














Du COVID-19 aux futures pandémies

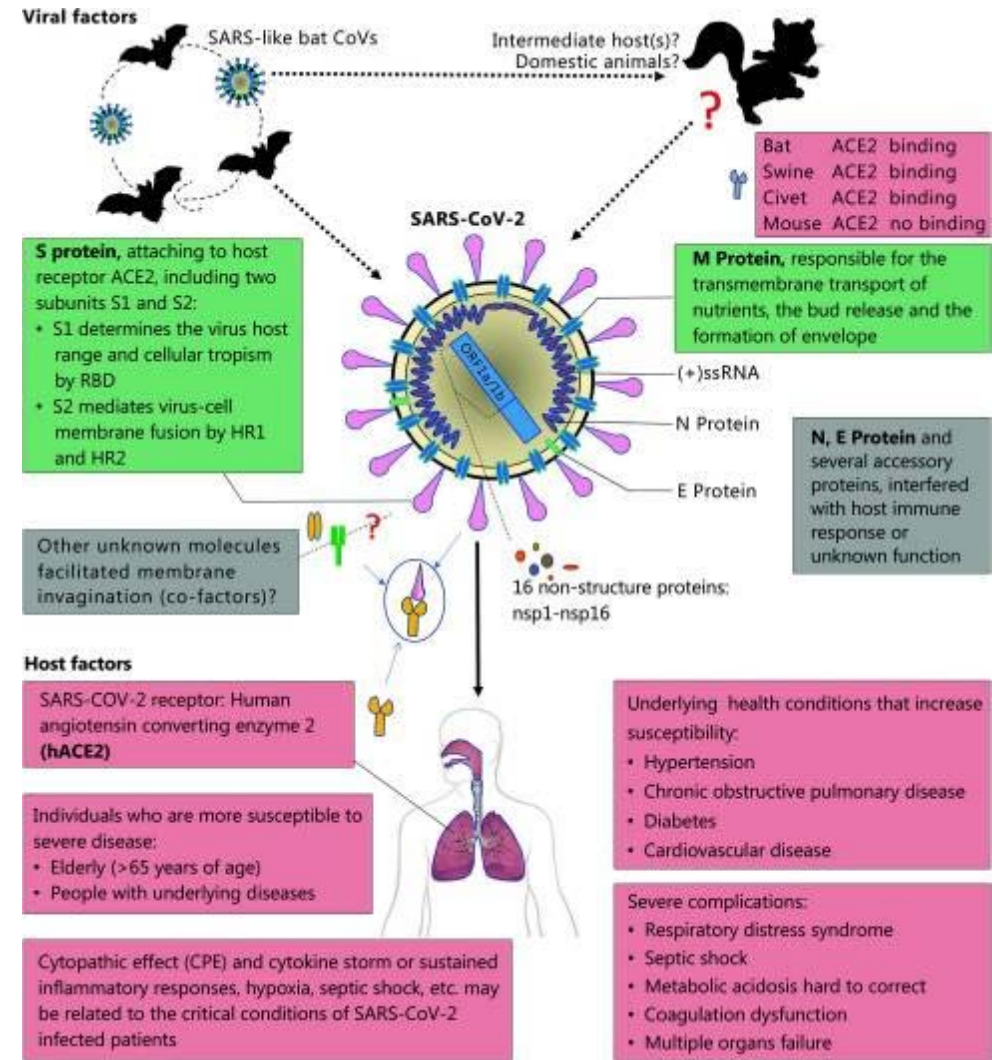
Bruno Lina

Laboratoire de Virologie, Institut des Agents Infectieux, Hôpital de la Croix-Rousse, Hospices Civils de Lyon, F-69004, Lyon
Virpath, CIRI, Université de Lyon, INSERM, CNRS, ENS de Lyon, UCBL, Faculté de Médecine Lyon Est, F-69372, Lyon

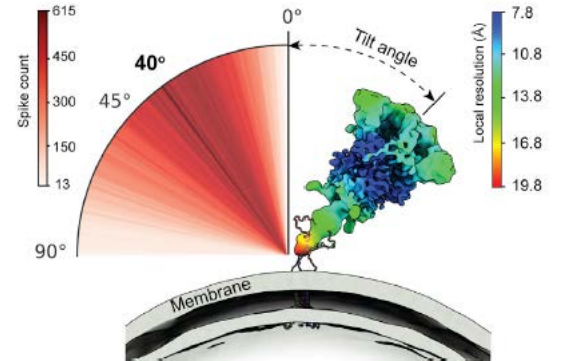
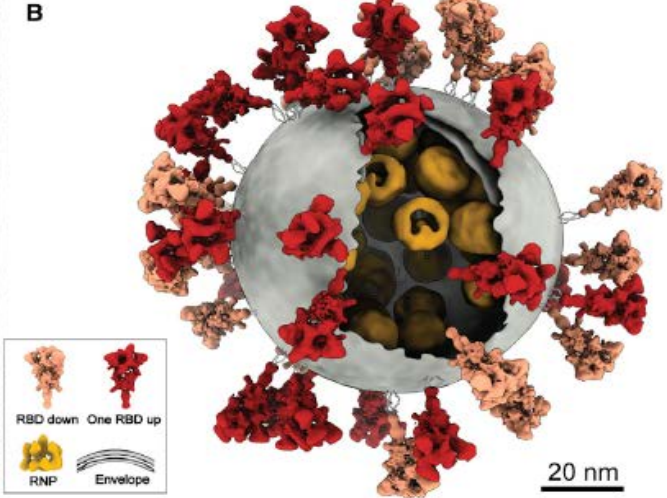
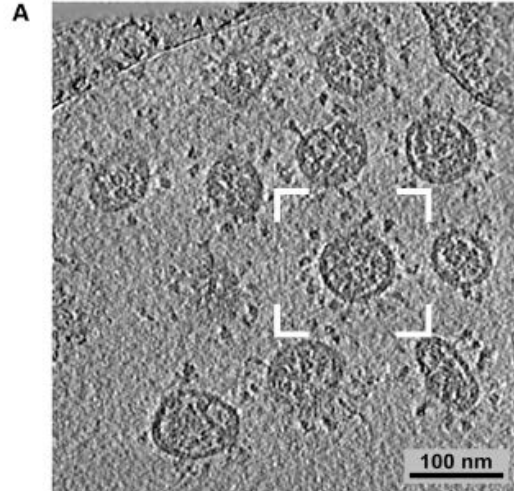
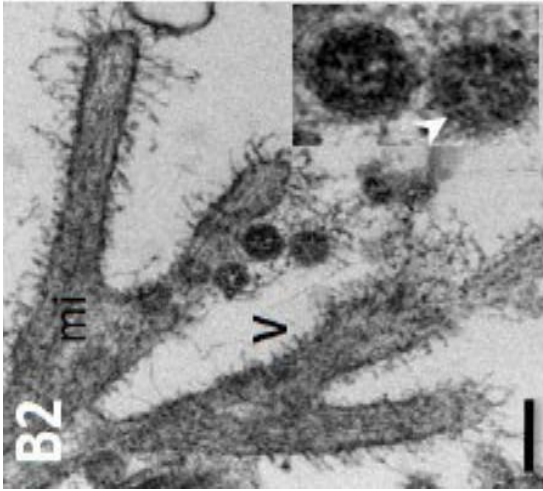
Historiques des pandémies de virus respiratoires : coronavirus

Coronavirus humain (HCoV)	Origine possible (hypothèse)	Hôte intermédiaire identifié	Date d'émergence (détermination du MRCA)	Circulation chez l'humain
HCoV-229E <i>Alphacoronavirus</i>		 Camelidae, <i>Alpaca</i> sp.	Début XIX ^e siècle	Ubiquitaire, saisonnier
HCoV-NL63 <i>Alphacoronavirus</i>		?	XIII ^e siècle	Ubiquitaire, saisonnier
HCoV-OC43 <i>Betacoronavirus</i> Clade A		 Bovidae	Fin XIX ^e siècle	Ubiquitaire, saisonnier
HCoV-HKU1 <i>Betacoronavirus</i> Clade A			?	Ubiquitaire, saisonnier
SARS-CoV <i>Betacoronavirus</i> Clade B		 <i>Paguma larva'a</i> (civette)	2002	Pandémie décembre 2002 – juillet 2003 Arrêt de la circulation
MERS-CoV <i>Betacoronavirus</i> Clade C		 <i>Camelus dromedarius</i>	2012	Circulation péninsule arabique. Risque pandémique lié aux voyages

La transmission à l'homme



Le virus SARS-CoV-2



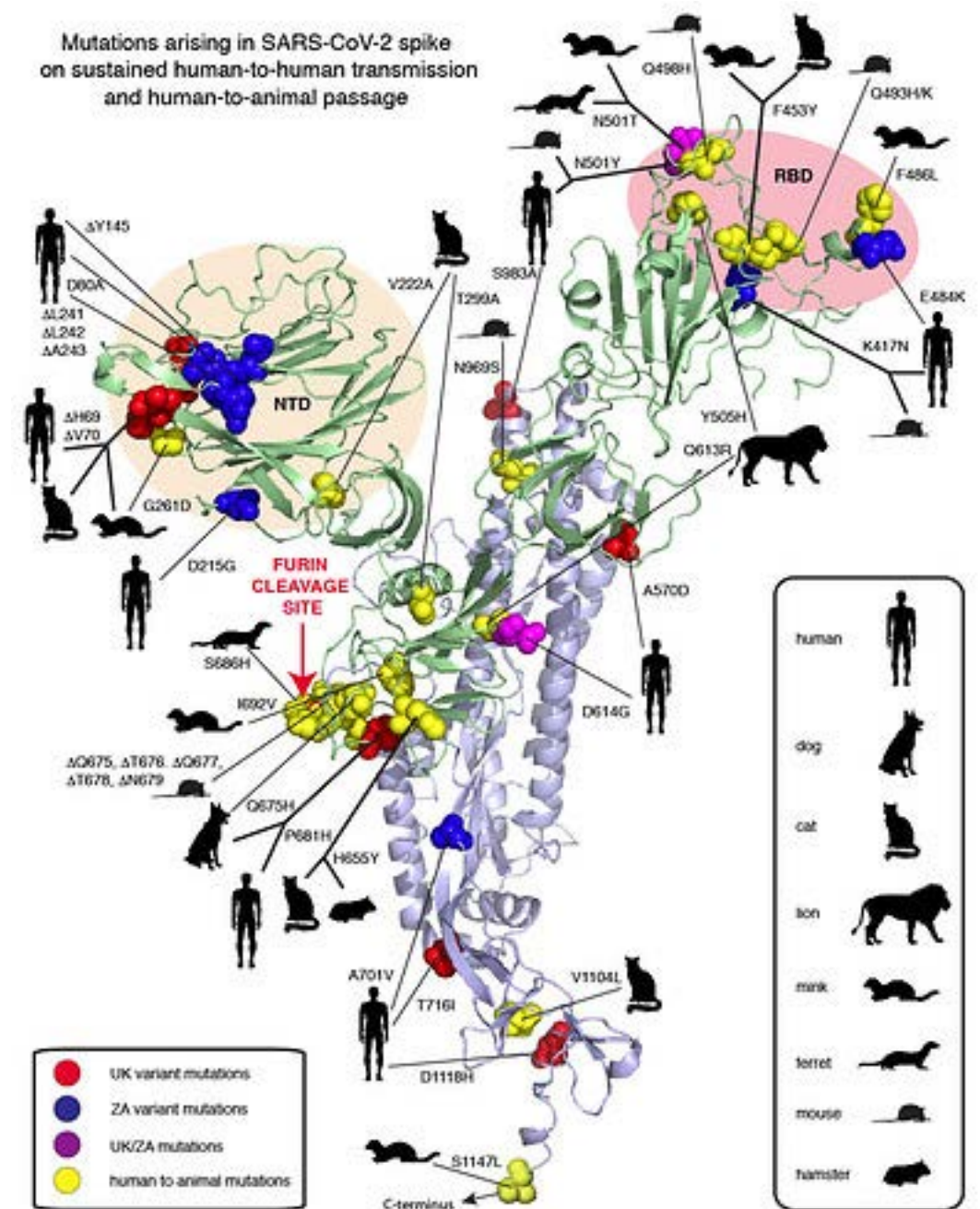
Mutations arising in SARS-CoV-2 spike on sustained human-to-human transmission and human-to-animal passage

Robert F. Garry^{1,2}

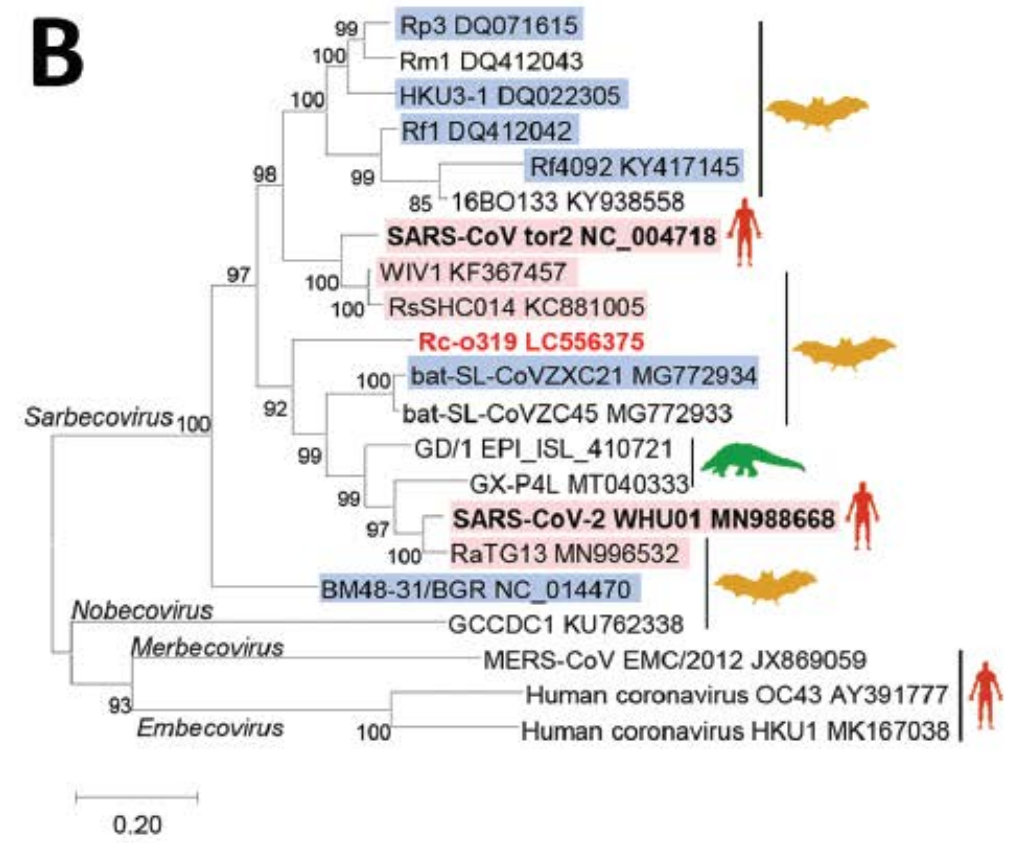
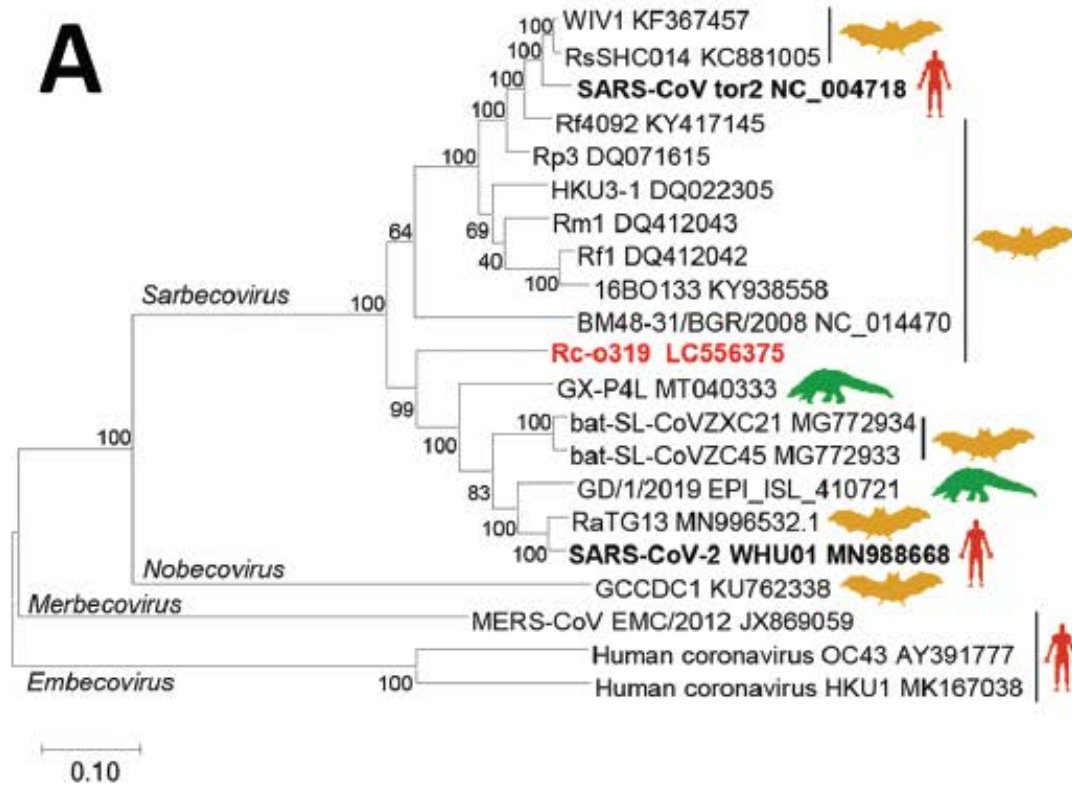
¹Department of Microbiology and Immunology,
Tulane University Medical Center, 1430 Tulane Avenue, New Orleans, Louisiana 70112 USA;

