

Modelling Covid-19 outspread dynamics involving geoclimatic and demographic factors

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Daniel Bernoulli's life

February 9th 1700 (Groningue, NL) – March 17th 1782 (Bâle, Switzerland)

- * Learning differential calculus of Leibnitz, with his father Jean and uncle Jacques (student of Leibnitz)
- * Receiving a M.D. degree (1721), after studying philosophy, logic, and medicine at universities of Heidelberg, Strasbourg, and Basel
- * Lecturing in St Petersburg until 1732, in medicine, mechanics, and physics
- * Returning to University of Basel, and accepting a post in anatomy and botany.



Bernoulli D (1760). Essai d'une nouvelle analyse de la mortalité causée par la petite vérole, et des avantages de l'inoculation pour la prévenir. Paris: Acad. Roy. Sci.

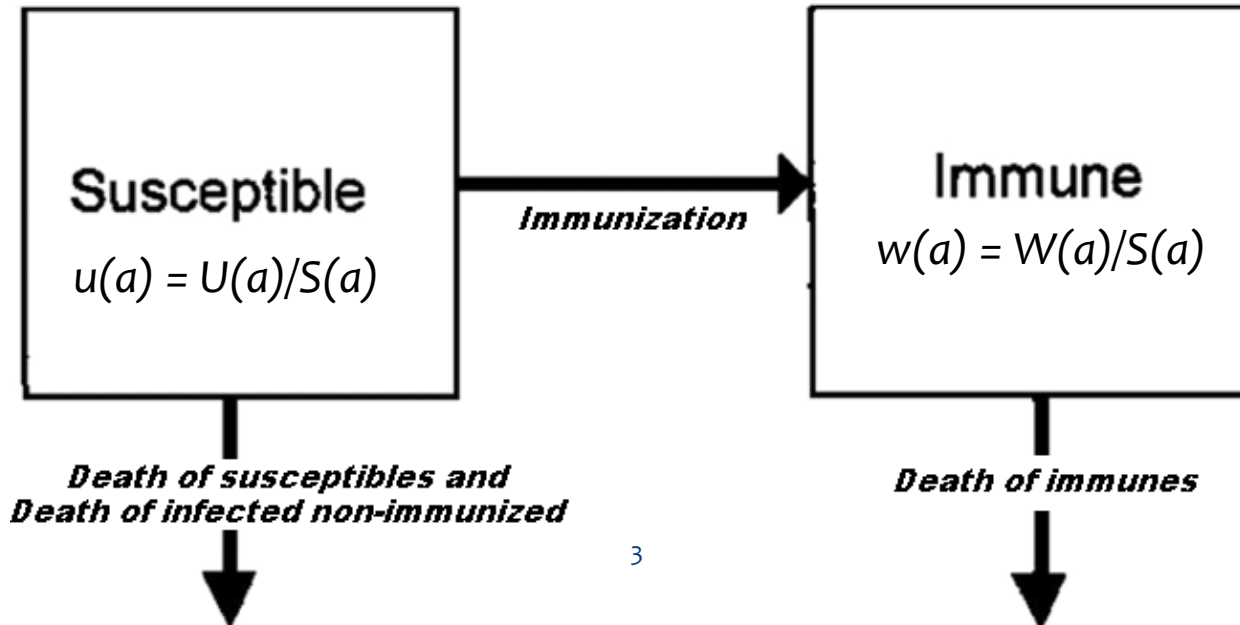
States variables 1760

Bernoulli, D. (1760). Essai d'une nouvelle analyse de la mortalité causée par la petite vérole, et des avantages de l'inoculation pour la prévenir. Mémoire Académie Royale des Sciences, Paris.

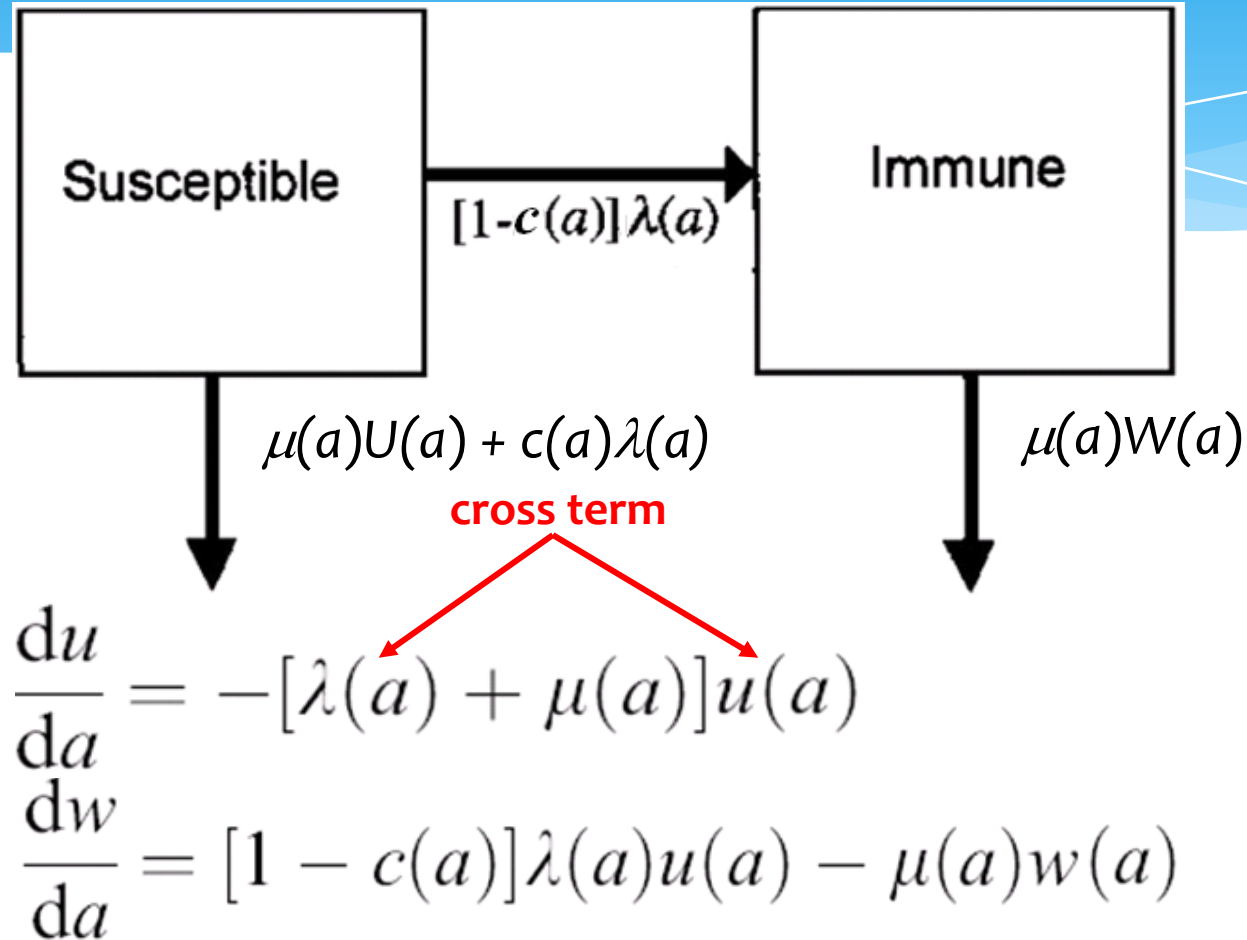
Population divided into: **susceptible**, not yet been infected, **infected** and **immune**, immunized for the rest of their life after one infection.

- * $u(a)$: probability for a newborn individual to be susceptible (and alive) at age a .
- * $w(a)$: probability to be immune (and alive) at age a .

$$S(a) = U(a) + \lambda(a) + W(a)$$



Differential equations 1760



SIRS model

Ross (1916) & McKendrick (1925)

Ronald Ross



Susceptible



Infected

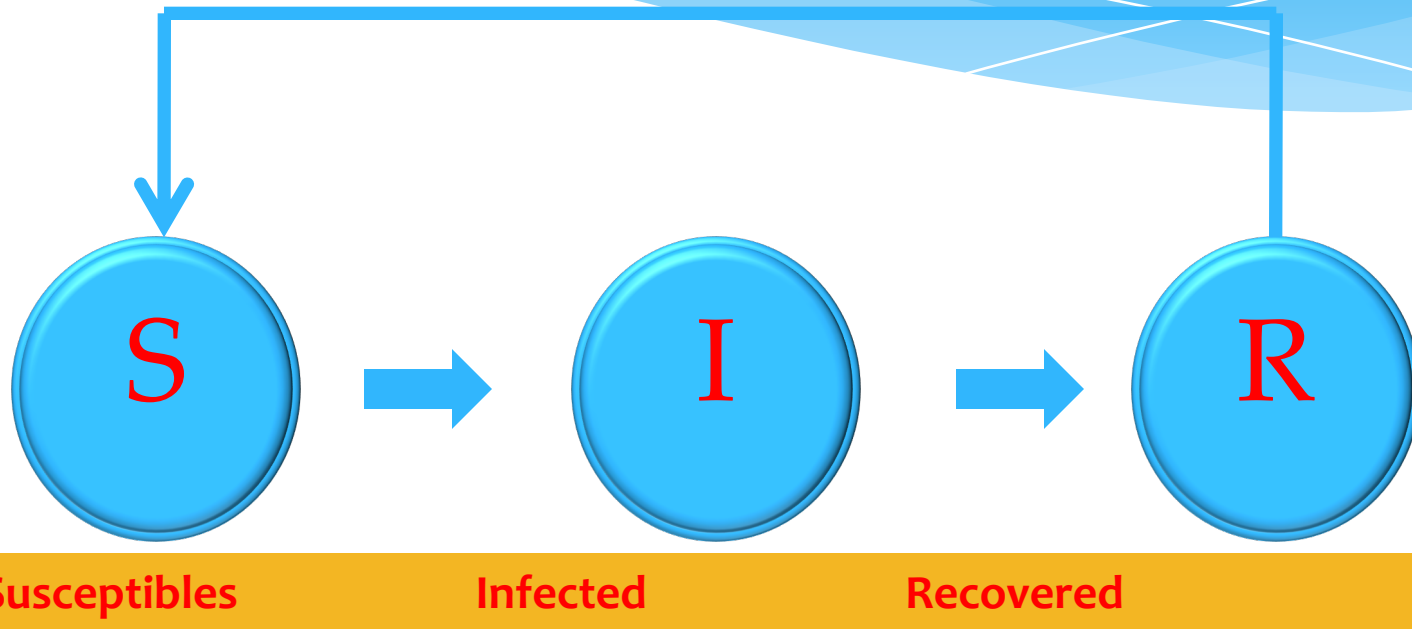
SIRS cycle



Recovered



The SIRS model



The SIRS model allows for a loss of immunity causing recovered individuals to become susceptible again.

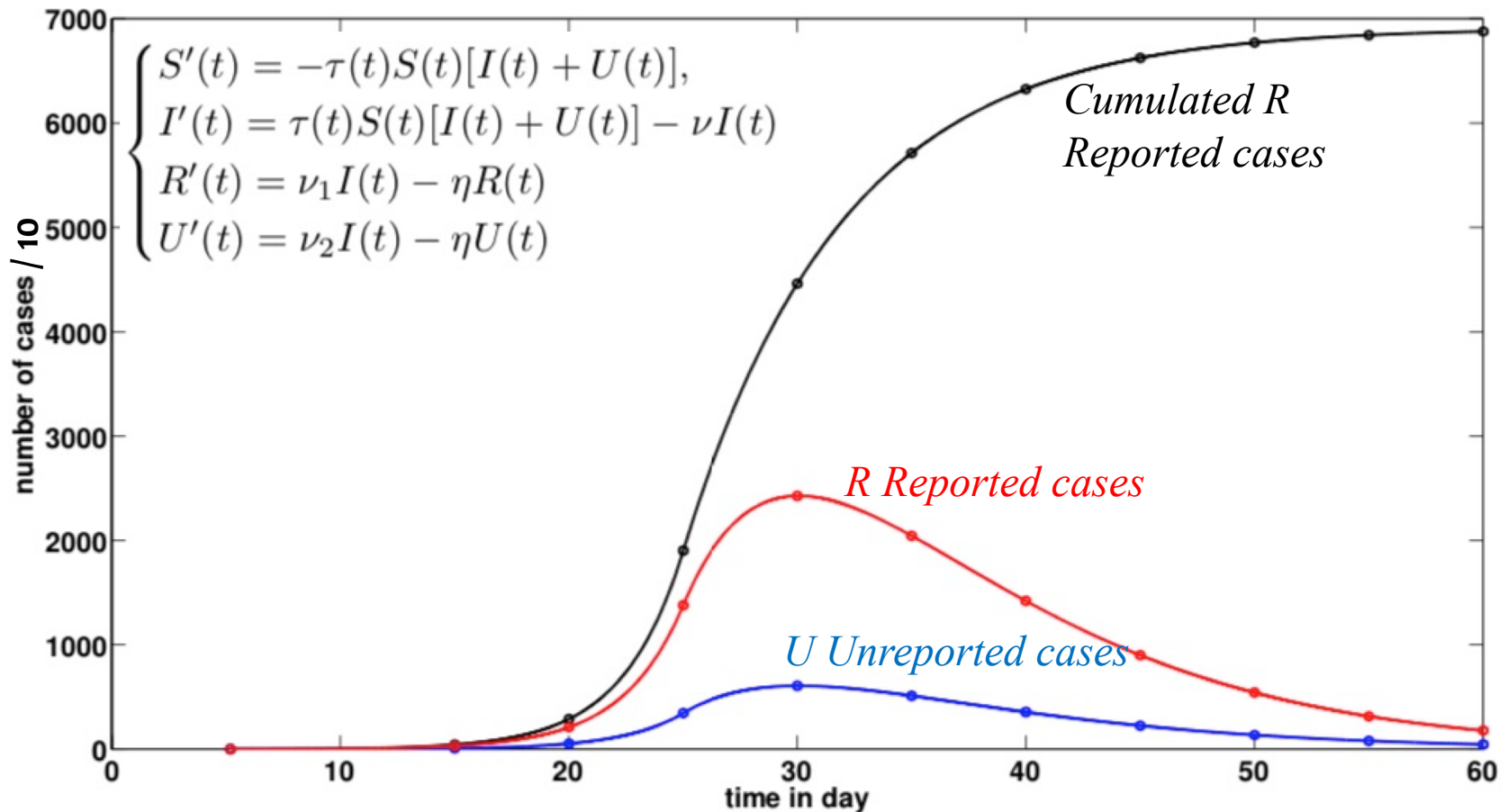
The SIRS Model Equations

$$dS/dt = fS - \nu SI - \mu S + \gamma R$$

$$dI/dt = \nu SI - cI - (1-c)I$$

$$dR/dt = (1-c)I - \gamma R$$

Covid-19 dynamics



[China](#) 4/5/2020

Cases 82,880

New cases +3

Deaths 4,633

Liu, Z.; Magal, P.; Seydi, O.; Webb, G. Understanding Unreported Cases in the COVID-19 Epidemic Outbreak in Wuhan, China, and the Importance of Major Public Health Interventions. *Biology* 2020, 9, 50.

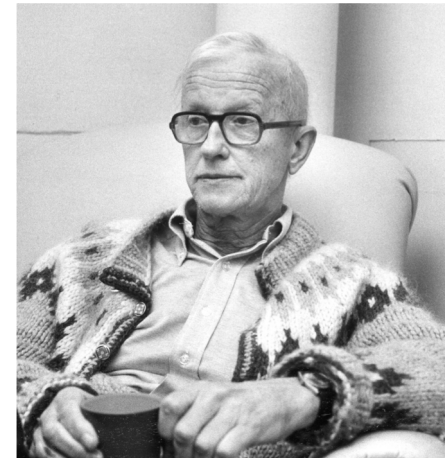
Probabilistic approach

At least one event (contact ν , birth f , death μ) in $(t, t+dt)$, where $I=N-S$:

$$P(S(t+dt)=k) = (1-\nu(N-k)dt) P(S(t)=k) + fdt P(S(t)=k-1) - \mu dt P(S(t)=k+1)$$

By multiplying by s^k and summing over k , we prove **if S and I are independent**, that they are Poisson, whose parameter $E(S)$ verifies (by multiplying by k and summing):

$$\begin{aligned} dE(S)/dt &\approx f E(S) - \nu E(SI) - \mu E(S) \\ &\approx -\nu E(S) E(I), \text{ if } f = \mu \end{aligned}$$



M. Delbrück 1940

Stability parameter = KS evolutionary entropy of the corresponding Markov process

M. DELBRÜCK. Statistical fluctuations in autocatalytic reactions. *Journal of Chemical Physics* **8**, 120–124 (1940)

C.J. RHODES & L. DEMETRIUS. Evolutionary entropy determines invasion success in emergent epidemics. *PloS ONE*, **5**, e12951 (2010).

J. DEMONGEOT & L. DEMETRIUS. Complexity and Stability in Biological Systems. *Int. J. Bifurcation & Chaos*, **25**, 40013 (2015).

