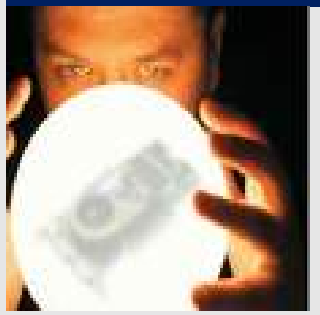
PREDICCION DE CARACTERISTICAS COMPLEJAS
en los tiempos de COVID-19



Daniel Gianola

Sewall Wright Emeritus Professor

of Animal Breeding and Genetics

University of Wisconsin

UW–MADISON
ANIMAL SCIENCES

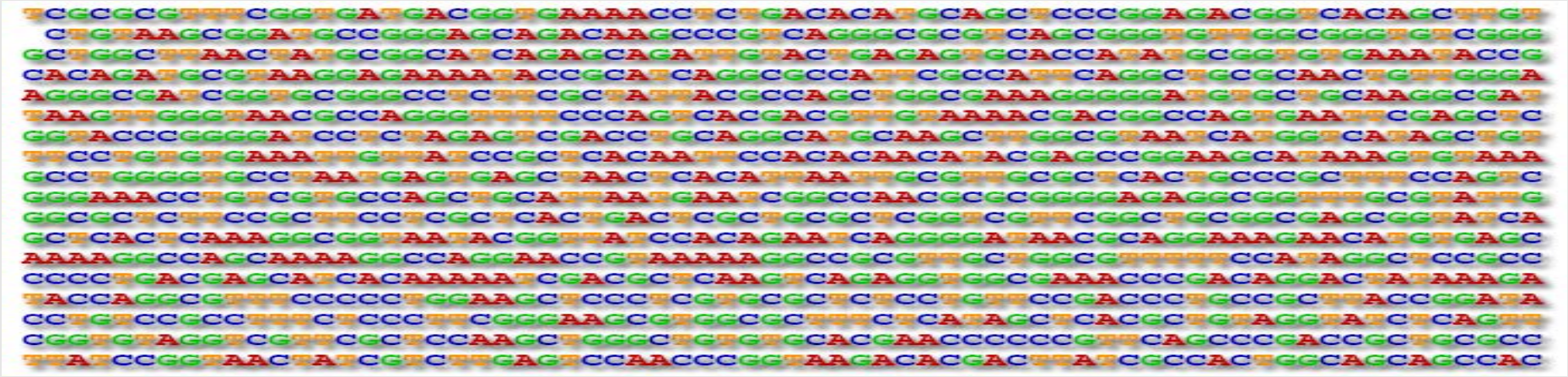
Dairy Science

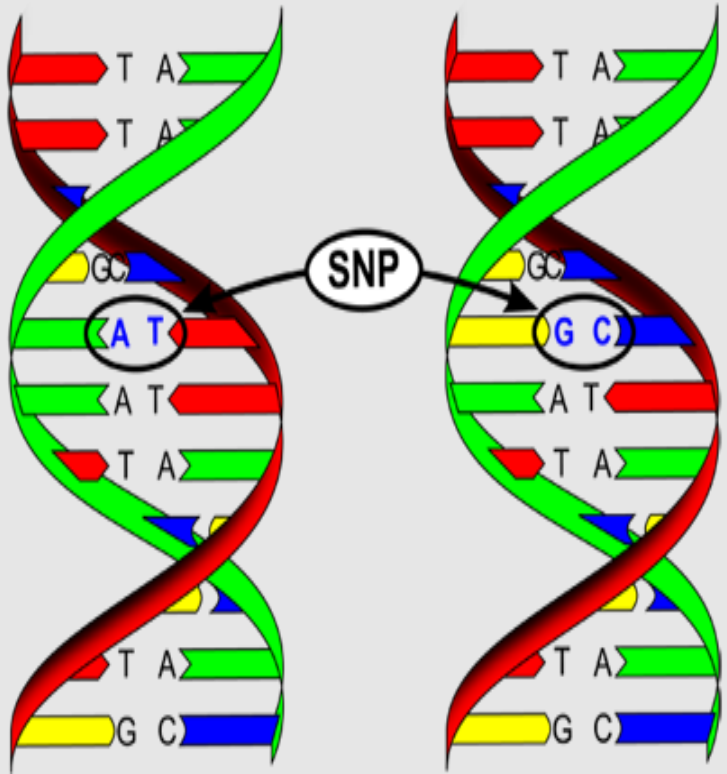
Fiddler on the Roof

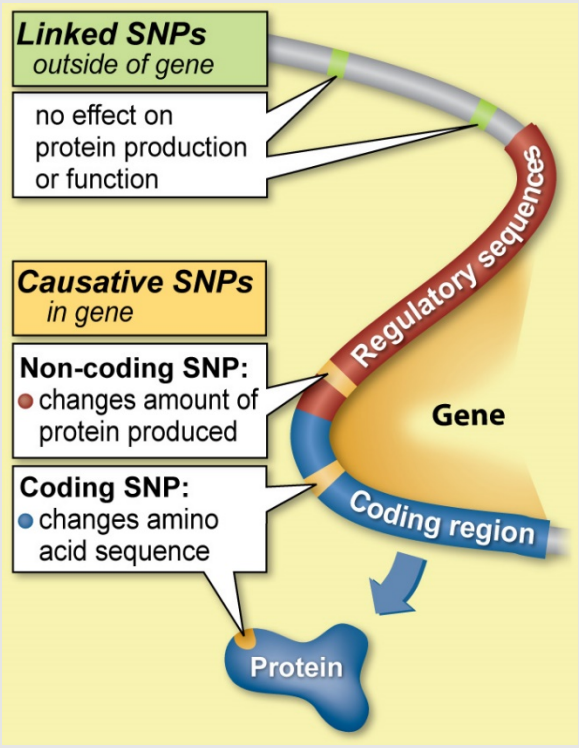
TOPICOS A DISCUTIR

- Perspectiva: metodos empleados en mejoramiento genetico animal
- Descripcion de la pandemia de COVID-19: 16 paises
- Uruguay y contexto regional
- Estimacion de “R” (numero de infecciones/infector)
- Modelo predictivo (simple) del numero de casos diarios
- Evaluacion de predicciones via “RANDEMIAS”
- Inmunidad de “rodeo” [si Uruguay fuera Suecia…]
- Comentarios miscelaneos

MASSIVE NUMBERS OF MOLECULAR MARKERS AVAILABLE: DNA sequences (cattle: 3 Gb; maize: 2500 Mb)