E-Mail: rfgarry@tulane.edu

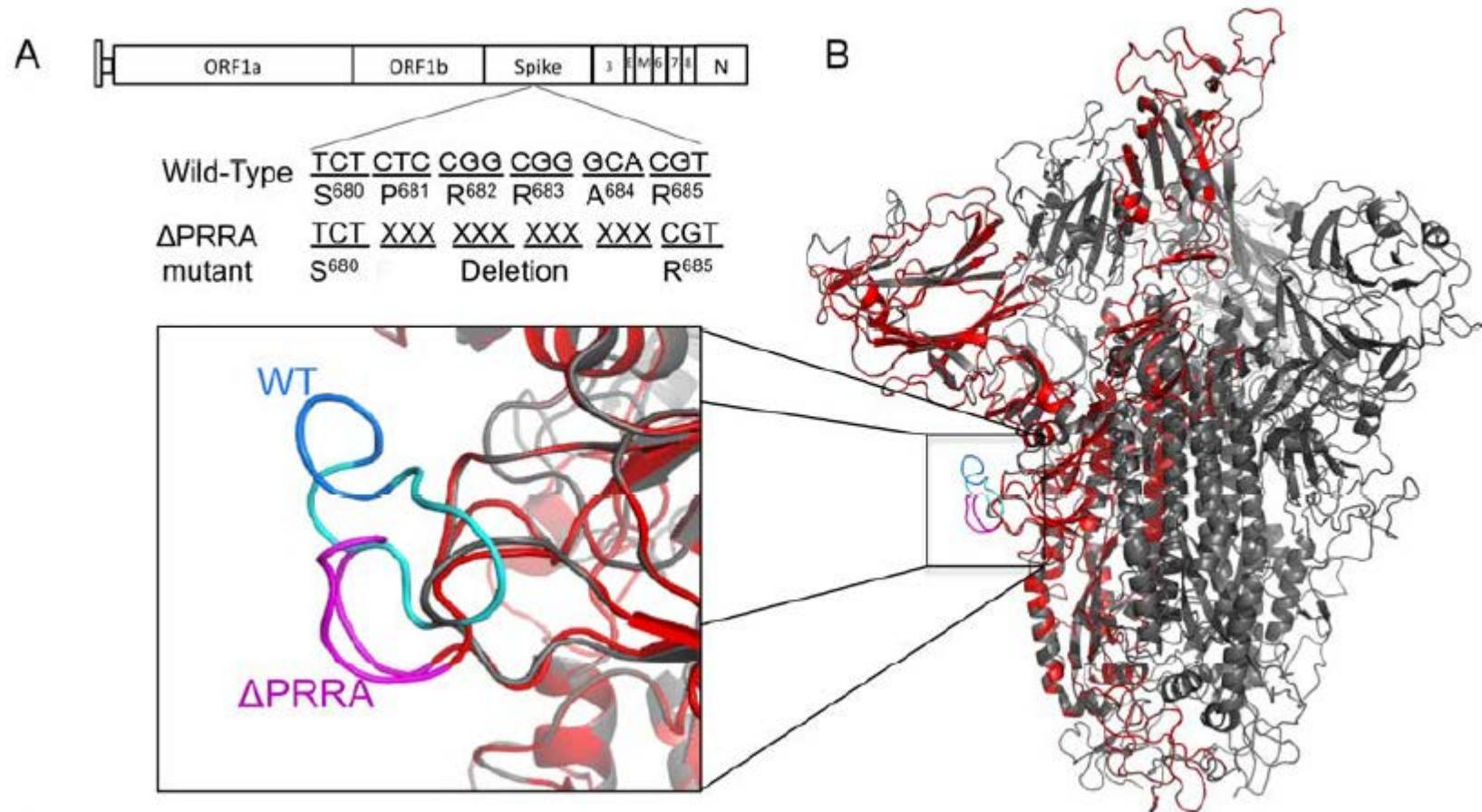
²Zalgen Labs, LLC, Germantown, MD, USA



Les virus précurseurs potentiels



The furin cleavage site: adaptation step to its new host?



Historiques des pandémies de virus respiratoires : influenzavirus



1918: "Spanish Flu"

H1N1

40-50 million



1957: "Asian Flu"

H2N2

1-4 million



1968: "Hong Kong Flu"

H3N2

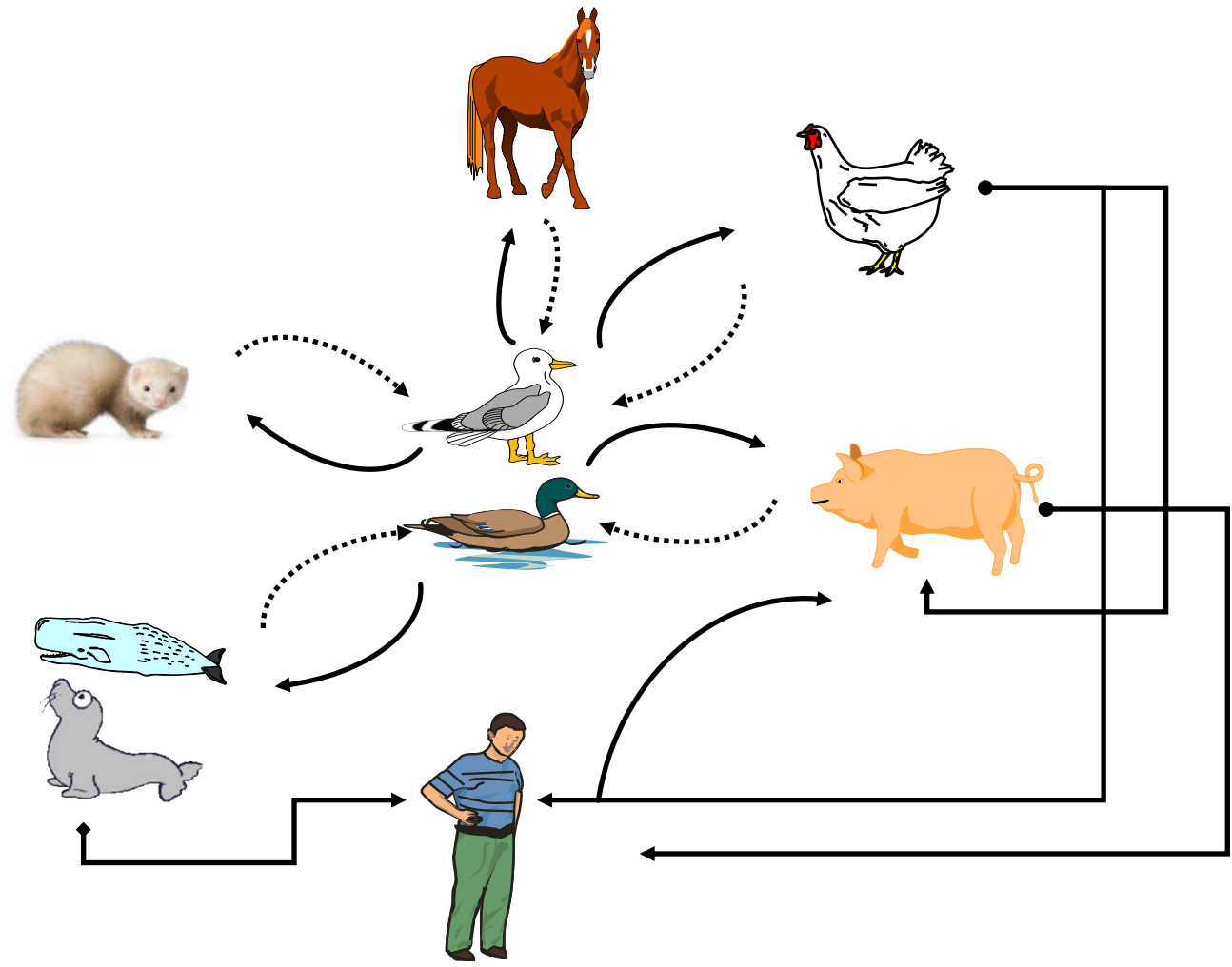
1 million

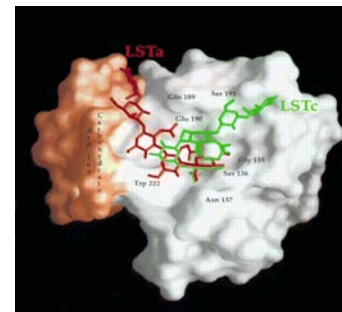
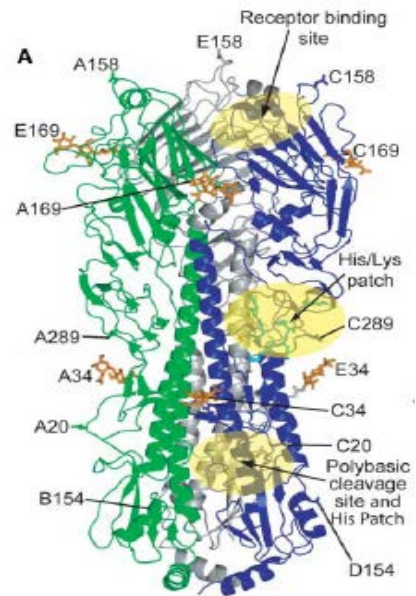
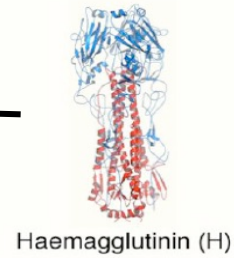
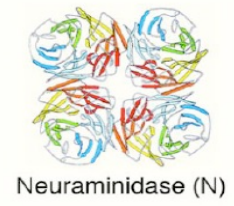
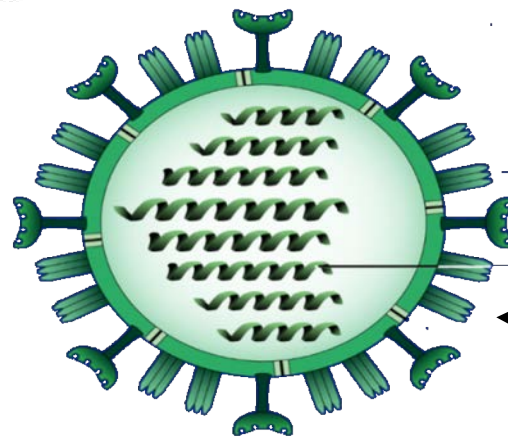
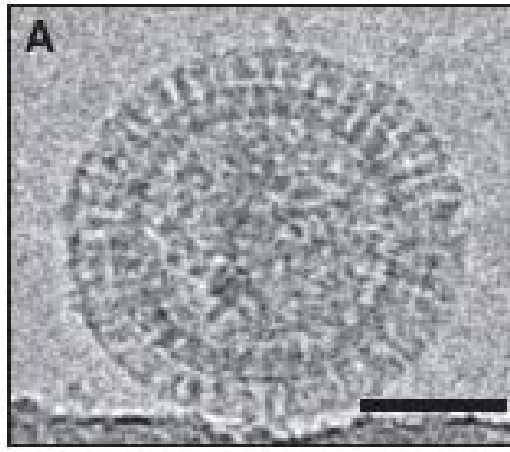


2009: "Swine Flu"

H1N1

0.7 million





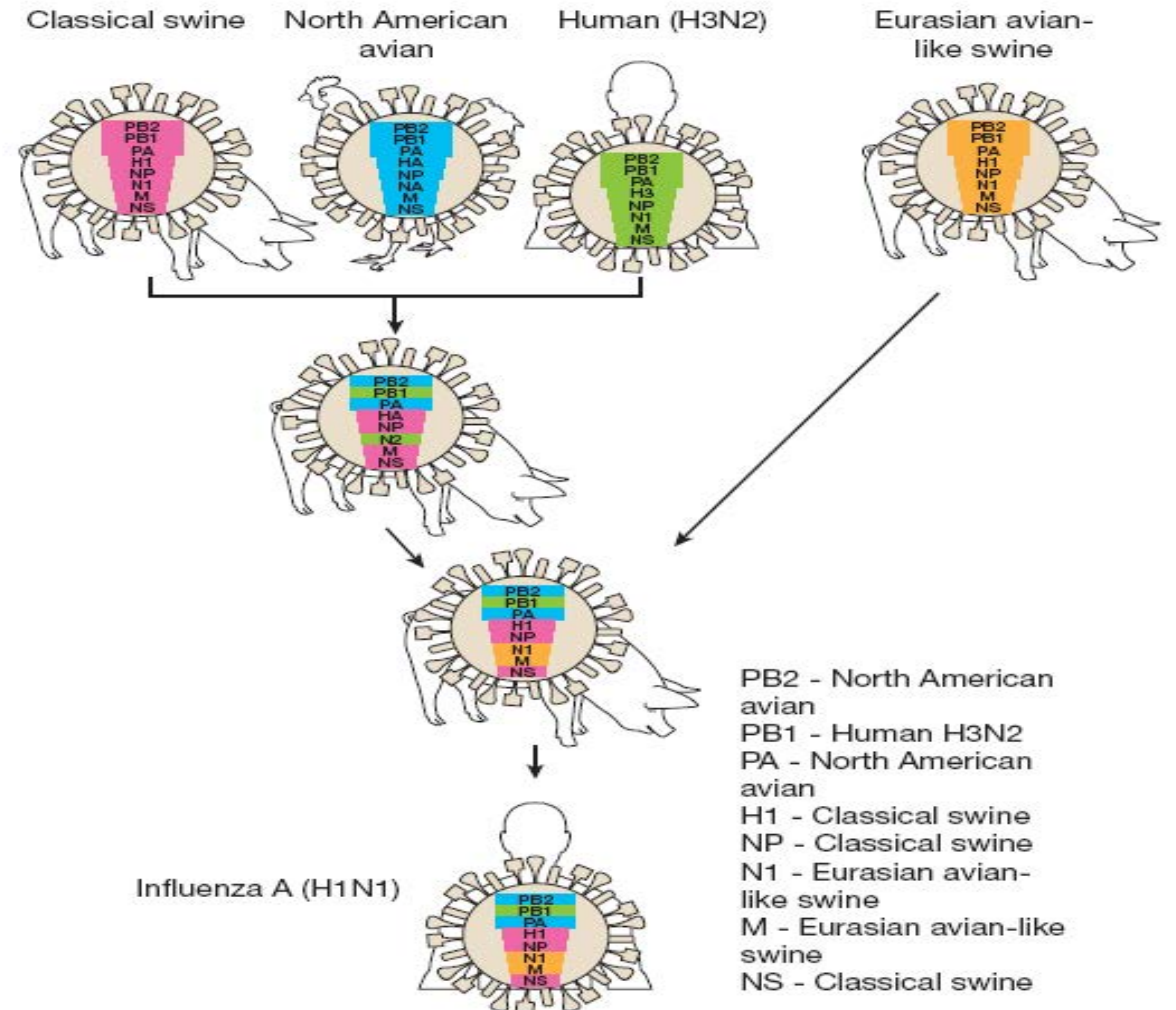
H1N1pdm09 en 2009 : un réassortiment génétique complexe



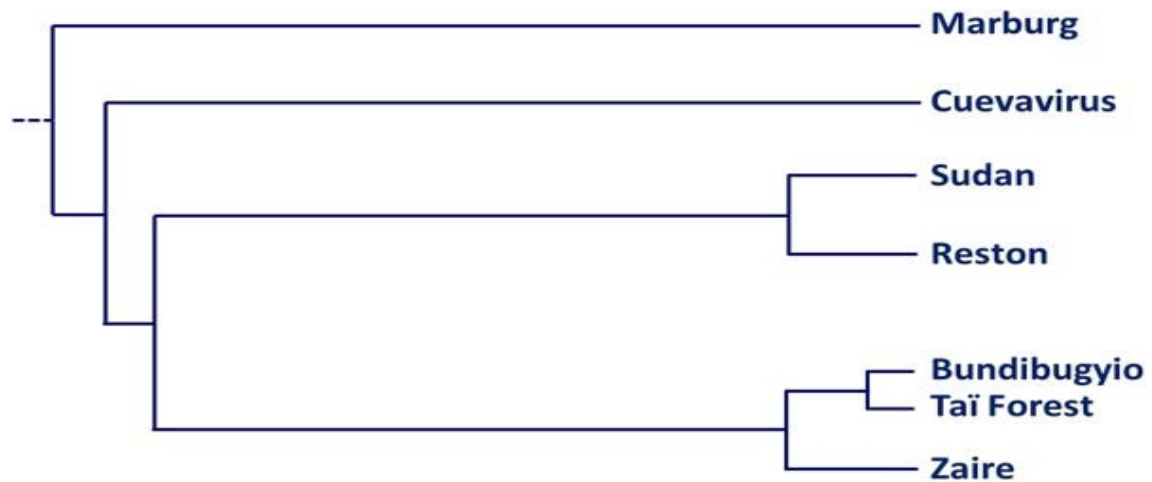
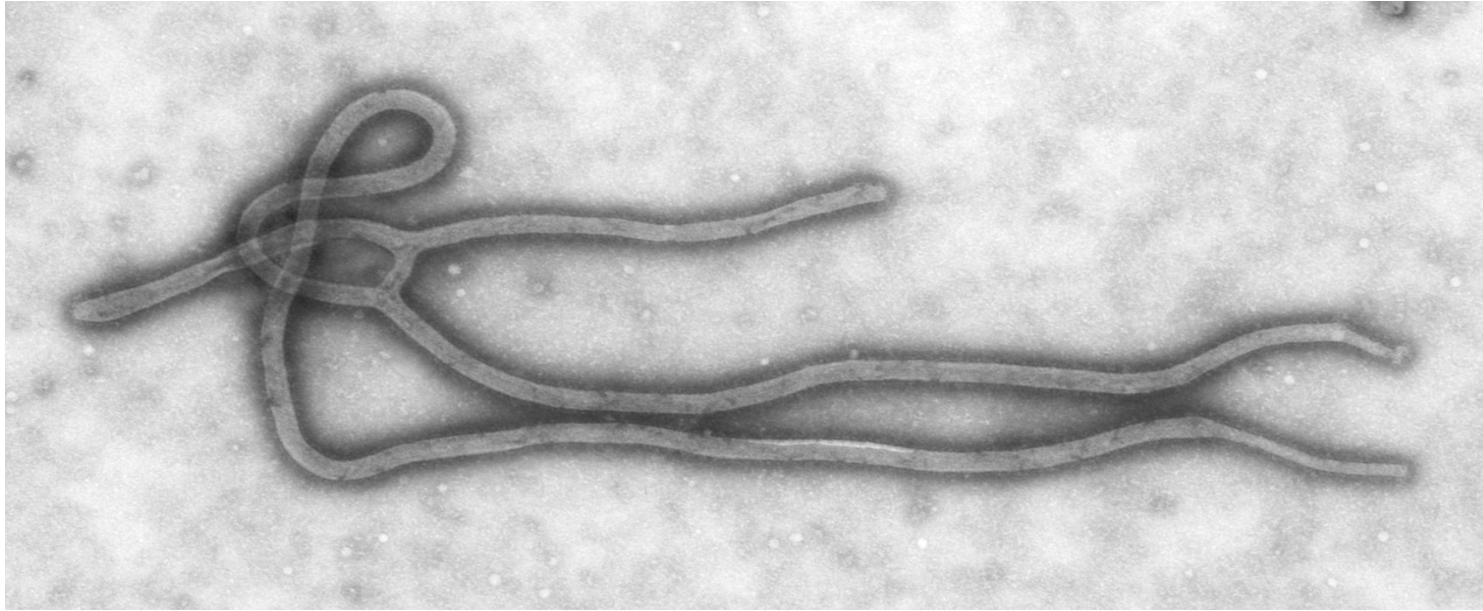
2009: "Swine Flu"

