Il punto clinico-epidemiologico e sulla vaccinazione

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SHORT COMMUNICATION

Early phylogenetic estimate of the effective reproduction number of SARS-CoV-2

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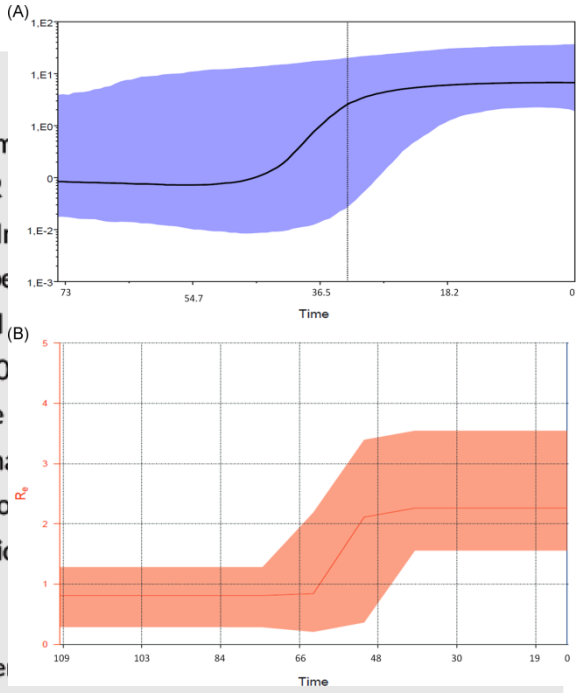
Abstract

To reconstruct the evolutionary dynam
causing an outbreak in Wuhan, China, 52
2020 at Global Initiative on Sharing All I
used to estimate the reproduction numbe
birth-death skyline method) indicated
7.8×10^{-4} subs/site/year (range, 1.1×10
root of 73 days. The estimated R value
0.8 to 2.4 in December 2019. The estima
between 3.6 and 4.1 days. This study pro
the surveillance of emerging new infecti

KEYWORDS

evolutionary dynamics, reproductive numbe



Science 2020;369: 1603–7, 25 September 2020

CORONAVIRUS

Adaptation of SARS-CoV-2 in BALB/c mice for testing vaccine efficacy

Hongjing Gu[1]*, Qi Chen[1]*, Guan Yang[2]*, Lei He[1]*, Hang Fan[1]*, Yong-Qiang Deng[1]*, Yanxiao Wang[2], Yue Teng[1], Zhongpeng Zhao[1], Yujun Cui[1], Yuchang Li[1], Xiao-Feng Li[1], Jiangfan Li[1], Na-Na Zhang[1], Xiaolan Yang[1], Shaolong Chen[1], Yan Guo[1], Guangyu Zhao[1], Xiliang Wang[1], De-Yan Luo[1], Hui Wang[1], Xiao Yang[2], Yan Li[3], Gencheng Han[3], Yuxian He[4], Xiaojun Zhou[5], Shusheng Geng[6], Xiaoli Sheng[6], Shibo Jiang[7]†‡, Shihui Sun[1]†‡, Cheng-Feng Qin[1]†‡, Yusen Zhou[1]‡§

The ongoing coronavirus disease 2019 (COVID-19) pandemic has prioritized the development of small-animal models for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We adapted a clinical isolate of SARS-CoV-2 by serial passaging in the respiratory tract of aged BALB/c mice. The resulting mouse-adapted strain at passage 6 (called MASCp6) showed increased infectivity in mouse lung and led to interstitial pneumonia and inflammatory responses in both young and aged mice after intranasal inoculation. Deep sequencing revealed a panel of adaptive mutations potentially associated with the increased virulence. In particular, the N501Y mutation is located at the receptor binding domain (RBD) of the spike protein. The protective efficacy of a recombinant RBD vaccine candidate was validated by using this model. Thus, this mouse-adapted strain and associated challenge model should be of value in evaluating vaccines and antivirals against SARS-CoV-2.

All but one of the newly-characterized genomes belonged to the lineage B.1 (D614G), the most frequently identified in European countries, including Italy. Only a single sequence was found to belong to lineage B.

tMRCA estimation confirmed the probable origin of the epidemic between the end of January and the beginning of February with a rapid increase in the number of infections between the end of February and mid-March. Since early February, an effective reproduction number (Re) greater than 1 was estimated, which then increased reaching the peak of 2.3 in early March, confirming the circulation of the virus before the first COVID-19 cases were documented.

Viruses 2020, 12, 798;doi:10.3390/v12080798

ARTICLES
https://doi.org/10.1038/s41564-020-00838-z

nature microbiology

Genomic epidemiology reveals multiple introductions of SARS-CoV-2 from mainland Europe into Scotland

Ana da Silva Filipe[1,17], James G. Shepherd[1,17], Thomas Williams[2,17], Joseph Hughes[1,17], Elihu Aranday-Cortes[1], Patawee Asamaphan[1], Shirin Ashraf[1], Carlos Balcazar[3], Kirstyn Brunker[1], Alasdair Campbell[4], Stephen Carmichael[1], Chris Davis[1], Rebecca Dewar[5], Michael D. Gallagher[6], Rory Gunson[7,8], Verity Hill[9], Antonia Ho[1], Ben Jackson[9], Edward James[10], Natasha Jesudason[1], Natasha Johnson[1], E. Carol McWilliam Leitch[1], Kathy Li[1], Alasdair MacLean[7], Daniel Mair[1], David A. McAllister[11,12], John T. McCrone[9], Sarah E. McDonald[1], Martin P. McHugh[5,13], A. Keith Morris[14], Jenna Nichols[1], Marc Niebel[1], Kyriaki Nomikou[1], Richard J. Orton[1], Áine O'Toole[9], Massimo Palmarini[1], Benjamin J. Parcell[15], Yasmin A. Parr[1], Andrew Rambaut[9], Stefan Rooke[8], Sharif Shaaban[11], Rajiv Shah[1], Joshua B. Singer[1], Katherine Smollett[1], Igor Starinskij[7], Lily Tong[1], Vattipally B. Sreenu[1], Elizabeth Wastnedge[5], The COVID-19 Genomics UK (COG-UK) Consortium[16]*, Matthew T. G. Holden[11,13,18], David L. Robertson[1,18], Kate Templeton[5,18] and Emma C. Thomson[1,17,18] ✉

Coronavirus disease 2019 (COVID-19) was first diagnosed in Scotland on 1 March 2020. During the first month of the outbreak, 2,641 cases of COVID-19 led to 1,832 hospital admissions, 207 intensive care admissions and 126 deaths. We aimed to identify the source and number of introductions of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into Scotland using a combined phylogenetic and epidemiological approach. Sequencing of 1,314 SARS-CoV-2 viral genomes from available patient samples enabled us to estimate that SARS-CoV-2 was introduced to Scotland on at least 283 occasions during February and March 2020. Epidemiological analysis confirmed that early introductions of SARS-CoV-2 originated from mainland Europe (the majority from Italy and Spain). We identified subsequent early outbreaks in the community, within healthcare facilities and at an international conference. Community transmission occurred after 2 March, 3 weeks before control measures were introduced. Earlier travel restrictions or quarantine measures, both locally and internationally, would have reduced the number of COVID-19 cases in Scotland. The risk of multiple reintroduction events in future waves of infection remains high in the absence of population immunity.

Relevant mutations and deletions: D614G

Spike mutation that favours the binding of virus to ACE-2 receptor

Evidence that D614G Increases Infectivity of the COVID-19 Virus

Bette Korber,[1,2,10,*] Will M. Fischer,[1] Sandrasegaram Gnanakaran,[1] Hyejin Yoon,[1] James Theiler,[1] Werner Abfalterer,[1] Nick Hengartner,[1] Elena E. Giorgi,[1] Tanmoy Bhattacharya,[1] Brian Foley,[1] Kathryn M. Hastie,[3] Matthew D. Parker,[4] David G. Partridge,[5] Cariad M. Evans,[5] Timothy M. Freeman,[4] Thushan I. de Silva,[5,6] on behalf of the Sheffield COVID-19 Genomics Group, Charlene McDanal,[7] Lautaro G. Perez,[7] Haili Tang,[7] Alex Moon-Walker,[3,8,9] Sean P. Whelan,[9] Celia C. LaBranche,[7] Erica O. Saphire,[3] and David C. Montefiori[7]

SARS-CoV-2 D614G variant exhibits efficient replication ex vivo and transmission in vivo

Yixuan J. Hou[1*], Shiho Chiba[2*], Peter Halfmann[2], Camille Ehre[3], Makoto Kuroda[2], Kenneth H. Dinnon III[4], Sarah R. Leist[1], Alexandra Schäfer[1], Noriko Nakajima[5], Kenta Takahashi[5], Rhianna E. Lee[3], Teresa M. Mascenik[3], Rachel Graham[1], Caitlin E. Edwards[1], Longping V. Tse[1], Kenichi Okuda[3], Alena J. Markmann[6], Luther Bartelt[6], Aravinda de Silva[4], David M. Margolis[4,6], Richard C. Boucher[3], Scott H. Randell[3], Tadaki Suzuki[5], Lisa E. Gralinski[1], Yoshihiro Kawaoka[2,7†], Ralph S. Baric[1,4†]