Bernoulli, 1760
d'Alembert, 1761
Lambert, 1772

Delbrück, 1940

Bartholomay, 1958

McQuarrie, 1967

Gillespie, 1970

Verhulst, 1838

Ronald Ross, 1916

McKendrick, 1925

Dr Pasteur Institute Kausali

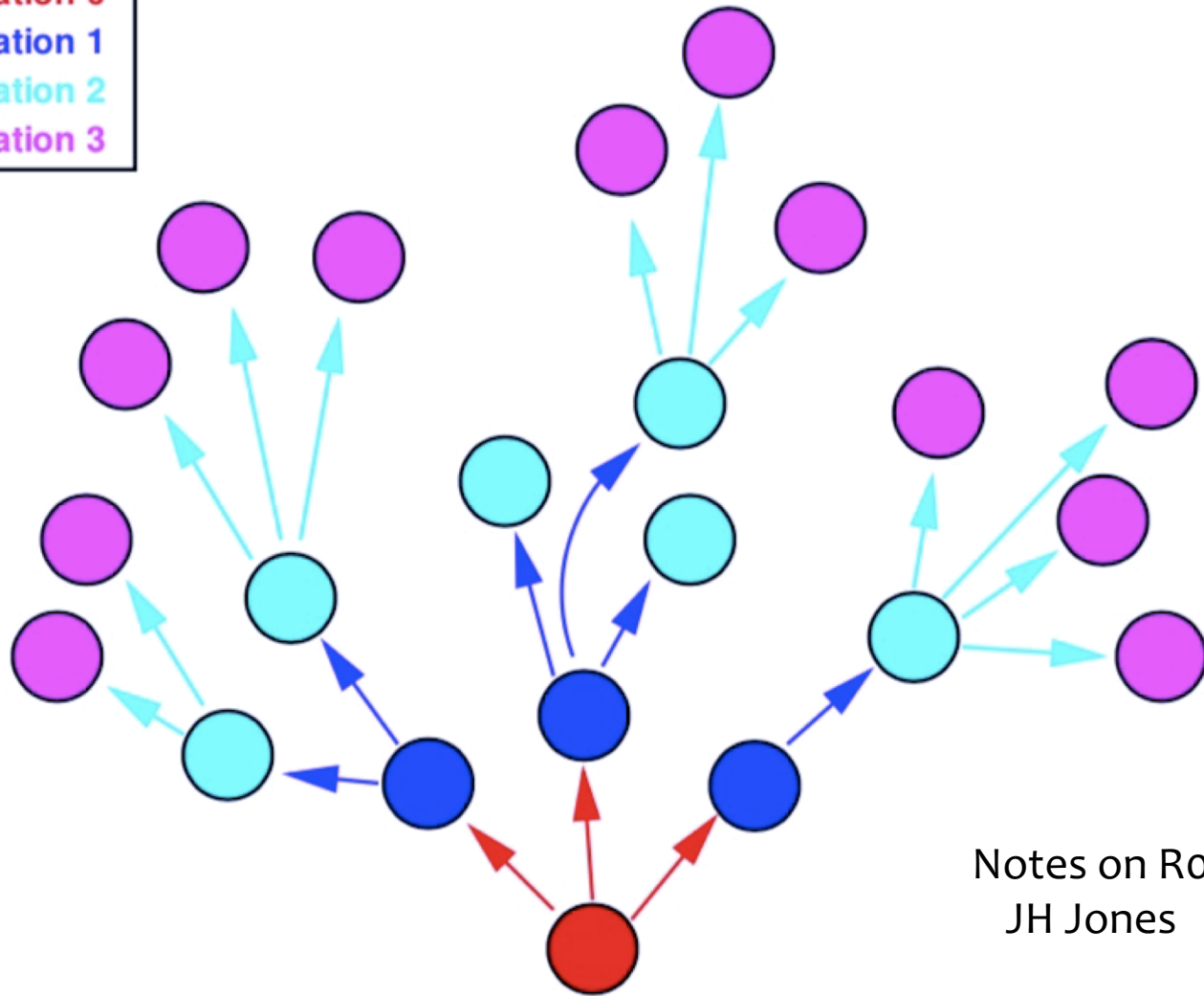
Ronald Fisher & KPP, 1937

Multi-agent or IBM discrete models

ODE or PDE continuous models

R₀

Generation 0
Generation 1
Generation 2
Generation 3



Notes on R₀
JH Jones

R_0

From The Editor

By Chris Evans, Editor

The best of *The Telegraph's* articles, sent by the Editor

Dear reader,

The Government's new "Stay Alert" message is now in full force and adverts are continually springing up to remind us of the importance of "controlling the R rate" to save lives. Sarah Knapton, our science editor, explains precisely what the R rate is [in this excellent piece](#) and analyses how reopening schools might impact on it.

R_0

The average number of secondary cases arising from an average primary case in an entirely susceptible population.

The basic reproduction number (basic reproductive rate, basic reproductive ratio R_0) of a contagious disease is the number of cases than a case of the disease generates (on an average) over the course of its infectious period in a susceptible population.

- * If $a \ll 1$, then $dI/dt = \nu SI$, $d\text{Log}I/dt = \nu S$, and if $I(0) = 1$ and S is quasi-constant at start of the epidemic:

$$\text{Log}(I(t)) = \nu \int_{[0,t]} S(\tau) d\tau \approx \nu \underline{S} t,$$

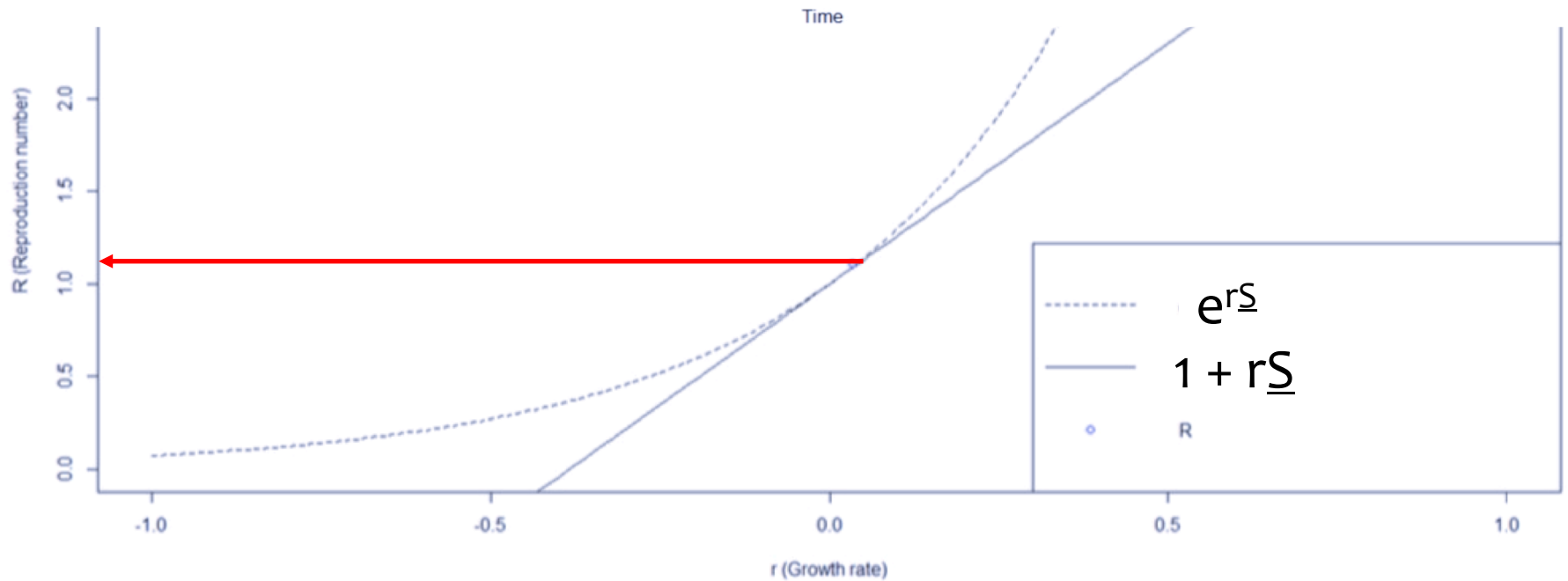
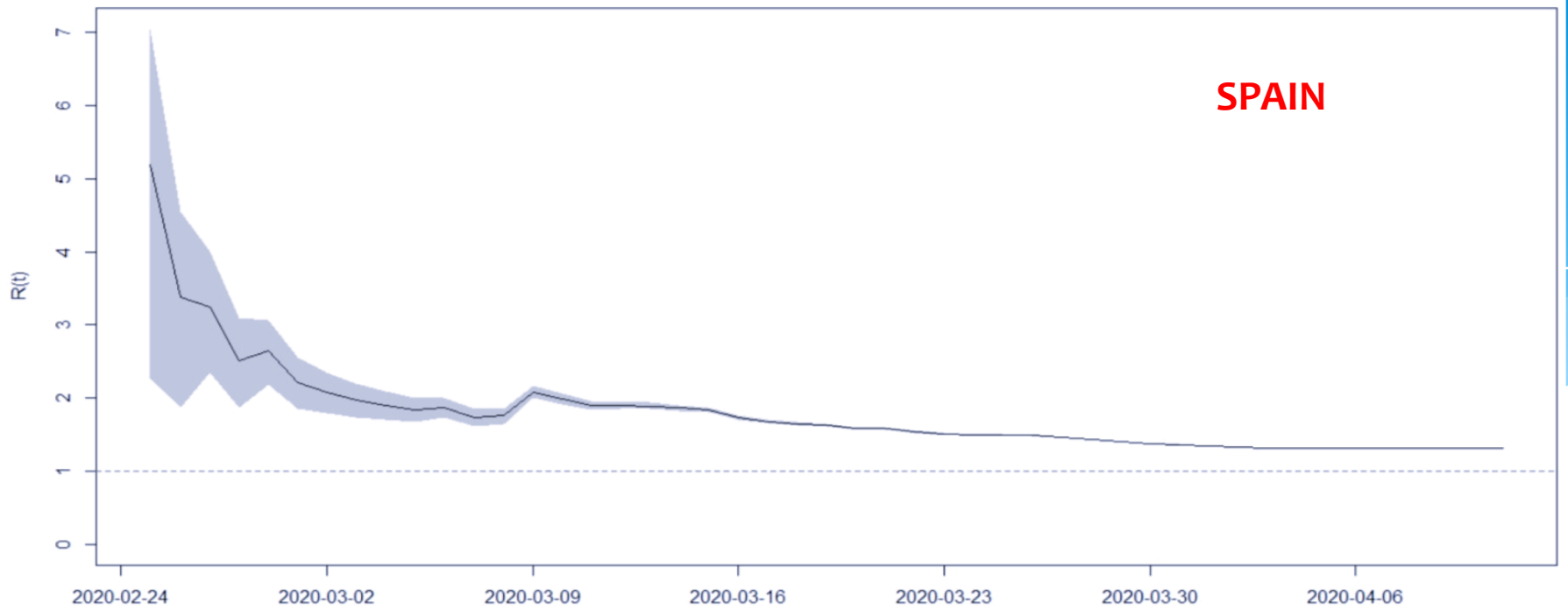
if $\text{Log}(I(t)) \approx \text{Log}(R_0)t$, then

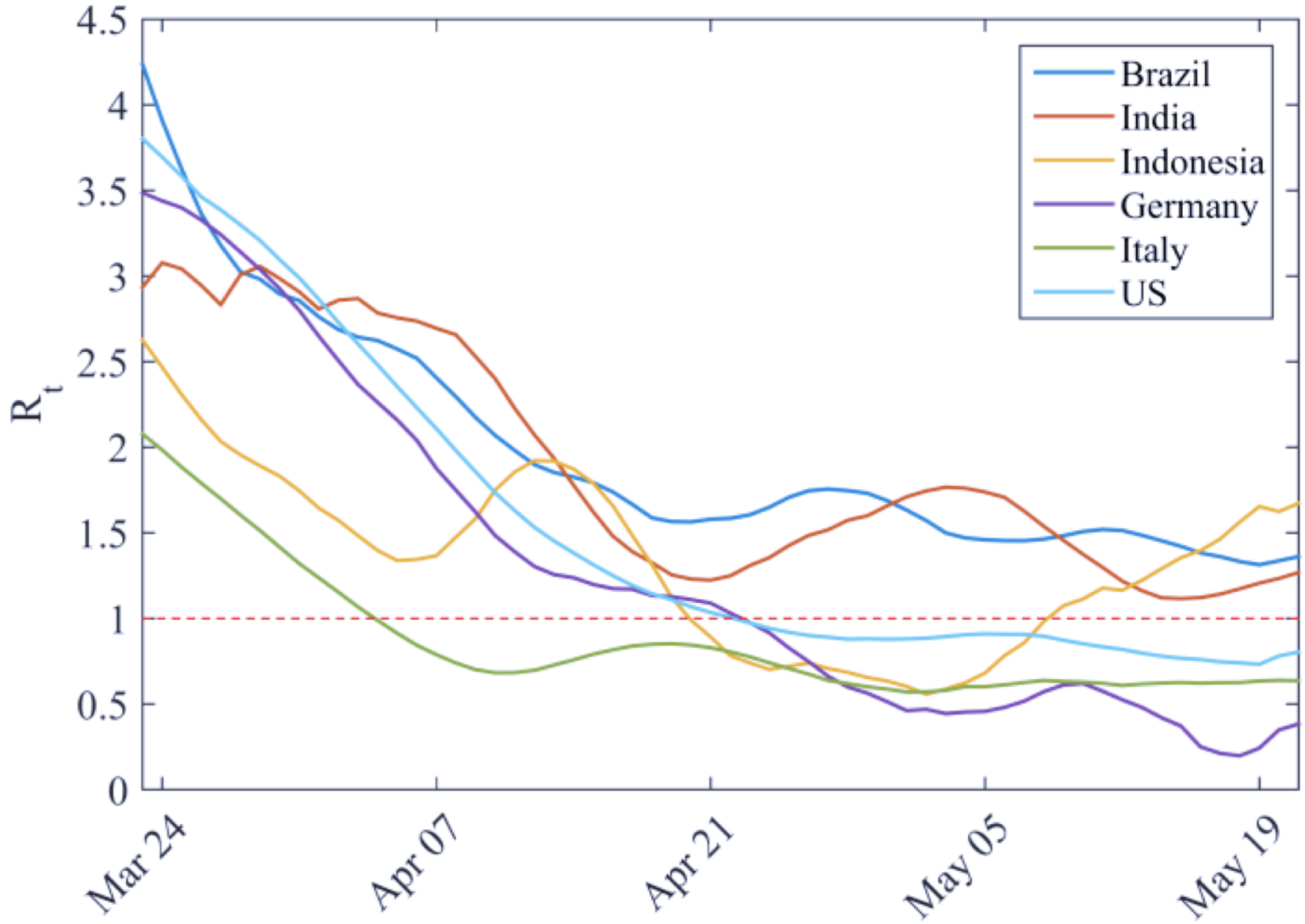
$$R_0 \approx e^{\nu \underline{S}} \approx 1 + \nu \underline{S}, \text{ if } \nu \underline{S} \ll 1$$

I. OUASSOU, L. HOBAD, M. ALAHIANE, J. GAUDART, S. IGGUI, M. RACHDI & J. DEMONGEOT

The ARIMA model to analyse incidence pattern and estimate short-term forecasts for retro-predicting the first wave of the COVID-19 outbreak. *Math. Population Studies* (submitted).

Reproduction number (Sequential Bayesian)





S. SOUBEYRAND, J. DEMONGEOT, L. ROQUES Towards unified and real-time analyses of outbreaks at country-level during pandemics. *One Health* (accepted).