H1N1

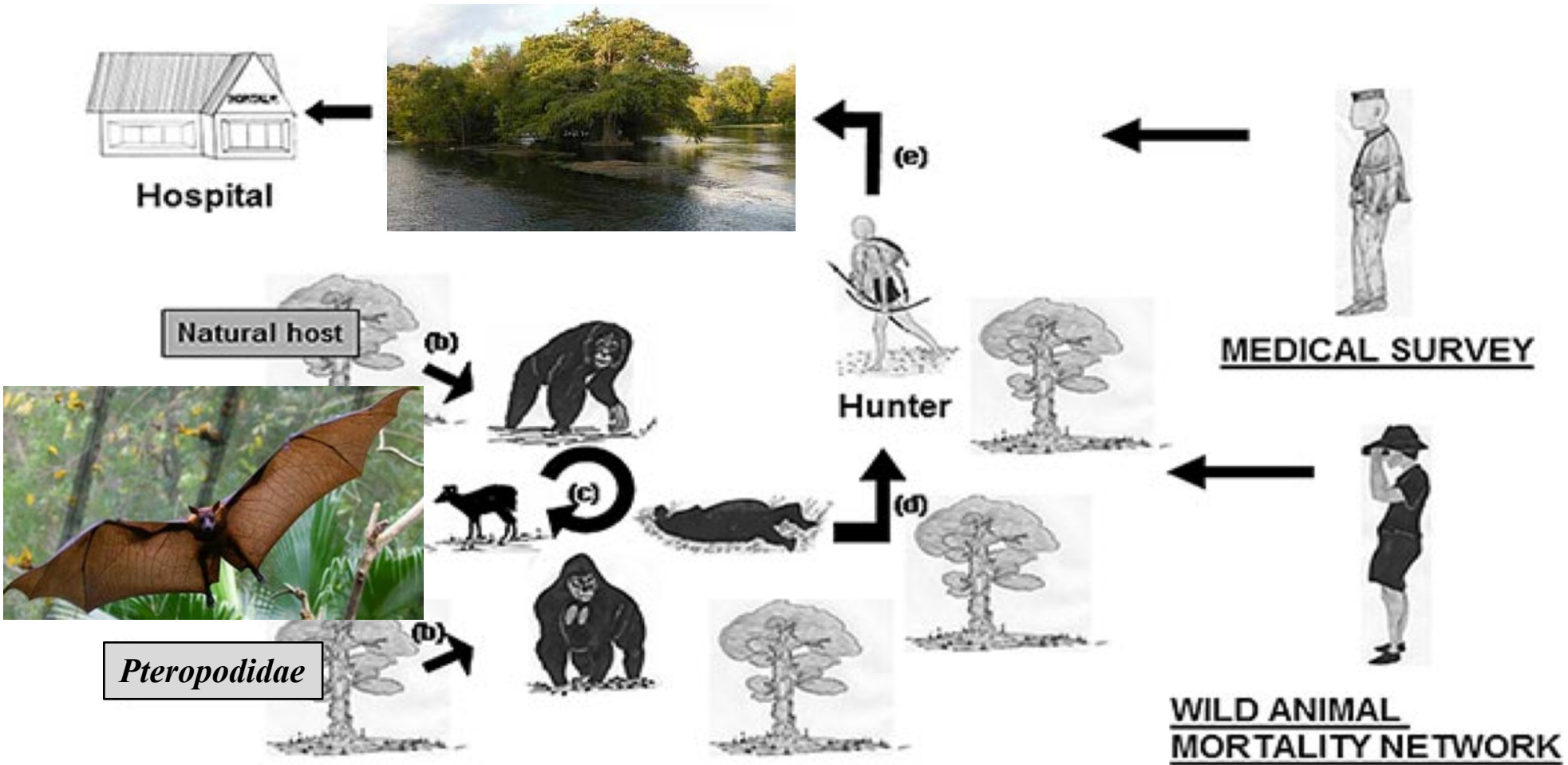
0.7 million



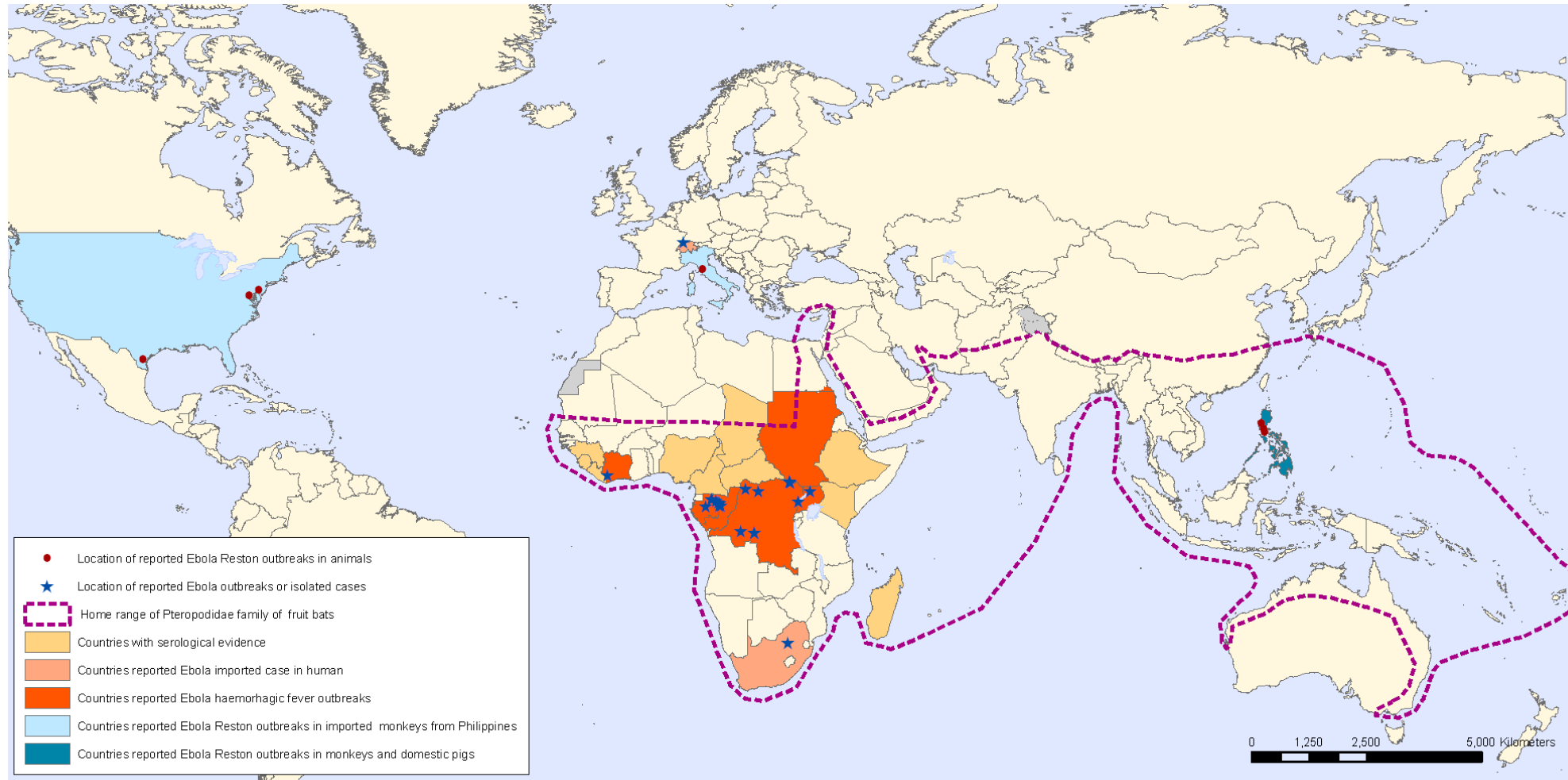
Les autres pandémies : la question Ebolavirus



Ebola : comment ca marche?



Epidémiologie du vecteur et des virus



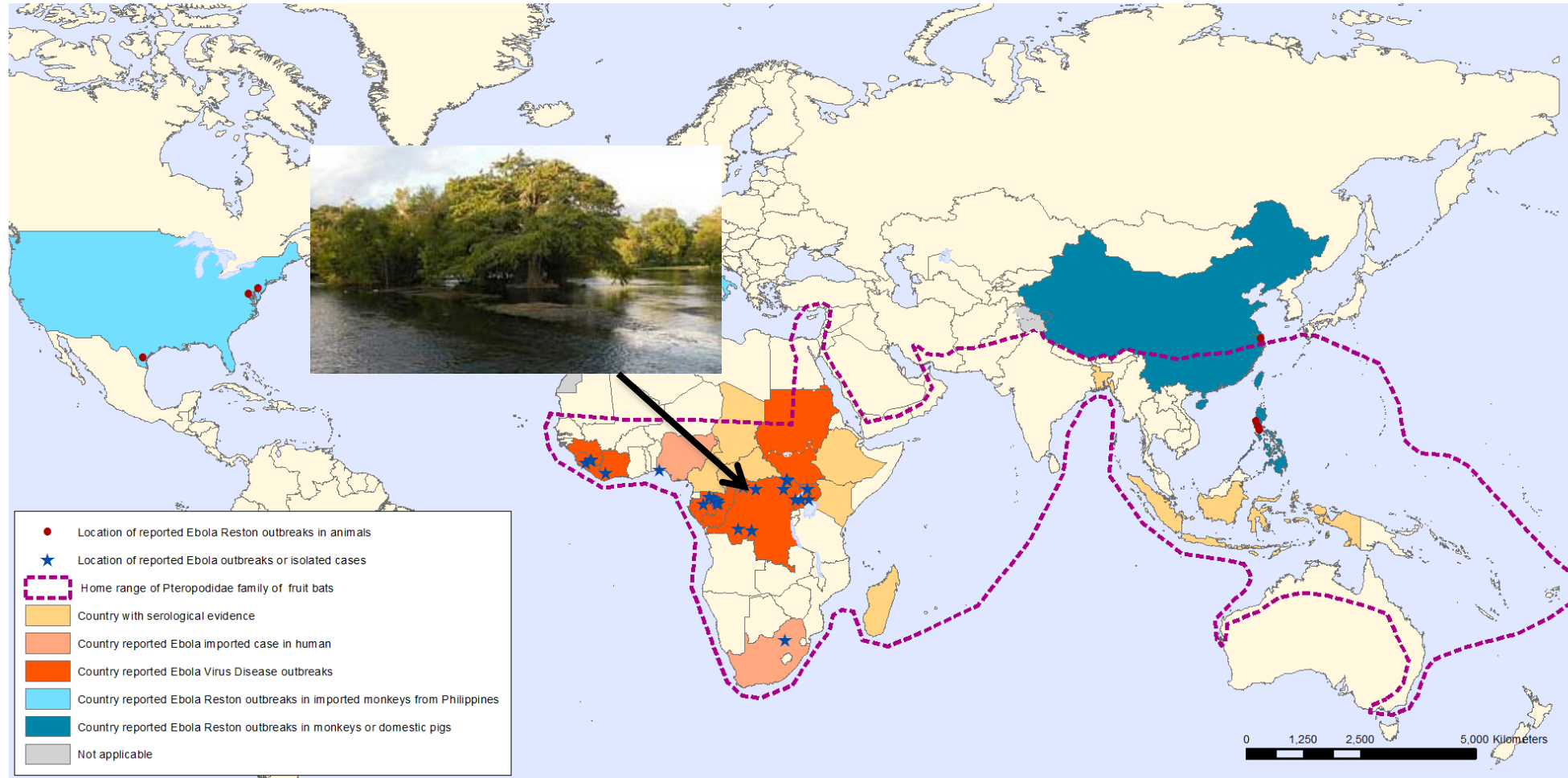
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Alert and Response Department
World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization



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Distribution géographique des virus Ebola et des cas/épidémies chez l'homme ou l'animal



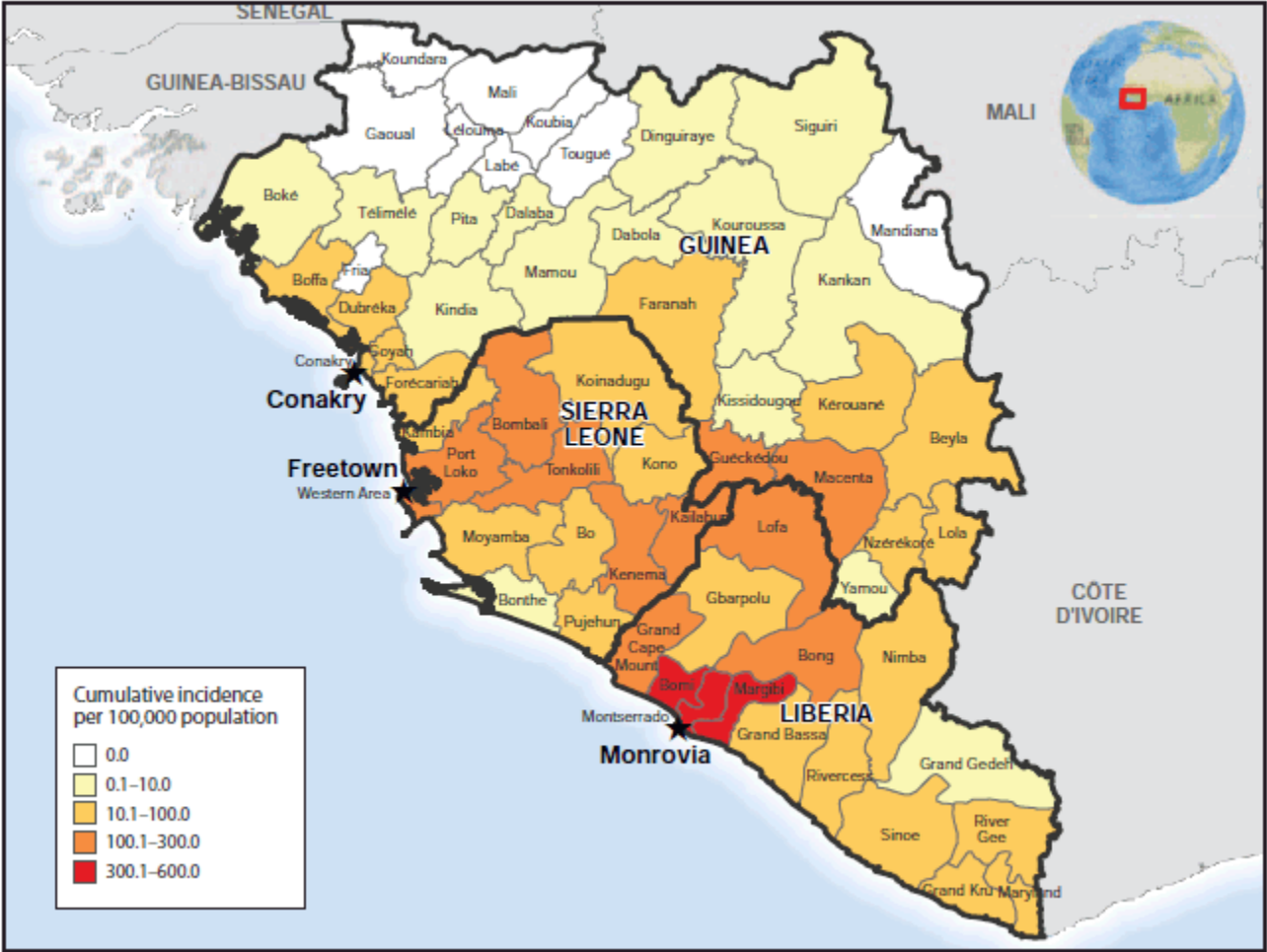
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

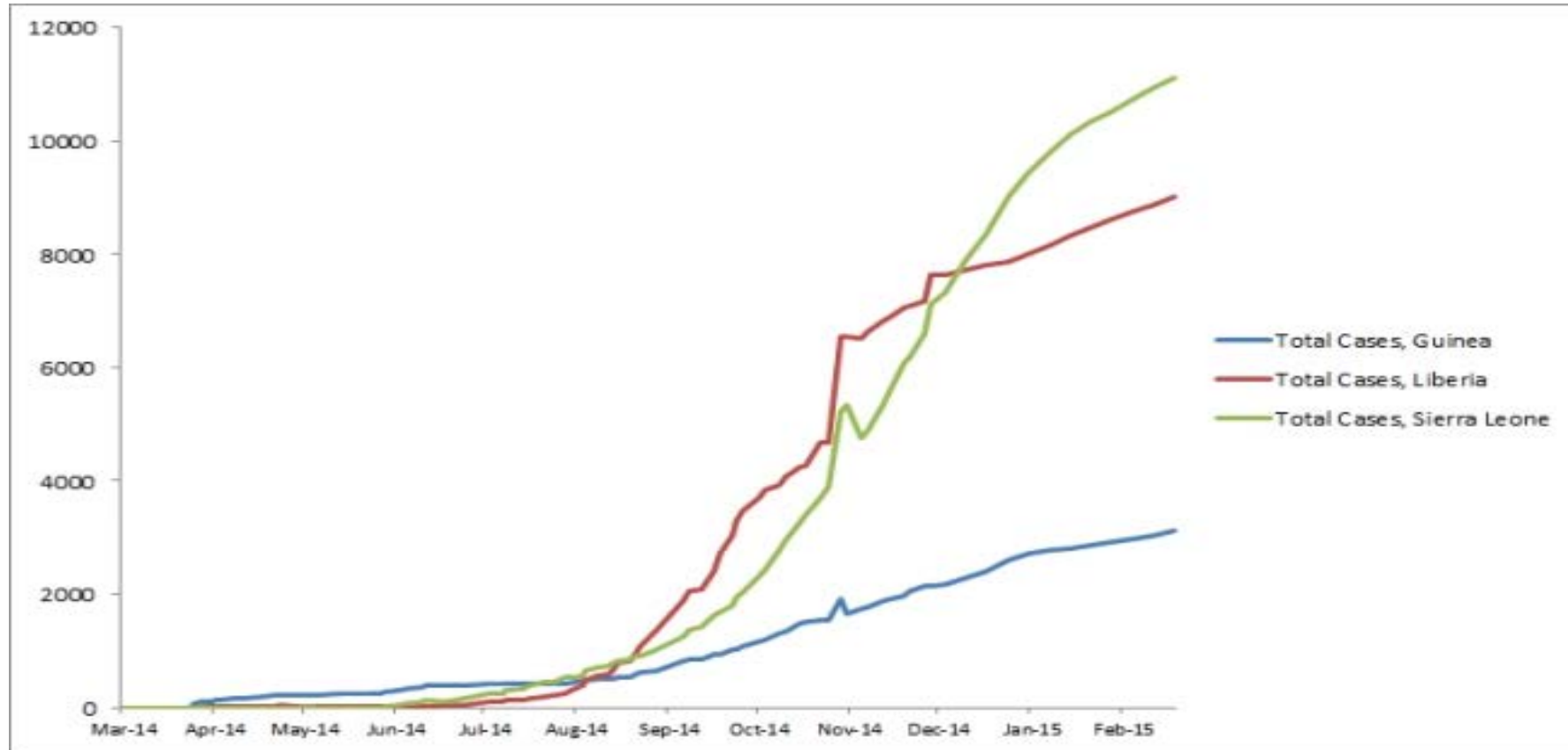


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Incidence cumulative des cas depuis février 2014



