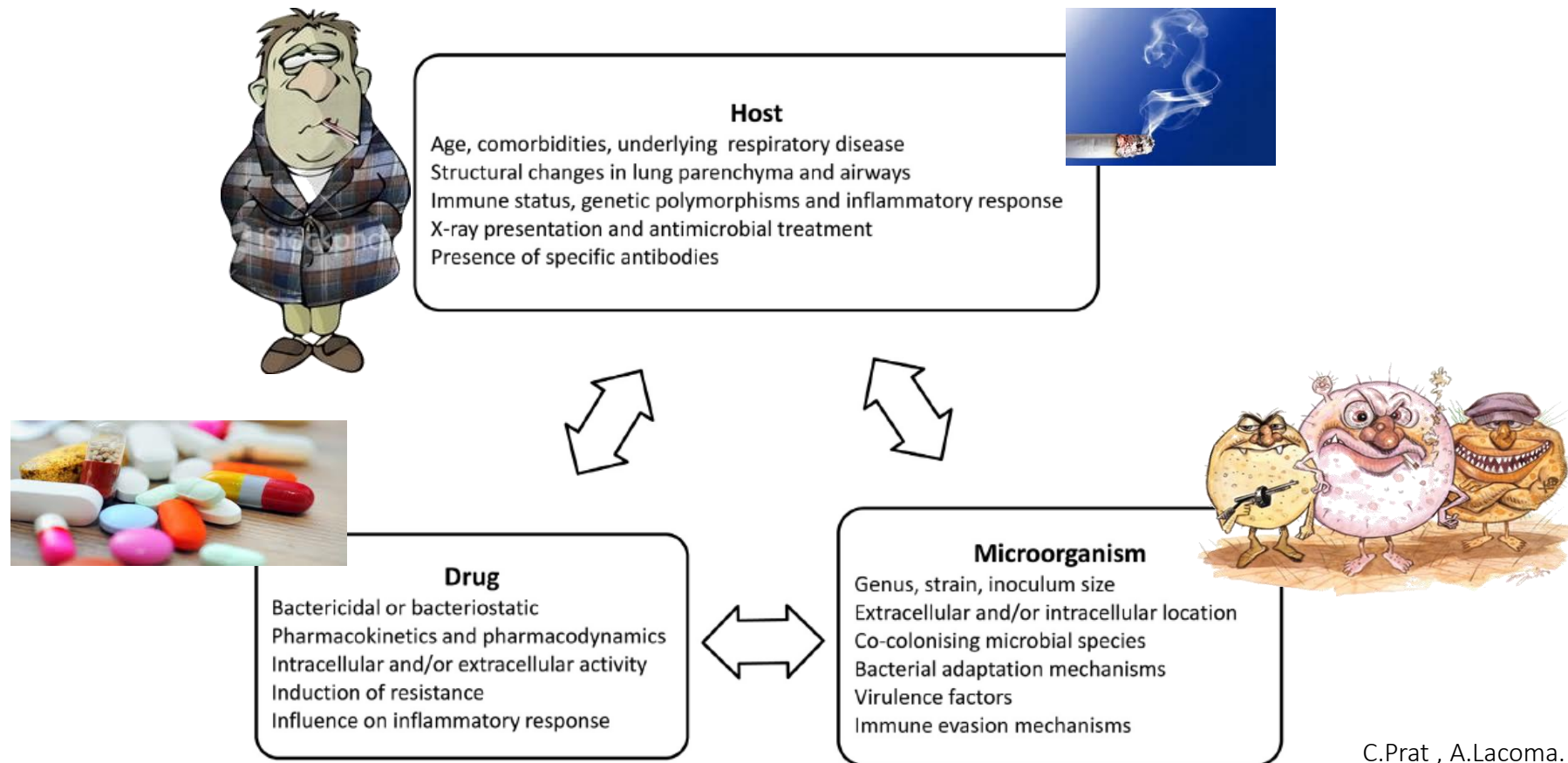


Figure 1. Key host, microorganism, and drug factors during colonization and infection in respiratory tract infections.

C.Prat , A.Lacoma. International Journal of Infectious Diseases 51 (2016)

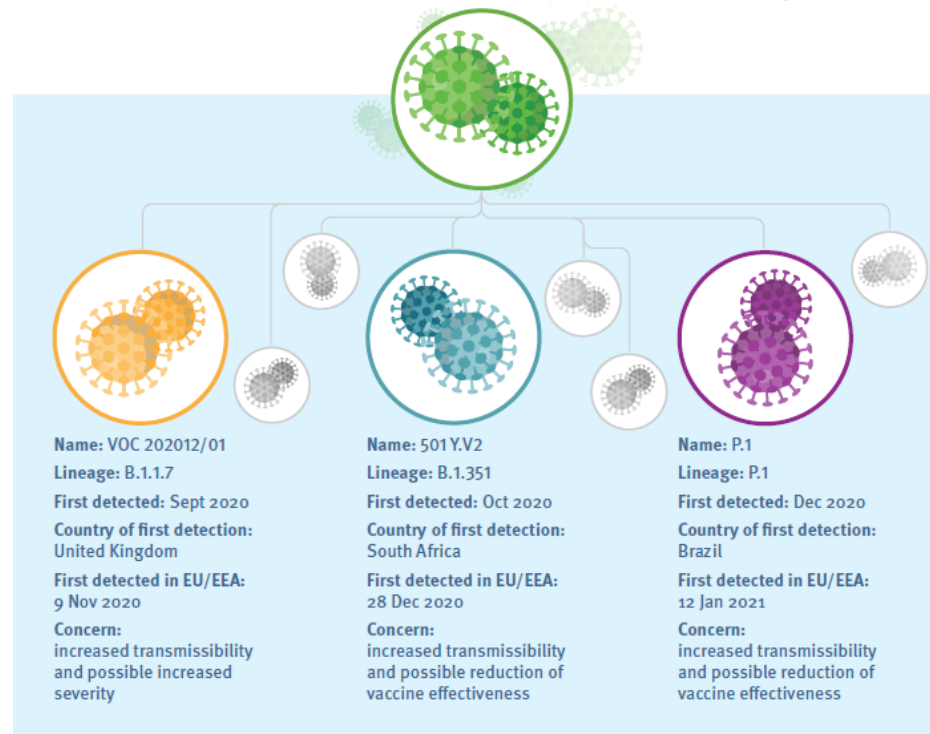
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## Pathogen genomics

### Mutation of SARS-CoV-2: current variants of concern

8 February 2021

Mutations of SARS-CoV-2 that cause COVID-19 have been observed globally. Viruses, in particular RNA viruses such as coronaviruses, constantly evolve through mutations, and while most will not have a significant impact, some mutations may provide the virus with a selective advantage such as increased transmissibility. Such mutations are cause for concern and need to be monitored closely.