Article Nature | www.nature.com

Spike mutation D614G alters SARS-CoV-2 fitness

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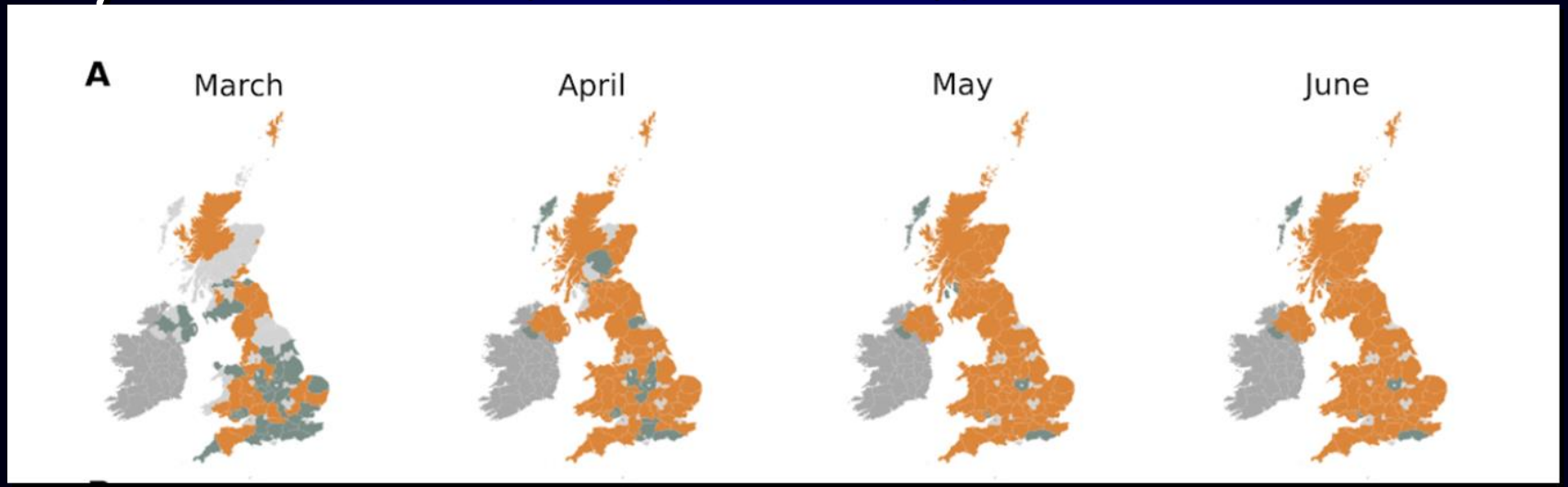
Accepted: 20 October 2020

Jessica A. Plante[1,2,3,12], Yang Liu[4,12], Jianying Liu[2,3,12], Hongjie Xia[4], Bryan A. Johnson[2], Kumari G. Lokugamage[3], Xianwen Zhang[4], Antonio E. Muruato[2,3], Jing Zou[4], Camila R. Fontes-Garfias[4], Divya Mirchandani[1,2,3], Dionna Scharton[1,2,3], John P. Bilello[5], Zhiqiang Ku[6], Zhiqiang An[6], Birte Kalveram[7], Alexander N. Freiberg[2,7,8,9], Vineet D. Menachery[2,3],

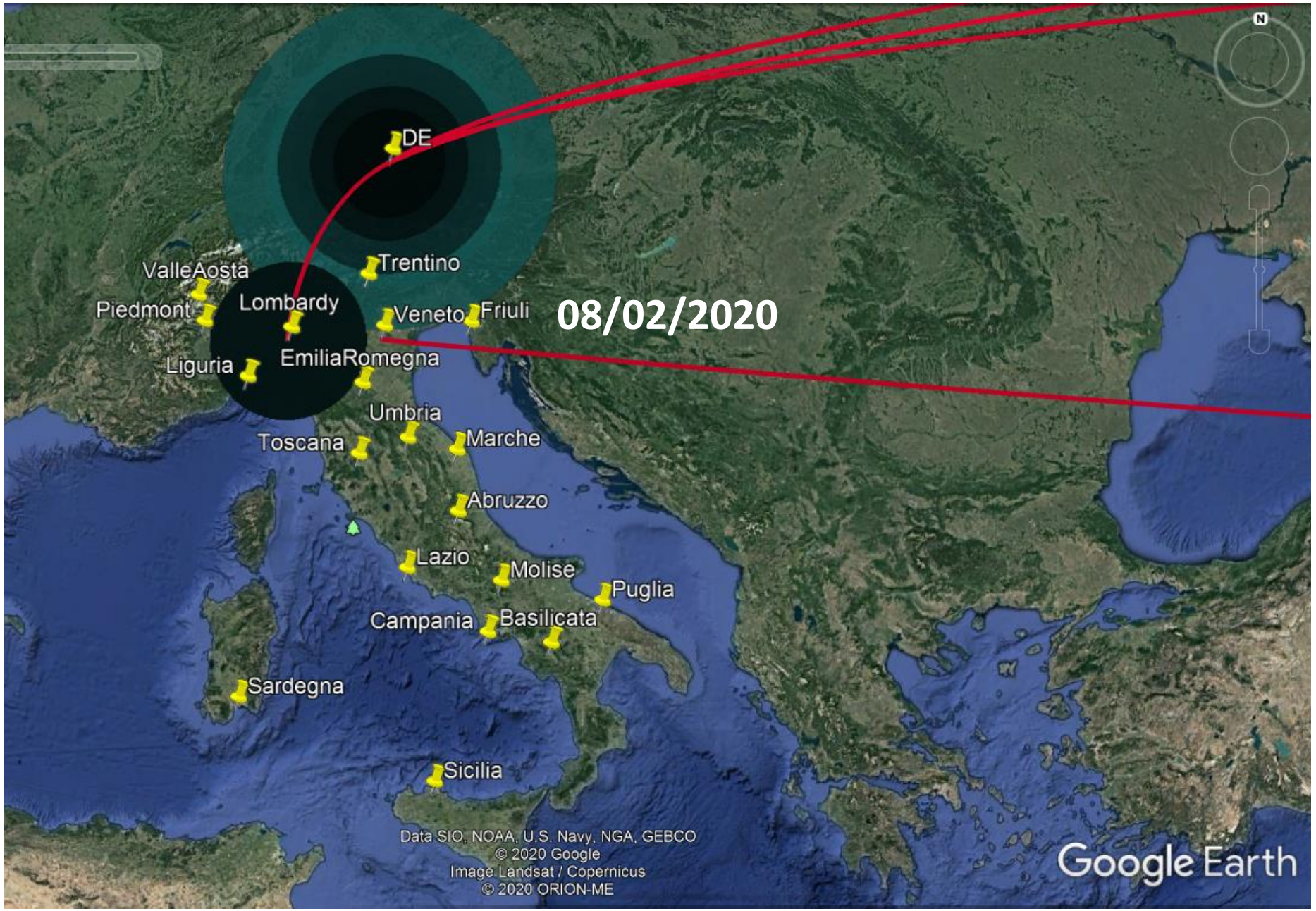
Evaluating the effects of SARS-CoV-2 Spike mutation D614G on transmissibility and pathogenicity

- More than 25,000 whole genome SARS-CoV-2 sequences collected by COVID-19 Genomics UK Consortium.



- Patients infected with the Spike 614G variant did not have higher COVID-19 mortality, but younger patients have slightly increased odds of 614G carriage.