Total cumulés des cas et depuis le 25 mars 2014 (Guinée, Libéria, Sierra Leone)



Ebola virus disease - tenth outbreak - Democratic Republic of the Congo - 2018-2019

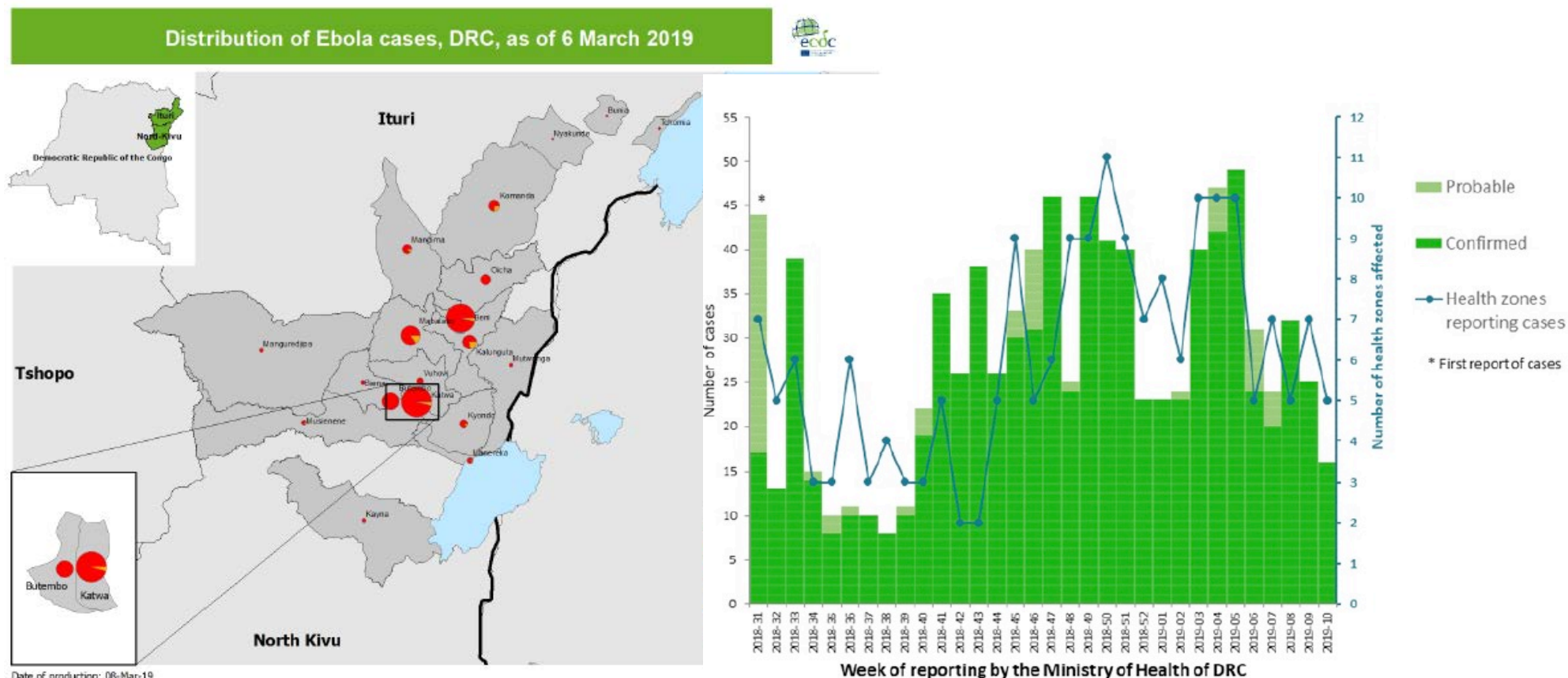
Opening date: 1 August 2018

Latest update: 8 March 2019

Epidemiological summary

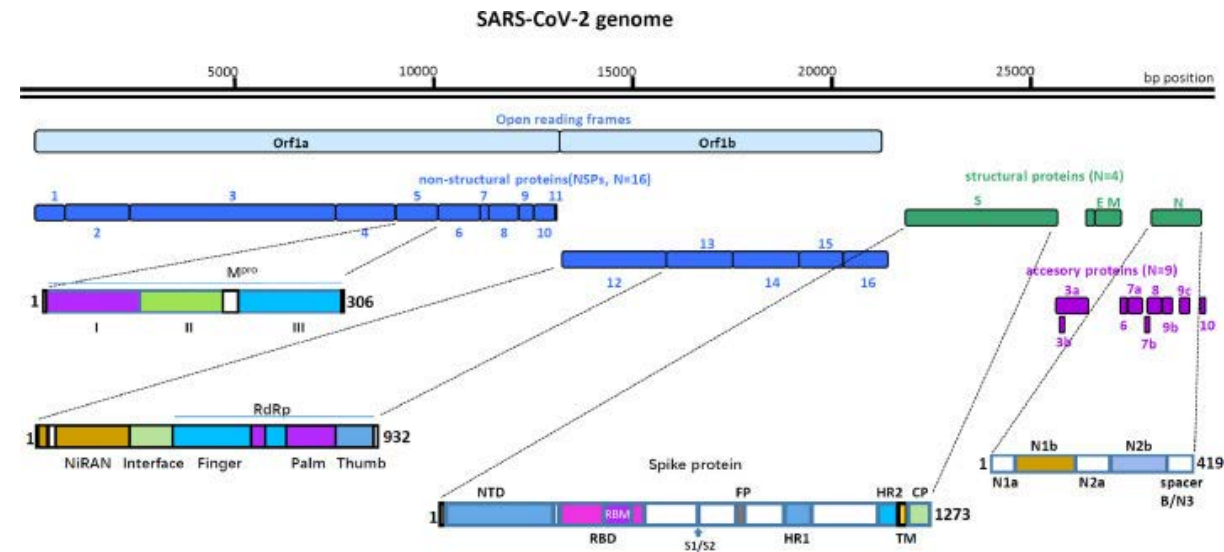
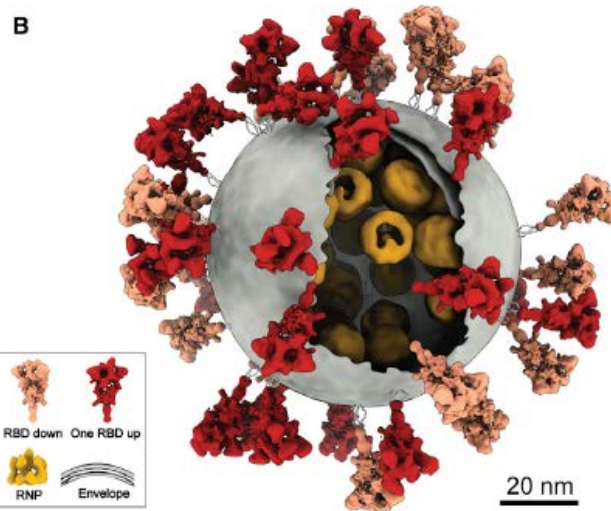
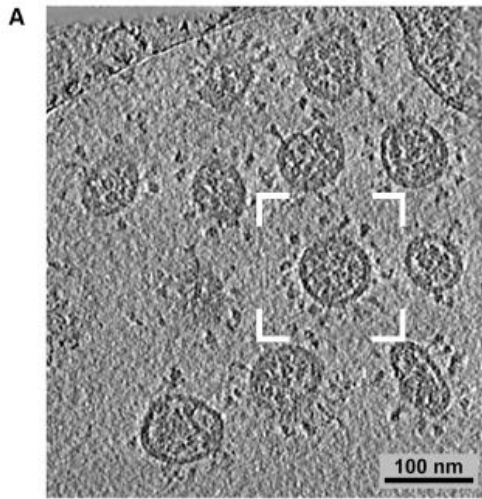
Since the beginning of the outbreak and as of 6 March 2019, there have been 913 cases (848 confirmed, 65 probable), including 574 deaths (509 confirmed, 65 probable), according to the Ministry of Health of the Democratic Republic of the Congo.

As of 2 March 2019 and according to the [WHO Regional Office for Africa External Situation Report 30](#), 72 healthcare workers have been infected, including 24 deaths.



Histoire du SARS-CoV-2

Histoire du SARS-CoV-2: une pandémie ... mémorable



Yao H et al, 2020

Phylogenie des precurseurs potentiels du SARS-CoV-2



- **New nearest bat precursor from Yunnan 2019 (high identity in Orf1ab, greatest difference in Spike protein, recombination or mixed viruses in metagenomic sample, not yet peer-reviewed)**
- **Nearest pangolin precursors from Guangdong (Southern China)**
- **Previous closest bat precursor also from Yunnan (Southern China) but sample from 2013**

Light Orange ... previous bat CoVs

Orange ... previous closest bat precursor (Yunnan 2013)

Red ... new bat CoVs (Yunnan 2019)

Light blue ... hCoV-19 2019-2020

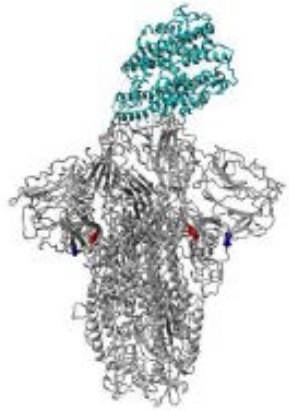
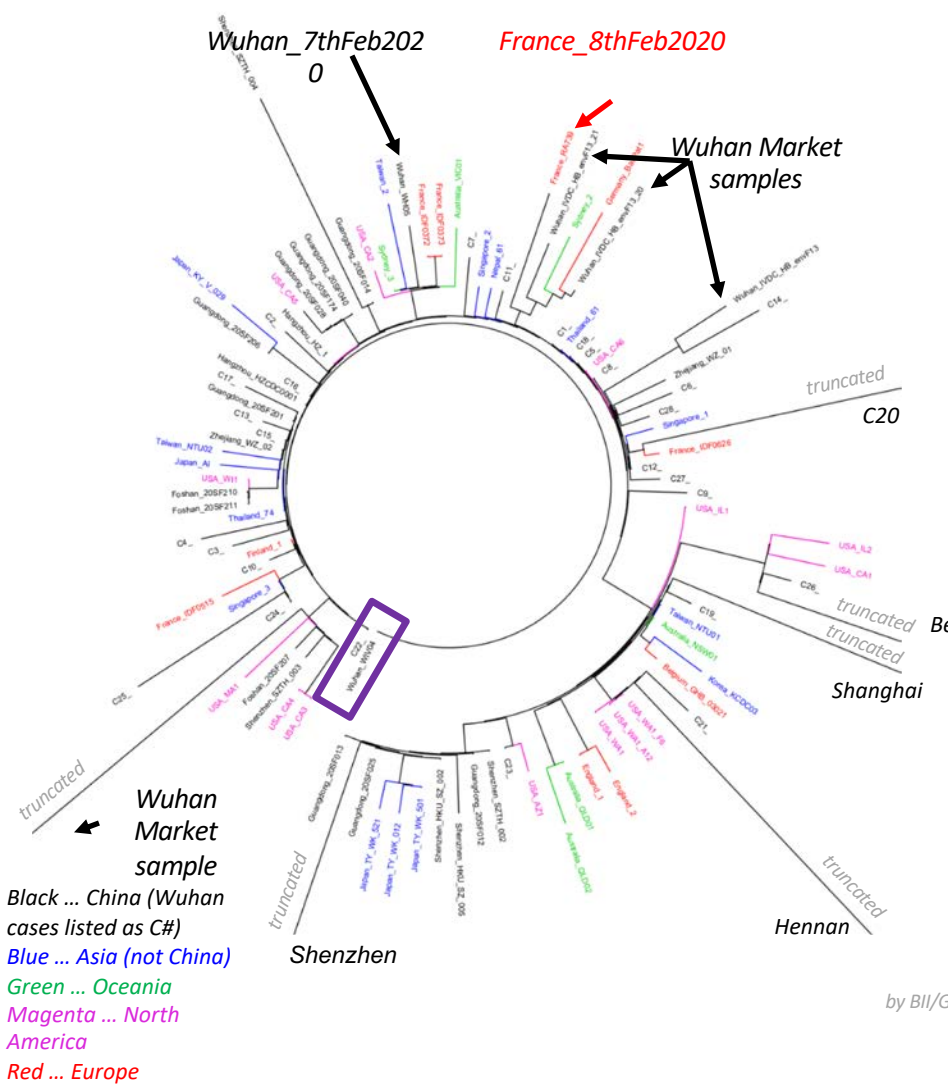
Green ... pangolin CoV (Southern China 2019)

Blue ... SARS CoV

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.



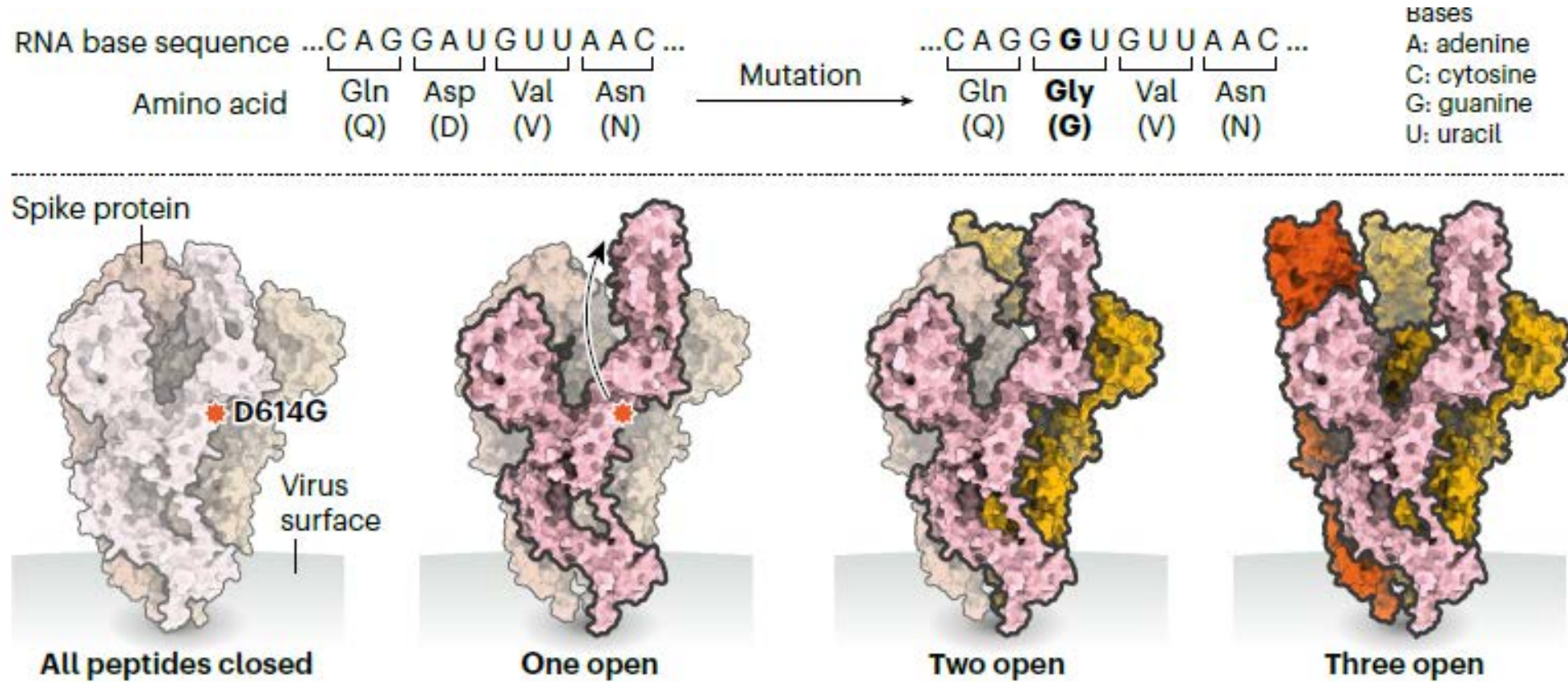
Virus du début de l'épidémie (fin janvier-début février)



Phylogenetic tree created with RAXML-NG (Maximum Likelihood tree search, 10 randomized parsimony starting trees, GTR model, Gamma distributed rates, 500 bootstrap) and visualized in FigTree

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.