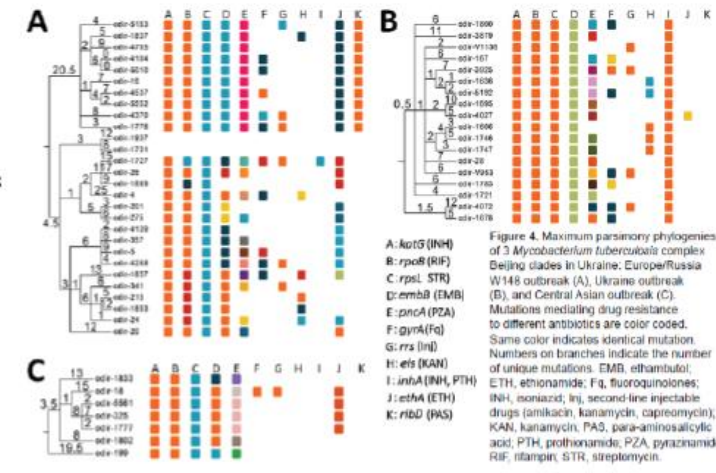
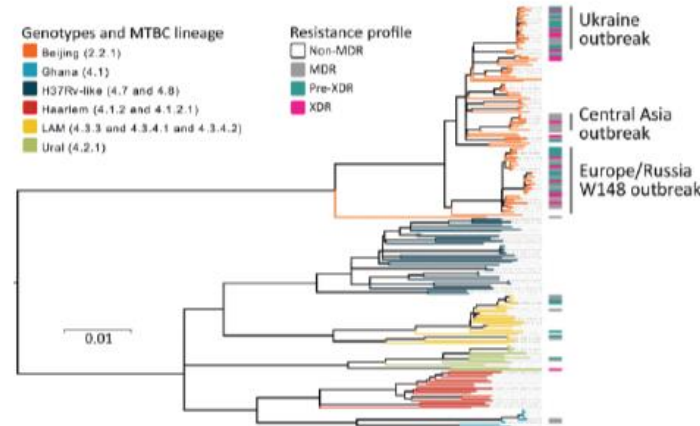


#COVID19

Learn more in the latest risk assessment by ECDC on SARS-CoV-2 variants of concern <http://bit.ly/RRAVariants1>



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## Multidrug- and Extensively Drug-Resistant *Mycobacterium tuberculosis* Beijing Clades, Ukraine, 2015

Matthias Merker, Elena Nikolaevskaya, Thomas A. Kohl, Barbara Molina-Moya, Oľha Pavlovskaya, Patrik Brännberg, Andrii Dudnyk, Valentyna Stokich, Ivan Barilar, Iryna Marynova, Tetiana Filipova, Cristina Prat, Anders Sjöstedt, Jose Dominguez, Oľena Rzhetspishevska, Stefan Niemann

Emerg Infect Dis. 2020 Mar;26(3):481-490.



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## Human (Host) genomics

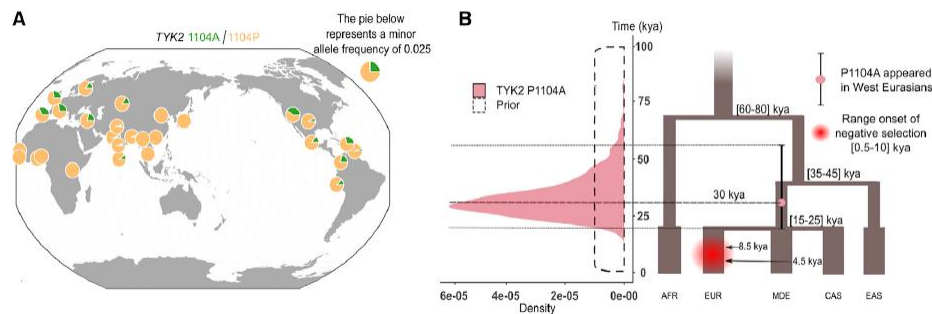


Figure 2. Present-day geographic distribution and age estimation of the *TYK2* P1104A mutation

### REPORT

Human ancient DNA analyses reveal the high burden of tuberculosis in Europeans over the last 2,000 years

Gaspard Kerner,<sup>1,2,3,\*</sup> Guillaume Laval,<sup>1</sup> Etienne Patin,<sup>1</sup> Stéphanie Boisson-Dupuis,<sup>2,3,4</sup> Laurent Abel,<sup>2,3,4</sup> Jean-Laurent Casanova,<sup>2,3,4,5,7</sup> and Lluís Quintana-Murci<sup>1,6,7,\*</sup>



Tuberculosis has killed more people in the past 2000 years than any other disease, and it has sickened many more, including these patients resting opposite the United Kingdom's Houses of Parliament in 1936. FOX PHOTOS/GETTY IMAGES