Restrictions :

- If $S(0)$ is very large and $I(0)$ small, then let use a saturation term $rSI/(1+S)$
- If the total population remains stable ($f=\mu$), then $S+I=N$ and S and I are not independent
- If the population is heterogeneous (e.g., if infectivity and susceptibility depends on age), then R_0 does not represent the initial exponential growth rate of infected

ARIMA model

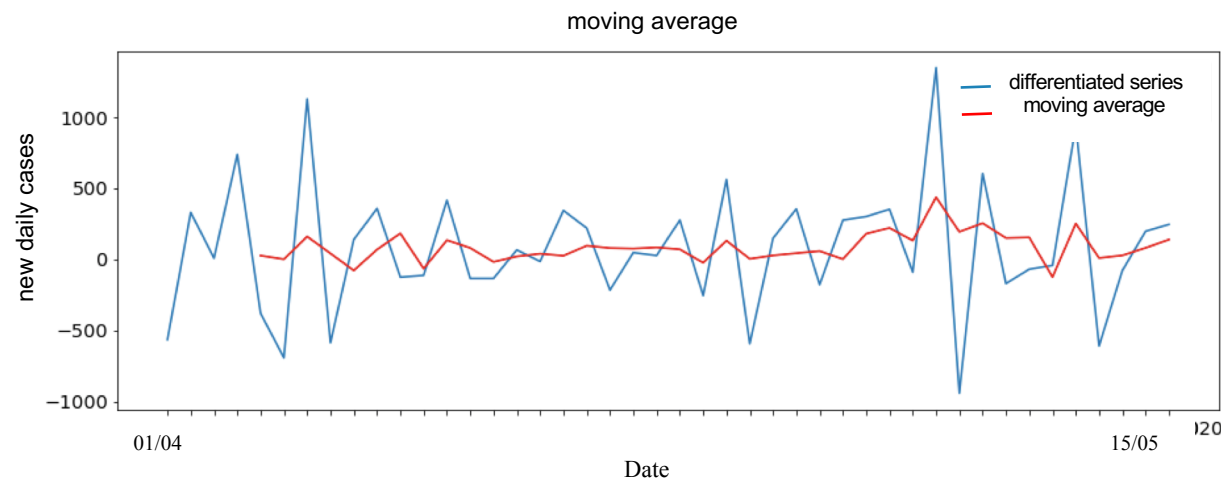
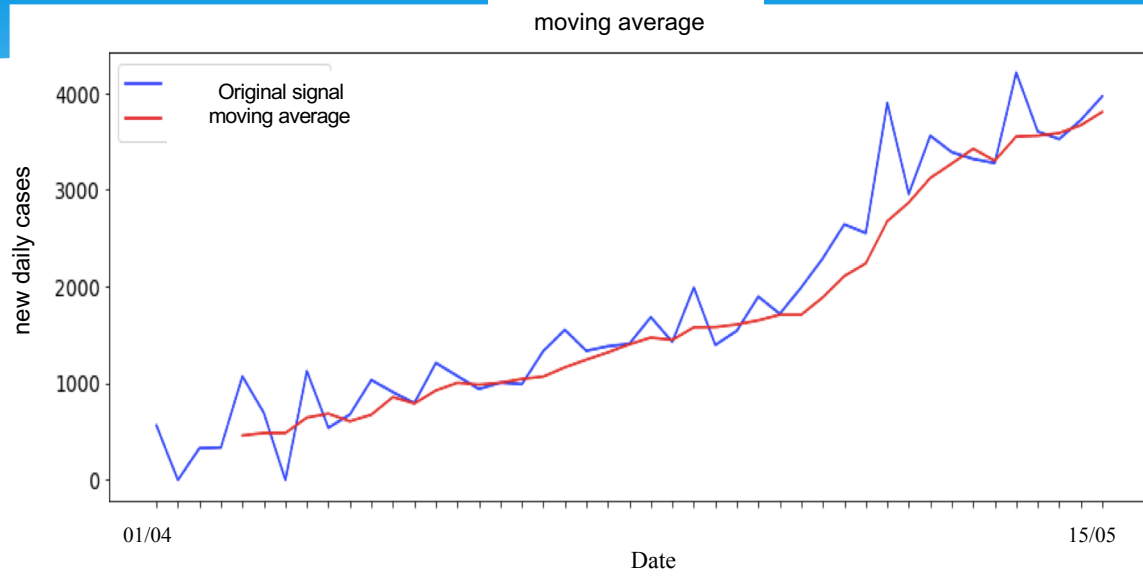
$$X_t - \alpha_1 X_{t-1} - \dots - \alpha_{p'} X_{t-p'} = \varepsilon_t + \theta_1 \varepsilon_{t-1} + \dots + \theta_q \varepsilon_{t-q},$$

or equivalently by

$$\left(1 - \sum_{i=1}^{p'} \alpha_i L^i\right) X_t = \left(1 + \sum_{i=1}^q \theta_i L^i\right) \varepsilon_t$$

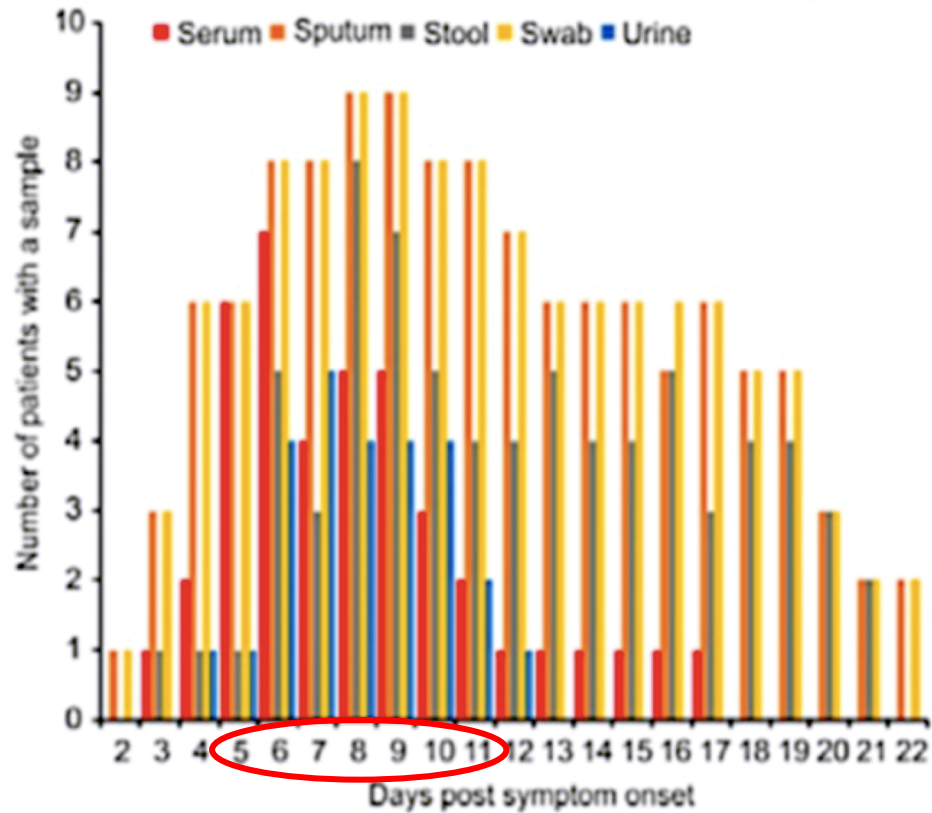
where L is the **lag operator**, the α_i are the parameters of the autoregressive part of the model, the θ_i are the parameters of the moving average part and the ε_t are error terms. The error terms ε_t are generally assumed to be **independent, identically distributed** variables sampled from a **normal distribution** with zero mean.

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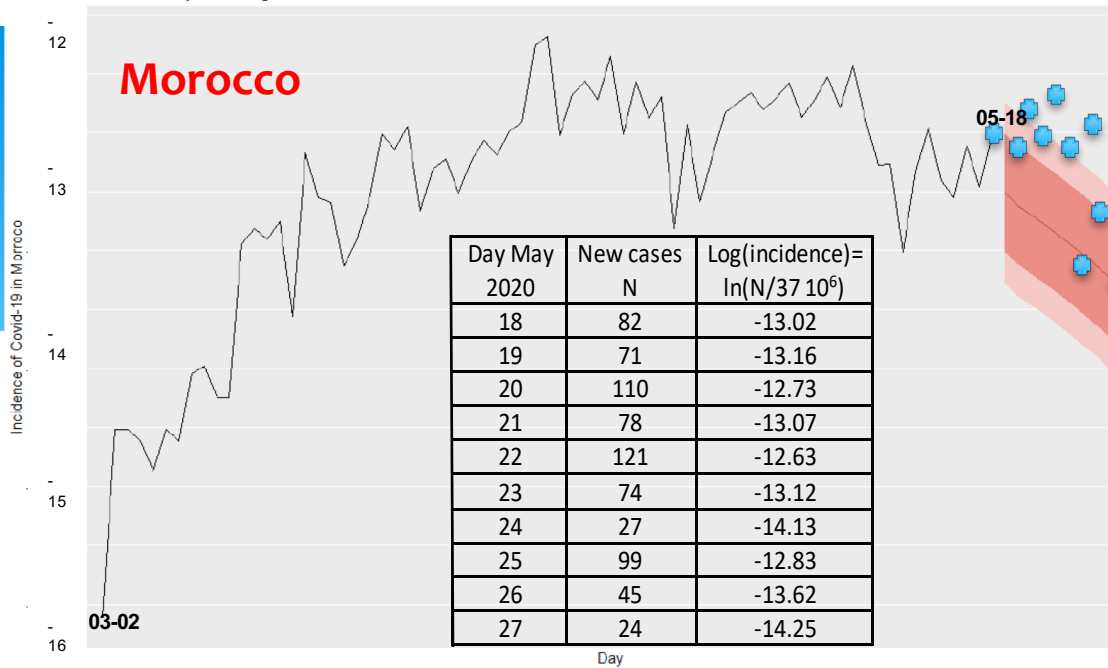
Top: New daily cases of the Covid-19 (in blue) with indication of the trend (in red) calculated by using the moving average method. Bottom: same series obtained by subtracting the trend (in blue) and indication of the moving average (in red).

| Country | ARIMA (3,1,0) Residual STD | ARIMA (4,1,0) Residual STD | ARIMA (5,1,0) Residual STD | ARIMA (6,1,0) Residual STD | ARIMA (3,1,1) Residual STD |
|---------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| France | 51.85 | 46.80 | 45.83 | 41.25 | 48.06 |
| Italy | 252.72 | 198.51 | | 184.90 | 230.10 |
| Germany | 99.98 | 99.97 | 99.96 | 95.54 | 99.97 |
| Chile | 1.99 | 2.00 | | 1.78 | |
| China | 361.52 | 344.30 | 343.50 | 342.61 | 349.15 |

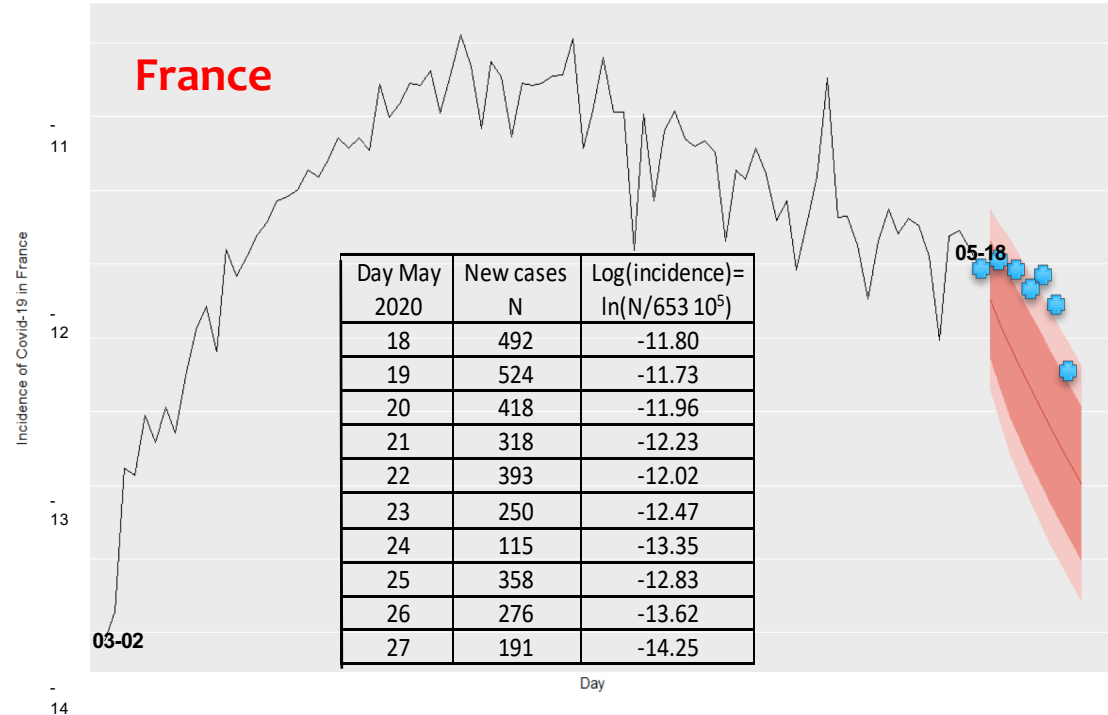


J. DEMONGEOT, Y. FLET-BERLIAC & H. SELIGMANN Temperature decreases spread parameters of the new covid-19 cases dynamics. *Biology (Basel)*, 9, 94 (2020).

Forecasts from Dynamic regression models



Forecasts from Dynamic regression models



Linear prediction before and after inflexion

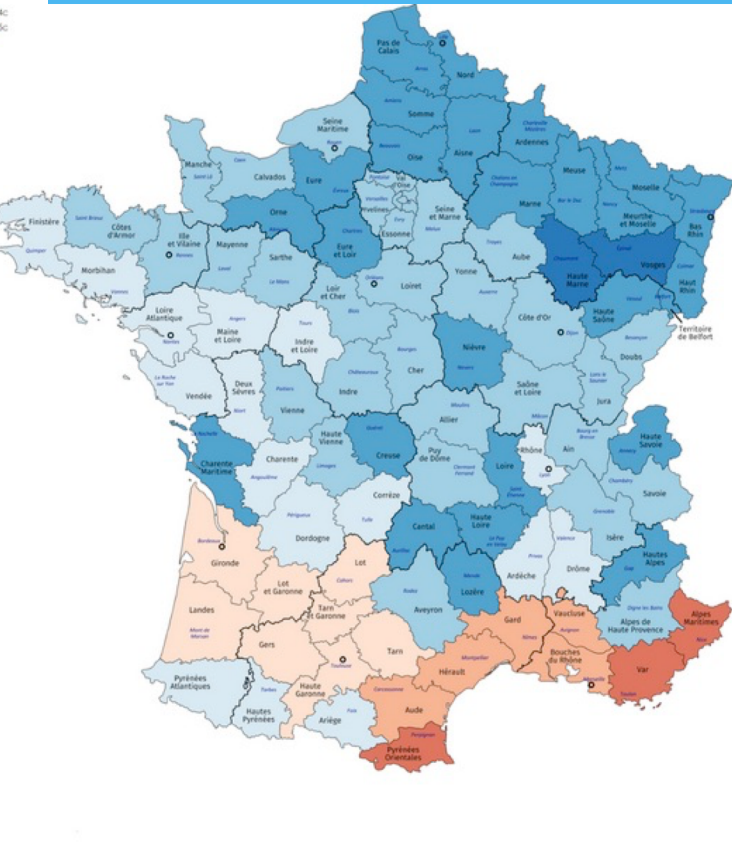
| | | Before resp. date (sd) | | After resp.date (sd) | |
|---------|--------------|------------------------|------------------|----------------------|----------------|
| Country | Trend change | Linear term | Quad. term | Linear term | Quad. term |
| Germany | 2020-04-04 | 0.3860(0.0322) | -0.0051(0.0008) | -0.0638(0.0091) | 3e-04(4e-04) |
| French | 2020-04-01 | 0.4094(0.0238) | -0.0054(0.0006) | -0.0508(0.0220) | 0(0) |
| Italy | 2020-03-22 | 0.3410 (0.0205) | -0.0045 (0.0006) | -0.0090 (0.0049) | -5e-04 (2e-04) |
| Morocco | 2020-04-17 | 0.1882(0.0382) | -0.0018(0.0011) | 0.0025 (0.0254) | -6e-04(7e-04) |
| UK | 2020-04-12 | 0.3403 (0.0169) | -0.0037 (0.0004) | 0.0230 (0.0101) | -9e-04 (3e-04) |
| USA | 2020-04-26 | 0.4489(0.0251) | -0.0048(0.0004) | -0.0092 (0.0217) | 1e-04 (8e-04) |
| Spain | 2020-04-01 | 0.3957(0.0267) | -0.0051(0.0006) | -0.0639 (0.0131) | 0 (3e-04) |



Dependence on air ambient temperature

Mean temperature in France

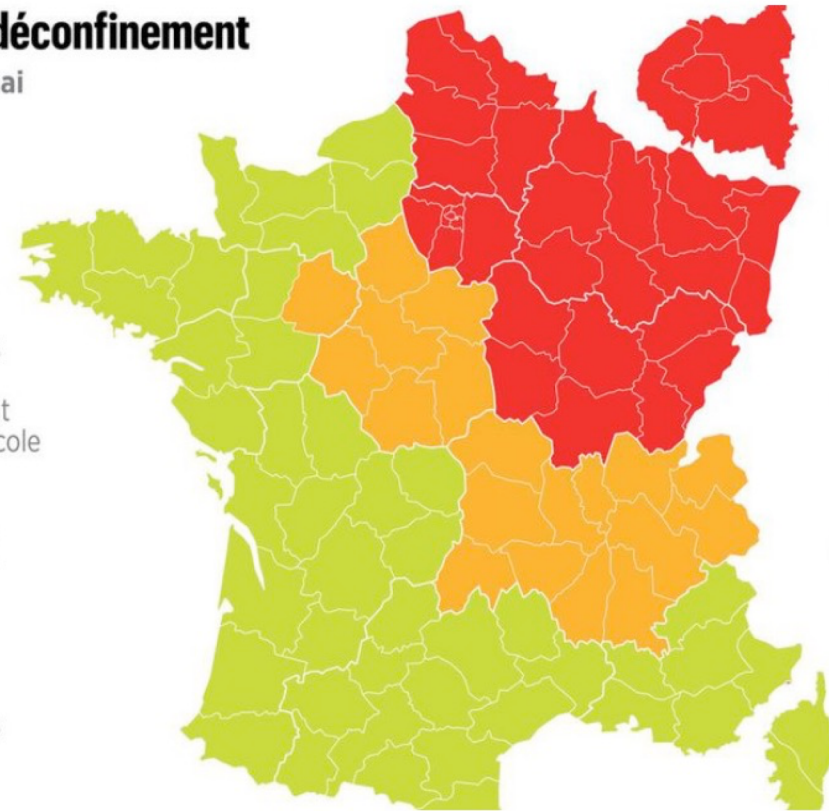
covid-19 spread



La carte du déconfinement

Situation au 3 mai

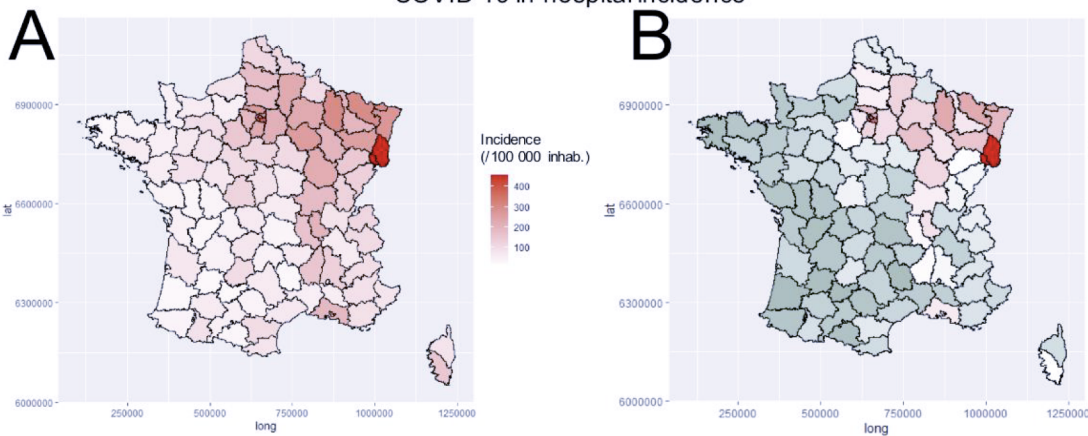
- Départements éligibles au déconfinement selon le protocole prévu
- Départements dont le déconfinement pourrait être durci
- Départements incertains