Volz et al.medRxiv preprint doi:https://doi.org/10.1101/2020.07.31.20166082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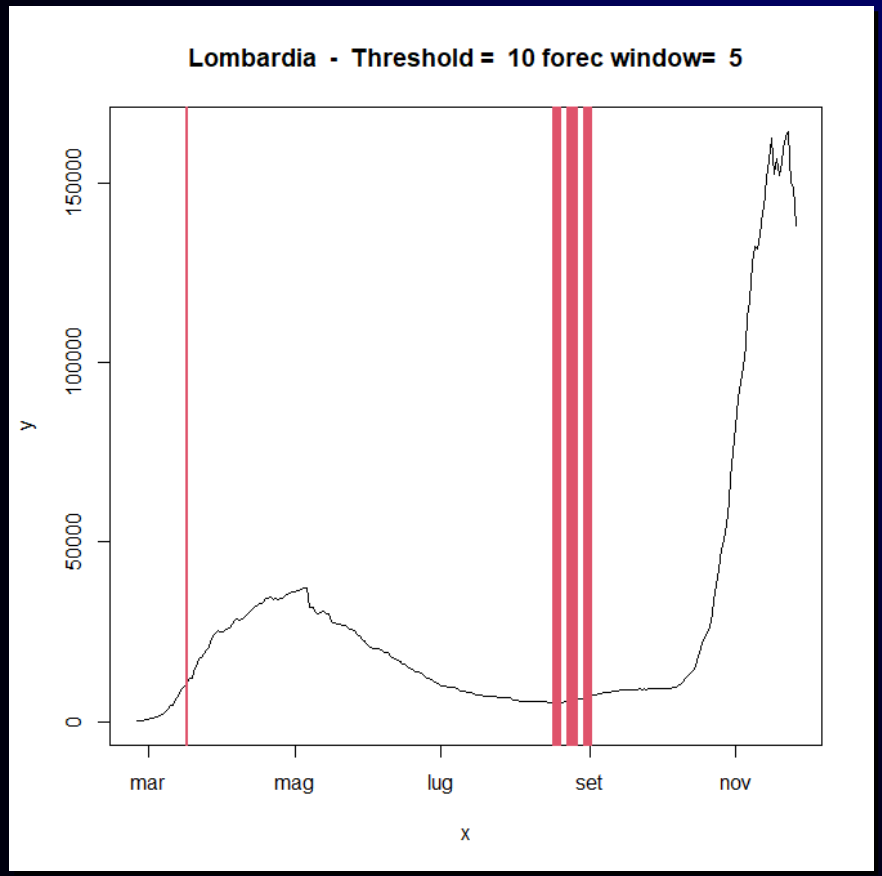
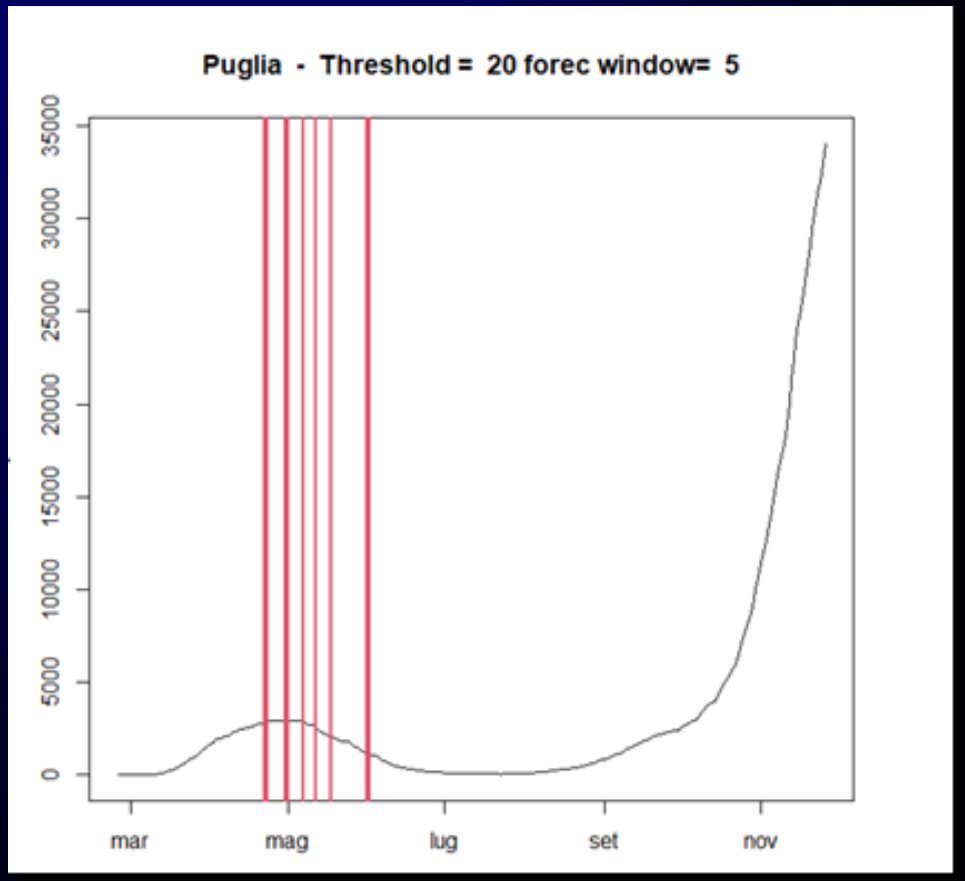
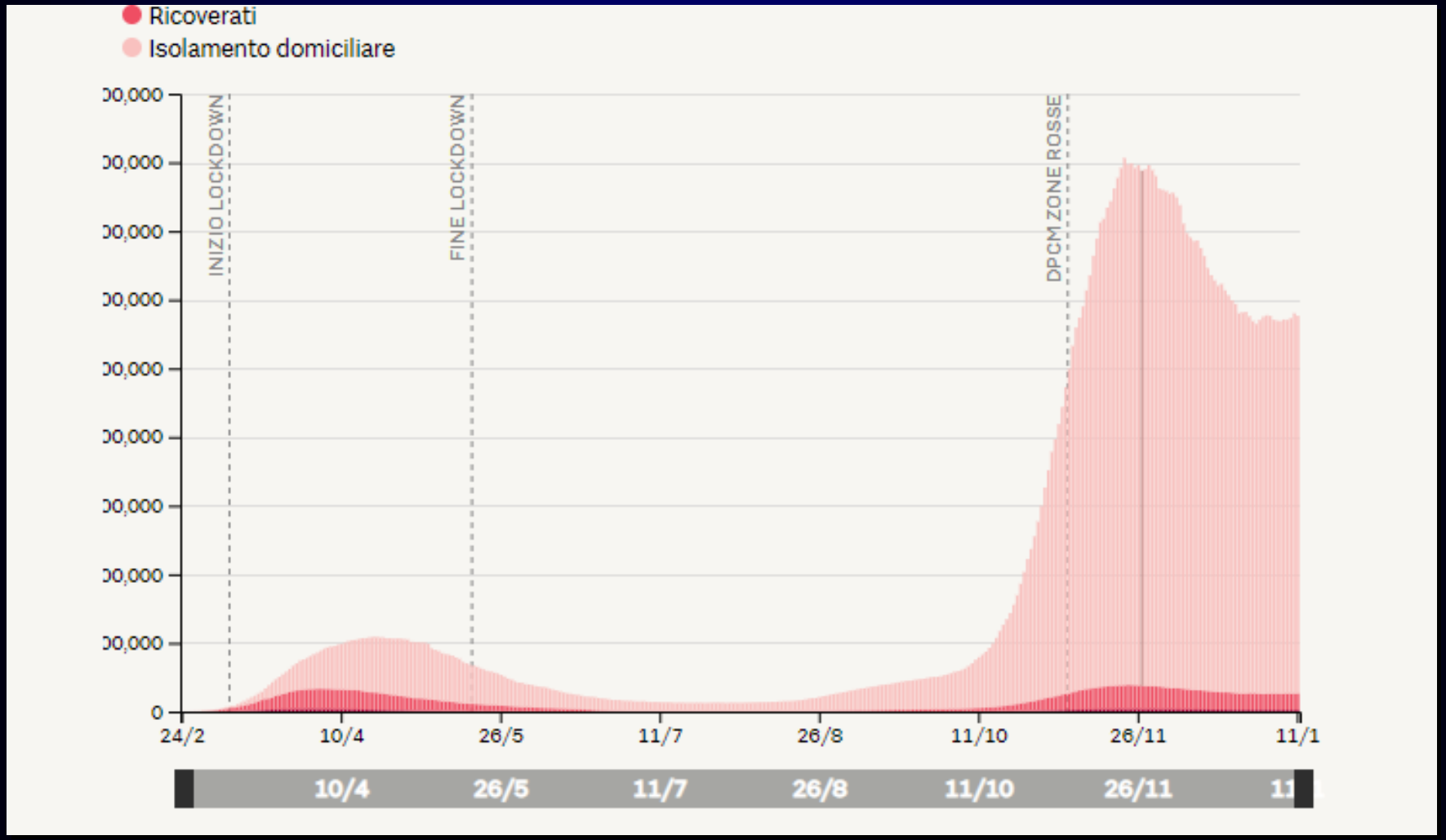
Analisi esplorativa regionale della serie dei positivi per l'individuazione di anomali incrementi.