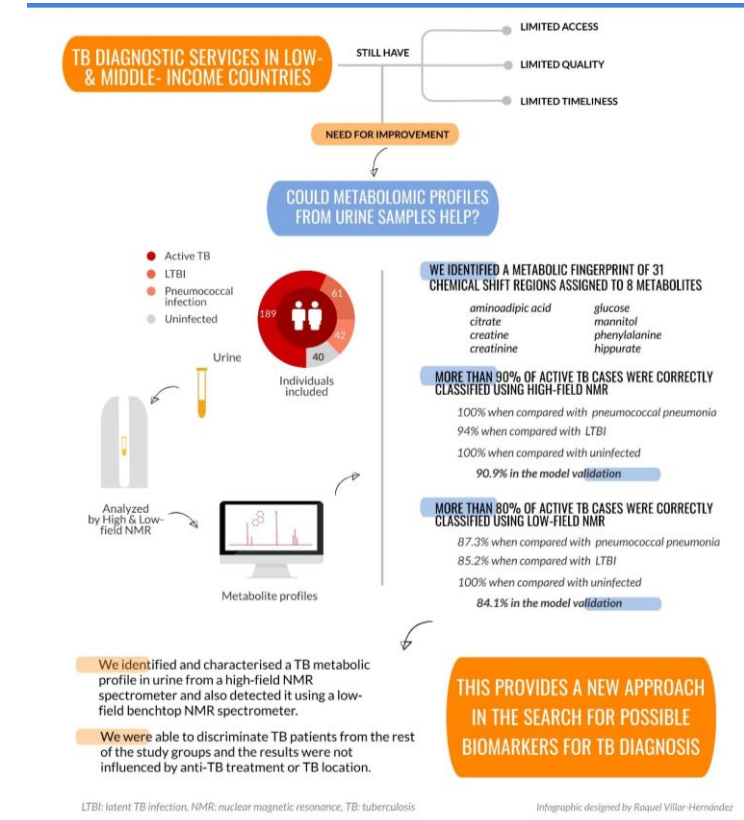
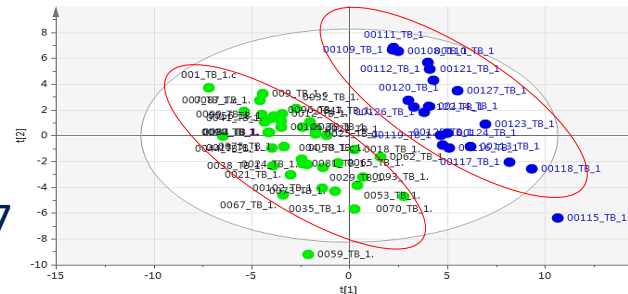
## How tuberculosis reshaped our immune systems

By **Ann Gibbons** | Mar. 4, 2021 , 11:00 AM

Host-Pathogen 'omics'  
e.g. metabolomics



FP7-PEOPLE-2012-IRSES 319007



# NGO INVOLVEMENT IN TB RESPONSE SYMPOSIUM СИМПОЗИУМ РОЛЬ НПО В ОТВЕТЕ НА ТУБЕРКУЛЕЗ

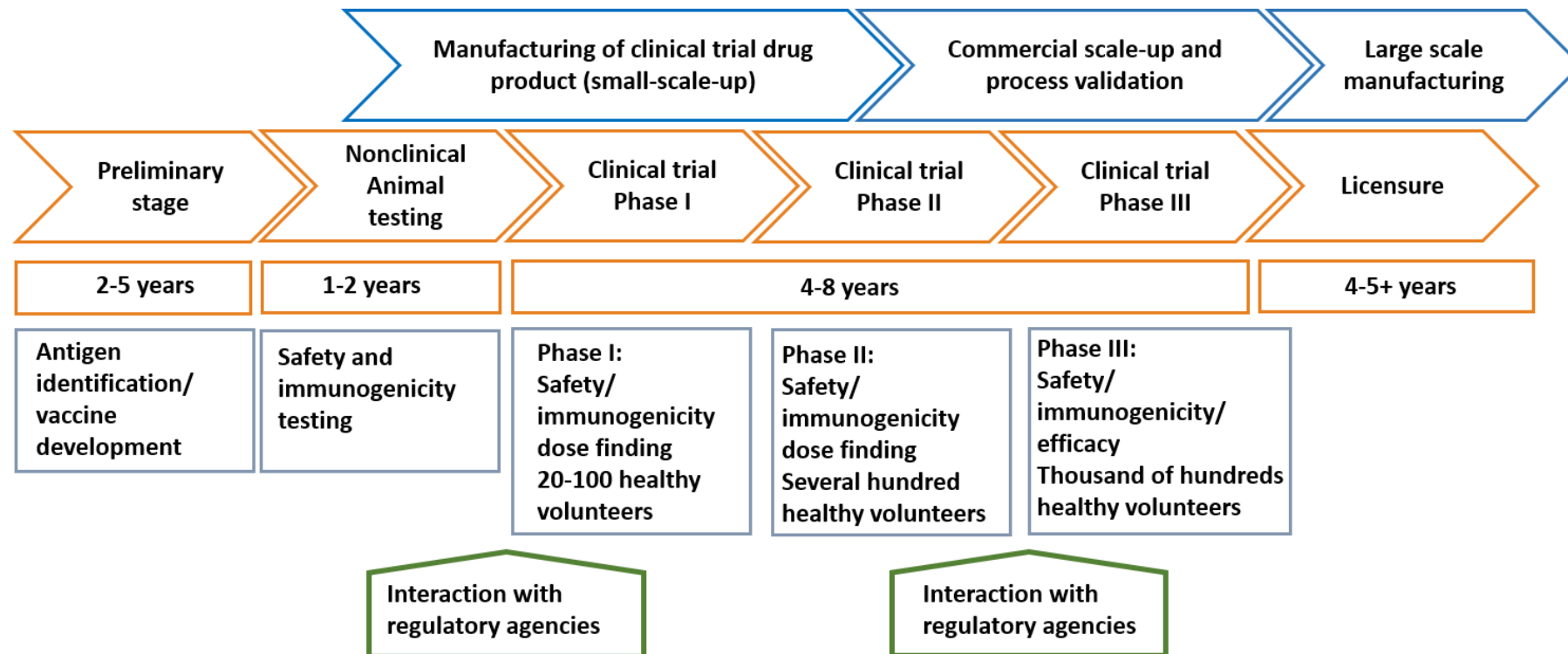


## Opportunity 5:

Well designed clinical trials are necessary.  
Ensure safety and good clinical practice is mandatory, even if learning by doing

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Need of global leadership and coordination  
Administrative, Regulatory and logistical



## Opportunity 6:

Unprecedented vaccine development

#vaccineswork



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Albert Calmette  
(1863-1933)



Camille Guérin  
(1872-1961)