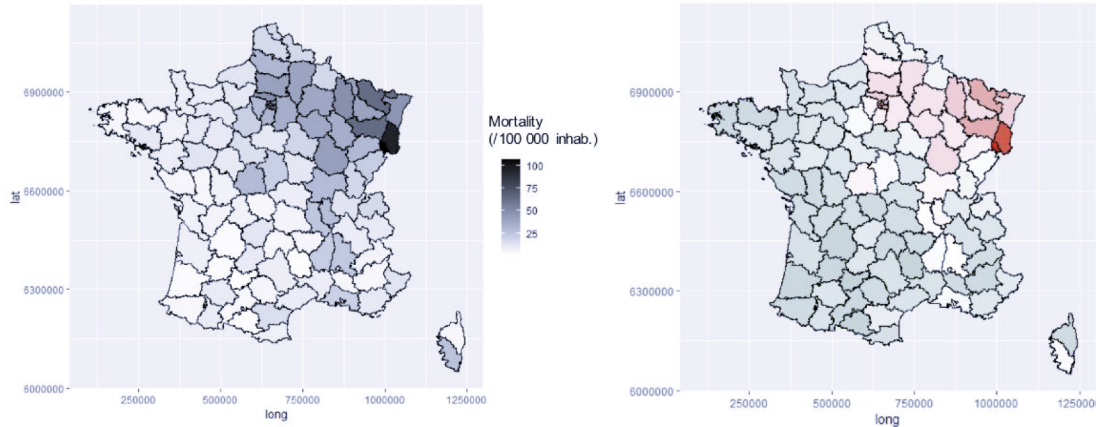
<https://www.reddit.com/r/MapPorn/comments/7rq6uh/average-annual-temperature-in-departments-of/>

<http://www.leparisien.fr/societe/coronavirus-135-deces-en-24-heures-une-nouvelle-carte-de-deconfinement-03-05-2020-8310096.php>

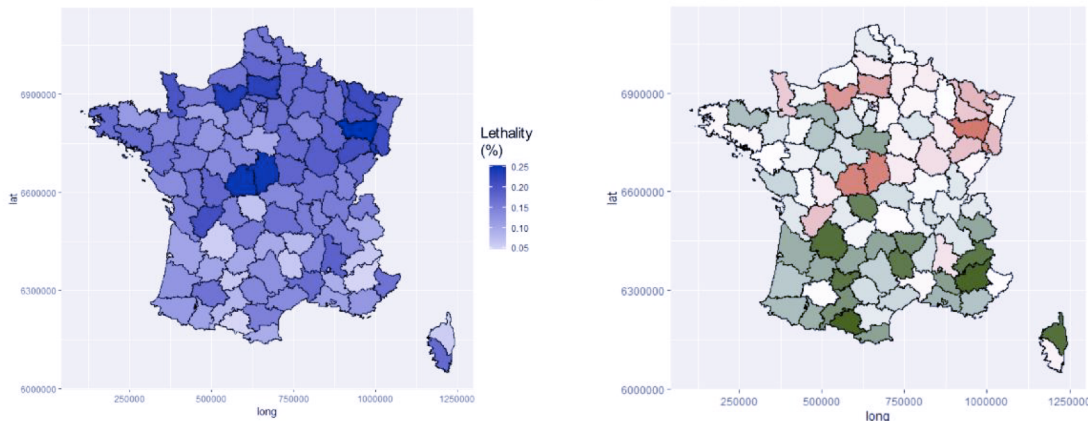
COVID-19 in-hospital incidence



COVID-19 in-hospital mortality



COVID-19 in-hospital lethality



Covid-19 in-hospital data

Gaudart et al. (2020)
The Lancet Public Health (submitted)

MedRxiv, doi.org/10.1101/2020.09.17.20196360doi (2020)

| French Regions | 2020 Temp | New Cases vs. Previous Day | | | | | | | |
|----------------------------|--------------|----------------------------|--------|--------|--------|-------|-------|-------|-------|
| | | 4III | 5III | 6III | 7III | 10III | 15III | 23III | 25III |
| Auvergne-Rhône-Alpes | 11.00 | 49 | 15 | 11 | 27 | 49.0 | 54.8 | 150.9 | 181.5 |
| Bourgogne-Franche-Comté | 10.00 | 16 | 23 | 39 | 51 | -2.0 | 67.6 | 110.8 | 111.0 |
| Bretagne | 11.53 | 23 | 6 | 3 | 8 | 14.3 | 27.0 | 34.0 | 56.5 |
| Centre-Val de Loire | 10.73 | 0 | 2 | 9 | 5 | 1.0 | 14.0 | 34.0 | 100.0 |
| Corse | 14.13 | 0 | 3 | 0 | 2 | 12.3 | 14.6 | 9.9 | 15.5 |
| Grand Est | 9.00 | 38 | 39 | 59 | 114 | 79.7 | 201.4 | 345.0 | 611.5 |
| Hauts de France | 10.40 | 65 | 9 | 23 | 76 | 25.3 | 58.0 | 91.3 | 242.0 |
| Ile de France | 10.80 | 55 | 21 | 13 | 15 | 121.3 | 275.6 | 545.6 | 724.5 |
| Normandie | 10.53 | 2 | 4 | 5 | 0 | 9.7 | 21.6 | 45.4 | 88.5 |
| Nouvelle-Aquitaine | 13.40 | 5 | 3 | 3 | 6 | 13.3 | 19.0 | 65.5 | 118.0 |
| Occitanie | 12.60 | 9 | 2 | 7 | 18 | 11.3 | 36.0 | 64.6 | 157.5 |
| Pays de la Loire | 11.40 | 7 | 1 | 8 | 2 | 4.3 | 15.4 | 23.1 | 37.5 |
| Provence-Alpes-Côte d'Azur | 11.80 | 13 | 5 | 8 | 12 | 24.0 | 56.2 | 139.9 | 208.5 |
| Pearson Rx100 | | -48.95 | -68.34 | -74.73 | -65.17 | -34.3 | -48.1 | -43.5 | -43.8 |

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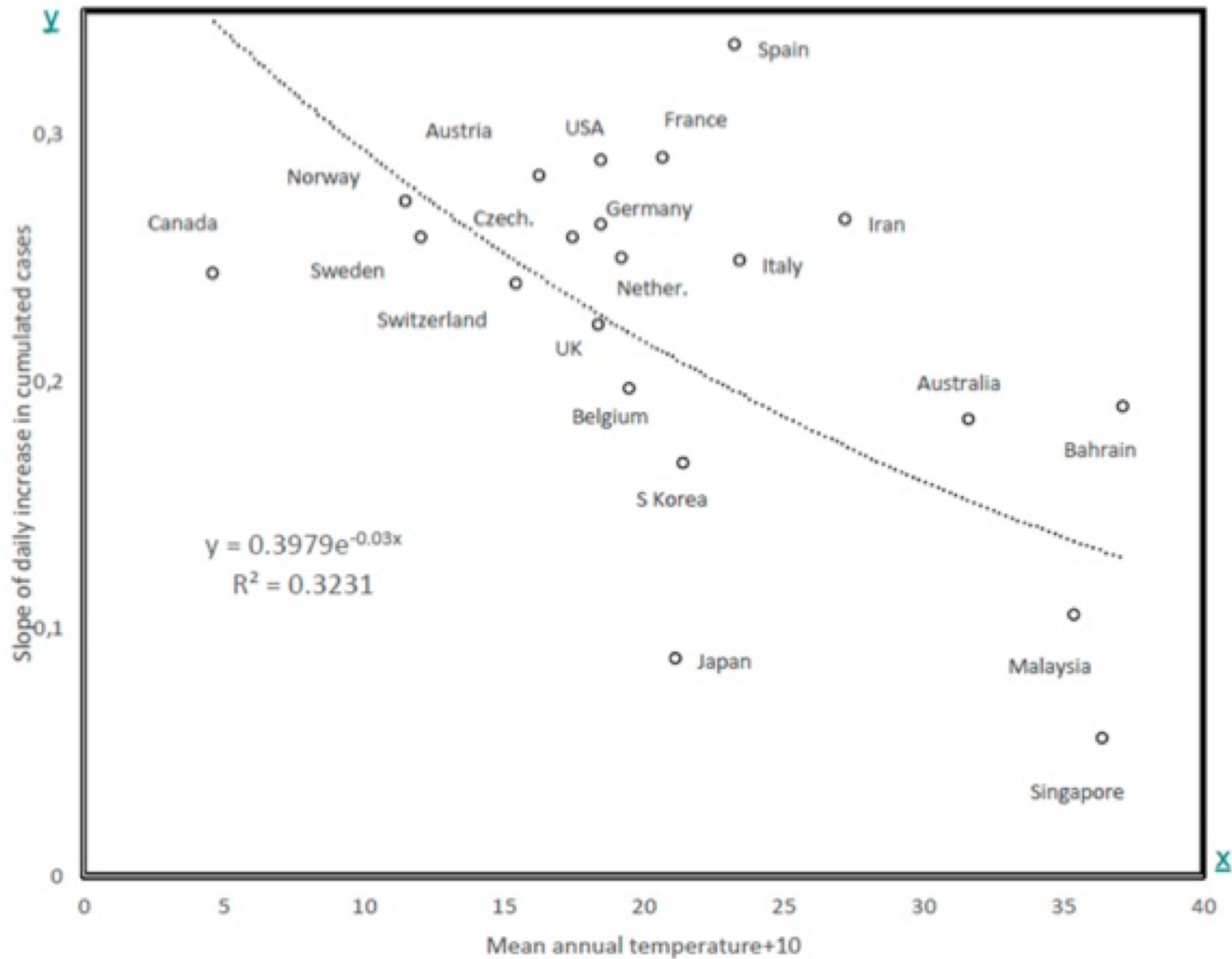


Figure 4. Slope of exponential model fitted to data in Table 3 as a function of mean annual temperature in that country. The Pearson correlation coefficient is $R = -0.568$, one-tailed $p = 0.0036$.

The second wave

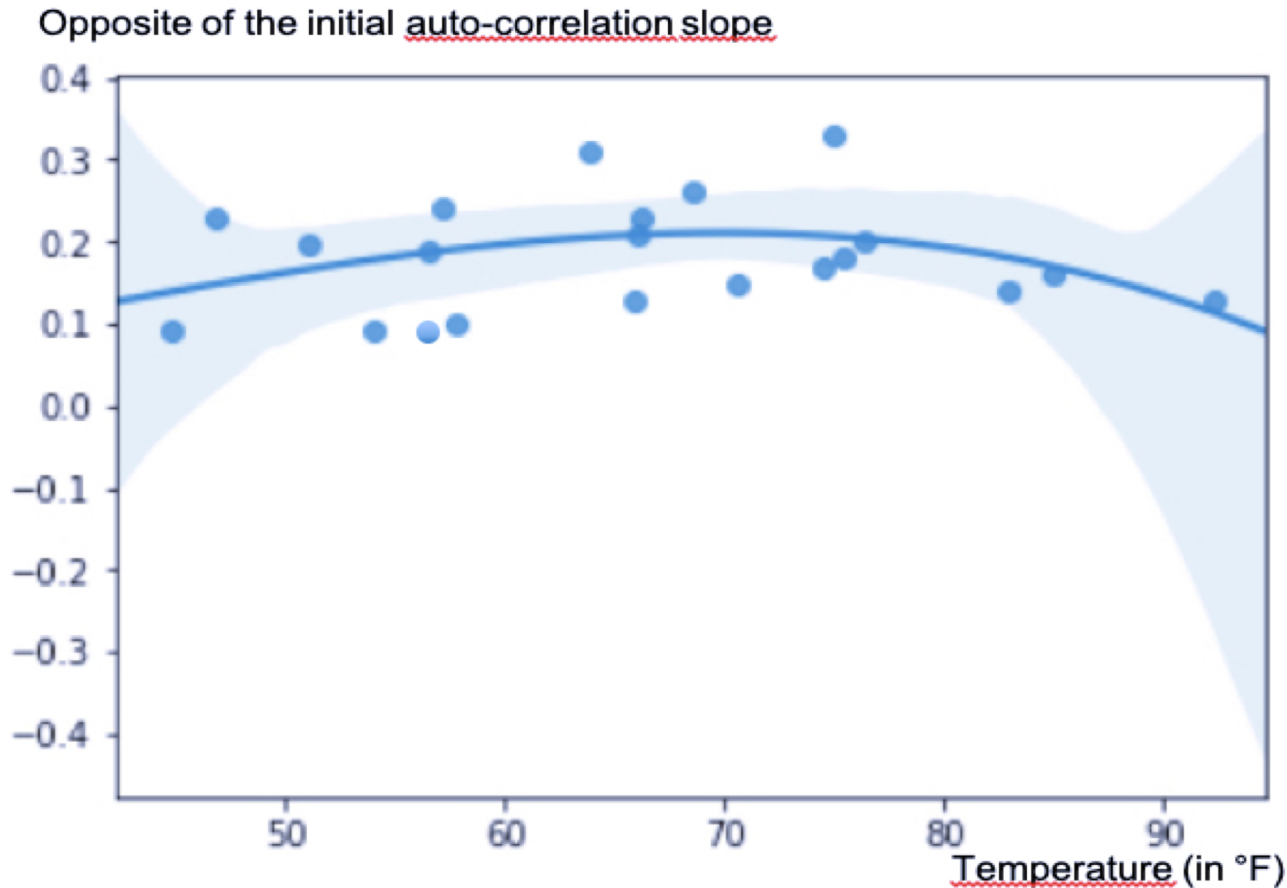
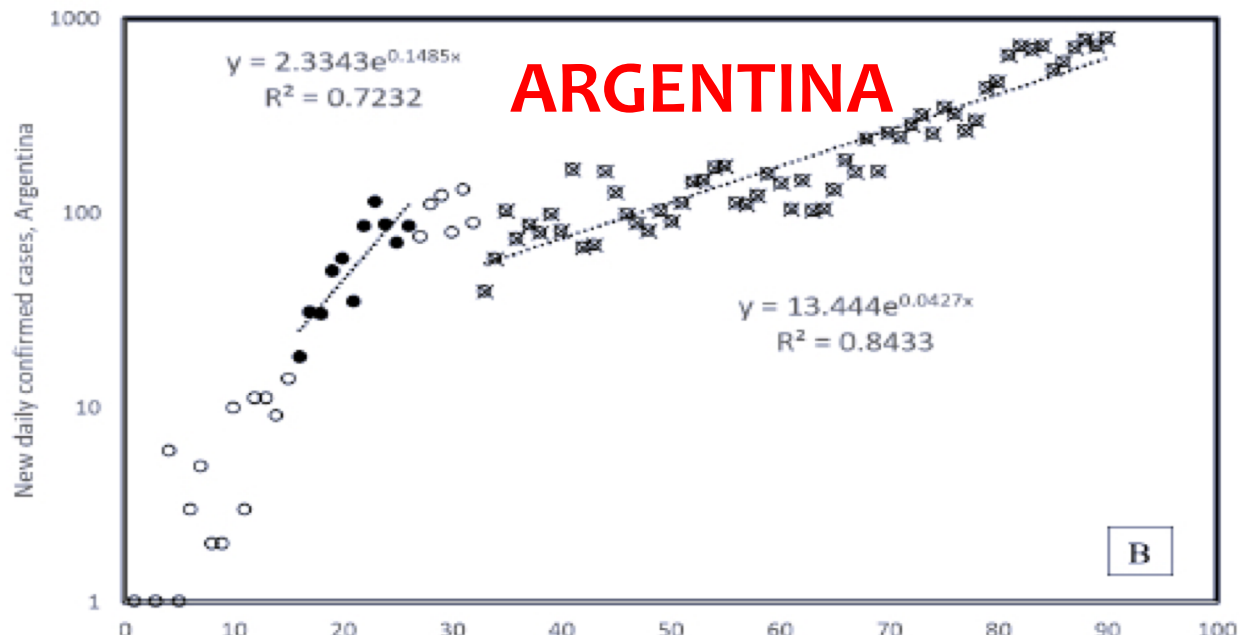
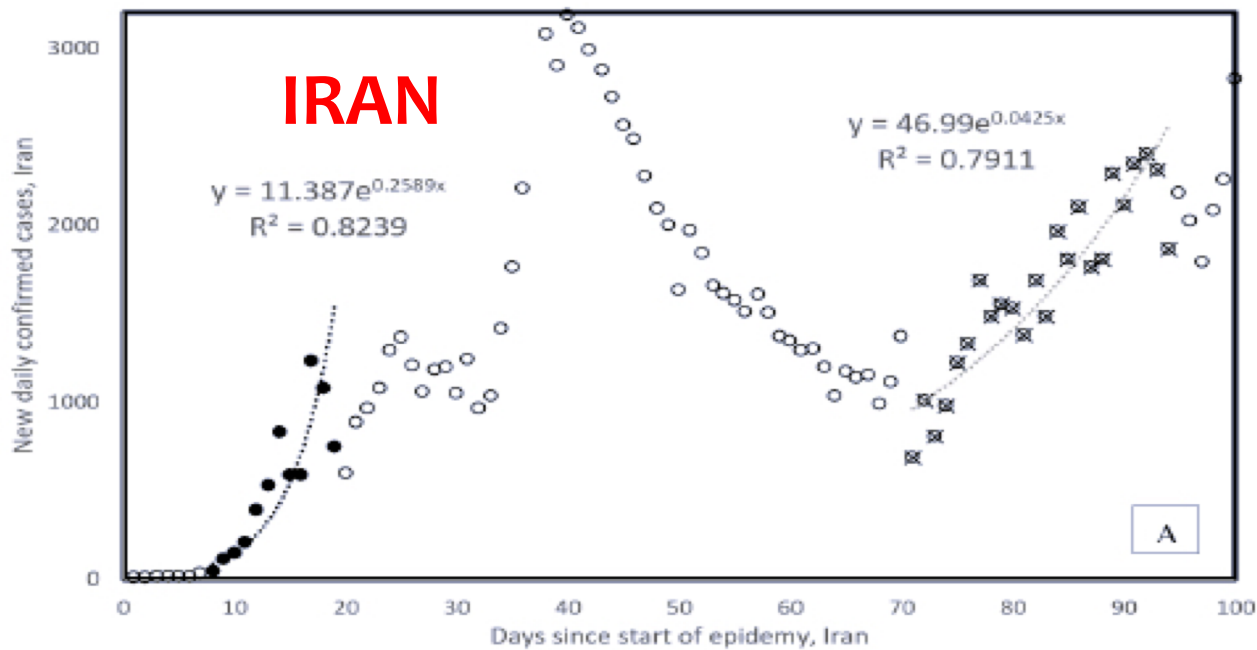