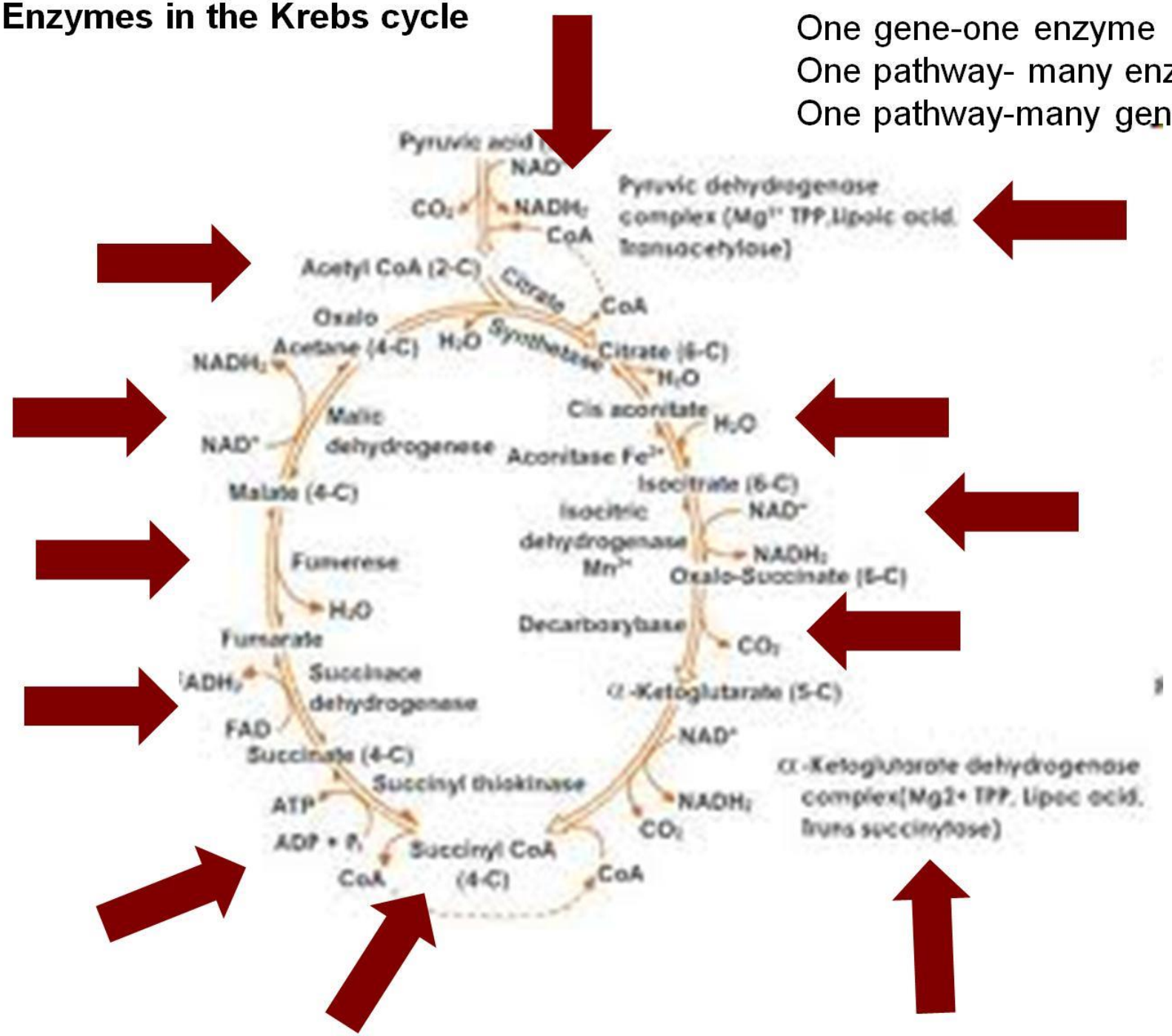




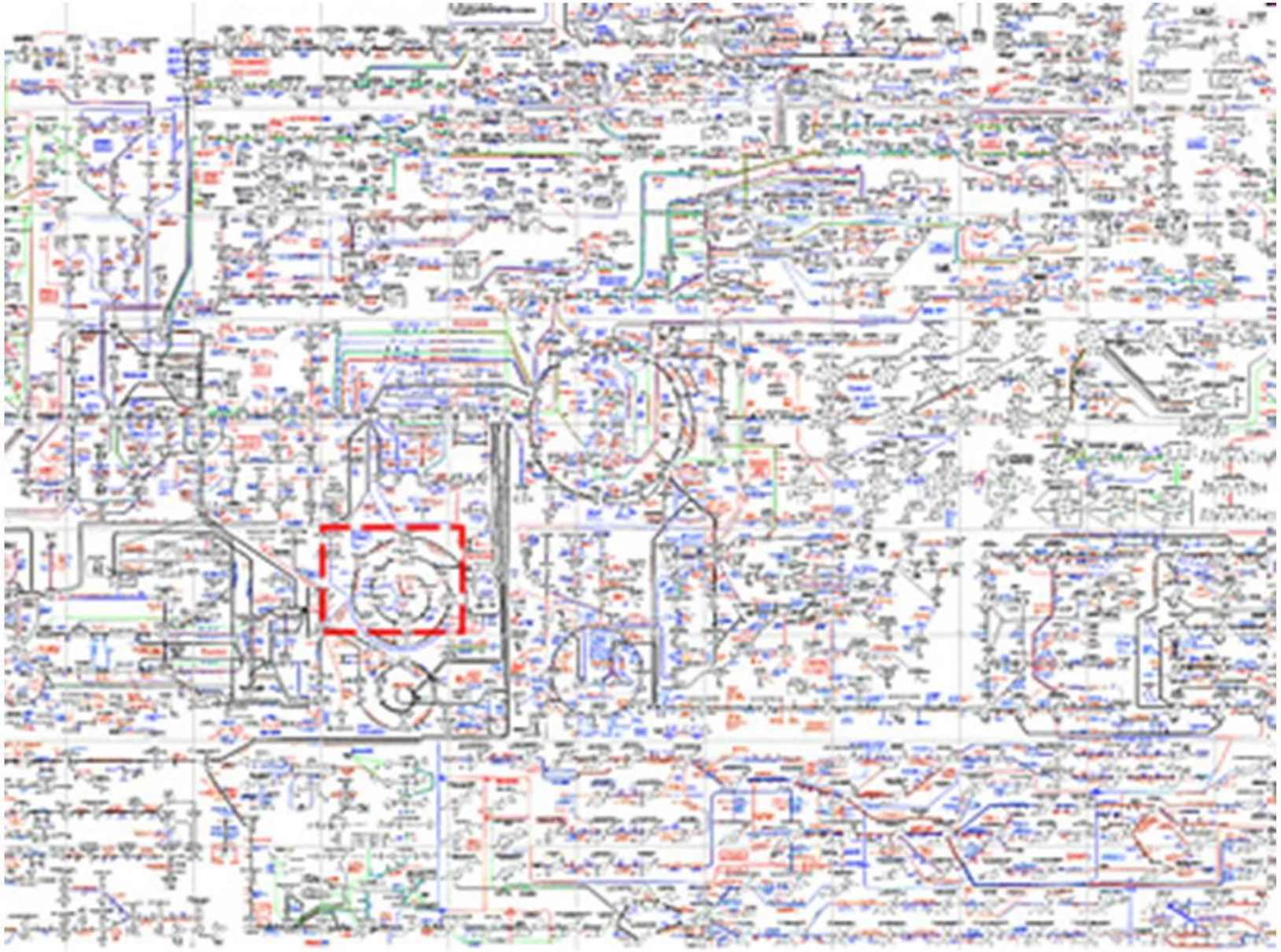


Enzymes in the Krebs cycle

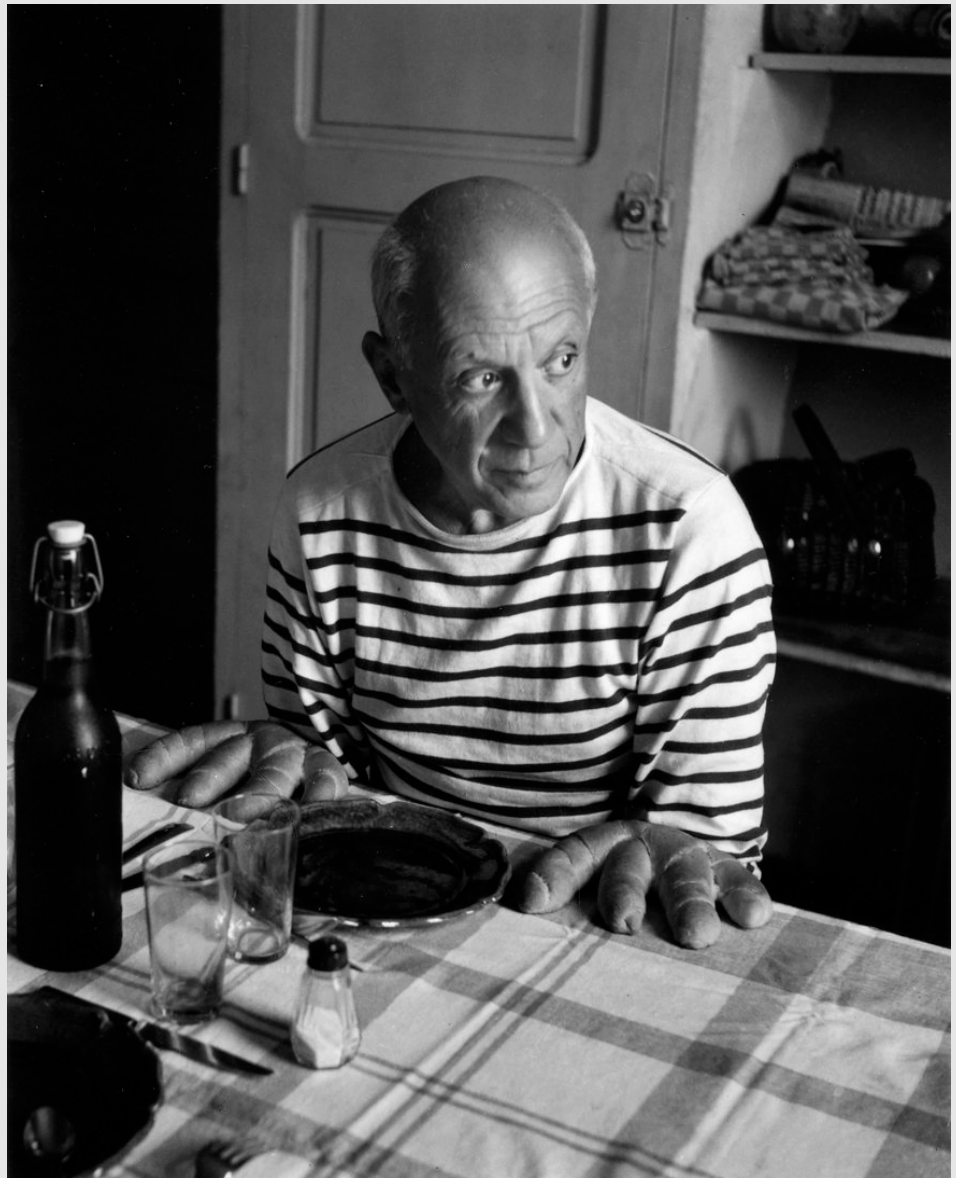
One gene-one enzyme
One pathway- many enzymes
One pathway-many genes



A “complex” trait involves many metabolic pathways: Roche’s Chart



BIOLOGIA-ABSTRACCIONES



Coping with complexity

(WELCOME TO THE WORLD OF ABSTRACTIONS)

First assumption: there is a genetic signal and an environmental signal
Second assumption: the joint effect translates into a phenotye **y**

$$Y = f(G, E)$$ For some **UNKNOWN** function *f*

Choices?

$$Y = G^E?$$
$$Y = E^G?$$
$$Y = G + E + GE?$$ → Is an assumption
$$Y = (G + E)^{GE}?$$
$$Y = G + E?$$ → Is an even a stronger assumption

Fisher, R. A. 1918. The correlation between relatives on the supposition of Mendelian inheritance. Transactions of the Royal Society of Edinburgh 52:399-433.

XV.—**The Correlation between Relatives on the Supposition of Mendelian Inheritance.** By **R. A. Fisher, B.A.** *Communicated by* Professor J. ARTHUR THOMSON. (With Four Figures in Text.)

(MS. received June 15, 1918. Read July 8, 1918. Issued separately October 1, 1918.)

CONTENTS.