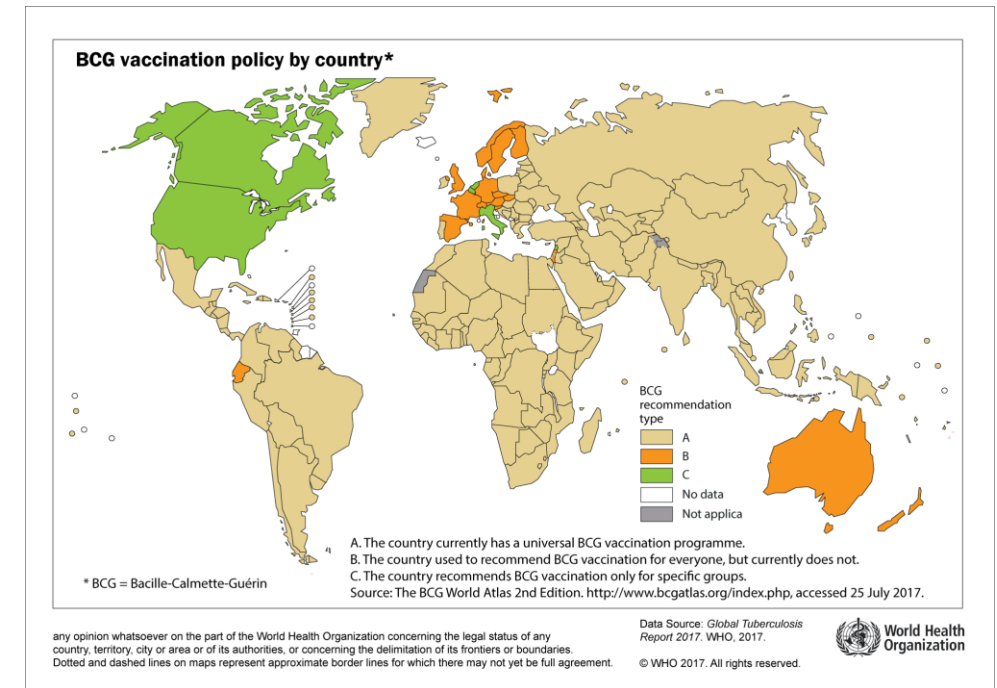
Albert CALMETTE & Camille GUÉRIN  
*Mycobacterium bovis* 1908-1921  
230 Passages

- BCG provides **strong protection against disseminated forms** of the disease (meningitis, miliar TB). Estimated to save 70.000 death every year
- **Variable protection against respiratory forms**, needs improvement
- BCG vaccination reduces all-cause mortality through beneficial **non-specific (heterologous) effects** in immune system

**1921:** first human administration

Currently:

**4 billion BCG-vaccinated individuals globally**  
100 million newborn BCG-vaccinated children every year.



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<https://clinicaltrials.gov/>

More than 20 trials evaluating efficacy of BCG vaccine in COVID-19



## Bacille Calmette-Guérin (BCG) vaccination and COVID-19

Scientific brief  
12 April 2020



### Use Only in clinical trials

*In the absence of evidence, WHO does not recommend BCG vaccination for the prevention of COVID-19. WHO continues to recommend neonatal BCG vaccination in countries or settings with a high incidence of tuberculosis.*



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## Tuberculosis vaccine candidates in the pipeline of clinical trials

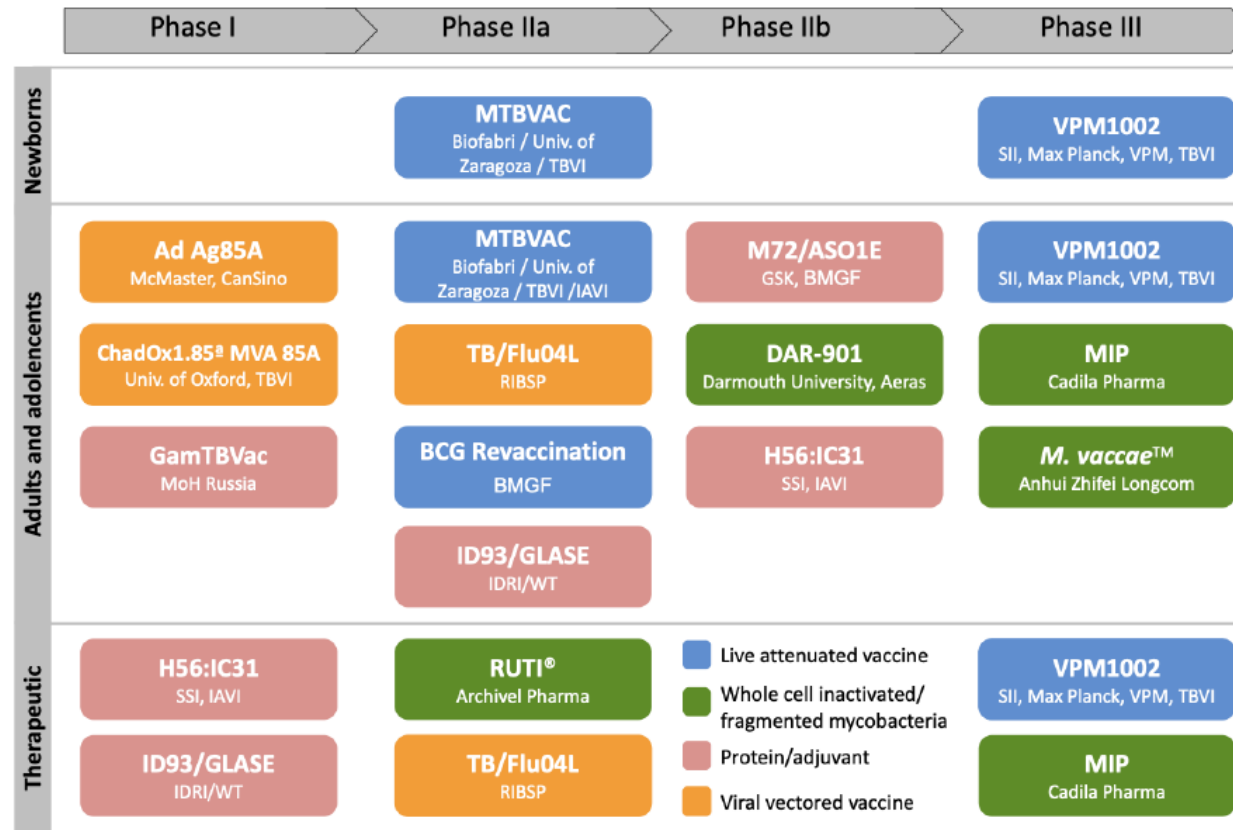






Figure 2. Tuberculosis (TB) vaccine candidates in the pipeline of clinical trials. The diagram shows the advance in clinical trials of the 14 vaccine candidates coloured according to each vaccine strategy.