Figure 11. Parabolic regression of the opposite of the initial slope vs temperature. The blue zone corresponds to the 95%-confidence set in the neighbourhood of the regression parabola.

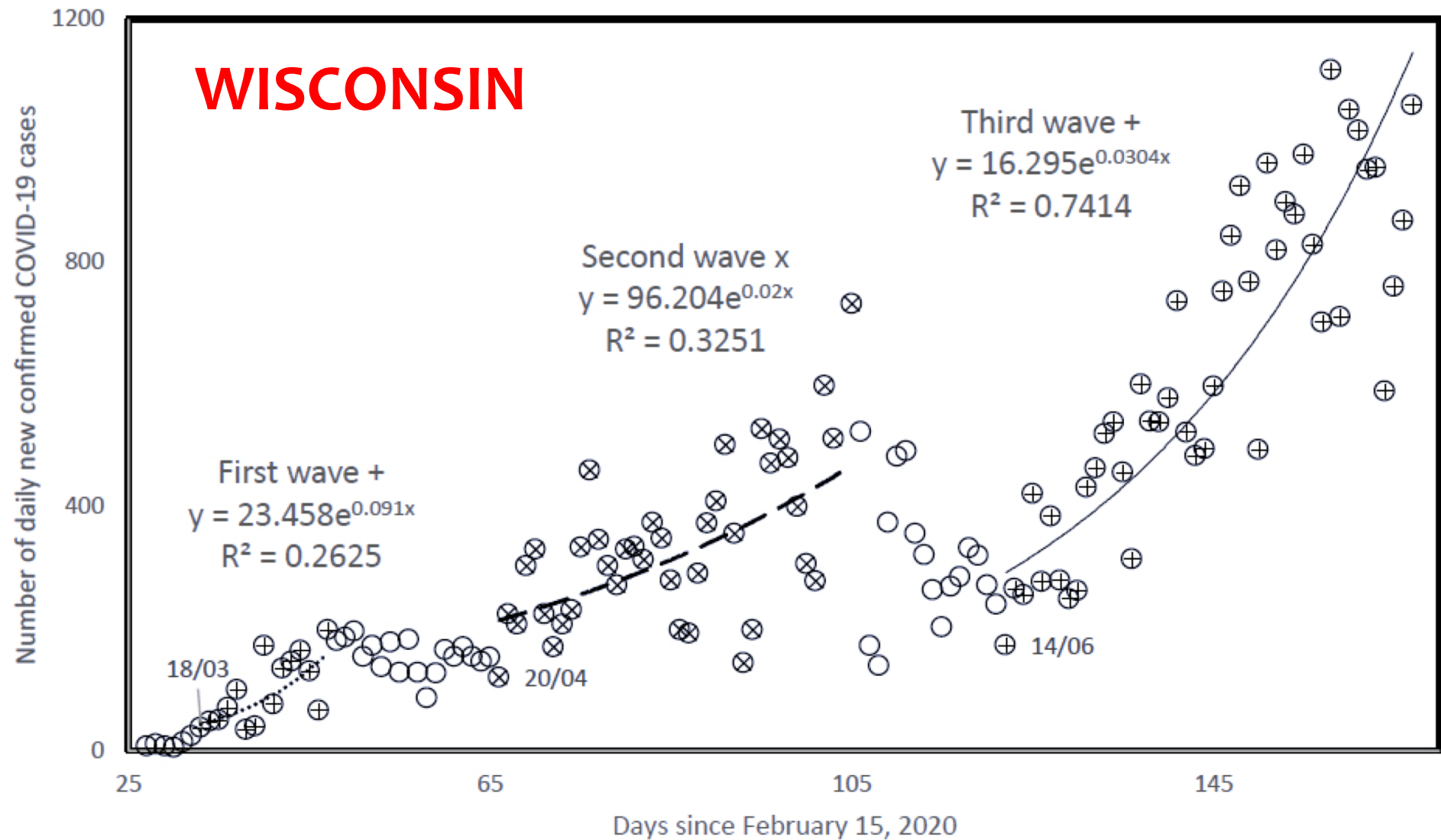
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H. SELIGMANN, S. IGGUI, M. RACHDI, N. VUILLERME & J. DEMONGEOT Inverted covariate effects for mutated 2nd vs 1st wave Covid-19: high temperature spread biased for young. *Biology*, 9, 226 (2020).

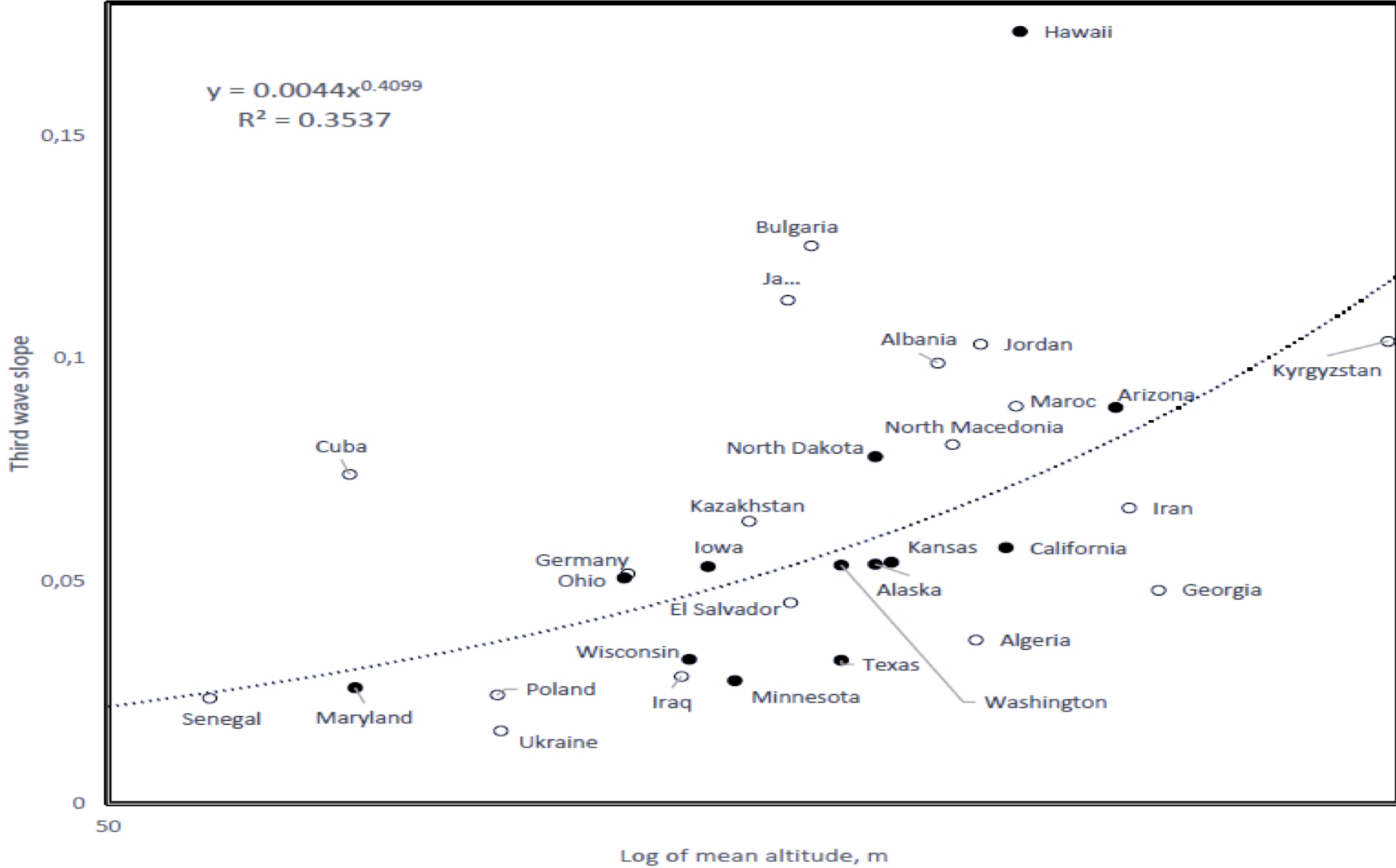
WISCONSIN



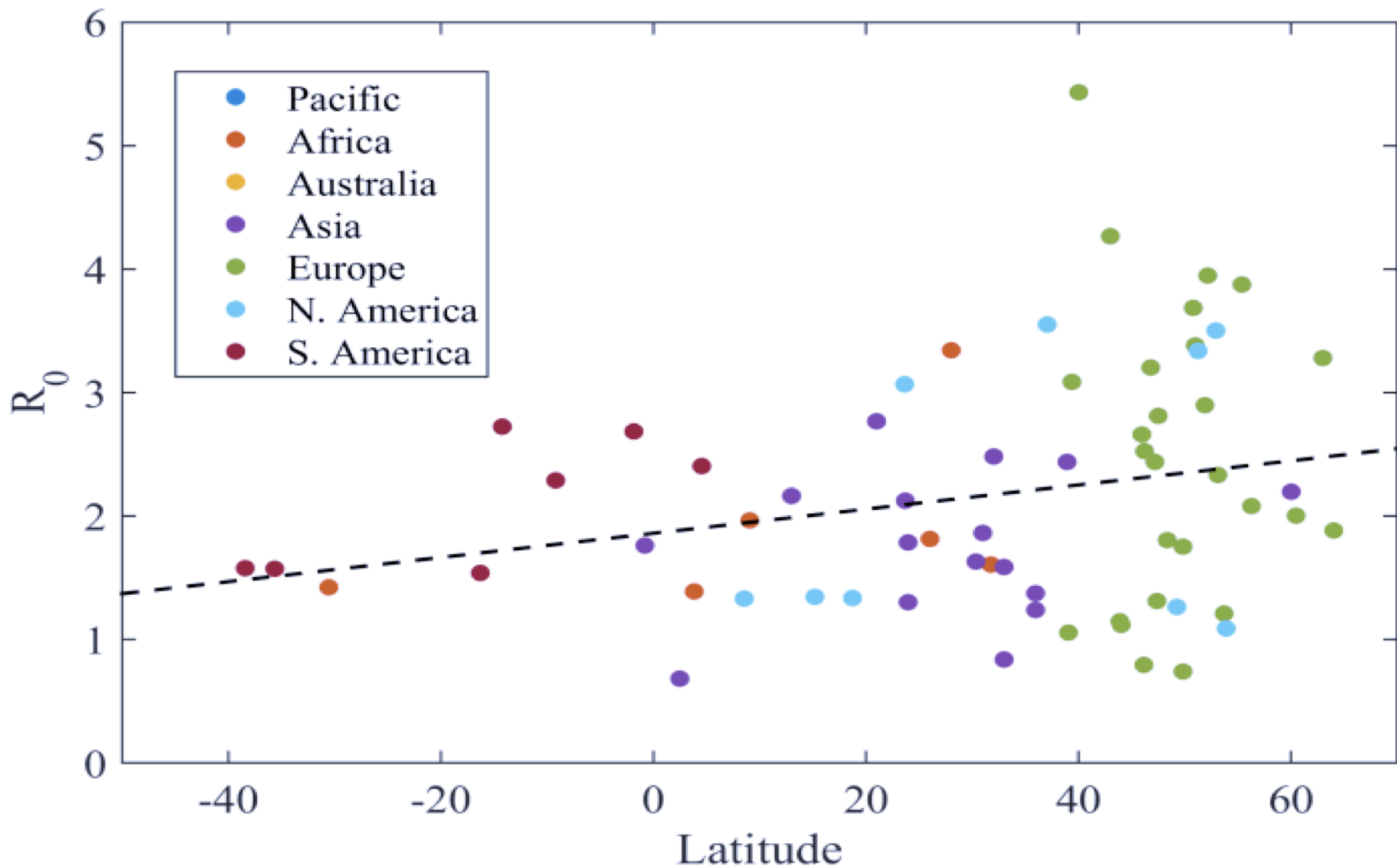
H. SELIGMANN, N. VUILLERME & J. DEMONGEOT Summer COVID-19 third wave like (winter) first wave, opposite to (spring) second wave: slower spread decreases with temperature, increases with population age. *Biology* (submitted). *MedRxiv*, doi.org/10.1101/2020.08.17.20176628 (2020)



Other geoclimatic parameters



H. SELIGMANN, N. VUILLERME & J. DEMONGEOT Summer COVID-19 third wave like (winter) first wave, opposite to (spring) second wave: slower spread decreases with temperature, increases with population age. *Biology* (submitted). *MedRxiv*, doi.org/10.1101/2020.08.17.20176628 (2020).