Fisher_Young_Man_Photograph courtesy of Professor A W F Edwards by kind permission of Joan Fisher Box.jpg

IX. *On the Mathematical Foundations of Theoretical Statistics.*

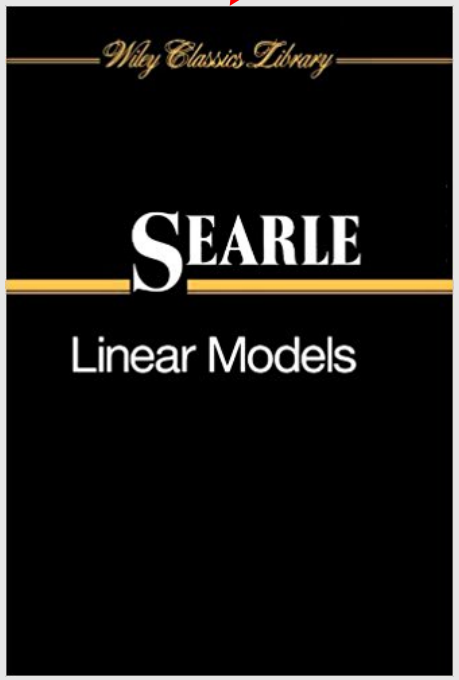
By R. A. Fisher, M.A., *Fellow of Gonville and Caius College, Cambridge, Chief Statistician, Rothamsted Experimental Station, Harpenden.*

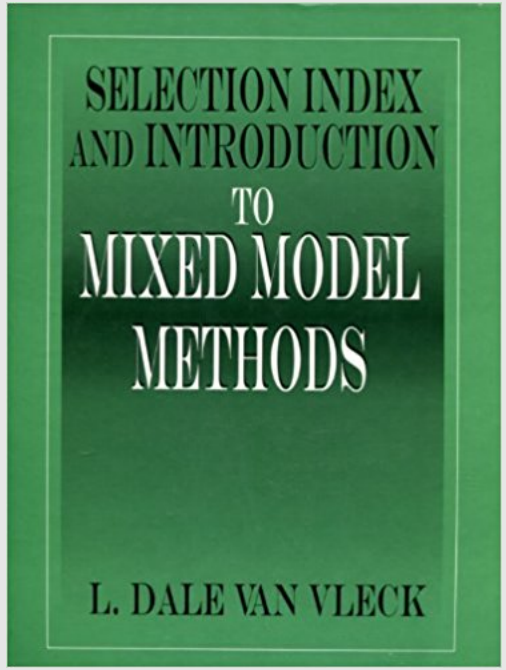
Communicated by Dr. E. J. Russell, F.R.S.

Received June 25,—Read November 17, 1921.

Contents.

Charles R. Henderson y DG
University of Illinois
Urbana, 1987





BAYESIAN INFERENCE AND THE NEO-BAYES-LAPLACE REVOLUTION (James-Stein, Lindley, Box, Zellner…)

Rev. Thomas Bayes

1702 London, England
1761 Tunbridge Wells, Kent, England

1763. “An essay towards solving a problem in the doctrine of chances”. *Philosophical Transactions of the Royal Society of London* **53**, 370-418.

Pierre-Simon Laplace

1749 Beaumont-en-Auge, France
1827 Paris, France

1774. "Mémoire sur la probabilité des causes par les événements“. *Savants étranges* **6**, 621-656. *Oeuvres* **8**, 27-65

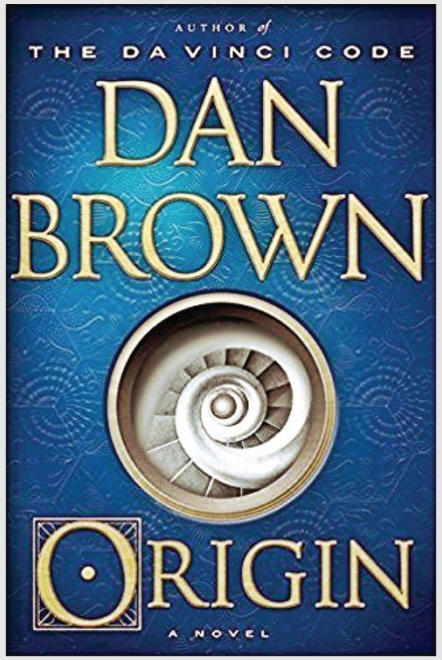
The era of machine learning and artificial intelligence

“BIG data”

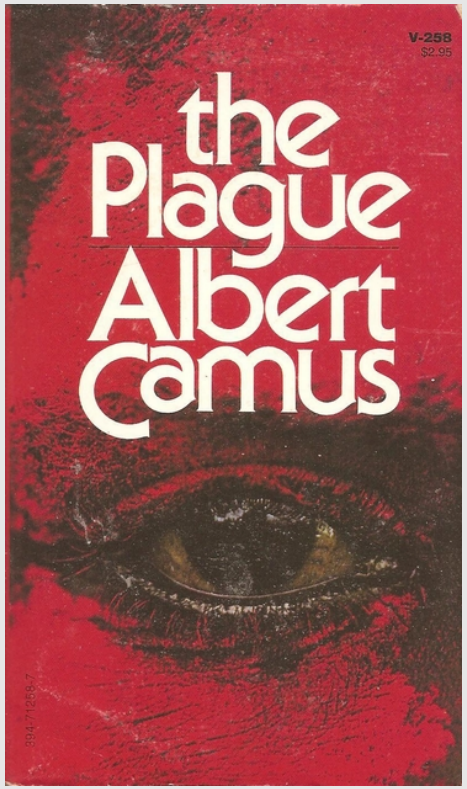
(largely non-parametric)