Update on TB Vaccine Pipeline.  
Martin C et al. *Appl. Sci.* 2020

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WHOLE CELL MYCOBACTERIA					ORIGIN	SOURCE	METHOD FOR ATTENUATION/ INACTIVATION	CONTENT IN <i>M. tuberculosis</i> T-CELL ANTIGENS
LIVE ATTENUATED	MTBVAC	<i>M. tuberculosis</i>		Double deletion of <i>phoP-fadD26</i> virulence genes	ALL present			
	BCG Revaccination	<i>M. bovis</i>		Loss of >100 genes within RD deletions	Epitopes in RD regions absent			
	VPM1002	<i>M. bovis</i>		Same than BCG with urease C deletion and listeriolysin insertion	Epitopes in RD regions absent			
INACTIVATED	<i>M. vaccae</i> <sup>TM</sup>	<i>M. vaccae</i>	Non-Tuberculous Mycobacteria	Heat	?			
	MIP	<i>M. indicus pranii</i>	Non-Tuberculous Mycobacteria	Heat	?			
	DAR-901	<i>M. vaccae</i> <i>M. obuense</i>	Non-Tuberculous Mycobacteria	Heat	?			
	RUTI	<i>M. tuberculosis</i>		Detoxified fragments of <i>M. tuberculosis</i> in a liposomal formulation	?			
	SUBUNITS	VIRAL VECTORED	<i>M. tuberculosis</i>	Adenovirus	Ag85A			
<i>M. tuberculosis</i>			ChadOx1 MVA 85A	Ag85A				
<i>M. tuberculosis</i>			TB/Flu041	ESAT-6 Ag85A				
ADJUVANTED		<i>M. tuberculosis</i>	ID93/GLASE	GLA-SE Glucopyranosyl Lipid A (GLA), in oil-in-water emulsion (SE)	Rv3620 Rv3619 Rv2608 Rv1813			
		<i>M. tuberculosis</i>	H56:IC31	IC31® antibacterial peptide and a synthetic oligonucleotide	ESAT-6 Rv2660 Ag85B			
	<i>M. tuberculosis</i>	M72/AS01E	AS01E Liposomal formulation of MPL and saponin QS-21	Rv0125 Rv1196				
	<i>M. tuberculosis</i>	GamTBVac	DEAE-dextran core and CpG oligonucleotide	ESAT-6 CFP-10 Ag85A				

**Figure 3.** The diversity of TB vaccine candidates in clinical trials. Schematic table showing the main characteristics of the vaccine candidates. The table is coloured according to vaccine strategies indicated in Figure 2 and contains representative information for each candidate, including the mycobacterial origin from each vaccine and their antigenic content.

Update on TB Vaccine Pipeline.  
Martin C et al. *Appl. Sci.* 2020

## Opportunity 7:

The world became global, but context still matters

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## Context matters

Healthcare system  
Clinical research resources  
Geographical location  
Social and cultural issues  
TB incidence

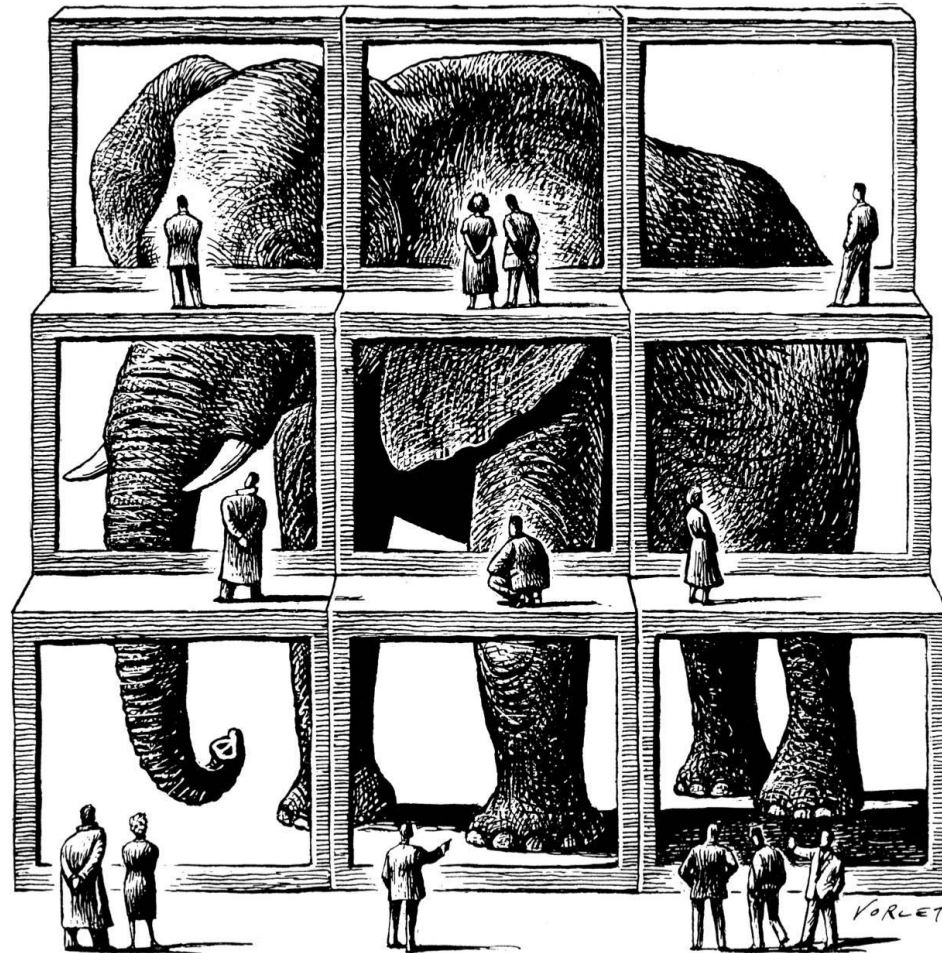


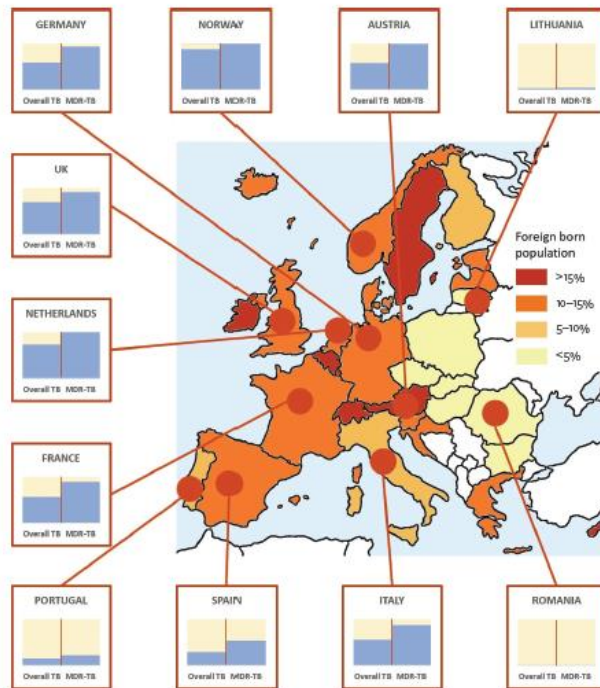
Illustration by [Christophe Vorlet](#).