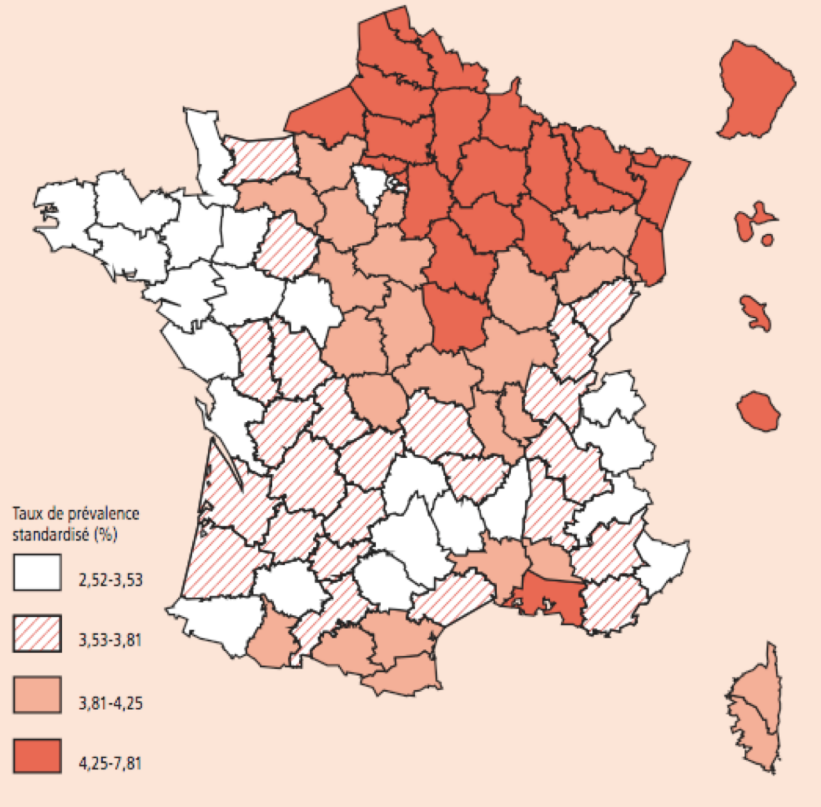
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Dependence on genomic factors of the susceptible population

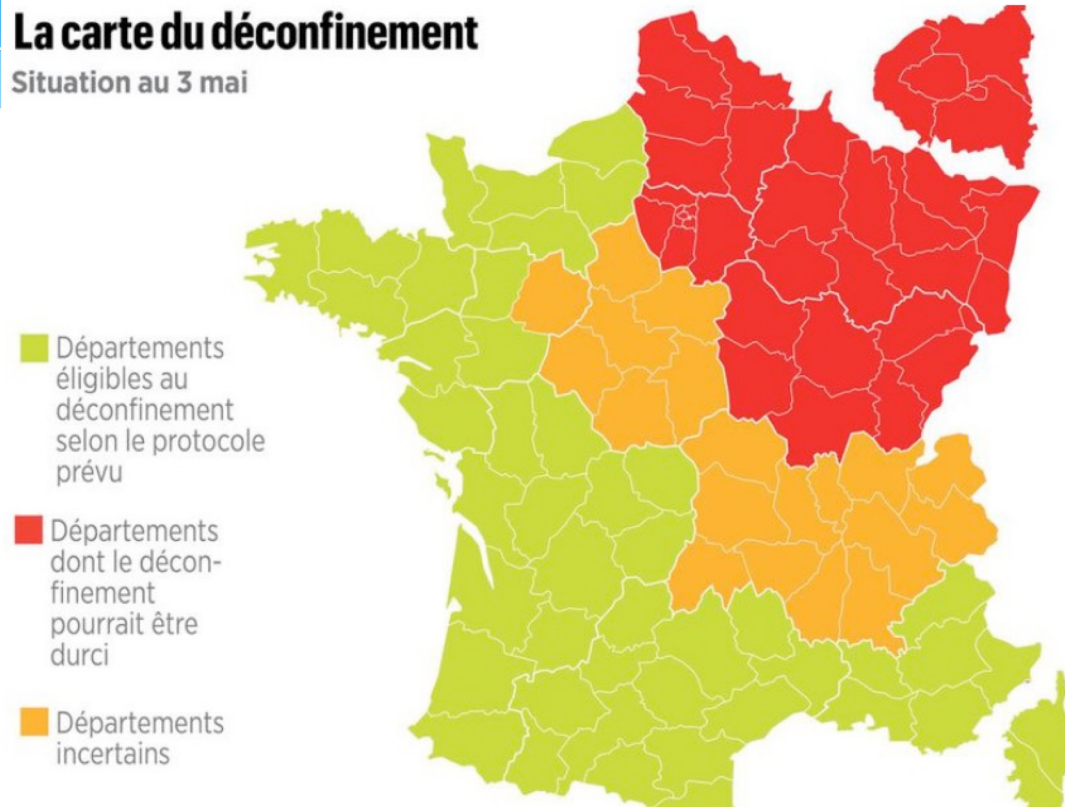
Type II diabetes in France

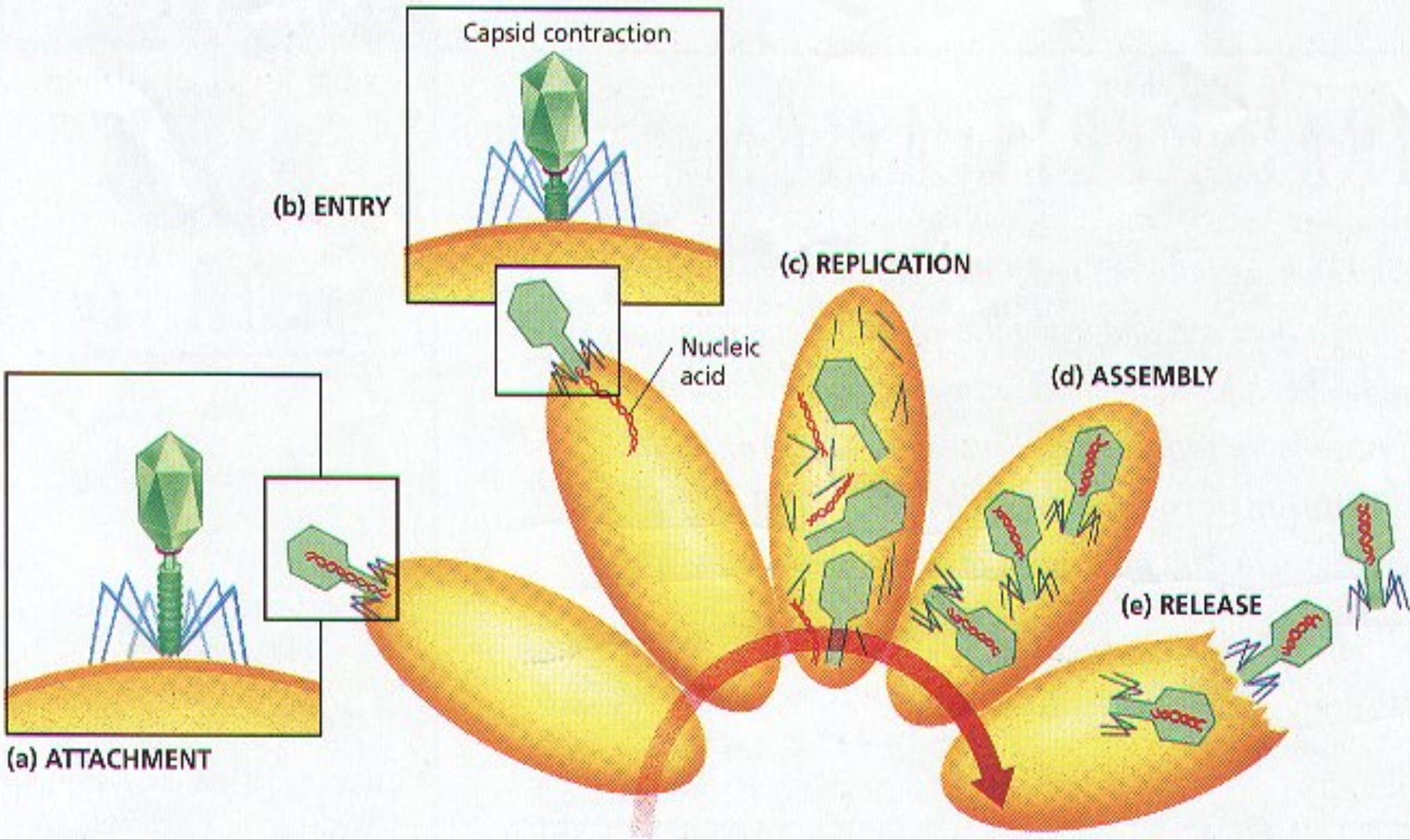
covid-19 spread

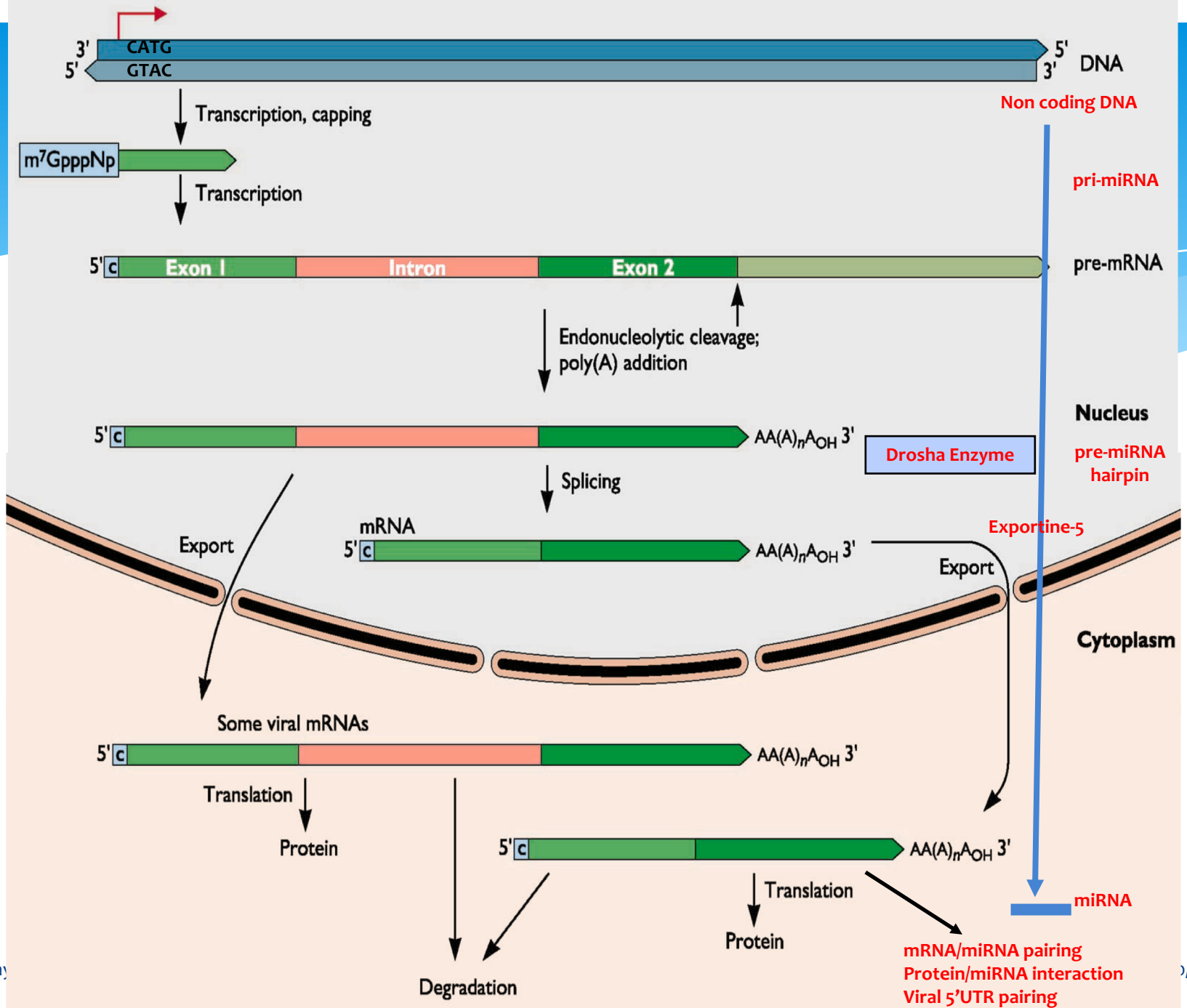


La carte du déconfinement

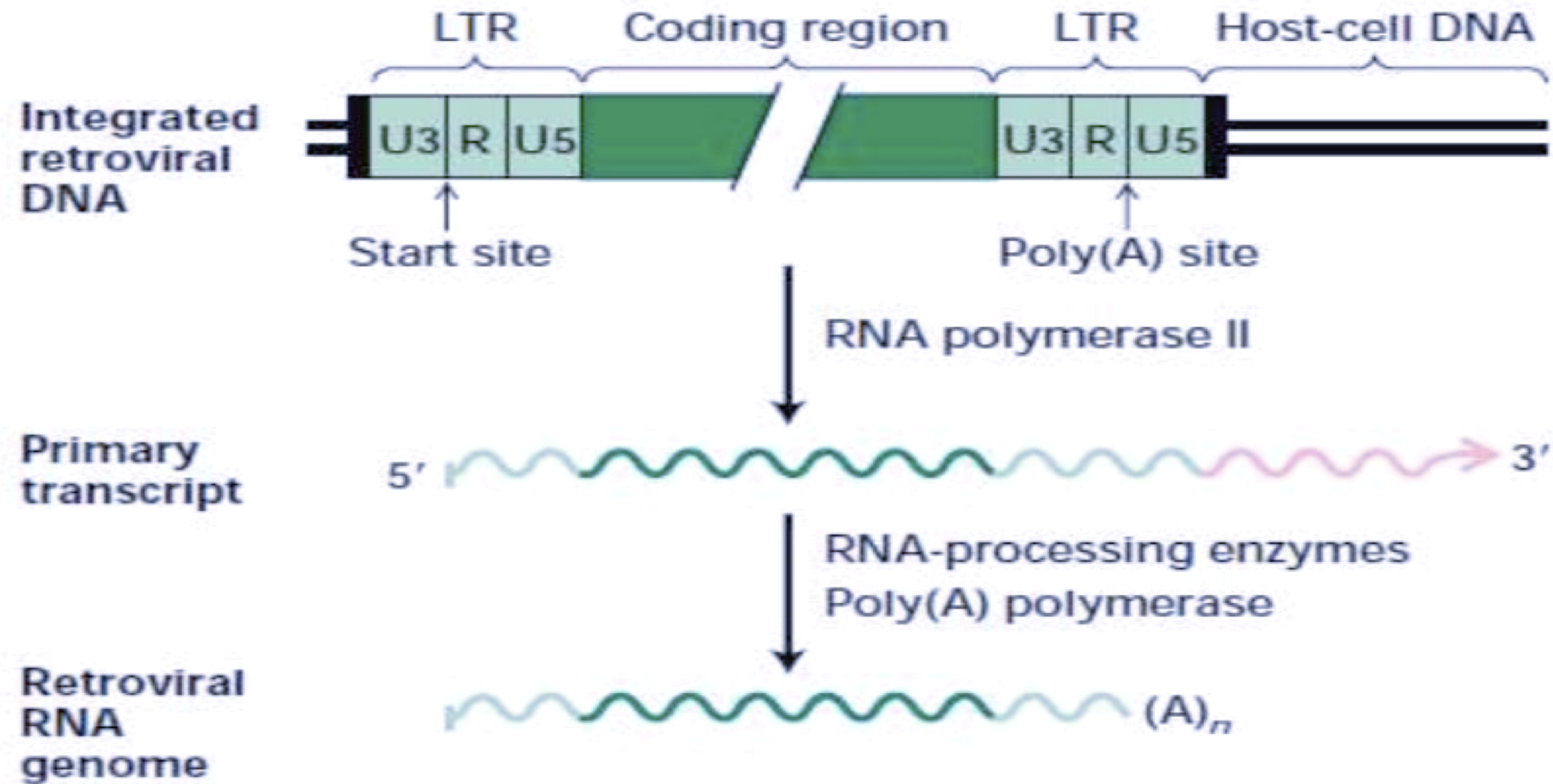
Situation au 3 mai







Generation of retroviral genomic RNA from integrated retroviral DNA



Ref: Molecular cell biology(Iodish et all. 2008)

Beneficial Functions of HERVs

- Enhancement and promotion of gene expression
- HERV-E LTR
 - enhancer for endothelin B receptor and apolipoprotein C- I
- HERV-H LTR
 - enhancer activities in embryonic and hematopoietic cells
- Would be considered as “foreign”
- Could trigger B-cells to produce antibodies against them
- **Cross-react** with other proteins of our bodies
- **Molecular mimicry** mechanism

ATGGGGCAAAC TAAAGTAAAAT TAAAAGTAAATATGCCTCTTATCTCAGCTTTATTAAAATTC TTTTAA
AAAGAGGGGGAGTTAAAGTATCTACAAAAATCTAATCAAGCTATTTCAAATAATAGAACAATTTTGCCC
ATGGTTTCCAGAACAAGGAAC TTTAGATCTAA AAGAT TGGAAAAGAAT TGGTAAGGAACTAAAACAAGCA
GGTAGGAAGGGTAATAT CATTCCACTTACAGTATGGAATGATTGGGCCATTATTAAAGCAGCTTTAGAAC
CATTTCAAACAGAAG AAGATAGCGTTTCAGTTTCTGATGCCCTTGGAAAGCTGTATAATAGATTGTAATGA
AAACACAAGGAAAAAATCC CAGAAAGAAACGGAAGGTTTACATTGCGAATATGTAGCAGAGCCGGTAATG
GCTCAGTCAACGCAAATGTTGACTATAATCAATTACAGGAGGTGATATATCCTGAAACGTTAAAATTAG
AAGGAAAAGGTCCAGAATTAGTGGGGCCATCAGAGTCTAAACCACGAGGCACAAGTCATCTTCCAGCAGG
TCAGGTGCCCGTAACATTACAACCTCAAAGCAGGTTAAAGAAAATAAGACCCAACCGCCAGTAGCCTAT
CAATACTGGCCTCCGGCTGAAC TTCAGTATCGGCCACCC CAGAAAGTCAGTATGGATATCCAGGAATGC
CCCAGCACCCACAGGGCAGGGC GCCATACCCTCAGCCGCCACTAGGAGACTTAATCCTACGGCACCCACC
TAGTAGACAGGGTAGTGAATTACATGAAATTATTGATAAA TCAAGA AAGGAAGGAGATACTGAGGCATGG
CAATTCCCAGTAACGTTAGAACCGATGCCACCTGGAGAAGGAGCCCAAGAGGGAGAGCCTCCACAGTTG
AGGCCAGATACAAGTCTTTTTCGATAAAAATGCTAA AAGATATGAAAGAGGGAGTAAAACAGTATGGACC
CAACTCCCCTTATATGAGGACATTATTAGATTCCATTGCTCATGGACATAGACTCATTCTTATGATTGG
GAGATTCTGGCAAATCGTCTCTCTCACCCTCTCAATTTT TACAATTTAAGACTTGGTGGATTGATGGG
TACAAGAACAGGTCCGAAGAAATAGGGCTGCCAATCCTCCAGTTAACATAGATGCAGATCAACTATTAGG
AATAGGTCAAATTTGGAGTACTATTAGTCAACAAGCATTAAATGCAAATGAGGCCATTGAGCAAGTTAGA
GCTATCTGCC TTAGAGCCTGGGAAAAAATCCAAGACCCAGGAAGTACCTGCCCTCATTTAATACAGTAA
GACAAGGTTCAA AAGAGCCCTATCCTGATTTTGTGGCAAGGCTCCAAGATGTTGCTCAAAGTCAATTGC
CGATGAA AAGCCCGTAAGGTCATAGTGGAGTTGATGGCATATGAAACGCCAATCCTGATGTCAATCAG
CCATTAAGCCATTAA

Observed 50 ancient pentamers (red) among 1481 possible = 3.4% (expected 2.1%±0.5%)

Figure 5. Complete RNA sequence of the Gag protein of the virus HERV-K102 [36]. The green subsequence of length 14 (271-285) is present in the RNA sequence of the protein S of the virus Covid-19 [22]. Red: pentamers belonging to ancient circular RNAs as measure of the genomic structure's age in evolution [7,8].