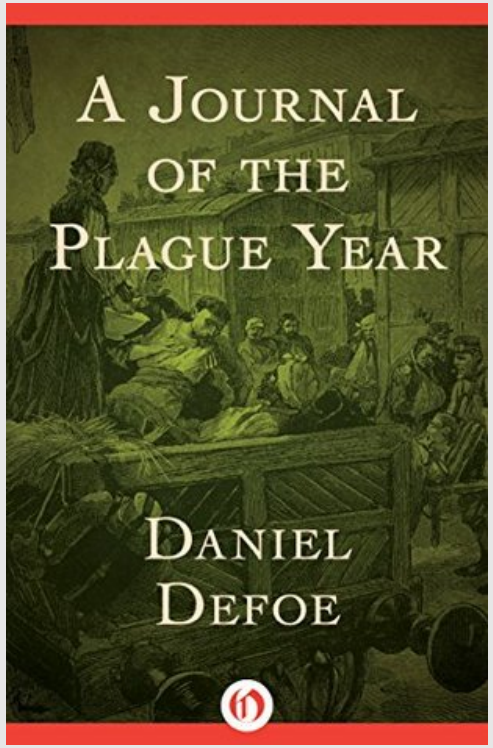
NEW METHODS COMING…

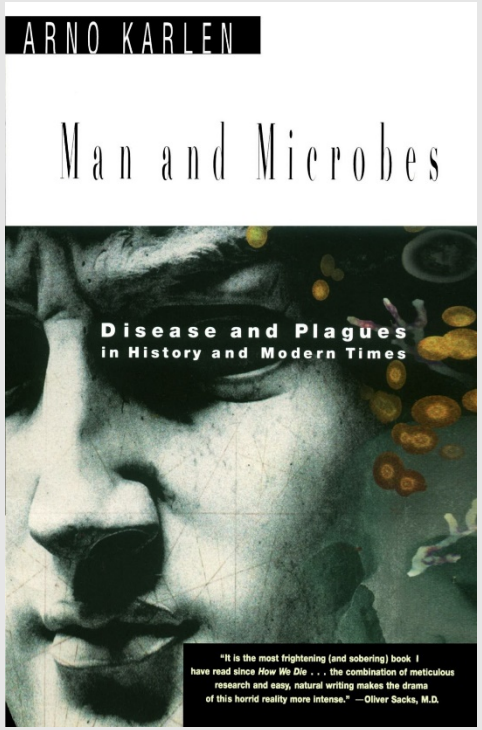
The return of the neural networks…



QUE HACEMOS DURANTE EL STAY-AT-HOME???







EPIDEMIOLOGIA CASERA!!!

COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)