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We live in a connected world where people (used to) travel for several reasons...

Fig. 4. MDR-TB among foreign-born individuals in certain European countries



Source: Reprinted from Clinical Microbiology and Infection 23(3), Hargreaves S, Lönnroth K, Nellums LB, Olaru ID, Nathavitharana RR, Norredam M et al. Multidrug-resistant tuberculosis and migration to Europe, 141-6. Copyright 2017, with permission from Elsevier (36).

Notes: Blue bars represent the proportion of infections that are in foreign-born individuals.



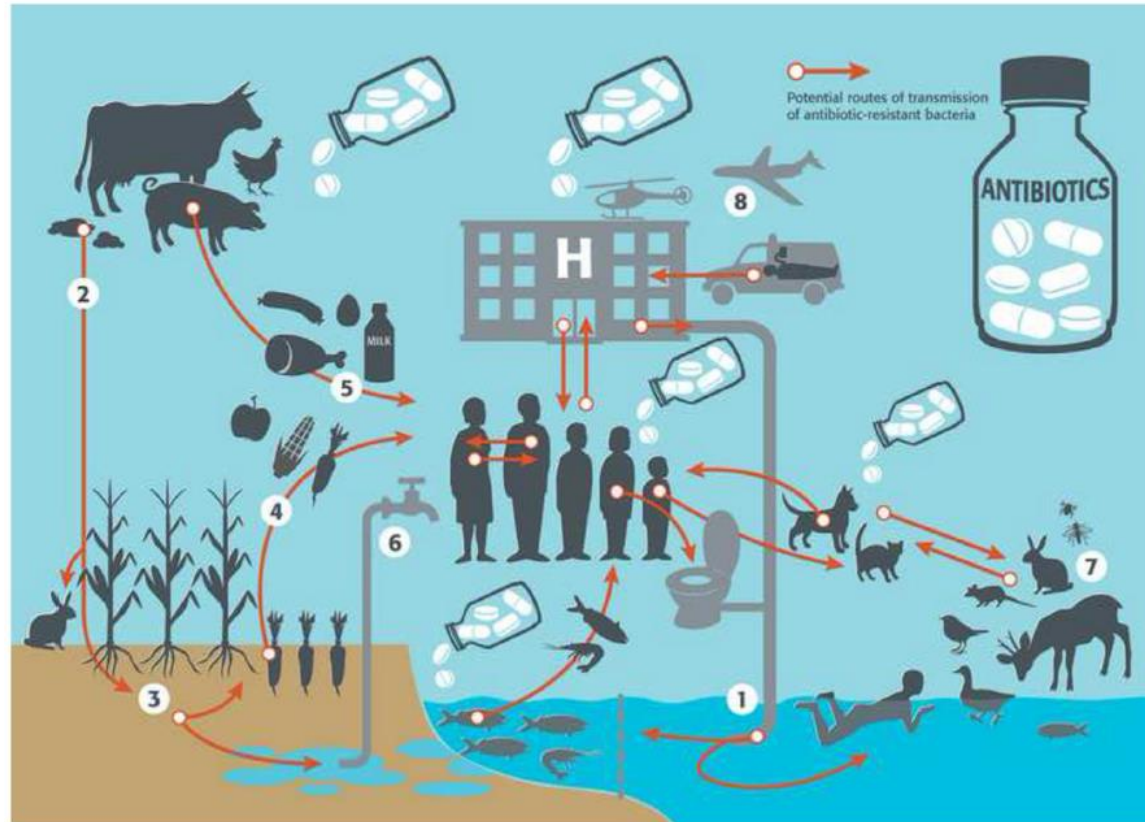
Although reducing HIV burden in some areas, novel risk groups are appearing ?

Ageing, immunosenescence, non communicable diseases ... and less awareness?

## Opportunity 8:

One health perspective:  
human, animal, enviromental

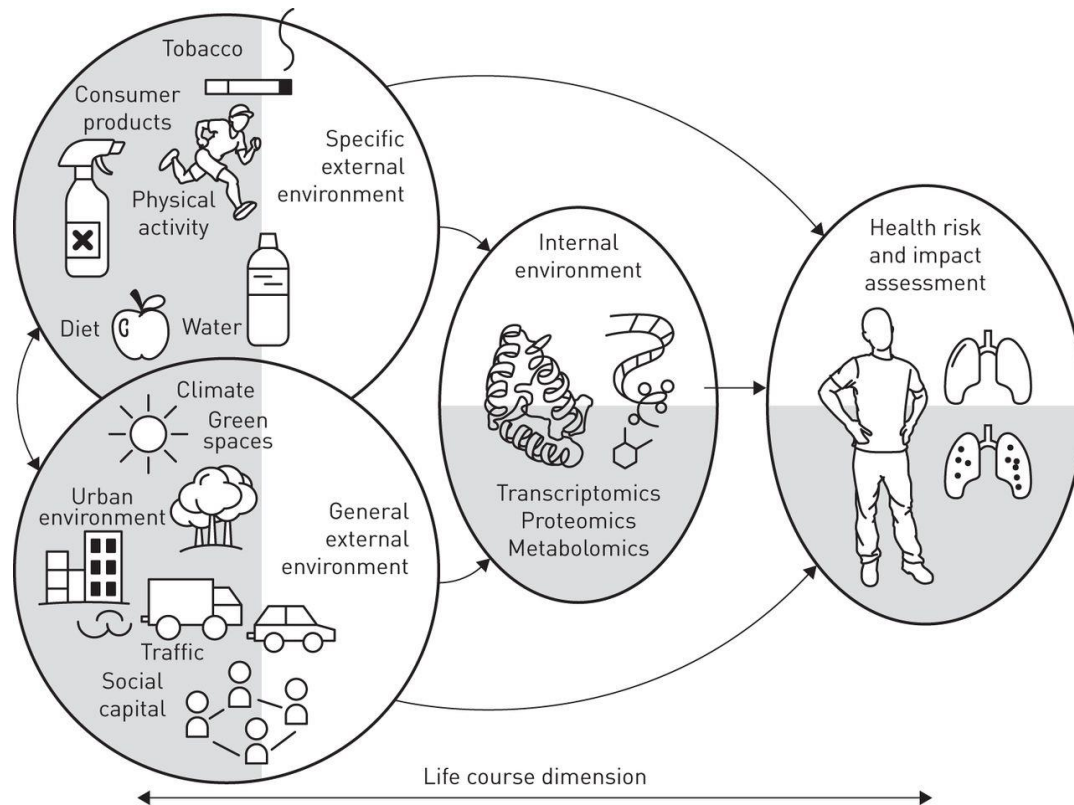
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Harbarth S, Balkhy HH, Goossens H, Jarlier V, Kluytmans J, Laxminarayan R, Saam M, Van Belkum A, Pittet D; for the **World Healthcare-Associated Infections Resistance Forum** participants.  
**Antimicrobial resistance: one world, one fight!** Antimicrob Resist Infect Control. 2015 Nov 18;4:49.  
Source graph bioMérieux)