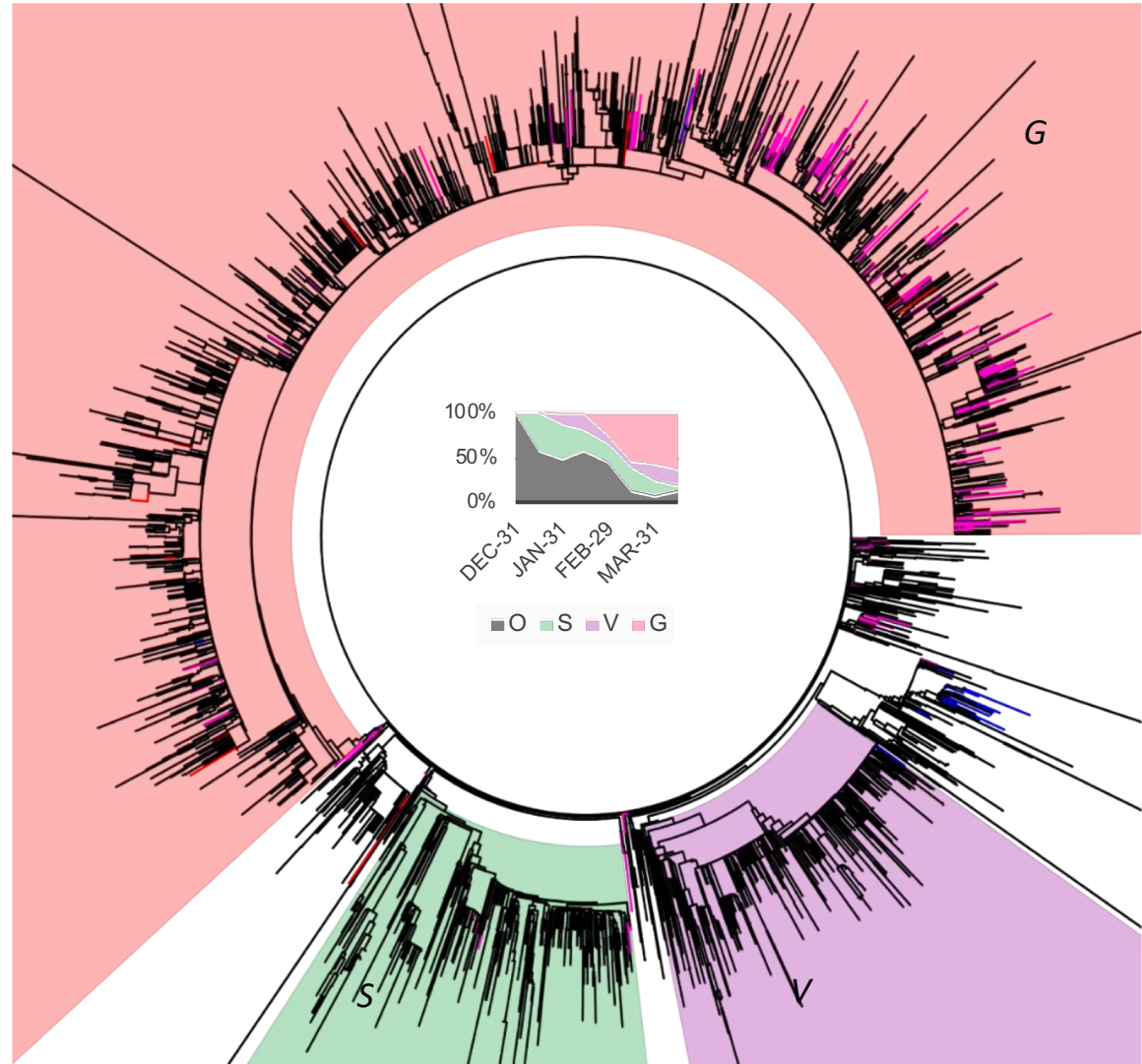
Impact de la substitution D614G : le premier pas evolutif



Phase d'extension (Avril-Mai 2020)

- 30-4-20
- Larger clades were named based on marker variants:
 - S ... ORF8-L84S*
 - G ... S-D614G*
 - V ... NS3-G251V*

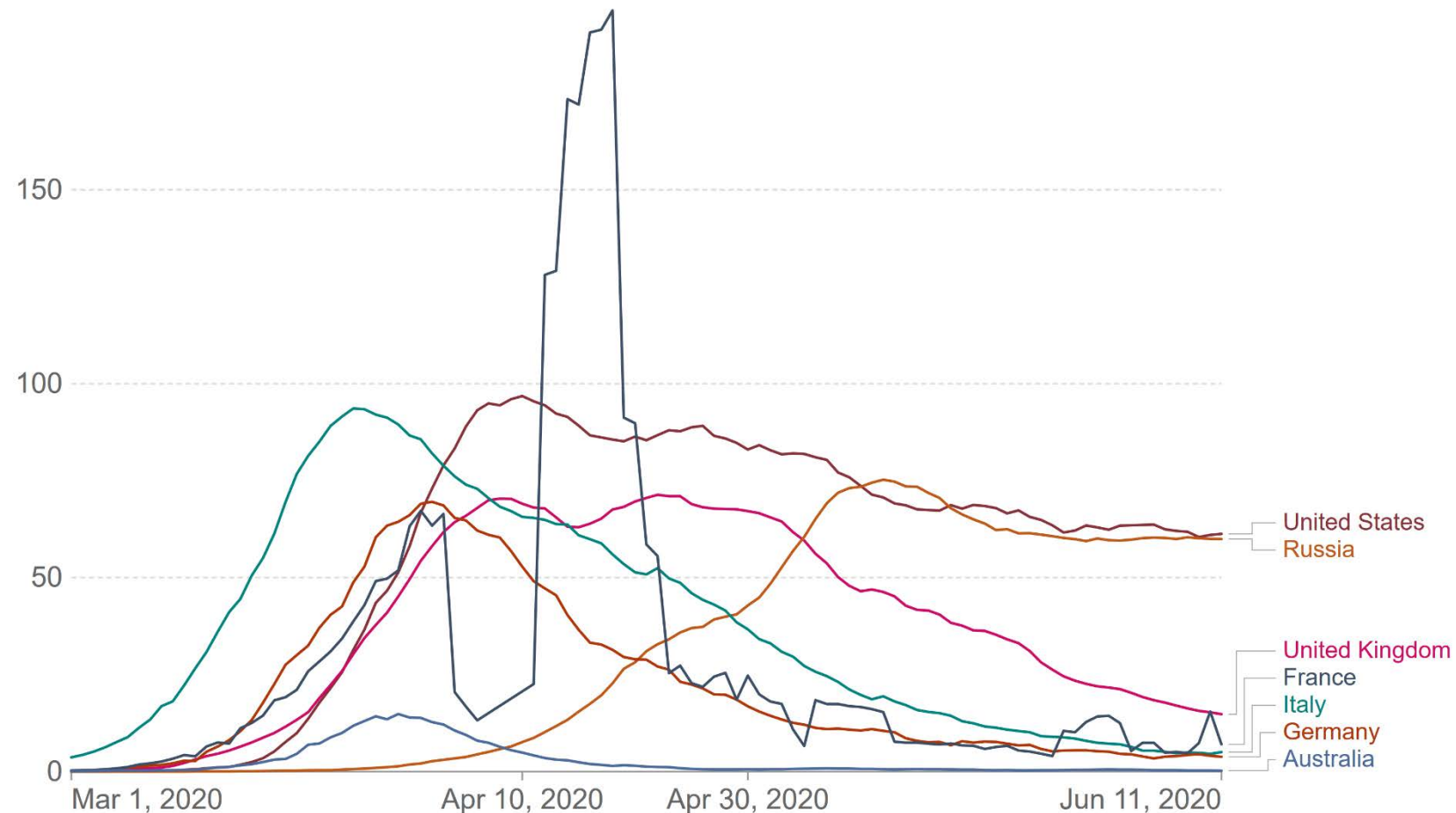
We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based



Premiere vague (Mars – mai 2020)

Daily new confirmed COVID-19 cases per million people

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.



Source: Johns Hopkins University CSSE COVID-19 Data

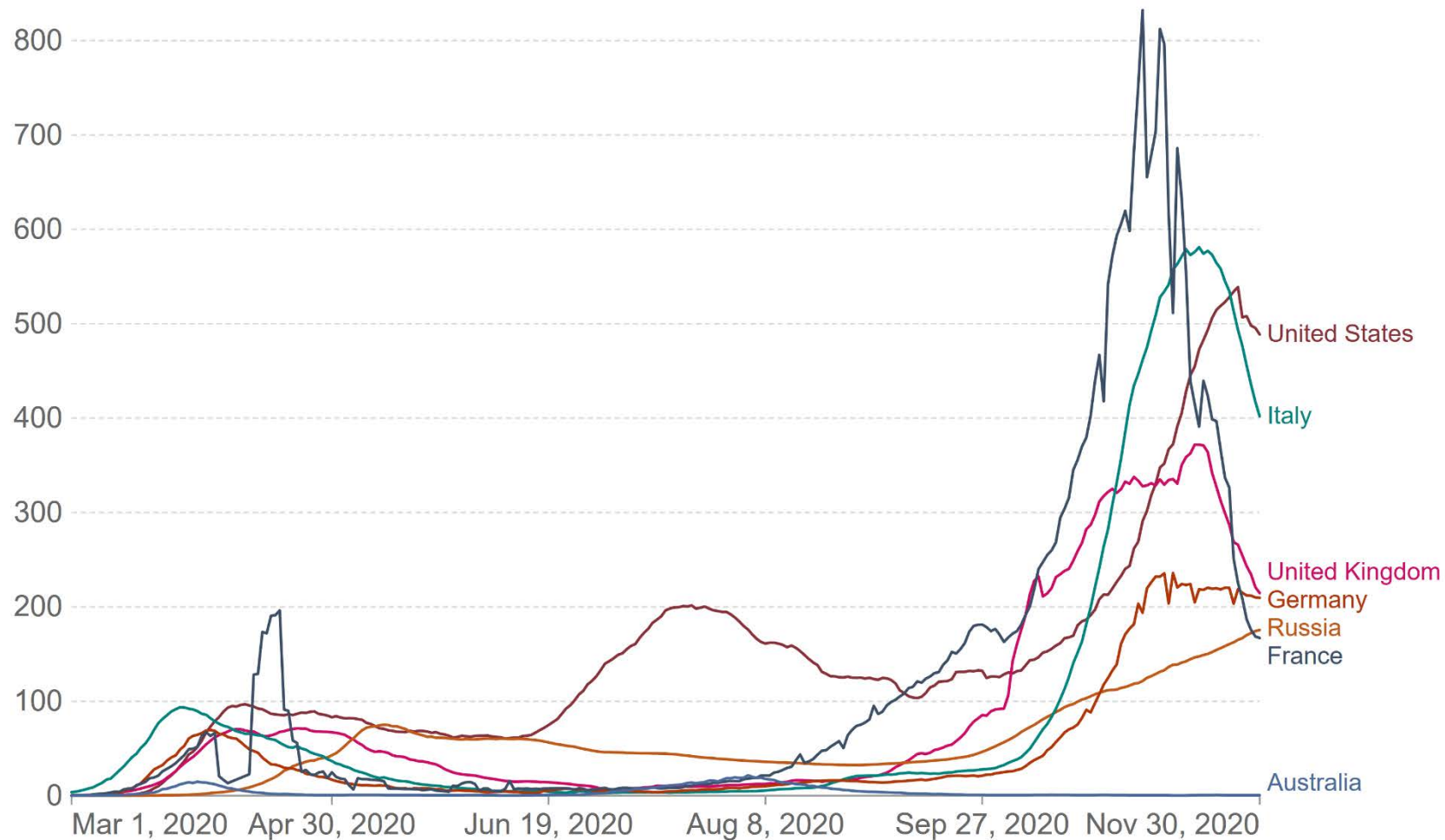
CC BY

Source: www.covidtracker.fr

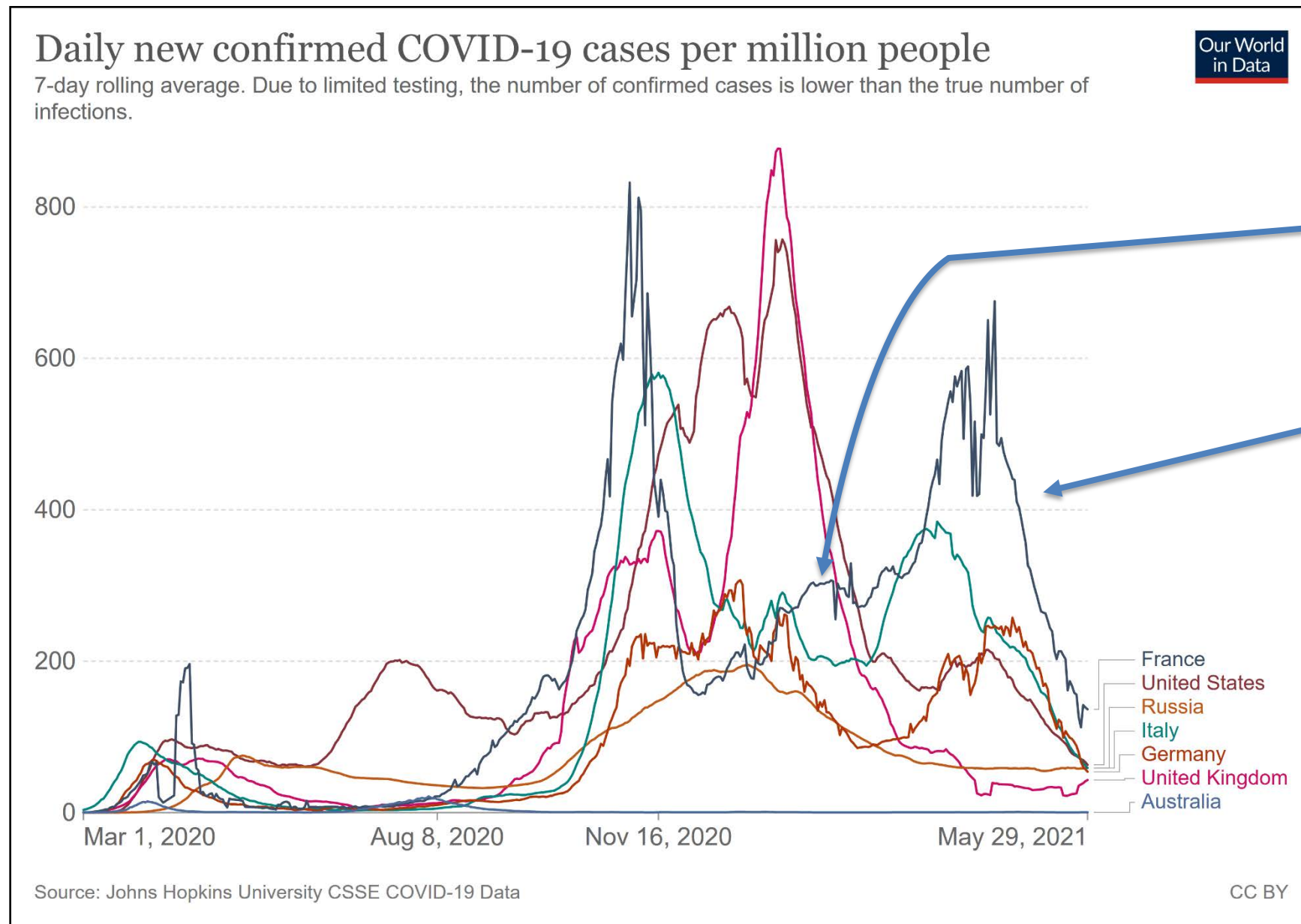
Seconde vague (Aout - Nov 2020)

Daily new confirmed COVID-19 cases per million people

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.



Troisième vague (avril - juin 2021)



Alpha

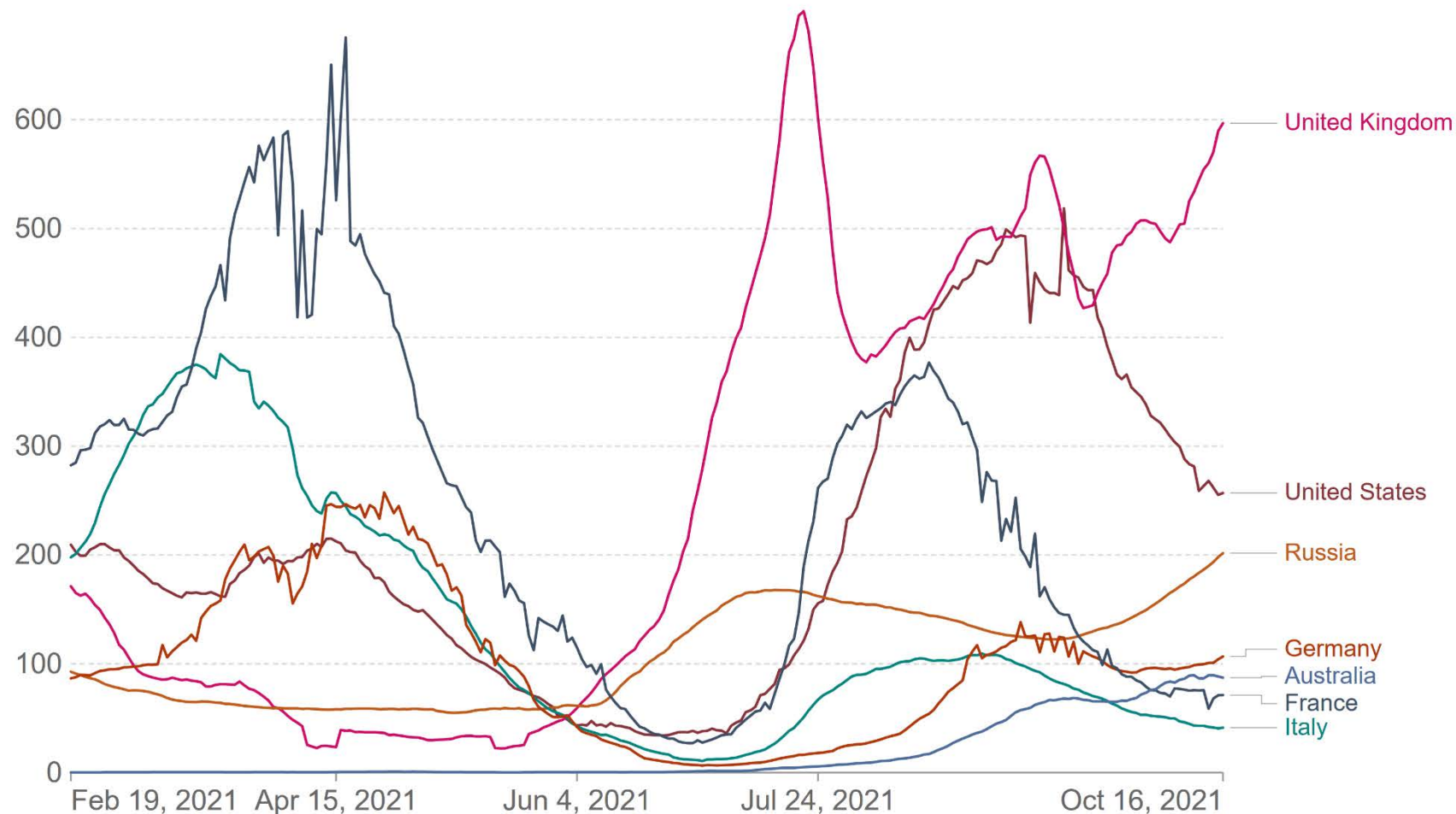
Delta

Quatrieme vague (depuis Oct 2021)

Daily new confirmed COVID-19 cases per million people

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.