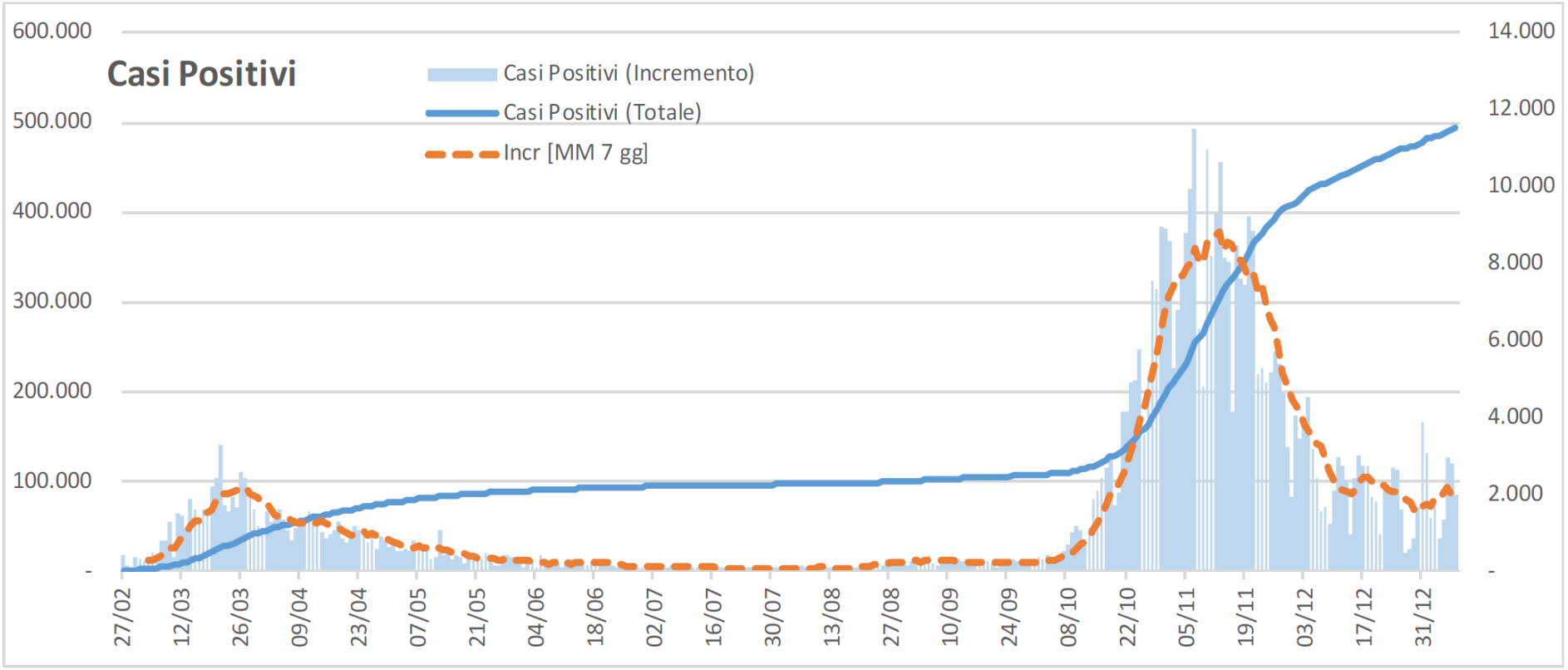


Cortesia di Livio Fenga ISTAT

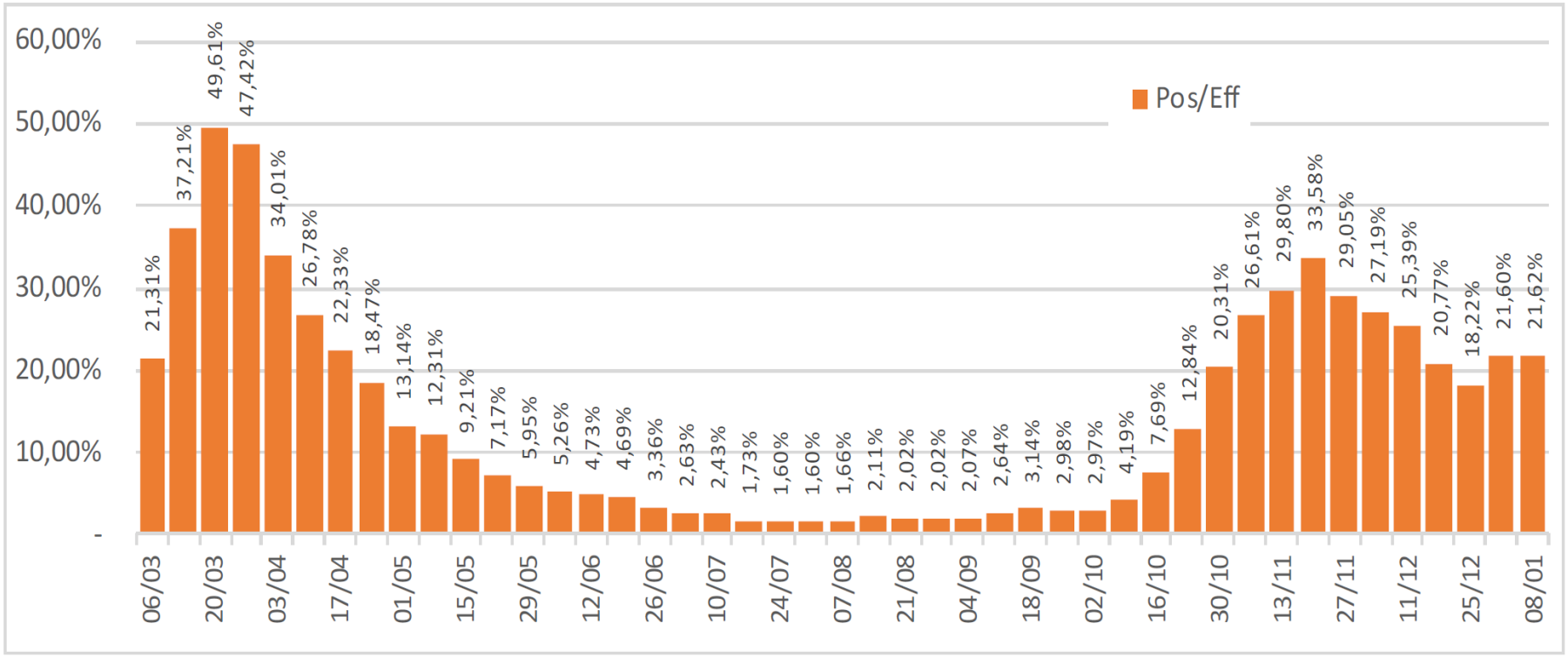
Isolamenti e ricoveri

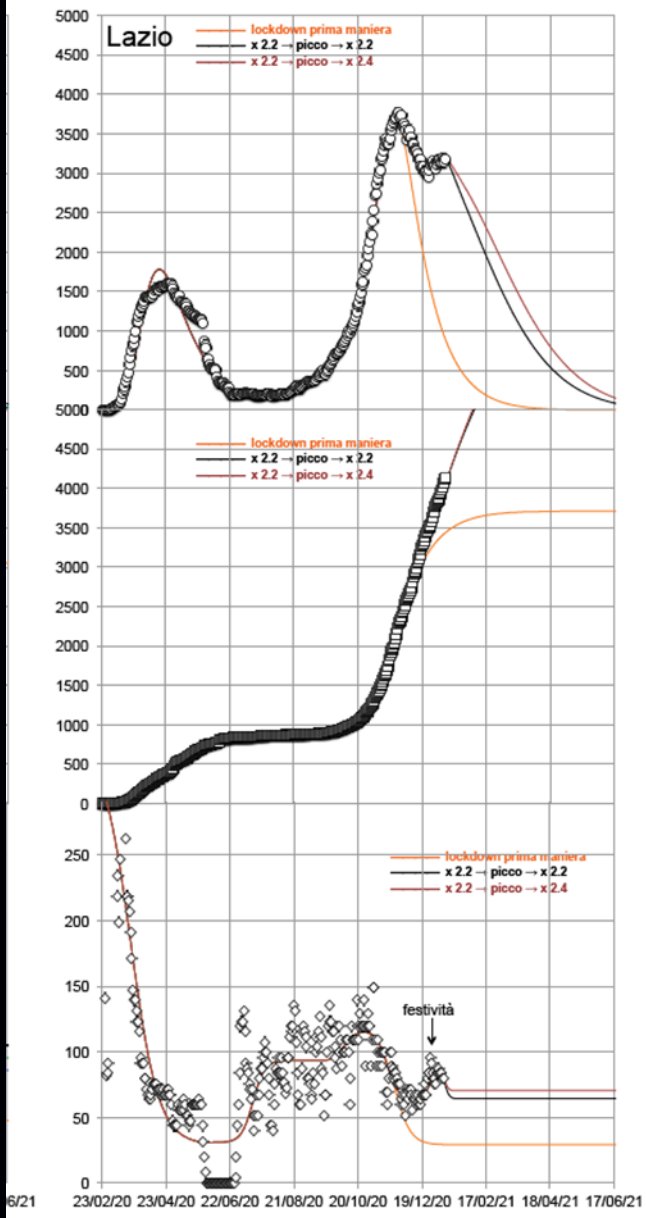


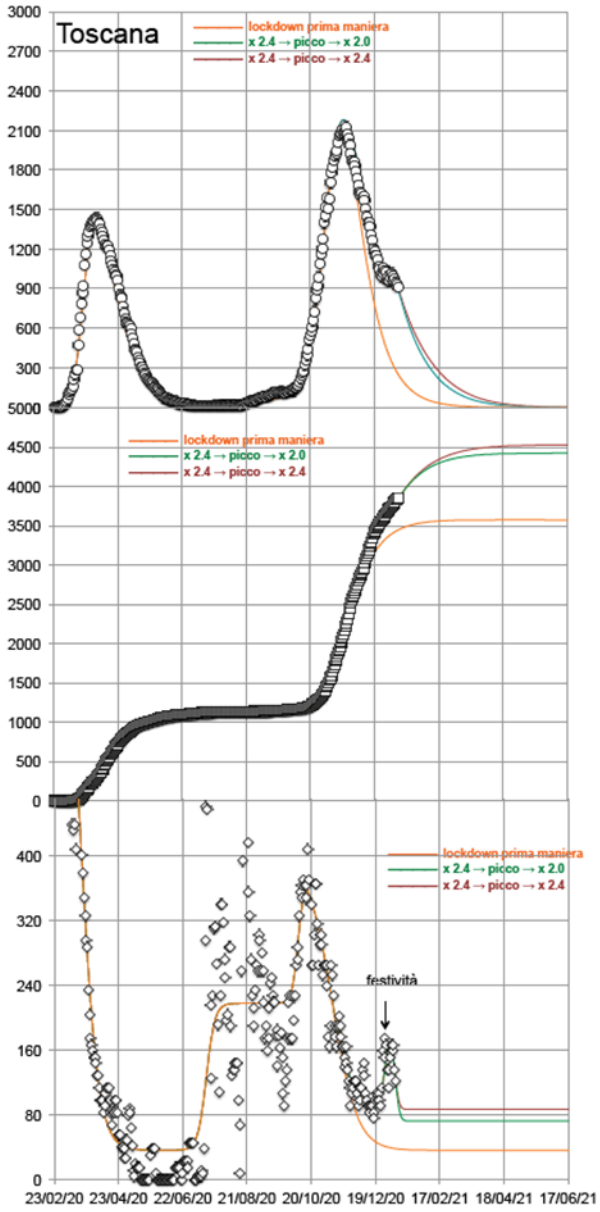
Casi positivi – Valore assoluto e incremento Giorno su Giorno

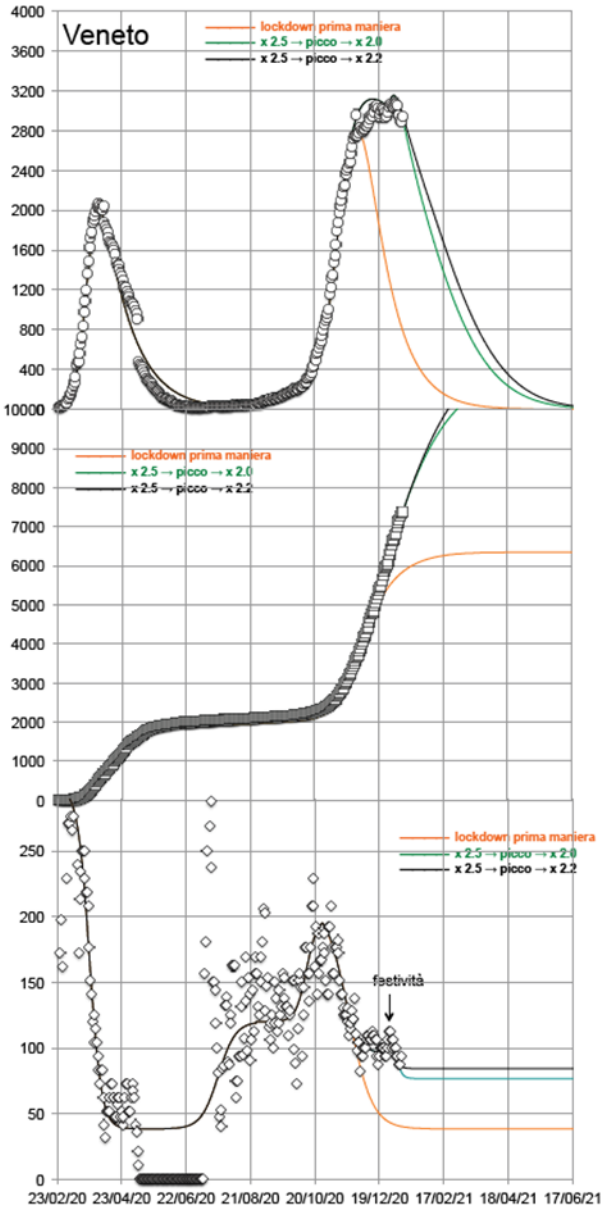


Numero tamponi positivi vs numero totale tamponi efficaci [perc sett su sett]









Cortesia di C.Spinella, CNR Roma

RANK	PAESI	TOTALI	% CONTAGI/ POPOLAZIONE	MORTI	TASSO LETALITÀ
1	Stati Uniti	**22.409.132**	6,770%	374.329	1,67%
2	India	**10.466.595**	0,758%	151.160	1,44%
3	Brasile	**8.105.790**	3,813%	203.100	2,51%
4	Russia	**3.366.715**	2,307%	60.963	1,81%
5	Regno Unito	**3.081.368**	4,539%	81.567	2,65%
6	Francia	**2.840.864**	4,352%	67.885	2,39%
7	Turchia	**2.326.256**	2,758%	22.807	0,98%
8	**Italia**	**2.289.021**	**3,792%**	**79.203**	**3,46%**