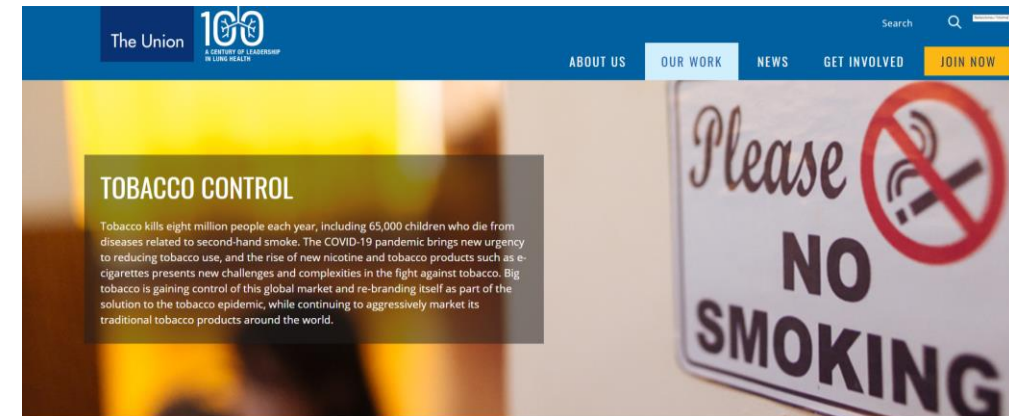


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Eur Respir Rev. 2016 Jun;25(140):124-9.

Diesel extract particles  
**Tobacco** (standard, e-cigarettes)  
Micro and nanoplastics



## Opportunity 9:

Handle the long-term effects.

Social science approach.

Gender equality.

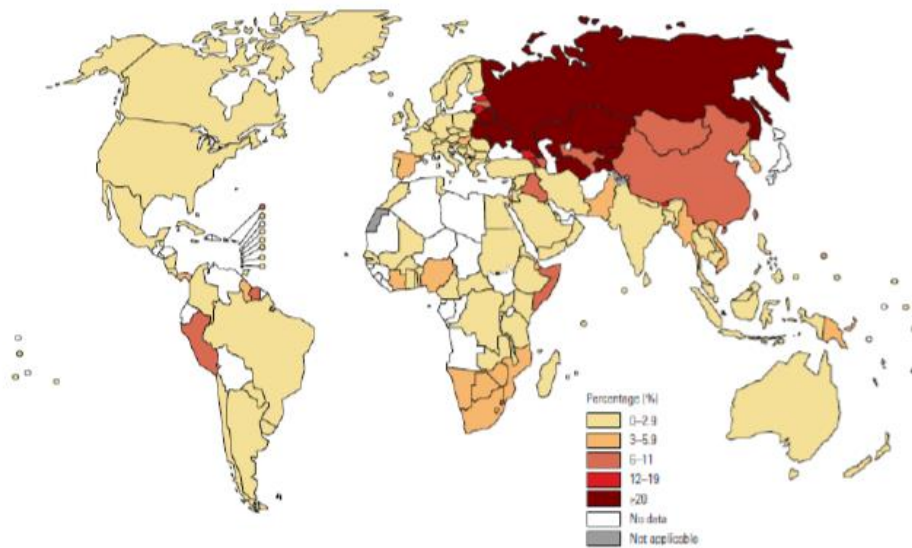
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## Different challenges in not so distant geographical areas:

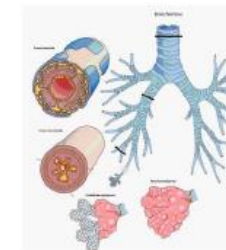
- Severe lung damage, long term functional disability
- Emerging non tuberculous mycobacteria in patients with fibrocavitary disease

FIG. 4.30

Percentage of new TB cases with MDR/RR-TB\*



\* Percentages are based on the most recent data point for countries with representative data from 2005 to 2020. Model-based estimates for countries without data are not shown. MDR-TB is a subset of RR-TB.



# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

## EDITORIALS



Oxford University Hospitals NHS Trust,  
Oxford, UK

emily.fraser@ouh.nhs.uk

Cite this as: *BMJ* 2020;370:m3001

<http://dx.doi.org/10.1136/bmj.m3001>

Published: 03 August 2020

## Long term respiratory complications of covid-19

Substantial population morbidity is likely

Emily Fraser *respiratory consultant*

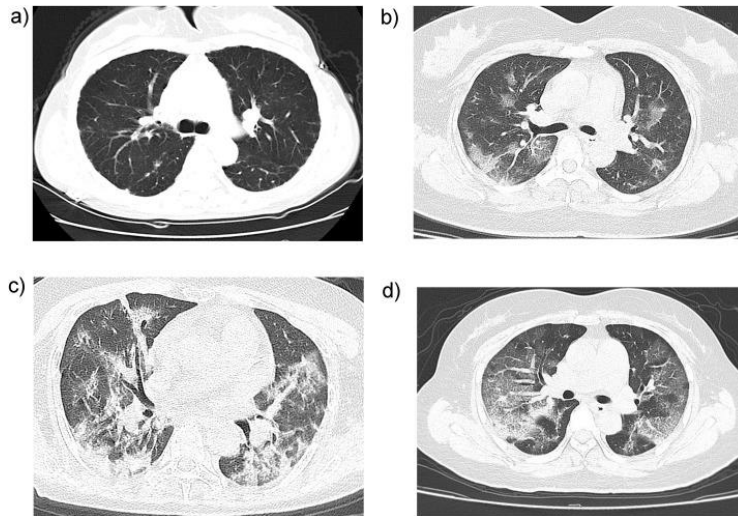
The extent and severity of the long term respiratory complications of covid-19 infection remain to be seen,