Our World
in Data



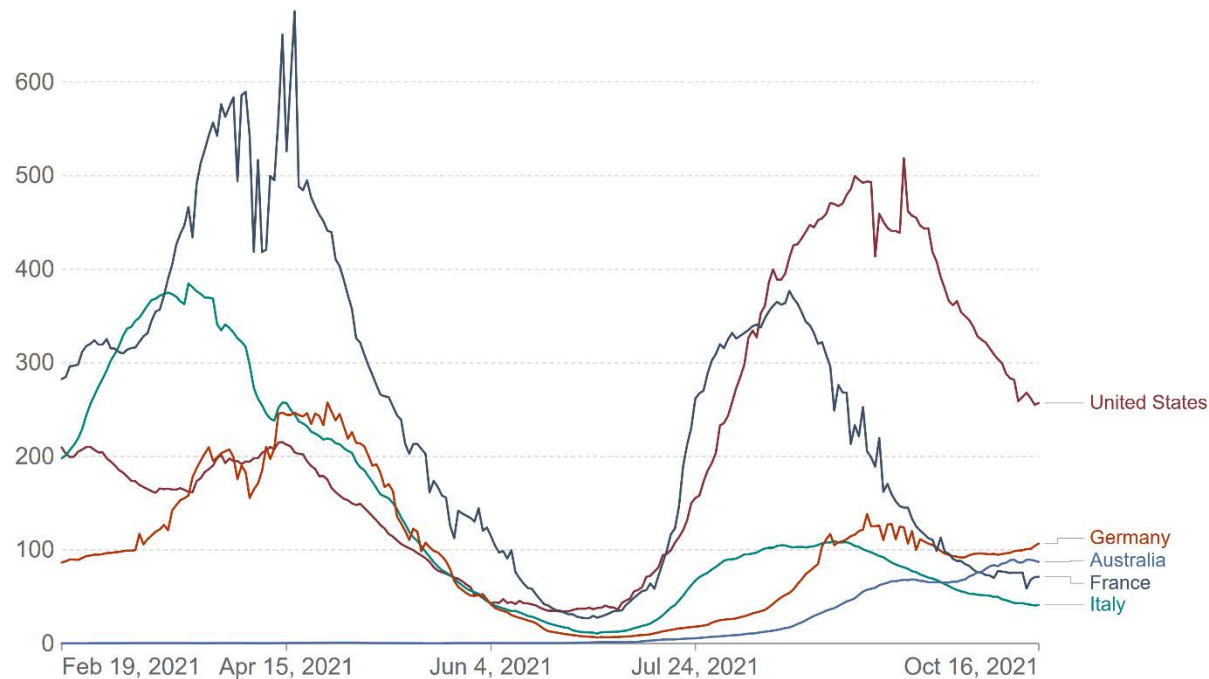
Source: Johns Hopkins University CSSE COVID-19 Data

CC BY Source: www.covidtracker.fr

Et la 5^e vague...

Daily new confirmed COVID-19 cases per million people

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.



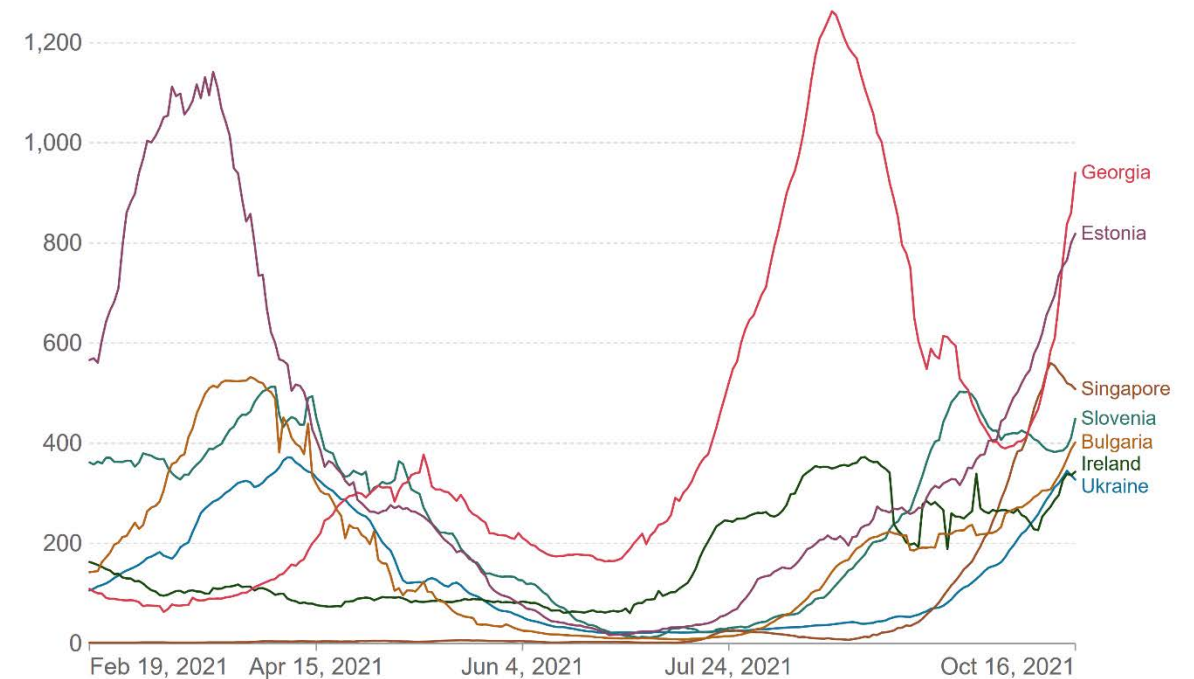
Source: Johns Hopkins University CSSE COVID-19 Data

Our World
in Data

CC BY

Daily new confirmed COVID-19 cases per million people

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.

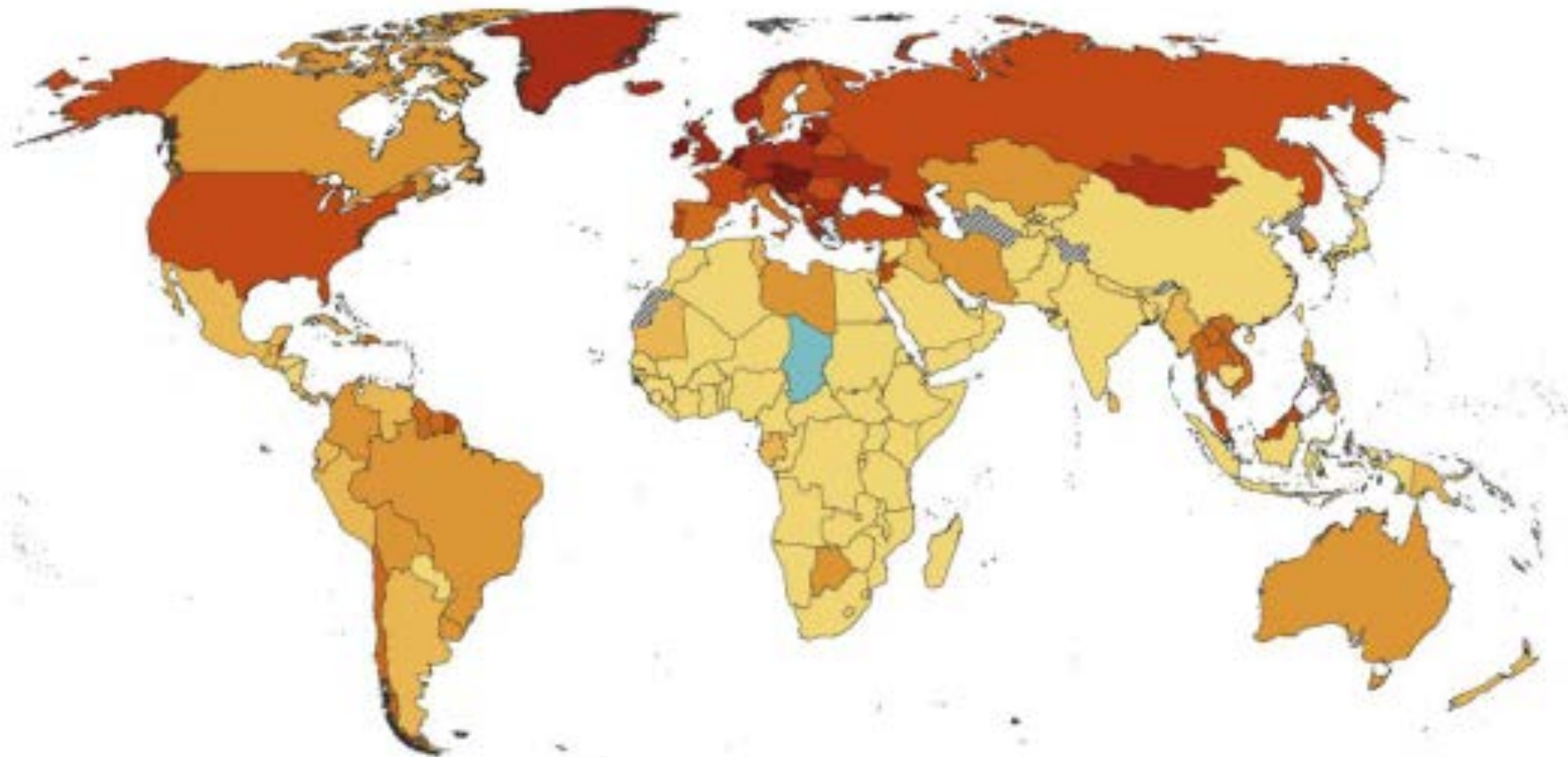


Source: Johns Hopkins University CSSE COVID-19 Data

Our World
in Data

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Situation internationale au 25 nov 2021



14-day COVID-19 case notification rate per 100 000, 2021-w45 to 2021-w46



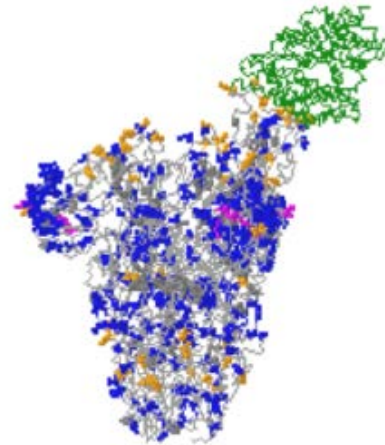
No cases reported by WHO and no cases identified in the public domain

Que s'est il passé ?

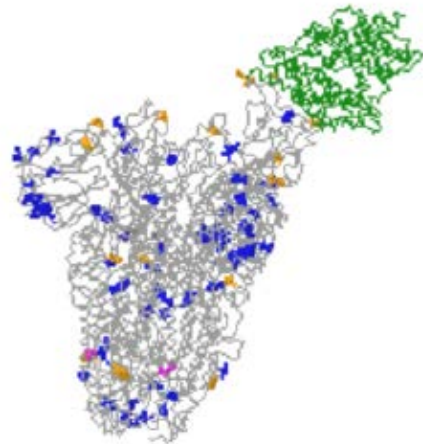
Tendance évolutive sur la Spike :

- 1 – modifications multiples
- 2 – évolution convergente

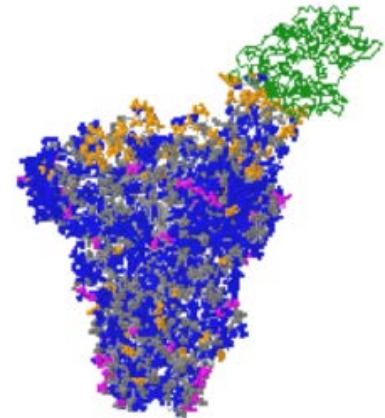
**K417T V445A N501Y E484K Y449H
T478K Y449S S494P F490S G485V**
in GR & GRY clade (B.1.1.1 & B.1.1.7)



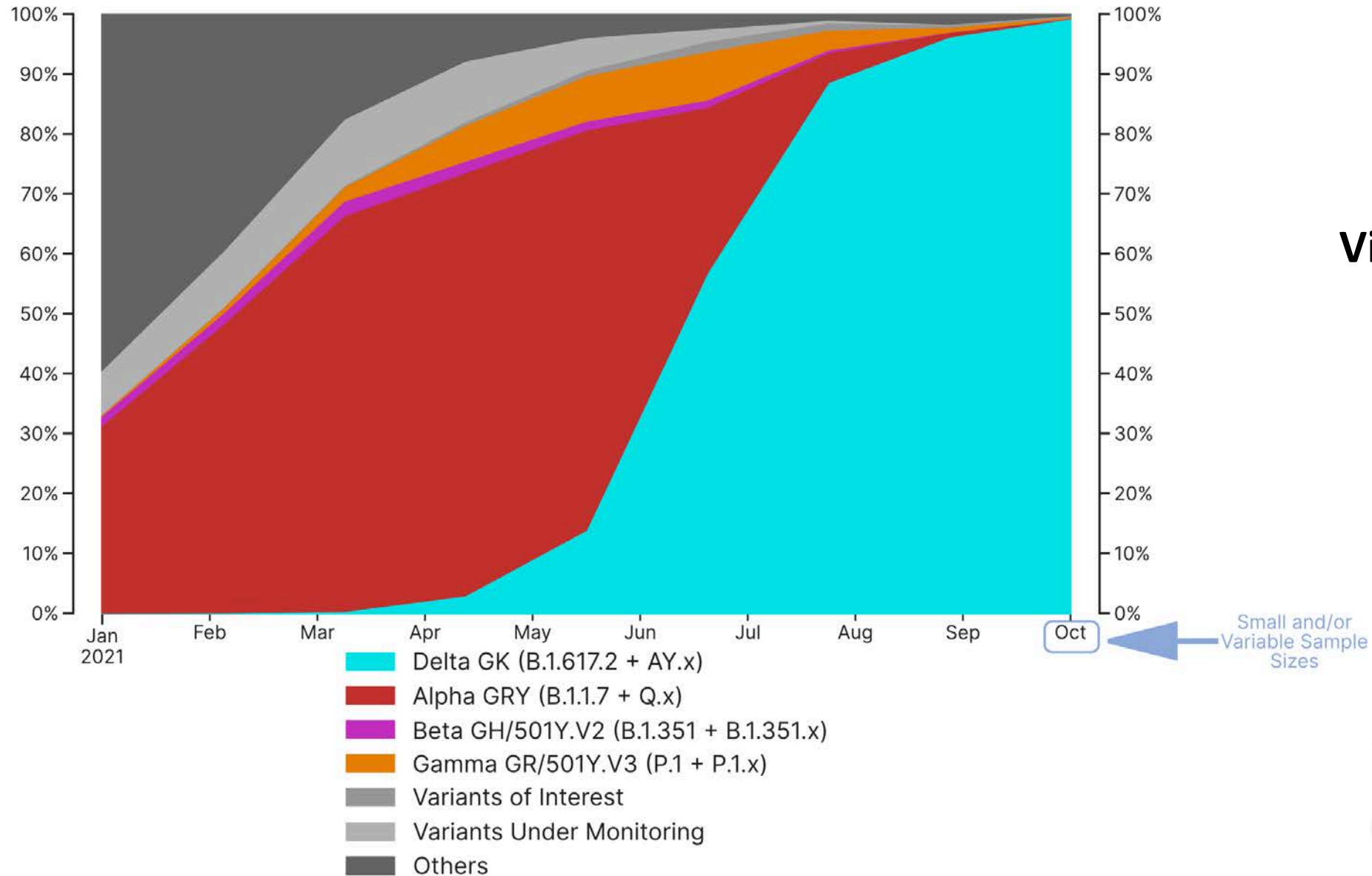
E484K T478K N501Y
in nonG clade (A, B & B.2)



**K458R G496V E484Q V445F V445A S494L
K458M F456L G446V S477N F490L G476S
N501T T478R G446A N501Y P499R E484K
E484V N437S G485R Q493L T478K S494P
E484G K417N N501I Q493E N439K S477G
A475V Q493P F490S S477I K417T R403K
L455F V445I G485S G446S E484D G446R**
in G, GK & GV clades (B.1, B.1.617.2, AY.* &
B.1.177)



Timecourse of variant distribution in all submitted sequences 02-11-21



Virus fitness matters!

We gratefully acknowledge the Authors from Originating and Submitting laboratories of sequence data on which the analysis is based.



by BII/GIS, A*STAR Singapore

Transmissibilité augmentée (Obermeyer et al, 2021)

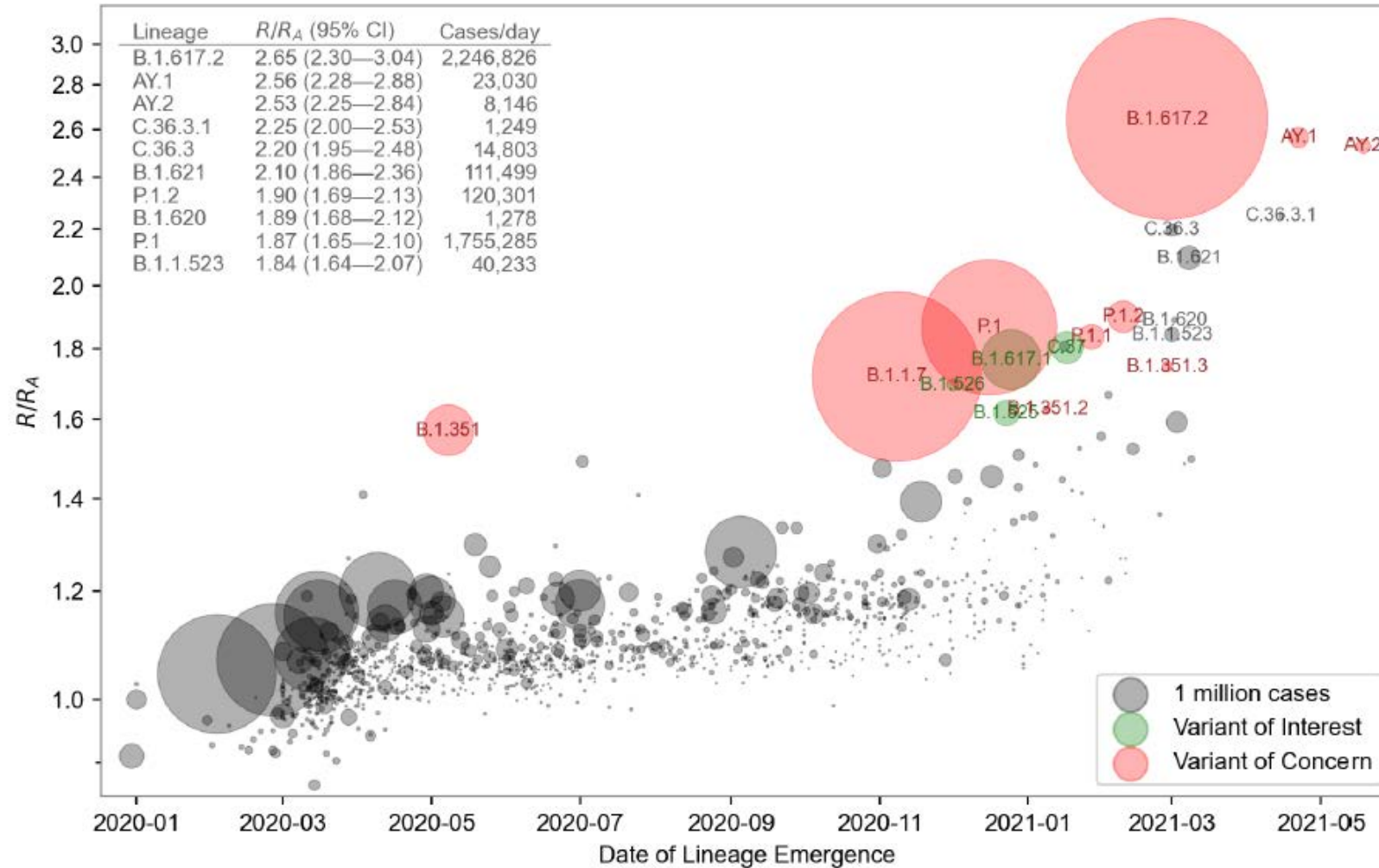


Figure 2. Growth rate versus date of lineage emergence. Circle size is proportional to cumulative case count inferred from lineage proportion estimates and confirmed case counts. Inset table lists the 10 most transmissible lineages inferred by the model. R/R_A : the fold increase in effective reproductive number over the Wuhan (A) lineage, assuming a fixed generation time of 5.5 days.