9	Spagna	**2.050.360**	4,385%	51.874	2,53%
10	Germania	**1.929.410**	2,303%	40.936	2,12%
11	Colombia	**1.786.900**	3,512%	46.114	2,58%
12	Argentina	**1.722.217**	3,811%	44.495	2,58%
13	Messico	**1.534.039**	1,190%	133.706	8,72%
14	Polonia	**1.385.522**	3,661%	31.189	2,25%
15	Iran	**1.286.406**	1,532%	56.171	4,37%
16	Sudafrica	**1.231.597**	2,077%	33.163	2,69%
17	Ucraina	**1.150.265**	2,630%	20.641	1,79%
18	Perù	**1.026.180**	3,112%	38.049	3,71%
19	Paesi Bassi	**885.098**	5,165%	12.461	1,41%
20	Repubblica Ceca	**831.165**	7,761%	13.115	1,58%

Fonte: Johns Hopkins University

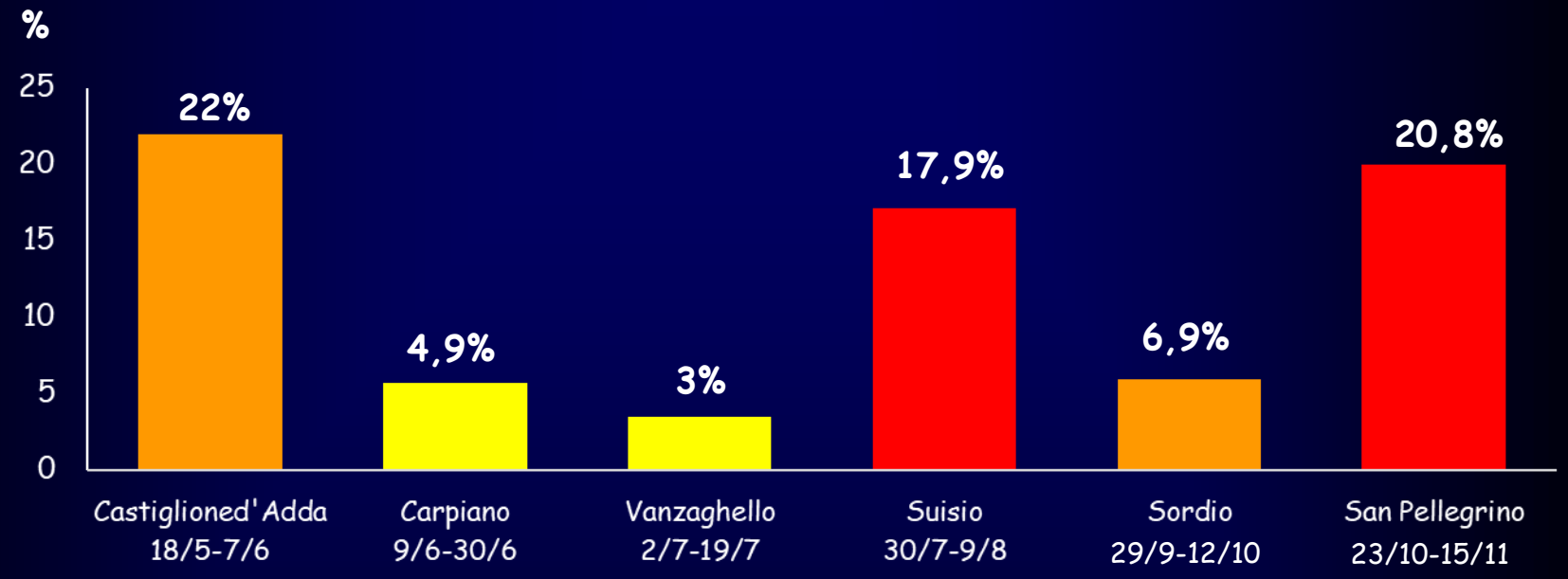
Letalità di Covid-19 in Italia: una questione di denominatori

date	casi	morti	%
21 febbraio-4 maggio	211.938	29.079	13,7
5 maggio -31 agosto	57.276	6.404	11,2
1 settembre -9 gennaio '21	1.988.652	42.911	2,1
Totali al 9 gennaio 2021	2.257.866	78.394	3,5