Total Confirmed

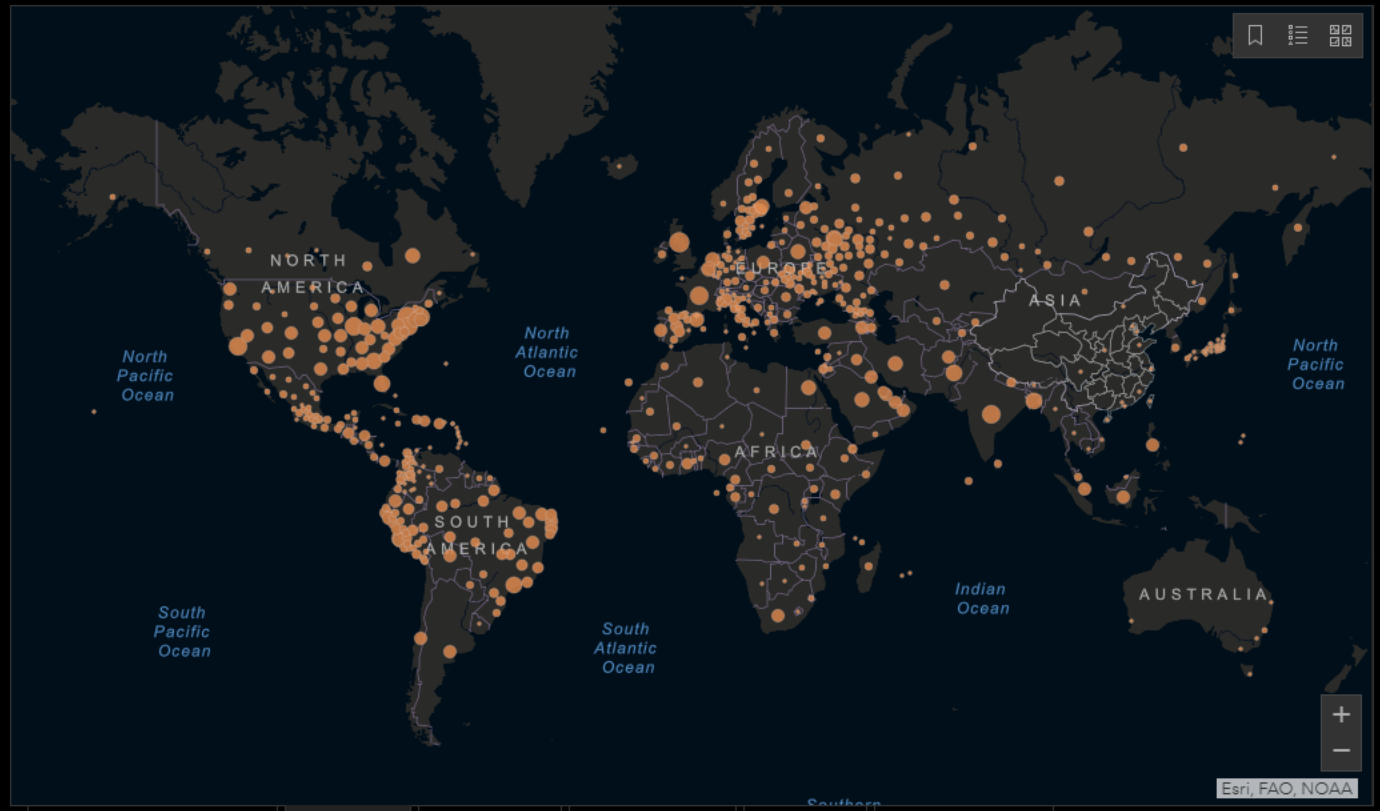
7,185,573

Confirmed Cases by Country/Region/Sovereignty

1,973,803	US
707,412	Brazil
484,630	Russia
290,576	United Kingdom
276,146	India
241,966	Spain
235,561	Italy
199,696	Peru
191,522	France
186,506	Germany
175,927	Iran
172,114	Turkey
142,759	Chile
120,102	Mexico
108,571	Saudi Arabia

Admin0 | Admin1 | Admin2

Last Updated at (M/D/YYYY)
6/9/2020, 3:33:25 PM



Cumulative Confirmed Cases | Active Cases | Incidence Rate | Case-Fatality Ratio | Testing Rate | Hospitalization Rate

188
countries/regions

Lancet Inf Dis Article: Here. Mobile Version: Here.
Lead by JHU CSSE. Technical Support: Esri Living Atlas team and JHU APL. Financial Support: JHU and NSF. Click *here* to **donate** to the CSSE dashboard team, and other JHU COVID-19 Research Efforts. FAQ. Read more in this blog. Contact US.

Global Deaths

408,954

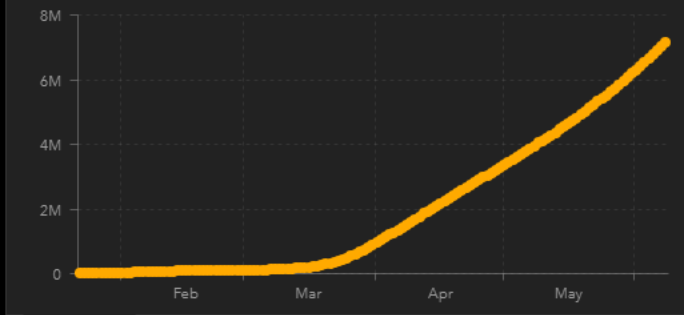
111,751 deaths	US
40,968 deaths	United Kingdom
37,134 deaths	Brazil
34,043 deaths	Italy
29,299 deaths	France
27,136 deaths	Spain
14,053 deaths	Mexico

Global Deaths | Global Recovered

US State Level Deaths, Recovered

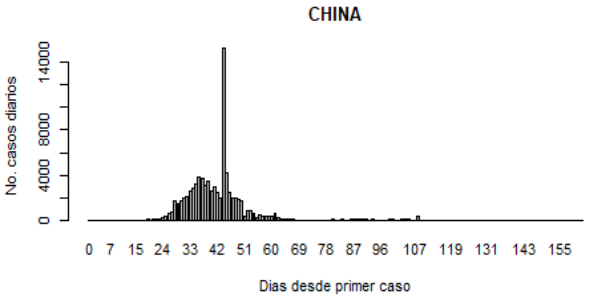
30,458 deaths, 67,687 recovered	New York US
12,303 deaths, 27,941 recovered	New Jersey US
7,353 deaths, recovered	Massachusetts US
6,018 deaths, recovered	Illinois US
6,014 deaths, 53,670 recovered	Pennsylvania US
5,912 deaths, 42,041 recovered	Michigan US
4,681 deaths, recovered	California US