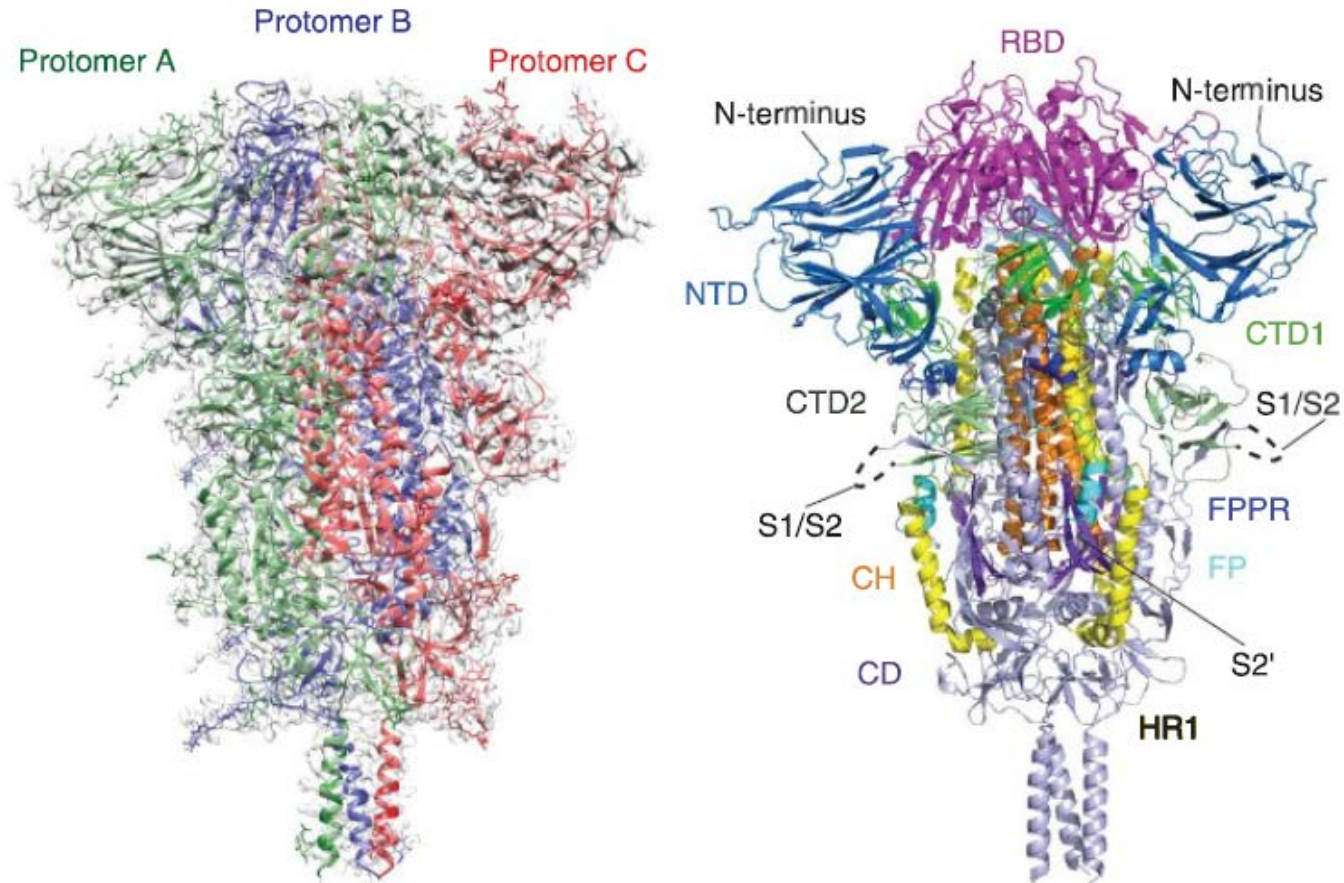
Pourquoi le Delta est plus transmissible

Rôle de la spike

CORONAVIRUS

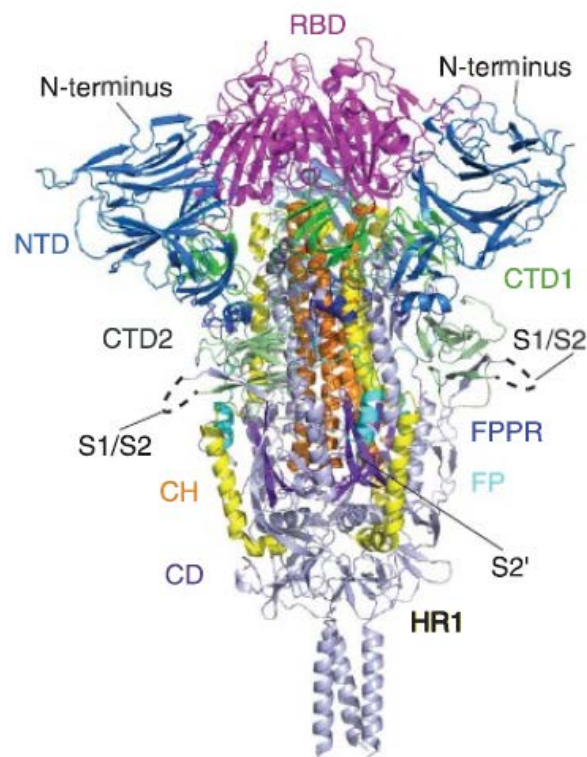
Distinct conformational states of SARS-CoV-2 spike protein

Yongfei Cai^{1,2*}, Jun Zhang^{1,2*}, Tianshu Xiao^{1,2}, Hanqin Peng¹, Sarah M. Sterling^{3,4}, Richard M. Walsh Jr.^{3,4}, Shaun Rawson^{3,4,5}, Sophia Rits-Volloch¹, Bing Chen^{1,2†}



Pourquoi le Delta est plus transmissible

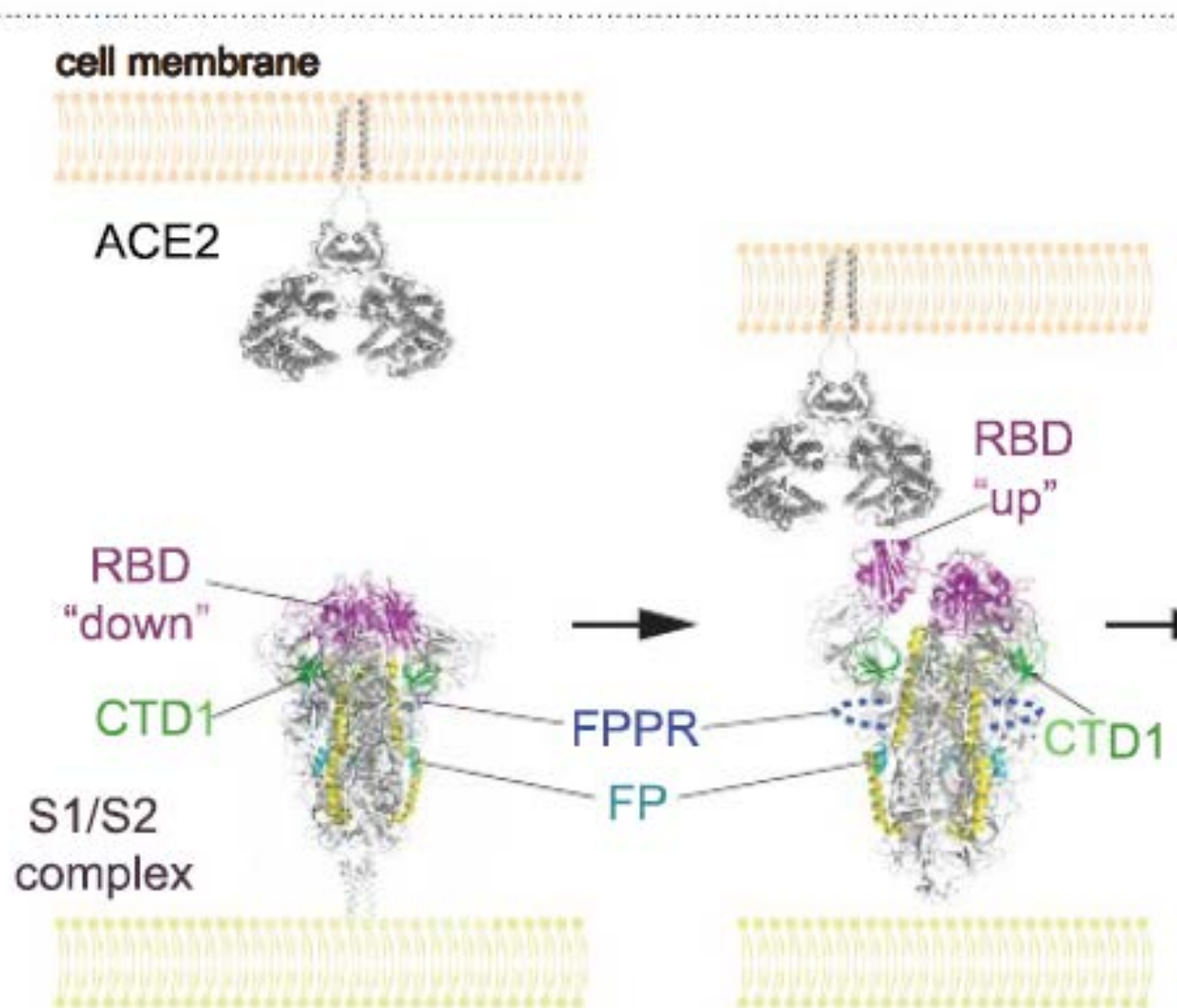
Rôle de la spike



CORONAVIRUS

Distinct conformational states of SARS-CoV-2 spike protein

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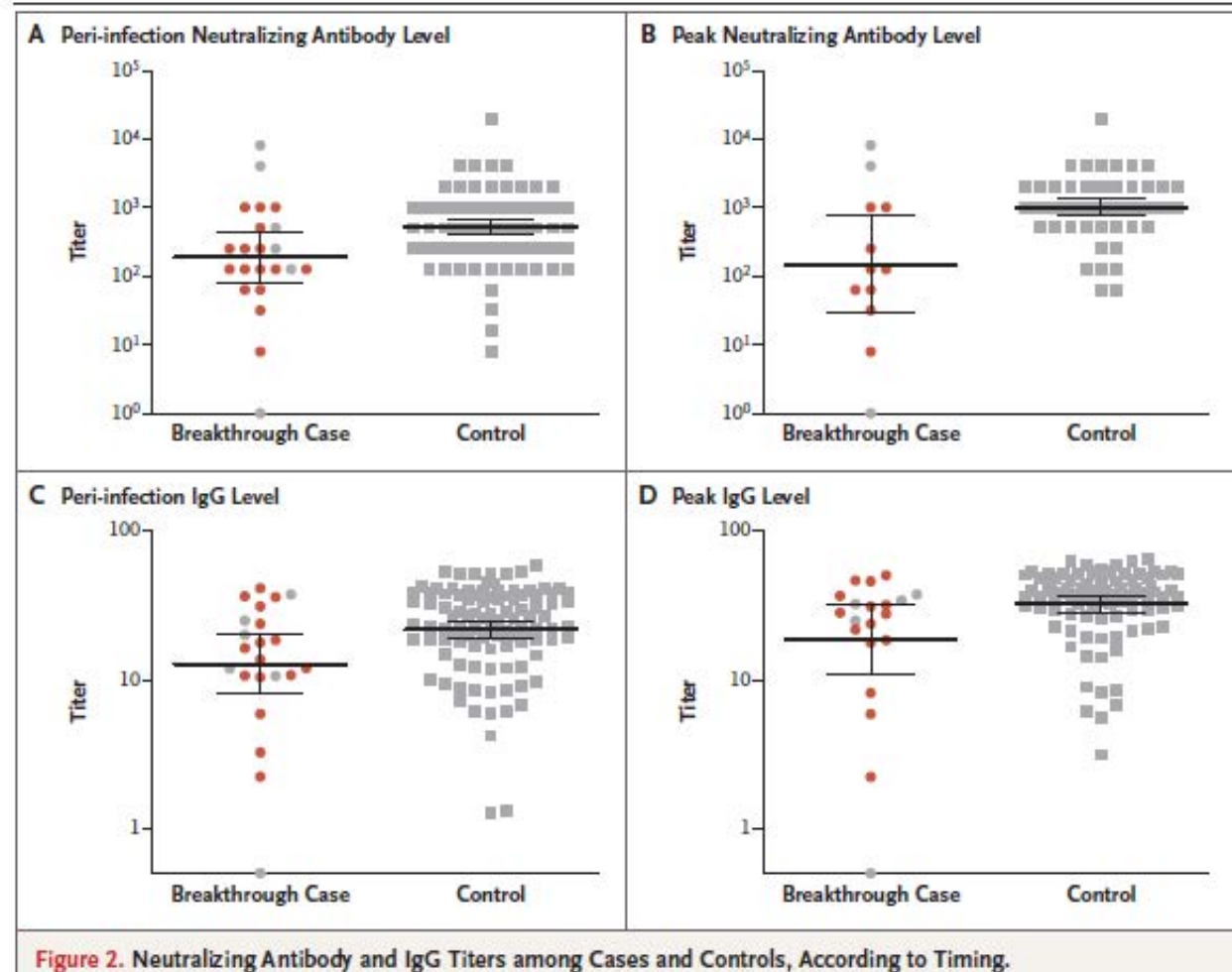
Et les vaccins dans tout ca?

Titre des anticorps post vaccinaux des infectés vs non infectés

ORIGINAL ARTICLE

Covid-19 Breakthrough Infections in Vaccinated Health Care Workers

Moriah Bergwerk, M.B., B.S., Tal Gonen, B.A., Yaniv Lustig, Ph.D., Sharon Amit, M.D.,
Marc Lipsitch, Ph.D., Carmit Cohen, Ph.D., Michal Mandelboim, Ph.D.,
Einav Gal Levin, M.D., Carmit Rubin, N.D., Victoria Indenbaum, Ph.D.,
Ilana Tal, R.N., Ph.D., Malka Zavitan, R.N., M.A., Neta Zuckerman, Ph.D.,
Adina Bar-Chaim, Ph.D., Yitshak Kreiss, M.D., and Gili Regev-Yochay, M.D.

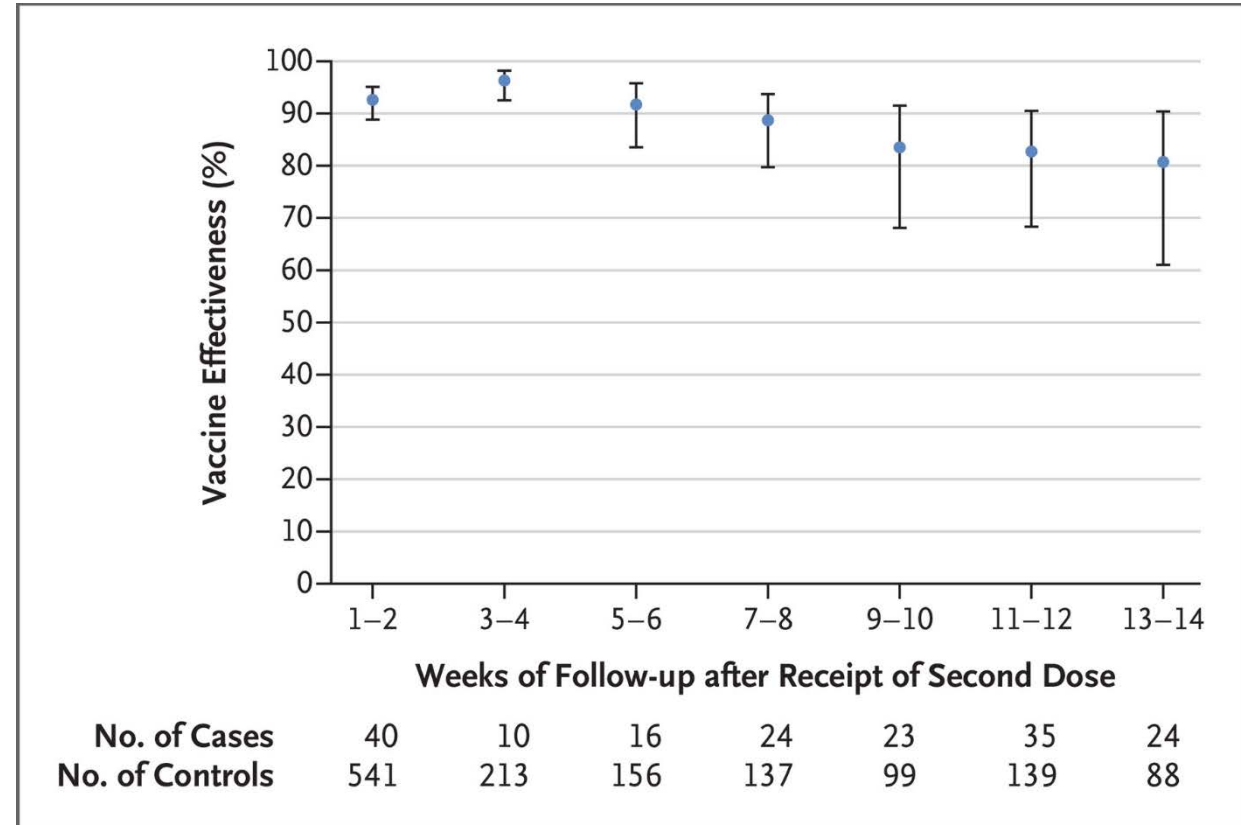


ORIGINAL ARTICLE

Effectiveness of mRNA Covid-19 Vaccine among U.S. Health Care Personnel

T. Pilishvili, R. Gierke, K.E. Fleming-Dutra, J.L. Farrar, N.M. Mohr, D.A. Talan, A. Krishnadasan, K.K. Harland, H.A. Smithline, P.C. Hou, L.C. Lee, S.C. Lim, G.J. Moran, E. Krebs, M.T. Steele, D.G. Beiser, B. Faine, J.P. Haran, U. Nandi, W.A. Schrading, B. Chinnock, D.J. Henning, F. Lovecchio, J. Lee, D. Barter, M. Brackney, S.K. Fridkin, K. Marceaux-Galli, S. Lim, E.C. Phipps, G. Dumyati, R. Pierce, T.M. Markus, D.J. Anderson, A.K. Debes, M.Y. Lin, J. Mayer, J.H. Kwon, N. Safdar, M. Fischer, R. Singleton, N. Chea, S.S. Magill, J.R. Verani, and S.J. Schrag, for the Vaccine Effectiveness among Healthcare Personnel Study Team*