Dati aggiornati al 29 dicembre

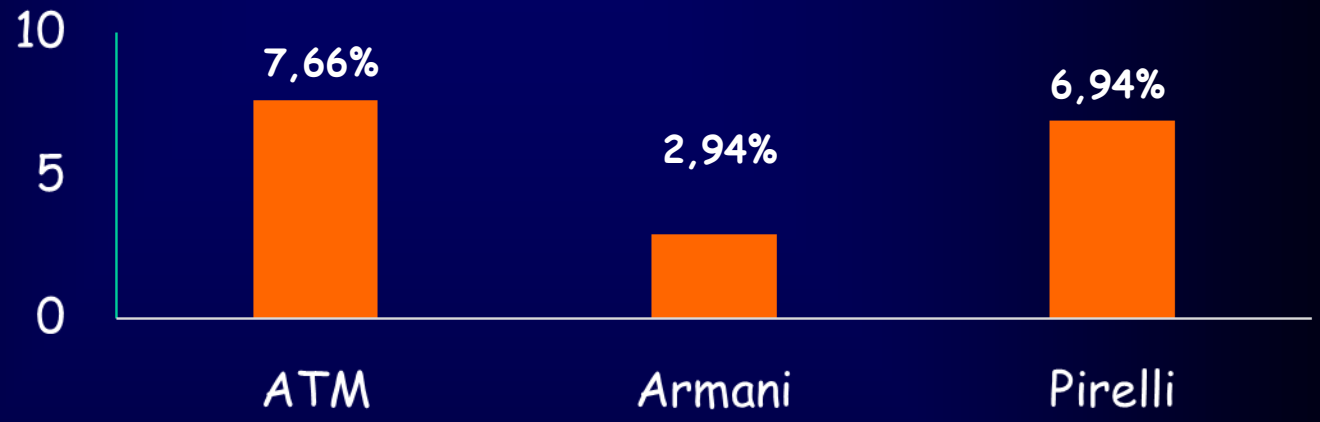
FASCIA D'ETÀ	MORTI	QUOTA %	LETALITÀ
0-9	9	0%	0,0%
10-19	10	0%	0,0%
20-29	35	0%	0,0%
30-39	150	0,2%	0,1%
40-49	602	0,9%	0,2%
50-59	2.376	3,4%	0,6%
60-69	6.818	9,6%	3%
70-79	17.493	24,7%	10,2%
80-89	29.224	41,3%	19,5%
>90	14.080	19,9%	24,3%
Non noto	2	0%	1,7%
Totale	70.799	100%	3,5%

Prevalenza delle IgG anti Covid-19 in sei Comuni Lombardi



Abitanti	4605	4168	5249	3828	3454	4790
Partecipanti (%)	4146 (90.0%)	1824 (43,8%)	2058 (39,2%)	1126 (29.4%)	1393 (40,3%)	2633 (54,9%)
IgG pos (%)	918 (22%)	89 (4,9%)	61 (3.0%)	201 (17.9%)	96 (6.9%)	549 (20.8%)
Tamponi (%)	26/1319 (1.5%)	8/435 (1.9%)	0/215 (0%)	5/289 (1,7%)	3/183 (1,64)	3/461 (0.6%)

Prevalenza di anticorpi anti Covid-19 IgG in Milano alla fine del lockdown di marzo-maggio 2020



Popolazione esaminata	Autisti mezzi di superficie	Dipendenti sedi di Milano	Dipendenti sedi di Milano
Periodo dello studio	6/5 -12/6	9/5 – 21/5	11/5 – 29/7
Numero totale	1852	1120	1023
Maschi/femmine	1752/100	650/470	ND
Età (anni: mediana e range)	45 (36-51)	40 (media)	ND
Tamponi +/-	1,07%	7,0%	0

Vaccines approaches being taken and the number of candidate vaccines in clinical and pre-clinical trials (20 August 2020).

Vaccine platform	Construct details	Number in pre-clinical trials	Number in clinical trials
Live attenuated virus	Codon-pair deoptimized live attenuated vaccines	3	0
Inactivated whole virus	Some combined with alum or CpG 1018 adjuvant	9	5
Protein/peptide subunit	Recombinant whole S protein, RBD or S1; 1 molecular clamp stabilized; 1 based on N protein; nanoparticle/VLP; peptides in LNP; 1 li-key peptide-based; OMV-based With or without adjuvant and/or fused with Fc subunit of IgG Most intramuscular delivery; 1 microneedle array, 1 oral construct	50	8
Non-replicating viral vectors	Chimp adenovirus 1; human adenovirus (Ad5, Ad 26); adeno-associated virus (AAV); influenza virus (H1N1); modified vaccinia Ankara (MVA); parainfluenza virus 5 (PIV5); rabies virus; Sendai virus With or without adjuvant Most intramuscular delivery; 1 subcutaneous and several oral constructs	19	5
Replicating viral vectors	Avian paramyxovirus; horsepox; influenza; measles; Newcastle disease virus (NDV); vesicular stomatitis virus (VSV); Yellow fever virus (YF17D) Most intramuscular delivery; 2 intranasal	17	1
DNA	DNA plasmid vaccines; mostly S protein or RBD-based, but 2 also with N protein With or without adjuvant Most intramuscular delivery; some with electroporation/needle free delivery; 1 oral vaccine (bacTRL-Spike)	12	4
RNA	LNP-encapsulated encoding spike protein or RBD; self-amplifying Most intramuscular delivery; 1 intranasal	16	6
Virus like particle (VLP)	Whole virus, protein and peptides inside or on surface; lentivirus, baculovirus, HIV-based vehicles Some with adjuvants	12	1

Adapted from WHO Draft Landscape of COVID-19 Vaccines [ref].

Leading Covid vaccines

Developer	Type	Phase	Status
Pfizer-BioNTech	mRNA	2/3	Approved
Moderna	mRNA	3	Approved
CanSino	Adenovirus	3	Limited use in China.
Gamaleya	Adenovirus	3	Early use in Russia.
Johnson & Johnson	Adenovirus	3	
Oxford-AstraZeneca	Adenovirus	2/3	
Novavax	Protein	3	
Vector Institute	Protein	1/2	Early use in Russia.
Sinopharm-Beijing	Inactivated	3	Approved in U.A.E.
Sinopharm-Wuhan	Inactivated	3	Limited use in U.A.E.
Sinovac	Inactivated	3	Limited use in China.

Researchers are currently testing 58 vaccines in clinical trials on humans, and 15 have reached the final stages of testing.
At least 85 preclinical vaccines are under active investigation in animals.

The NEW ENGLAND JOURNAL of MEDICINE
DOI: 10.1056/NEJMoa2034577

ORIGINAL ARTICLE

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose).

BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 fulllength spike protein.

The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety.

Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (1,7411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

* The total population without baseline infection was 36,523; total population including those with and those without prior evidence of infection was 40,137.

† The surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.

‡ The credible interval for vaccine efficacy was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

§ Posterior probability was calculated with the use of a beta-binomial model with prior beta (0.700102, 1) adjusted for the surveillance time.

Polack et al. NEJM December 10, 2020

Vaccine Efficacy Overall and by Subgroup in Participants without Evidence of Infection before 7 Days after Dose 2.

Efficacy End-Point Subgroup	BNT162b2 (N=18,198)		Placebo (N=18,325)		Vaccine Efficacy, % (95% CI)†
	No. of Cases	Surveillance Time (No. at Risk)*	No. of Cases	Surveillance Time (No. at Risk)*	
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0 (90.0–97.9)
Age group					
16 to 55 yr	5	1.234 (9,897)	114	1.239 (9,955)	95.6 (89.4–98.6)
>55 yr					93.7 (80.6–98.8)
≥65 yr					94.7 (66.7–99.9)
≥75 yr					100.0 (–13.1–100.0)
Sex					
Male					96.4 (88.9–99.3)
Female					93.7 (84.7–98.0)
Race or ethnic group‡					
White					95.2 (89.8–98.1)
Black or African Am					100.0 (31.2–100.0)
All others					89.3 (22.6–99.8)
Hispanic or Latinx	3	0.605 (4,764)	53	0.600 (4,746)	94.4 (82.7–98.9)
Non-Hispanic, non-Latinx	5	1.596 (12,548)	109	1.608 (12,661)	95.4 (88.9–98.5)
Country					
Argentina	1	0.351 (2,545)	35	0.346 (2,521)	97.2 (83.3–99.9)
Brazil	1	0.119 (1,129)	8	0.117 (1,121)	87.7 (8.1–99.7)
United States	6	1.732 (13,359)	119	1.747 (13,506)	94.9 (88.6–98.2)

Similar vaccine efficacy (generally 90 to 100%) was observed across subgroups defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions.

* Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from 7 days after the second dose to the end of the surveillance period.
† The confidence interval (CI) for vaccine efficacy is derived according to the Clopper–Pearson method, adjusted for surveillance time.
‡ Race or ethnic group was reported by the participants. "All others" included the following categories: American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported.

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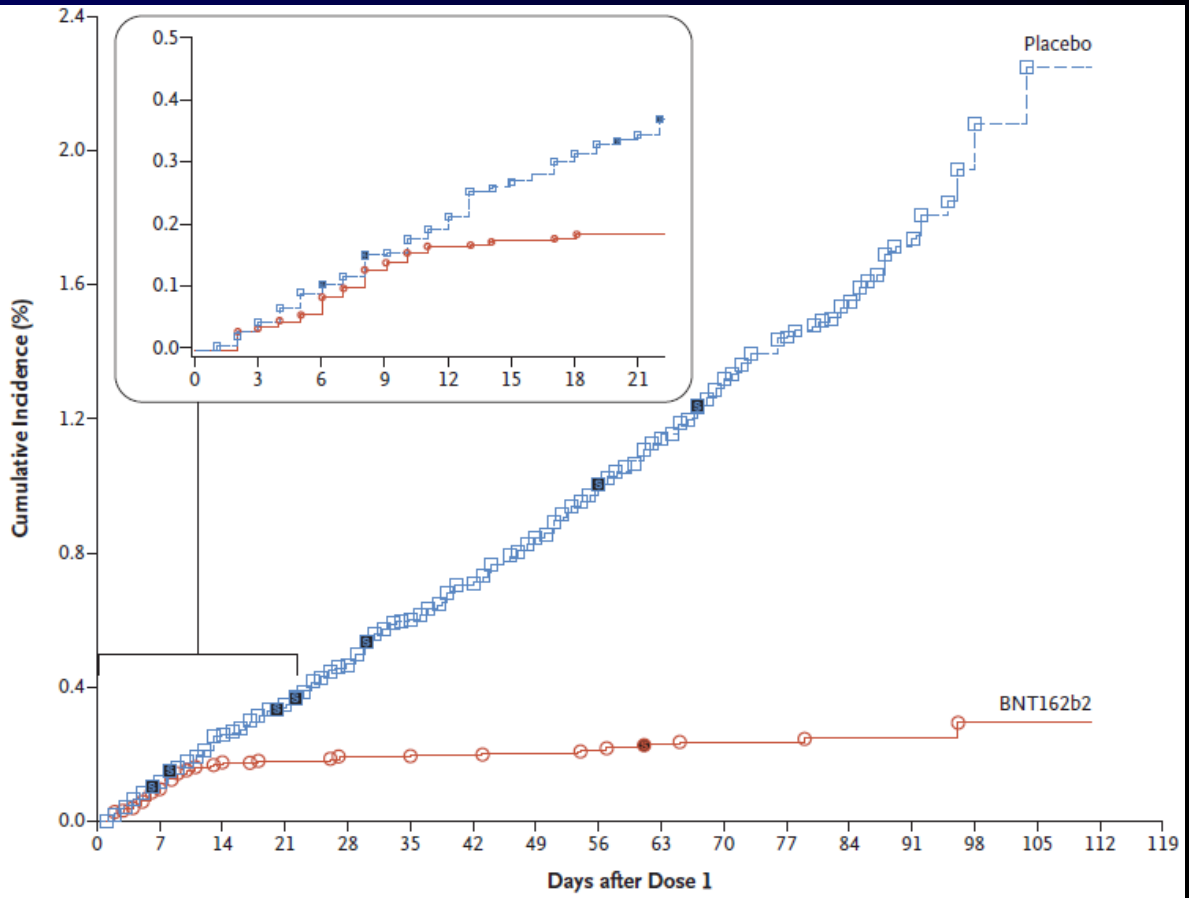
Efficacy of BNT162b2 against Covid-19 after the First Dose.

- Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases.
- The inset shows the same data on an enlarged y axis, through 21 days.
- The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

- Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient.

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Local adverse events

- The safety profile of BNT162b2 was characterized by short-term, mild-to-moderate pain at the injection site, fatigue, and headache.
- Pain at the injection site was assessed according to the following scale: mild, does not interfere with activity; moderate, interferes with activity; severe, prevents daily activity; and grade 4, emergency department visit or hospitalization.
- Redness and swelling were measured according to the following scale: mild, 2.0 to 5.0 cm in diameter; moderate, >5.0 to 10.0 cm in diameter;severe, >10.0 cm in diameter; and grade 4, necrosis or exfoliative dermatitis (for redness) and necrosis(for swelling).
- The incidence of serious adverse events was low and was similar in the vaccine and placebo groups.

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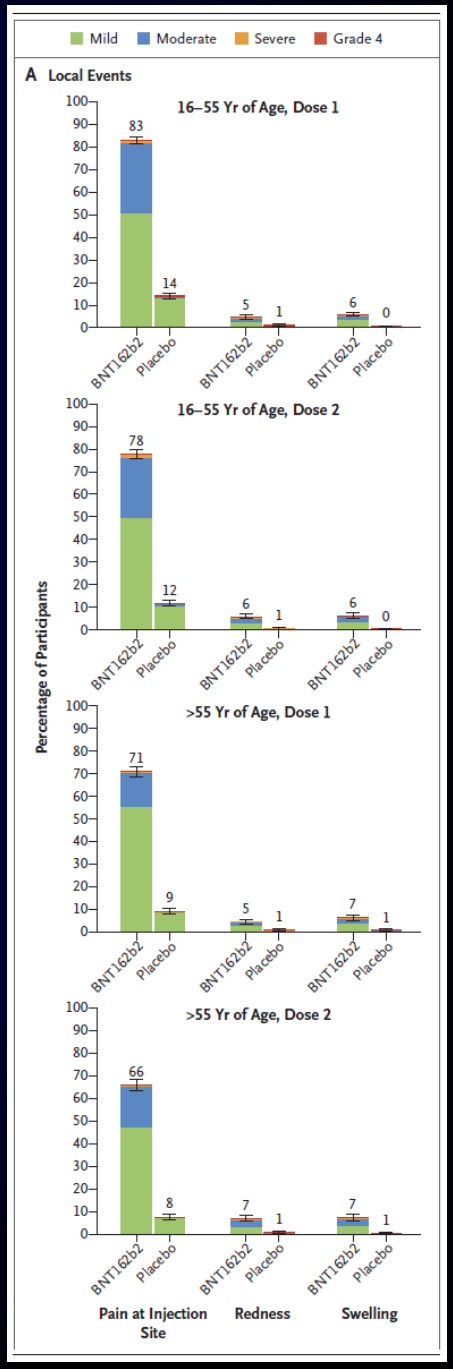
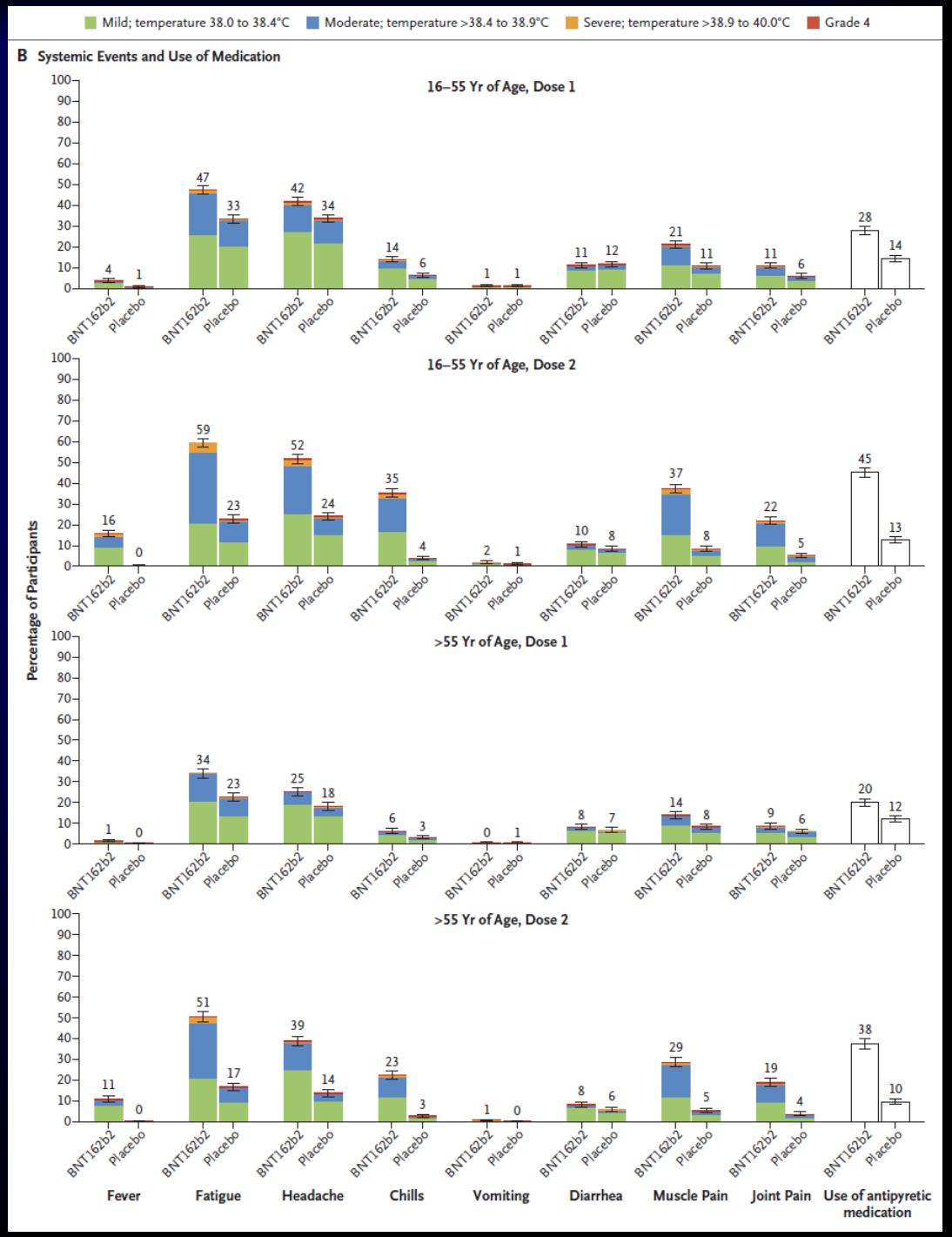