## COVID-19 rapid guideline: managing the long-term effects of COVID-19

NICE guideline

Published: 18 December 2020

[www.nice.org.uk/guidance/ng188](http://www.nice.org.uk/guidance/ng188)



Eur J Radiol. 2020



Recently added

RECOVER Scientific Publications



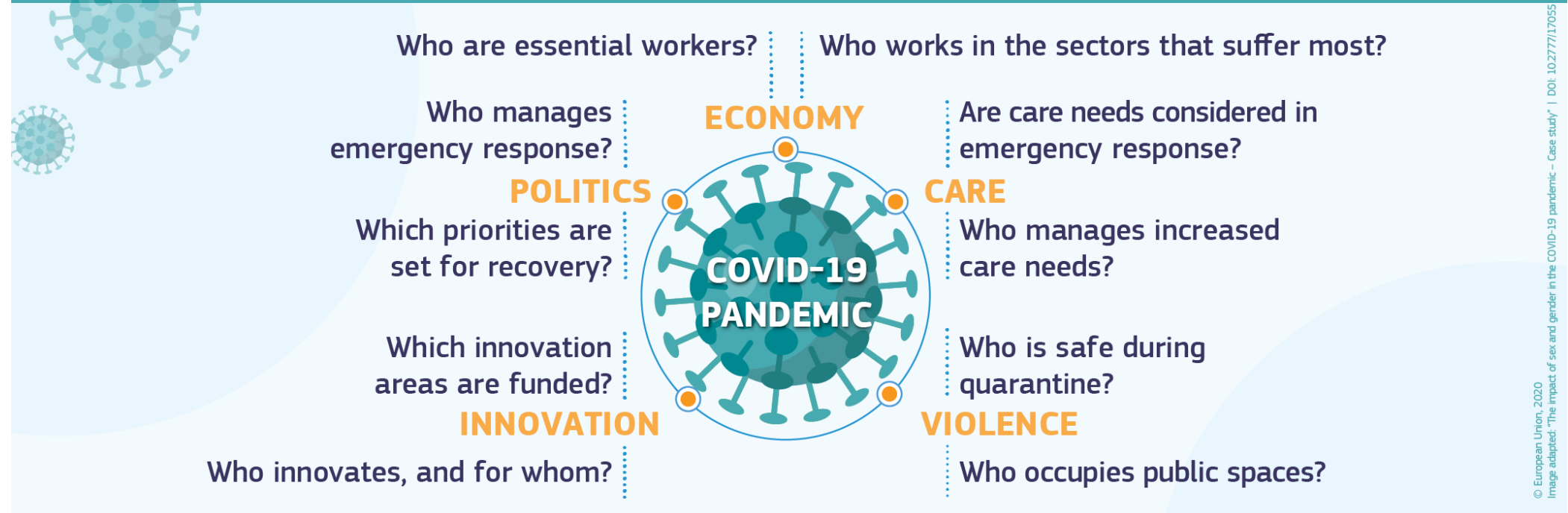
The project will provide surveillance, inform decision making, deliver evidence-based management during COVID-19 pandemic

Social Science Studies



# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

## Gender-sensitive impact of the COVID-19 pandemic



#UnionOfEquality #GenderEquality  
#UnitedAgainstCoronavirus



European  
Commission

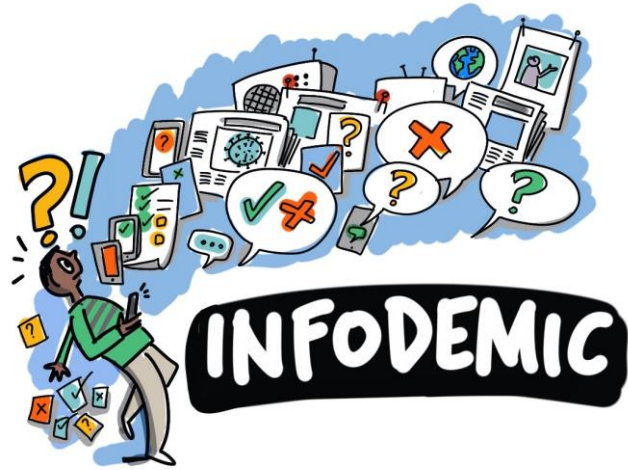


## Opportunity 10:

Communication channels  
to be used with critical spirit

# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

Never before so easy to communicate as now  
Never before so easy to misscommunicate



**WHO definition:** An **infodemic** is **too much information including false or misleading information** in digital and physical environments during a disease outbreak. It causes confusion and risk-taking behaviors that can harm health. It also leads to mistrust in health authorities and undermines the public health response.



## Top tips for navigating the infodemic



### 1. Assess the source:

Who shared the information with you and where did they get it from? Even if it is friends or family, you still need to vet their source.



### 2. Go beyond headlines:

Headlines may be intentionally sensational or provocative.



### 3. Identify the author:

Search the author's name online to see if they are real or credible.



### 4. Check the date:

Is it up to date and relevant to current events? Has a headline, image or statistic been used out of context?



### 5. Examine the supporting evidence:

Credible stories back up their claims with facts.



### 6. Check your biases:

Think about whether your own biases could affect your judgment on what is or is not trustworthy.



### 7. Turn to fact-checkers:

Consult trusted fact-checking organizations, such as the International Fact-Checking Network and global news outlets focused on debunking misinformation.

# Impact of COVID-19 on tuberculosis: turn challenges into opportunities

Healthcare workers and scientific community needed **continuous learning**, global communication, daily updates



**Responsability at the Academic level:** Social awareness of the importance of research. Prevent infodemics, prevent non constructive competition, communicate honestly.

## Scientists, keep an open line of communication with the public

The COVID-19 pandemic has opened up a direct channel between scientists and the public. Keeping it open must become part of scientists' mission.

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