Durée de la protection vaccinale



Durabilité des protection en fonction des vaccins

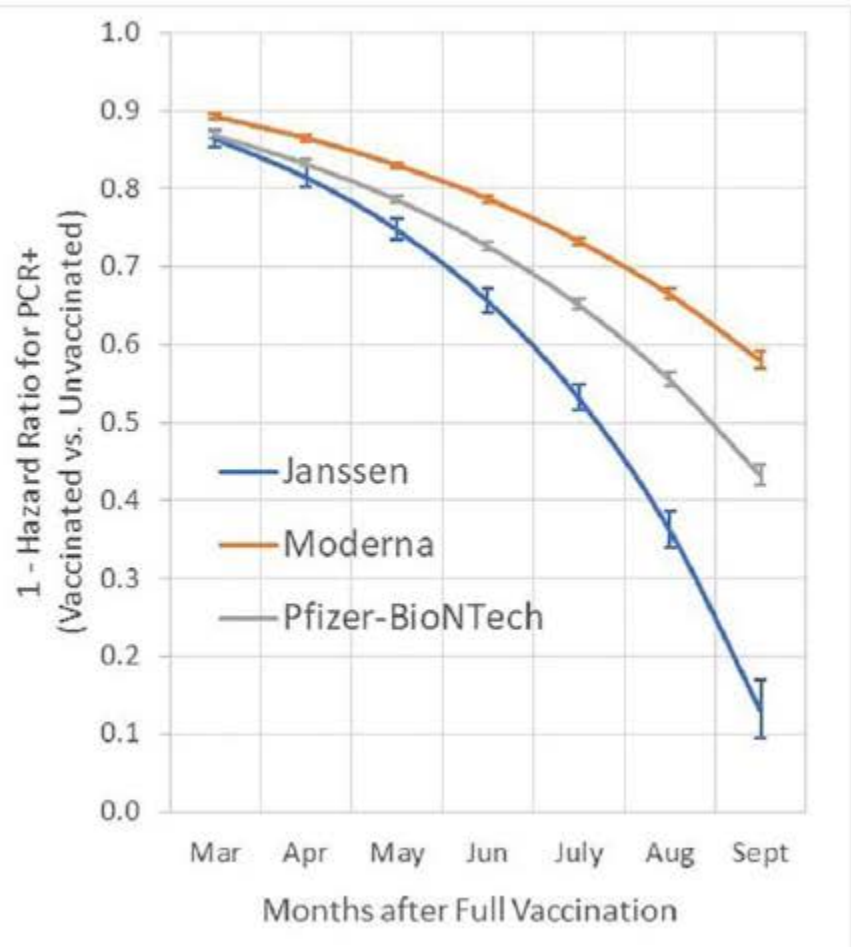


Fig. 1. Time dependent vaccine effectiveness against SARS-CoV-2 infection as estimated from Cox proportional hazards models, adjusted for age, race, ethnicity, sex, and comorbidity score. Vaccine effectiveness presented as $(1 - \text{hazard ratio} \times 100)$ and 95% confidence intervals. Effectiveness for each month was estimated from contrasts using product terms for vaccination status by time to most recent RT-PCR assay.

Vaccination hétérologue

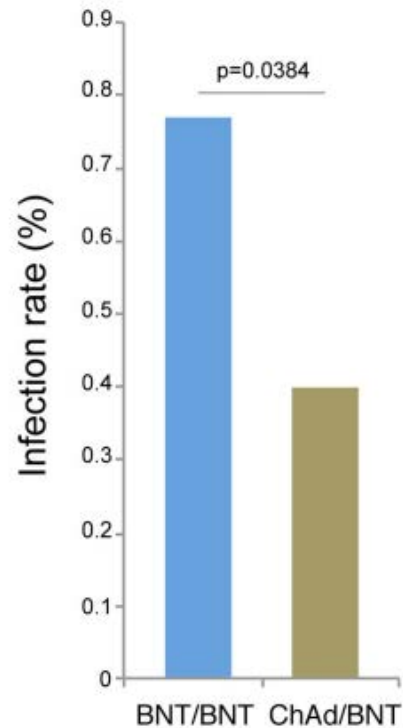


Fig. 1 | Incidence of SARS-CoV-2 infection after different vaccination regimens. Histograms show the infection rate (as documented by positive SARS-CoV-2 RT-PCR) among groups of healthcare workers who were vaccinated with the homologous BNT/BNT combination (n=81/10609) within the recommended 4-week timeframe between the two doses, or with the BNT boost after receiving the first ChAd dose (n=10/2512) approximately 12 weeks before, as recorded by the service of occupational medicine, Hospices Civils de

nature

<https://doi.org/10.1038/s41586-021-04120-y>

Accelerated Article Preview

Immunogenicity and efficacy of heterologous ChadOx1/BNT162b2 vaccination

VIEW

Vaccination hétérologue

Immunogenicity and efficacy of heterologous ChadOx1/BNT162b2 vaccination

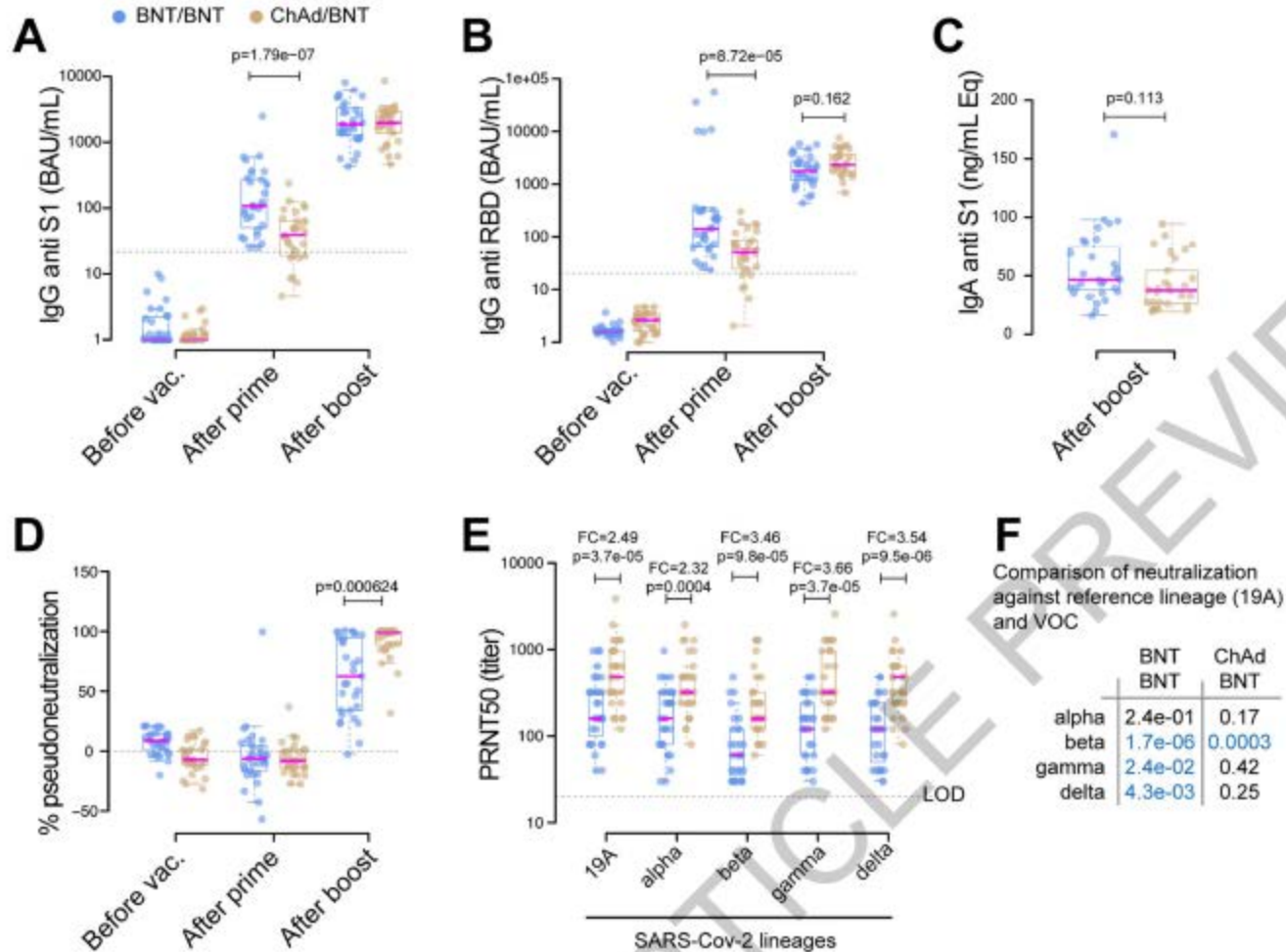


Fig. 2 | Heterologous vaccination induces higher neutralizing antibody against different SARS-CoV-2 strains (E-F), as indicated. Data show the % of

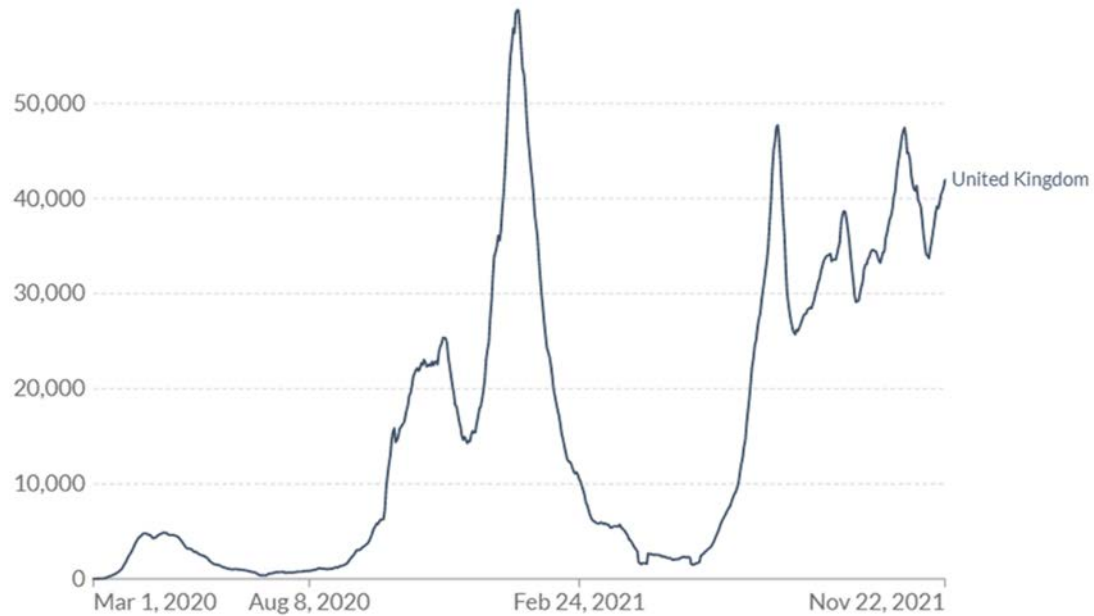
Situation dans le UK

Daily new confirmed COVID-19 cases

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.

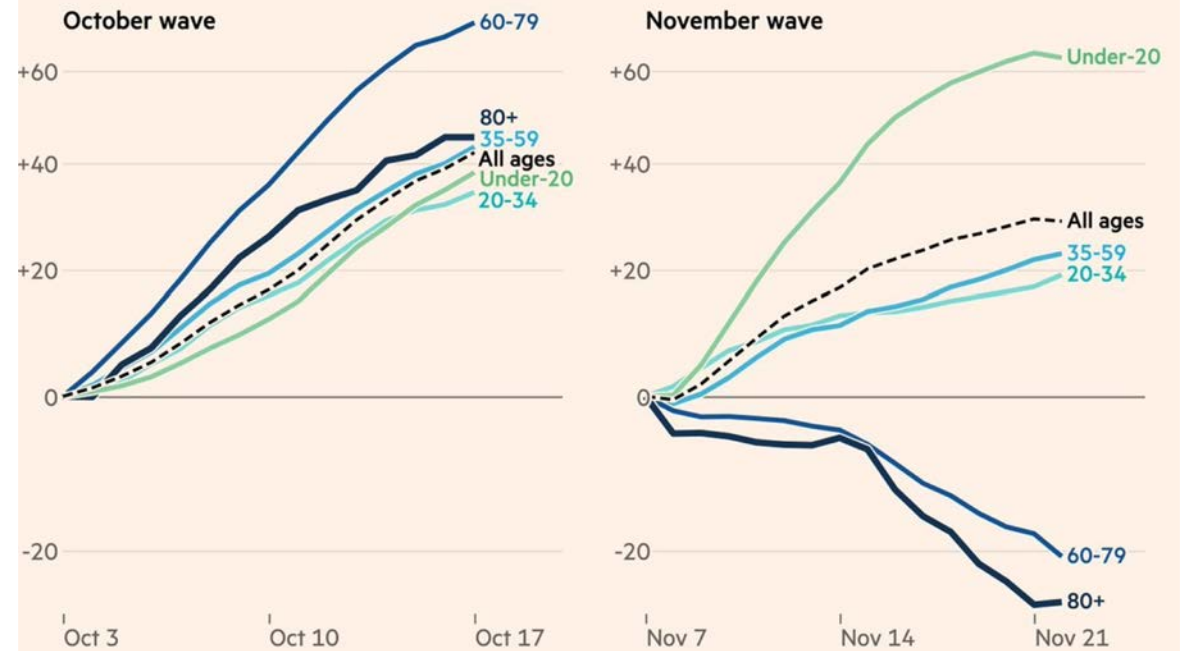
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Unlike in recent waves, cases among England's elderly are now falling while younger age groups' rates rise

Percentage change in case rate since start of increase, by age group



Source: FT analysis of UK government Covid-19 dashboard
© FT

Effet de la 3^e dose sur la transmission (données Israël)

Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study

Noam Barda*, Noa Dagan*, Cyrille Cohen, Miguel A Hernán, Marc Lipsitch, Isaac S Kohane, Ben Y Reist, Ran D Balicer†

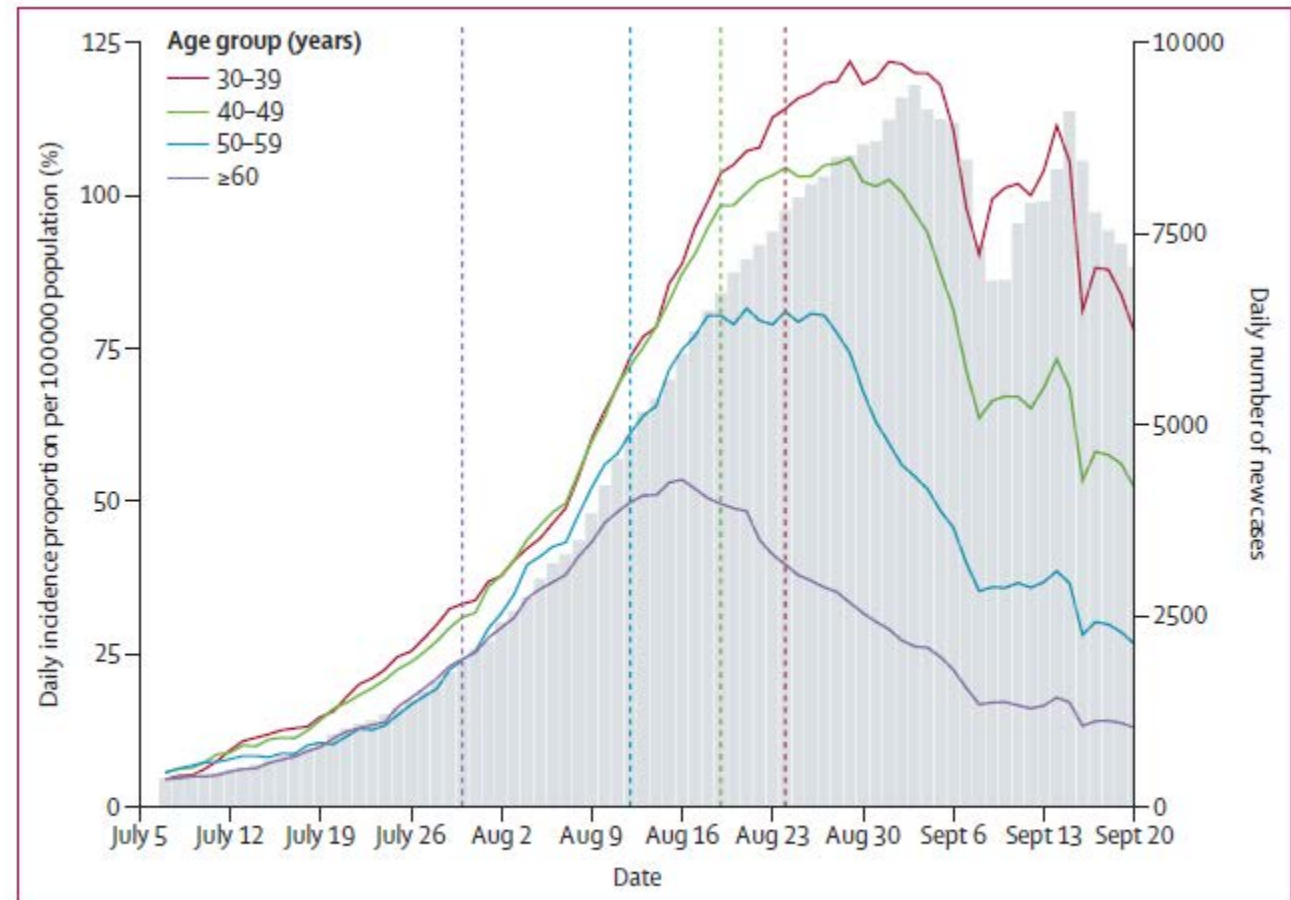


Figure 2: Daily incidence of SARS-CoV-2 infection for different age groups around initiation of third dose vaccination

Les questions actuelles

- La vaccination va-t-elle être suffisante
 - Nouvelle souche vaccinale
 - Nouveau schéma vaccinal
- Comment va évoluer l'épidémie
 - Nouveau variant
 - Persistance ou non du virus
 - Quid des autres virus respiratoires
- Comment gérer les mesures de contrôle
 - Maintien de toutes les mesures de contrôle
 - Renforcement de la vaccination

Oui	Non

Bien	Mal

Oui	Non

Et il y en aura d'autres, des phénomènes pandémiques...

Il convient juste d'être préparé a l'imprevisible



MERCI

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**GENomique
EPIdémologique
des maladies
Infectieuses**



Public SARS-CoV-2 databases

GISAID

NextStrain

COV-GLUE

Covidtracker

ECDC

Ressource documentaire

Pr Odile Launay

Pr Alain Fischer

Pr Marie-Paule Kieny

Pr Derek Smith

HCL
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