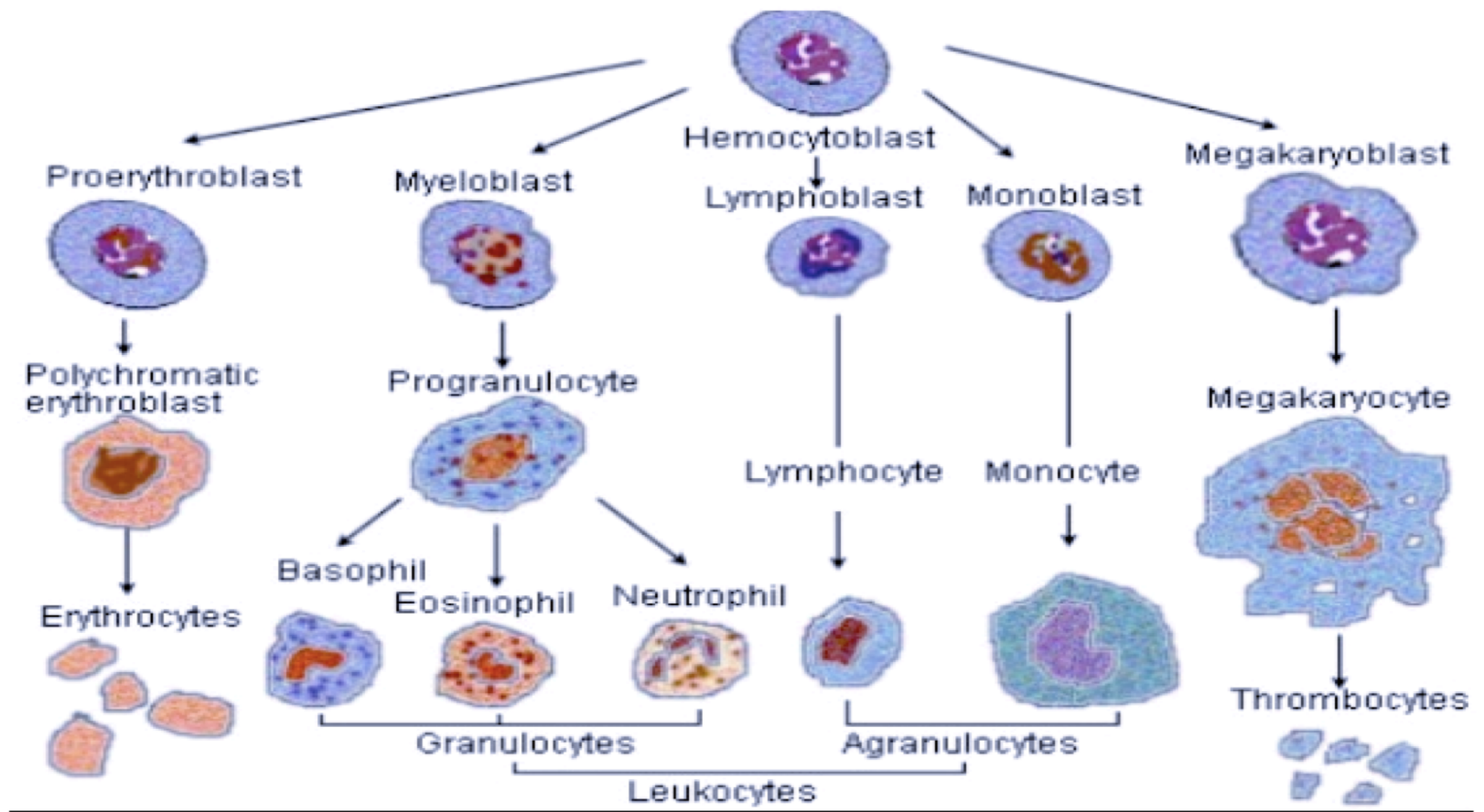
Covid-19 dynamics depends on genomic factors like retro-viruses

5' - **TGAGGTATTGTGAATTTTCACCTTTTA** - 3' **Protein S Covid-19**

3' - **GGCTTTATTCTGCAAGCAATCAA**ATAAT - 5' **Homo sapiens HBG2**

5' - CCCGGGCT**TGAGGTAGGAGGTTGTATAGTT**GAGGAGGACACCCAAGGAGATCACTATACG - 3'
**Homo sapiens microRNA let-7e (MIRLET7E), microRNA NCBI Reference
Sequence: NR_029482.1**

- J. DEMONGEOT, E. DROUET, A. MOREIRA, Y. RECHOUM & S. SENÉ.** Micro-RNAs: viral genome and robustness of the genes expression in host. *Phil. Trans. Royal Soc. A*, **367**, 4941-4965 (2009).
- J. DEMONGEOT & H. SELIGMANN.** Covid-19 and miRNA-like inhibition power. *Medical Hypotheses*, **144**, 110245 (2020).



Homo sapiens erythropoietin (EPO), mRNA [NCBI Reference Sequence: NM_000799.4](#)

TTTTCACCTTTTACTACGCC Protein S Covid-19

CCTTTCCCAGATAGCACGCTCCGCCAGTCCCAAGGGTGC GCAACCGGCTGCACTCCCCTCCCGCGACCCA
 GGGCCCGGGAGCAGCCCCCATGACCCACACGCACGTCTGCAGCAGCCCCGCTCACGCCCCGGCGAGCCTC
 AACCCAGGCGTCT**CTGCC**CCTGCTCTGACCCCGGGTGGCCCCCTACCCCTGGCGACCCCTCACGCACACAGC
 CTCTCCCCACCCCCACCCGCGCACGCACACATGCAGATAACAGCCCCGACCCCCGGCCAGAGCCCGCAGA

ACGGGCGGCTCCTTTAATCAG Protein S Covid-19

GTCCCTGGGCCACCCCGGCGCTCGCTGCGCTGCGCCGCACCGCGCTGTCCTCCCGGAGCCGGACCGGGG
 CCACCGCGCCCGCTCTGCTCCGACACCGCGCCCCCTGGACAGCCGCCCTCTCCTCCAGGCCCGTGGGGCT
 GGCCCTGCACCGCCGAGCTTCCCGG**GATGA**GGGCCCCCGGTGTGGTCAACCGGCGCGCCCCAGGTGCGCTG

TTTTCACCTTTTACTACGCC Protein S Covid-19

AGGGACCCCGGCCAGGCGCGG**AGATG**GGGGTGCAC**GAATG**TCT**CTGCC**TGGCTGTGGCTTCTCCTGTCCCT

| First author (year) | Region | Study period | Sample size | Categorisation of haematological factors | Main findings |
|----------------------------|---|---|-------------|--|--|
| Guan (2020) ¹⁶ | 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China | December 11, 2019 - January 31, 2020 | 1099 | Lymphocytopenia: lymphocyte count of less than 1500 cells/mm ³ | Lymphocytopenia was present in 83.2% of patients on admission. 92.6% (50/54) of patients with the composite primary endpoint (admission to an intensive care unit, use of mechanical ventilation, or death) presented with lymphocytopenia vs. 82.5% (681/825) of patients without the primary endpoint (p=0.056 ^a). Severe cases presented lymphocytopenia more frequently (96.1%, 147/153) vs. non-severe cases (80.4%, 584/726); p<0.001 ^a |
| Huang (2020) ¹⁷ | Jinyintan Hospital, Wuhan, China | December 16, 2019, to January 2, 2020 | 41 | Low lymphocyte count of <1.0 x10 ⁹ lymphocytes per litre | 85% (11/13) of patients needing ICU care presented low lymphocyte count vs. 54% (15/28) of patients that did not need ICU care (p=0.045). |
| Wang (2020) ¹⁹ | Zhongnan Hospital, Wuhan, China | January 1 to February 3, 2020 | 138 | Lymphocytes treated as a continuous variable, x10 ⁹ per L | ICU cases presented with lower lymphocyte count (median:0.8, IQR: 0.5-0.9) vs. non-ICU cases (median: 0.9, IQR: 0.6-1.2); p=0.03. Longitudinal decrease was noted in non-survivors. |
| Wu (2020) ²⁰ | Jinyintan Hospital, Wuhan, China | December 25, 2019, to February 13, 2020 | 201 | Lymphocytes treated as a continuous variable, x10 ⁹ /mL in a bivariate Cox regression model | Lower lymphocyte count was associated with ARDS development (HR=0.37, 95%CI: 0.21-0.63, p<0.001 in the incremental model); the association with survival did not reach significance (HR=0.51, 95%CI: 0.22-1.17, p=0.11) |
| Young (2020) ²¹ | 4 hospitals in Singapore | January 23 to February 3, 2020 | 18 | Lymphocytes treated as a continuous variable, x10 ⁹ per L; lymphopenia was defined as <1.1 x10 ⁹ /L. | Lymphopenia was present in 7 of 16 patients (39%). Median lymphocyte count was 1.1 (IQR: 0.8-1.7) in patients that required supplemental O ₂ and 1.2 (IQR:0.8-1.6) in those that did not; no statistical comparison was undertaken. |

Blood routine parameters of patients with COVID-19 on admission.

| | Median (IQR) | | <i>P</i> value |
|-----------------------------------|----------------------------|---------------------------|----------------|
| | All patients (n = 116) | Controls (n = 100) | |
| Age, Median(IQR),Range, years | 50.0 (41.0–57.0), 20–93 | 48.5(37.3–59.8), 21–90 | 0.397 |
| Sex | | | 0.739 |
| Male(%) | 60 (51.7%) | 53 (53.0%) | |
| Female(%) | 56 (48.3%) | 47 (47.0%) | |
| Blood routine | | | |
| Leucocytes($\times 10^9$ per L) | 4.60 (3.76–6.40) | 5.95 (5.13–6.88) | < 0.001 |
| Neutrophils($\times 10^9$ per L) | 3.10 (2.33–4.30) | 3.20 (2.70–3.88) | 0.456 |
| Lymphocytes($\times 10^9$ per L) | 1.00 (0.72–1.40) | 2.10 (1.80–2.40) | < 0.001 |
| Monocyte($\times 10^9$ per L) | 0.39 (0.29–0.49) | 0.40 (0.34–0.47) | 0.372 |
| Eosinophil($\times 10^9$ per L) | 0.02 (0.01–0.05) | 0.10 (0.06–0.16) | < 0.001 |
| Hemoglobin(g/L) | 132.5 (122.3–145.8) | 146.5 (135.0–156.0) | < 0.001 |
| Platelet($\times 10^9$ per L) | 180.5 (145.5–229) | 240.0 (202.8–274.8) | < 0.001 |
| MLR | 0.37 (0.27–0.56) | 0.19 (0.17–0.23) | < 0.001 |
| NLR | 2.91 (1.87–4.83) | 1.58 (1.34–1.98) | < 0.001 |
| PLR | 169.0 (123.5–245.6) | 113.0 (95.1–138.2) | < 0.001 |

Homo sapiens hemoglobin subunit beta (HBB), mRNA NCBI Reference Sequence: NM_000518.5

ACATTTGCTTCTGACACAACCTGTGTTCACTAGCAACCTCAAACAGACACCATGGTGCATCTGACTCCTGA
GGAGAAGTCTGCCGTTACTGCCCTGTGGGGCAAGGTGAACGTGGATGAAGTTGGTGGTGAGGCCCTGGGC
TGGGAGCAGCAAGAGAACCGT mir-451b
AGGCTGCTGGTGGTCTACCCTTGGACCCAGAGGTTCTTTGAGTCCTTTGGGGATCTGTCCACTCCTGATG
TACAGTATAGATGATGTACT miR-144-3p
CTGTTATGGGCAACCCTAAGGTGAAGGCTCATGGCAAGAAAGTGCTCGGTGCCTTTAGTGATGGCCTGGC
TCACCTGGACAACCTCAAGGGCACCTTTGCCACACTGAGTGAGCTGCACTGTGACAAGCTGCACGTGGAT
AAACCGTTACCATTAC
CCTGAGAACTTCAGGCTCCTGGGCAACGTGCTGGTCTGTGTGCTGGCCCATCACTTTGGCAAAGAATTCA
TGAGTT mir-451a **TATTGCACTTGTCCCGGCCTGT miR-92a-3p**
CCCCACCAGTGCAGGCTGCCTATCAGAAAGTGGTGGCTGGTGTGGCTAATGCCCTGGCCACAAGTATCA
5'-TTTTCACCTTTTACTACGCC-3' Protein S Covid-19
CTAAGCTCGCTTTCTTGCTGTCCAATTTCTATTAAAGGTTCCCTTTGTTCCCTAAGTCCAACACTAAACT
AGGTTGGGATCGGTTGCAATG miR-92a-1-5p
GGGGGATATTATGAAGGGCCTTGAGCATCTGGATTCTGCCTAATAAAAAACATTTATTTTCATTGCAA

Figure 2. Human beta-globin gene [24] potentially targeted by a subsequence from Covid-19 protein S [23] (in blue), by microRNA miR-93a known for inhibiting its translation [25] (in green) and by microRNAs involved in erythrocyte maturation [26-31] (in red).

J. DEMONGEOT & H. SELIGMANN Covid-19 and miRNA-like inhibition power. *Medical Hypotheses*, **144**, 110245 (2020).

Neanderthal effect

Zeberg, H. et al. The major genetic risk factor for severe COVID-19 is inherited from Neanderthals. Nature <https://doi.org/10.1038/s41586-020-2818-3> (2020).

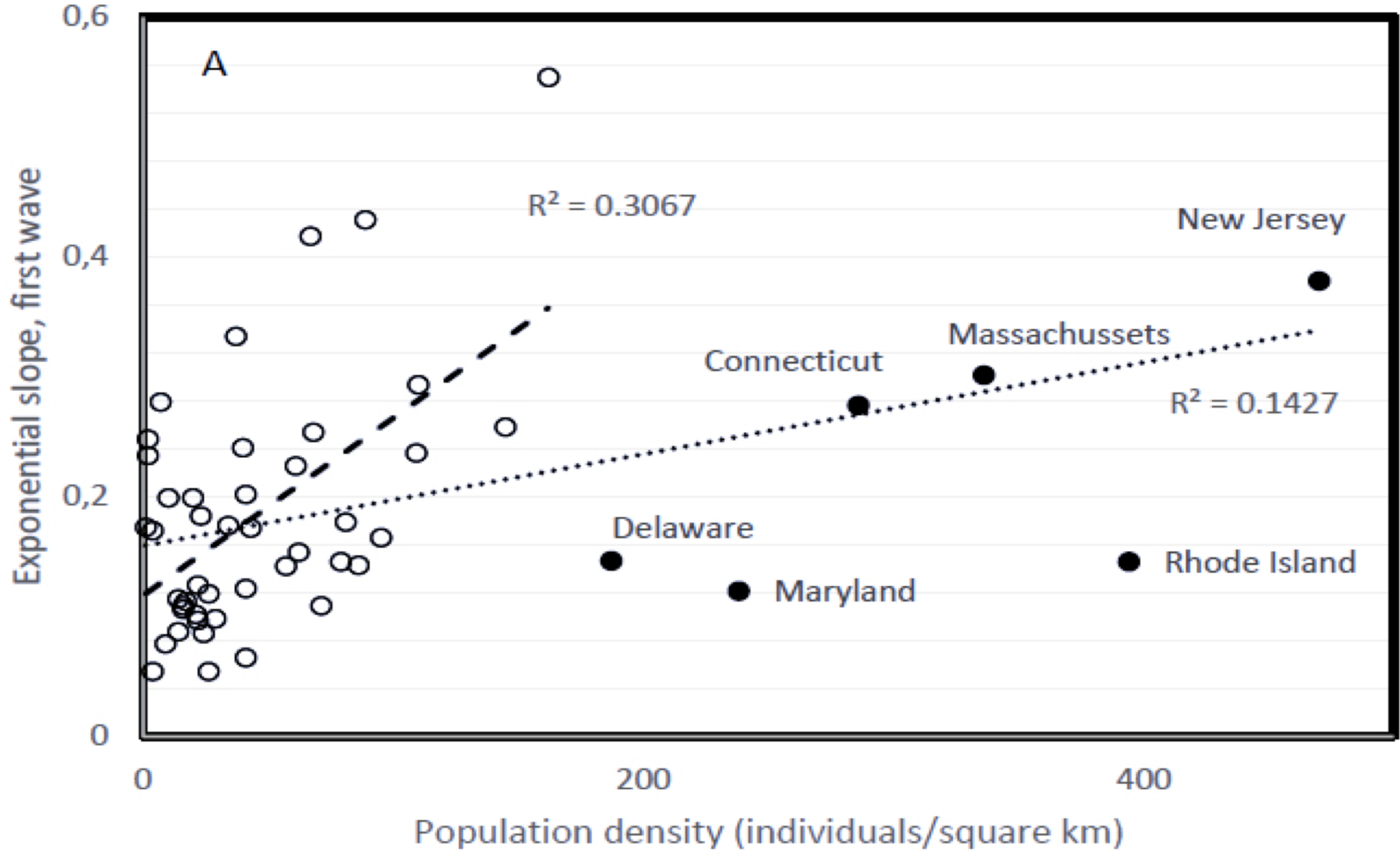
Homo sapiens isolate Altai intergenic region 10B genomic sequence GenBank: KF469167.1