Systemic adverse events

- Systemic events were reported more often by younger vaccine recipients and more often after dose 2 than dose 1.
- The most commonly reported systemic events were fatigue and headache (59% and 52%, respectively, after the second dose, among younger vaccine recipients; 51% and 39% among older recipients), although fatigue and headache were also reported by many placebo recipients (23% and 24%, respectively, after the second dose, among younger vaccine recipients; 17% and 14% among older recipients)



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

An mRNA Vaccine against SARS-CoV-2 — Preliminary Report

L.A. Jackson, E.J. Anderson, N.G. Rouphael, P.C. Roberts, M. Makhene, R.N. Coler, M.P. McCullough, J.D. Chappell, M.R. Denison, L.J. Stevens, A.J. Pruijssers, A. McDermott, B. Flach, N.A. Doria-Rose, K.S. Corbett, K.M. Morabito, S. O'Dell, S.D. Schmidt, P.A. Swanson II, M. Padilla, J.R. Mascola, K.M. Neuzil, H. Bennett, W. Sun, E. Peters, M. Makowski, J. Albert, K. Cross, W. Buchanan, R. Pikaart-Tautges, J.E. Ledgerwood, B.S. Graham, and J.H. Beigel, for the mRNA-1273 Study Group*

Moderna

N Engl J Med 2020;383:1920-31.

November 16: Moderna announced that mRNA-1273 met its primary efficacy endpoint in the first interim analysis of the Phase 3 COVE study with a vaccine efficacy of 94.5%

The Lancet: Published online December 8, 2020

- From 21 days after the first dose, there were ten cases hospitalised for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death.
- There were 74 341 person-months of safety follow-up (median 3·4 months, IQR 1·3–4·8): 175 severe adverse events occurred in 168 participants, 84 events in the ChAdOx1 nCoV-19 group and 91 in the control group.
- Three events were classified as possibly related to a vaccine: one in the ChAdOx1 nCoV-19 group, one in the control group, and one in a participant who remains masked to group allocation.

Comparing Oxford/AstraZeneca's and CanSino's vaccine candidates

- When comparing the NAb response between the two adenoviral vector-based vaccine candidates, it was shown that while Oxford/AstraZeneca's AZD1222 has demonstrated a high NAb level in 91% of individuals following the first dose, and in all individuals following a booster dose, only 59% of individuals in CanSino's vaccine demonstrated a Nab.
- This indicates that a good proportion of participants did not develop an effective immune response due to the presence of pre-existing immunity against human adenoviruses.
- Oxford/AstraZeneca were able to prevent this outcome by utilizing a genetically modified chimpanzee-derived adenovirus against which humans do not have pre-existing immunity.
- However, CanSino plans to offers its vaccine at a low cost which, combined with its moderate efficacy, may prove advantageous for some countries.

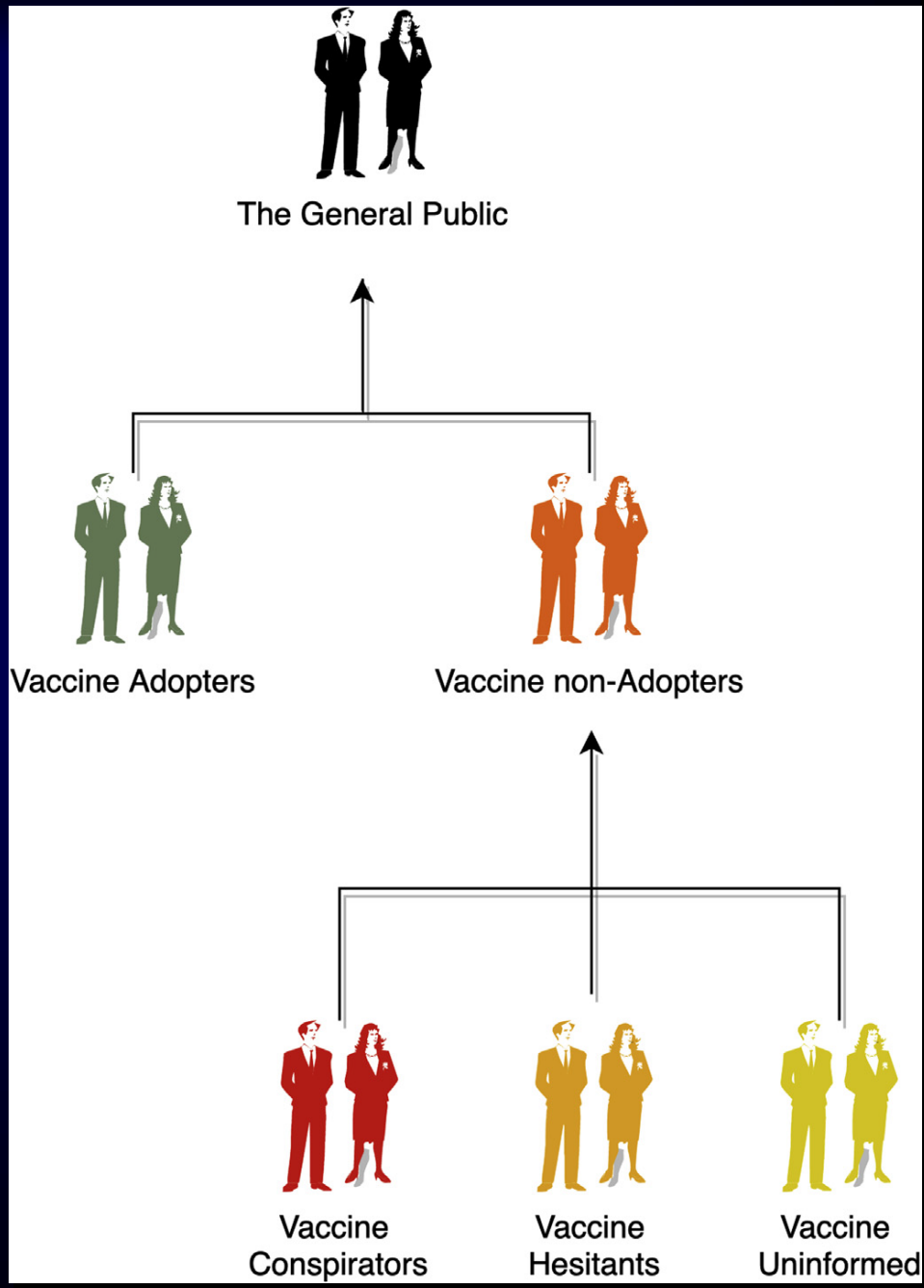
JNJ-78436735

November 15, 2020

- The Phase 3 ENSEMBLE study of the single-dose regimen of JNJ-78436735, the investigational vaccine candidate for the prevention of COVID-19 being developed by the Janssen Pharmaceutical Companies of Johnson & Johnson, continues to enroll and vaccinate study participants.
- ENSEMBLE is proceeding to enroll up to 60,000 participants worldwide.

Vaccine non-adopters

- Vaccine conspirators:
  people who possess too much misinformation to adopt the vaccine
- Vaccine uninformed
  people who possess insufficient information to adopt the vaccine
- Vaccine hesitants
  people who are considering adopting the vaccine but lack the right conditions or context to do so



Su et al. Brain, Behavior, & Immunity - Health 9 (2020) 100159

Grazie per l'attenzione