ACAGTATTAGTTTCCTTTTTTTTTGTTTTTTTTACATTACCTCCCCCTCTGGTCAAATAATTGTTGGAAGG
AGTG**TGCCA**GTGAAACAGTCCTGAGTCCTTCCTTGAGCATTTAAAA**AATTAGA**ACTAAGAAGGCCCTAT
TGTATCCTGATAAGGTTGACAACGTGAACTGGGAGTACTAGTAGGCATAATTTCCAC**AATGGTAATGA**
AATCAATAAGCAAAGAGAGAAATCCTGT**TGGTA**TTTAACCCCATAT**TGCCR**GAGGTCGTAGAACTAGTT
CCAAATCTTTTTTGTTCATTTTTATTAAATAATTTGCCTTTTATCTCTTGTATTATAGGTATTTCTA
TCTC**CAAG**GCAGAA**ATTCAA****TAATTCTTACTG**TTGTTAGCAGATAGGAGTTATCTATTT**GTACTG**TTT
TTTATTTAAATATATTTAAATTATCATTTTCATTATTTTTAATTGTTTAATTATTATCACAGAGCCAAATT
TATTTAGACACAGTTAATTTTA**AAGAT**CACATCTCAAATGATTGATTAATGCCTTTGTGATAATGTTGT
TATTTATAAATCTAAAACGATCAATCCT**TGGTA**ATTTTTTAAAACAATATAAAAATCACAAAATAAAAT
TTTAACTTGACATATAATAAACATACCAAACAAACACAGTTAGAAATGTGAGCAATATGCAACATTTTTA
GGATCTA**AAGAT**TAAATAGGTAGAATCCCTAAGCTGAAGTTTCCCAATG**CATTC**CTAGAGGAAGAGAGAT
TGTCAGAG**GAATG**CATAATAGTTAAACTGTGAGTTTTTAAAA**AAGAT**CTAATTTTTGTAGAAATTACAATA
AGCATAAAGTTGTCCATATGTTAT**CATTC**TCATGCAC**CAAGAT**TTATGTT**AATGG**GCAGAAAGAGGAGCT
GAGCTAGAGCTAGGACAACCAGAAAAT**ATTC**AATAG

24 942 **2.6 In green, sequences common with miRN-like parts of protein S**



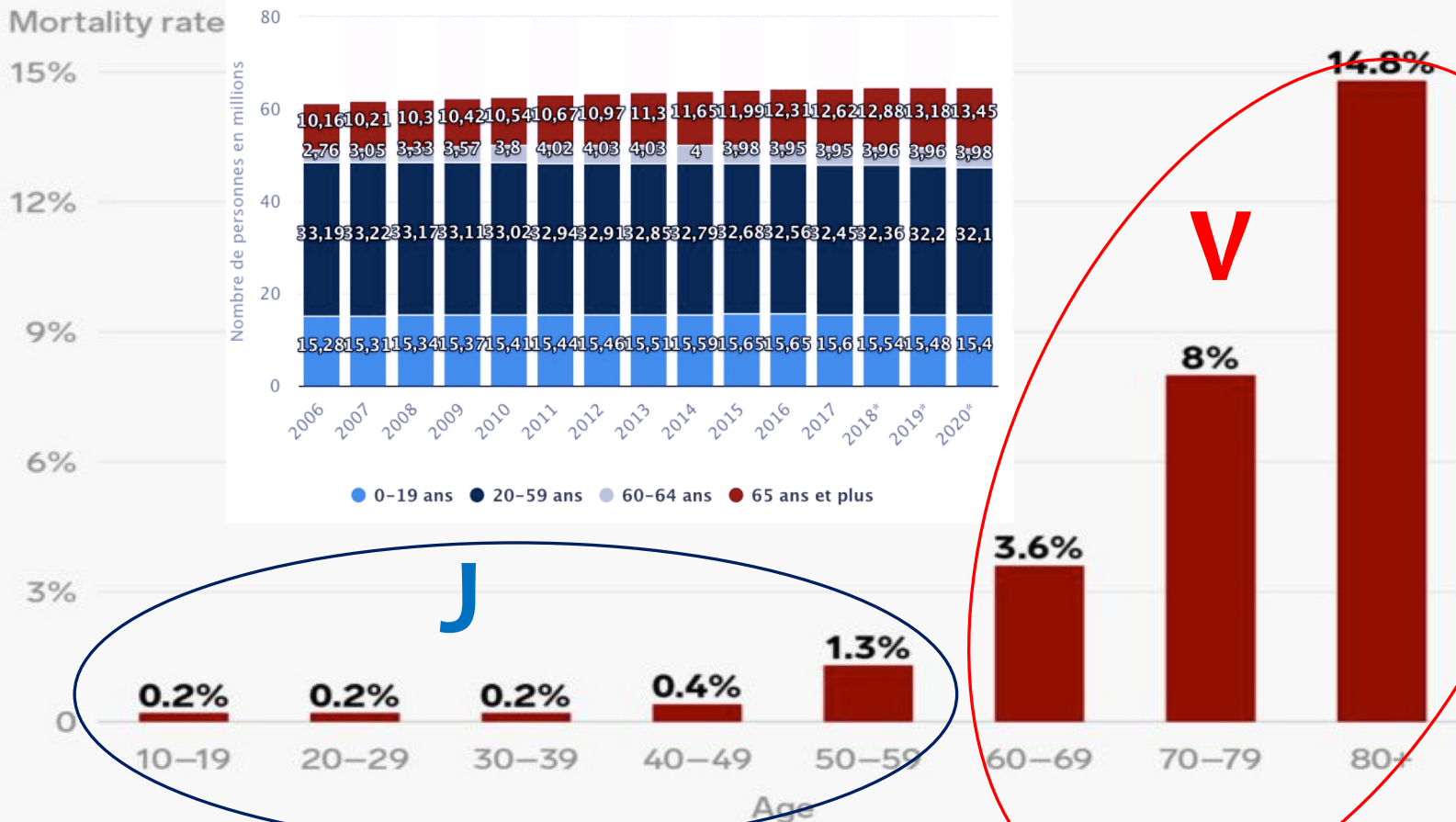
Dependence on demographic factors of the susceptible population



H. SELIGMANN, N. VUILLERME & J. DEMONGEOT Summer COVID-19 third wave like (winter) first wave, opposite to (spring) second wave: slower spread decreases with temperature, increases with population age. *Biology* (submitted). *MedRxiv*, doi.org/10.1101/2020.08.17.20176628 (2020)

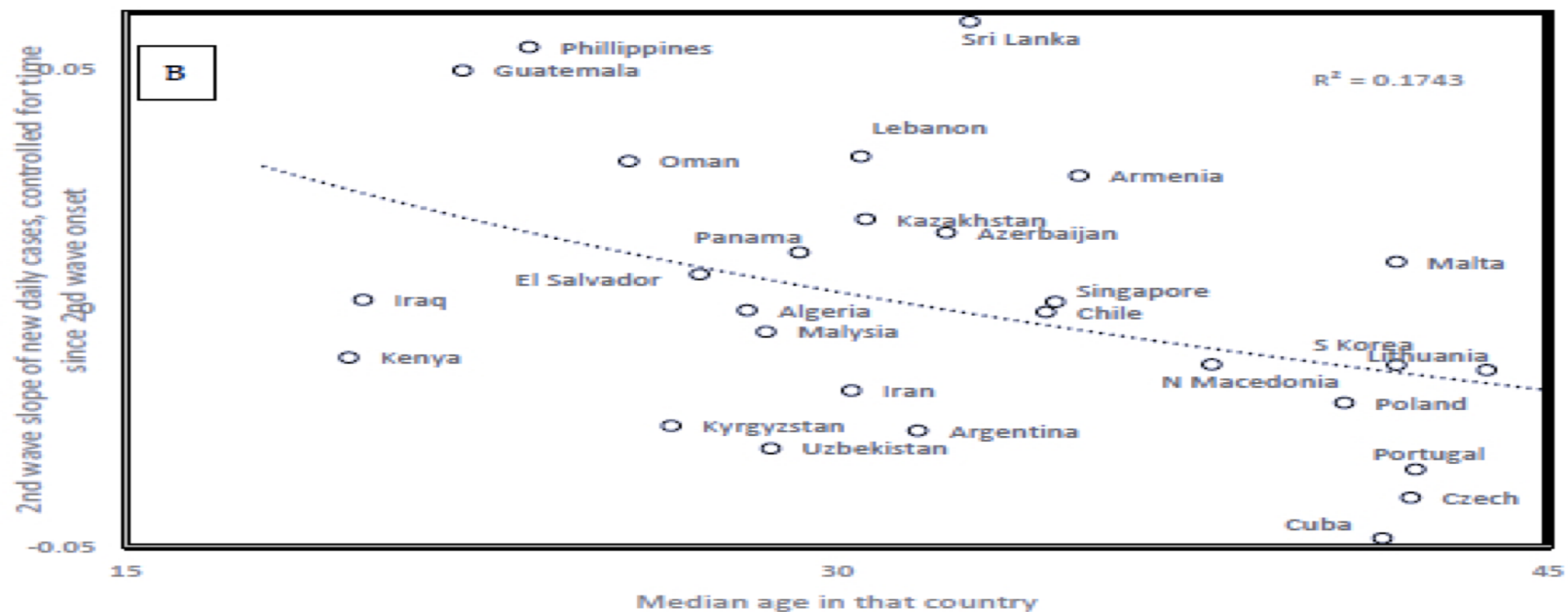
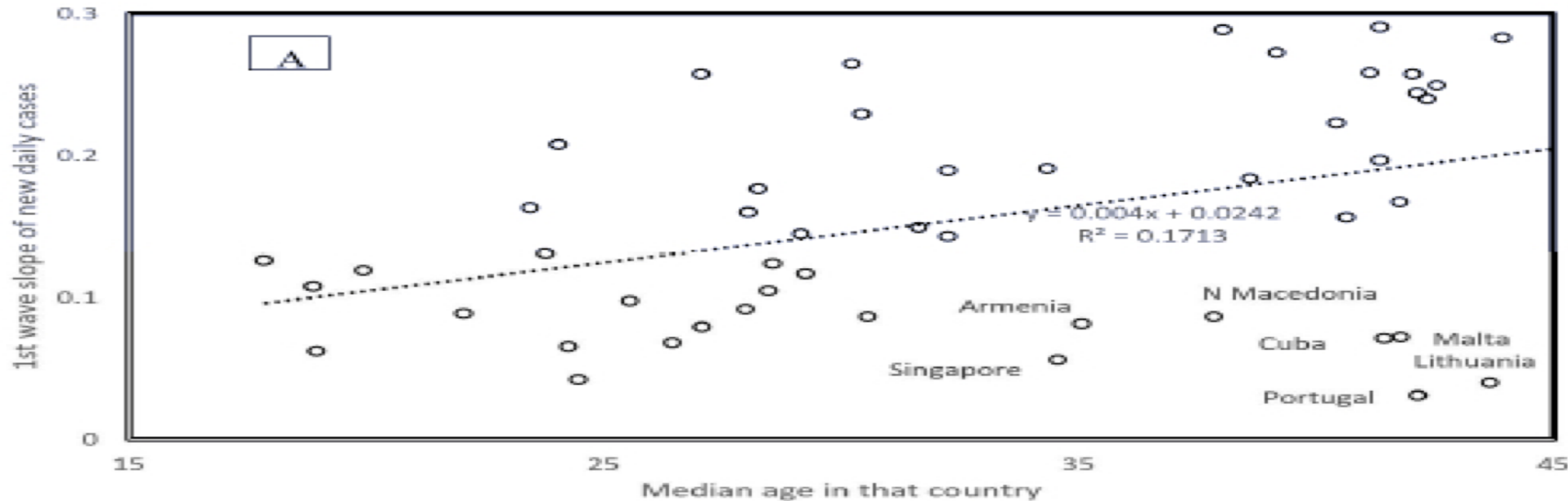
Covid-19 dynamics depends on age

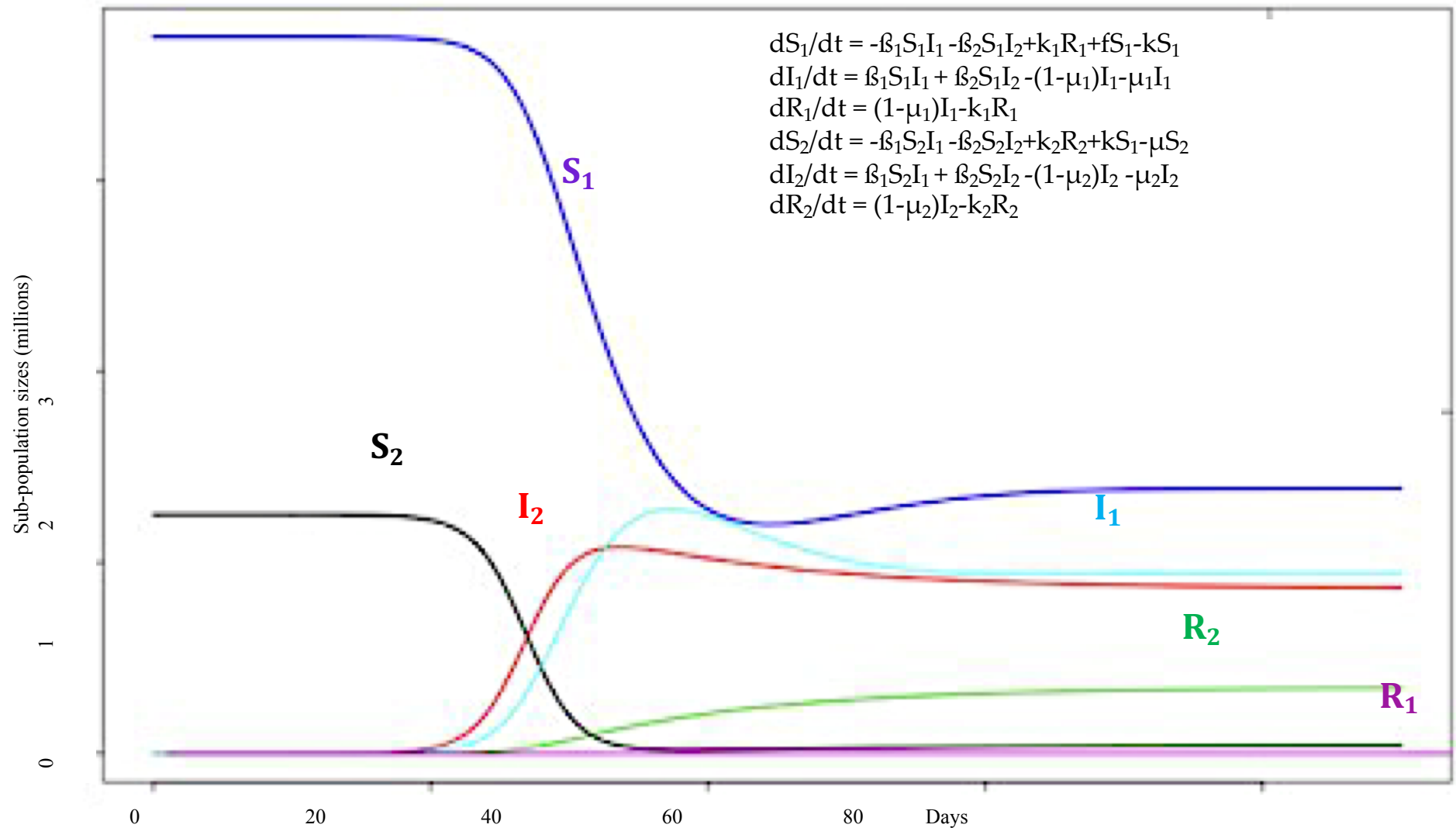
COVID-19 mortality rate by age



Source: Chinese Center for Disease Control and Prevention

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J. DEMONGEOT, O. HANSEN, H. HESSAMI, A.S. JANNOT, J. MINTSA, M. RACHDI & C. TARAMASCO Random modelling of contagious diseases. *Acta Biotheoretica*, **61**, 141-172 (2013).

I. OUASSOU, L. HOBAD, M. ALAHIANE, J. GAUDART, S. IGGUI, M. RACHDI & J. DEMONGEOT The ARIMA model to analyse incidence pattern and estimate short-term forecasts for retro-predicting the first wave of the COVID-19 outbreak. *Math. Population Studies* (submitted).



Thanks for your attention !