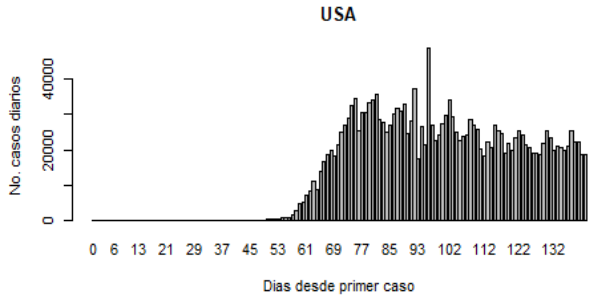
US Deaths, Recovered

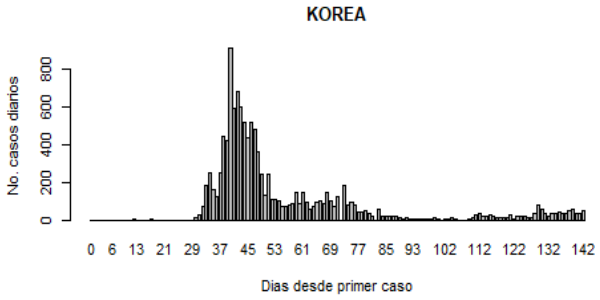


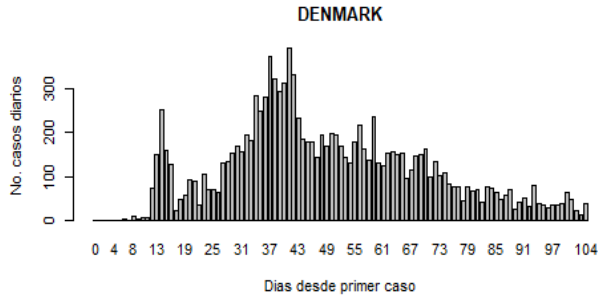
Confirmed | Logarithmic | Daily Cases

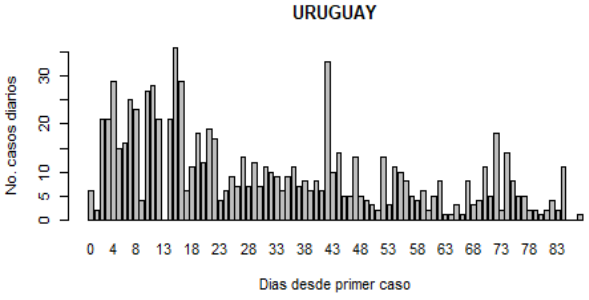
PANDEMIA EN 16 PAISES: 10 DE JUNIO- 2020 10:45 CST

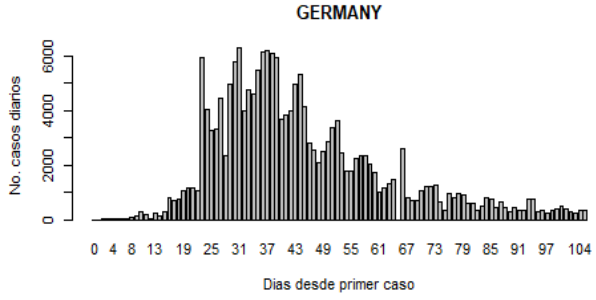


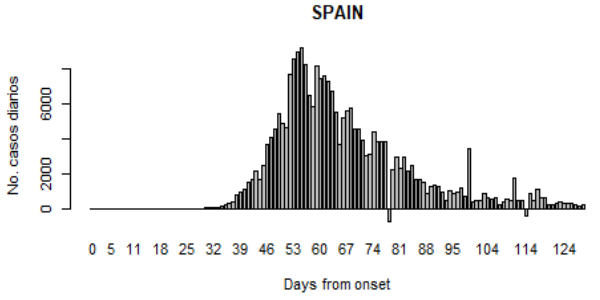


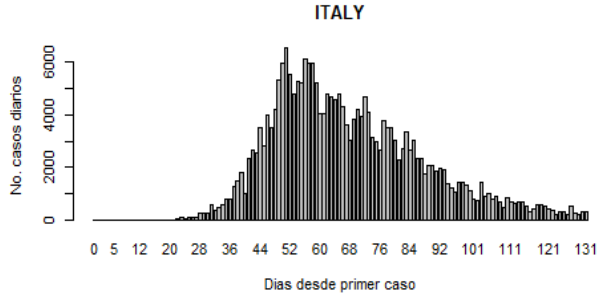


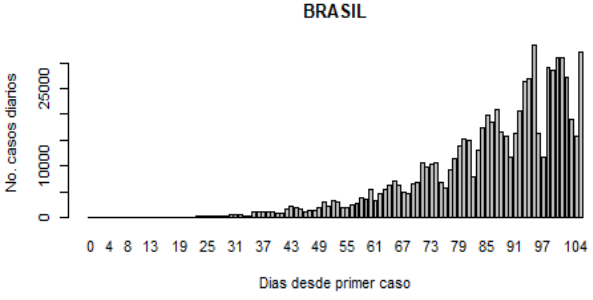


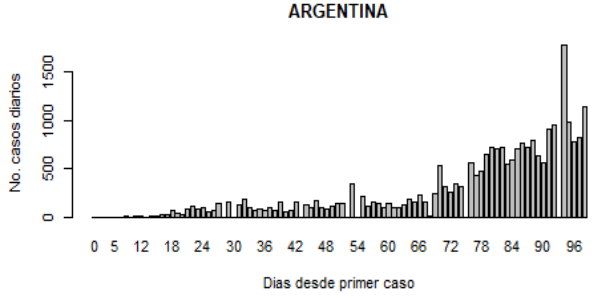


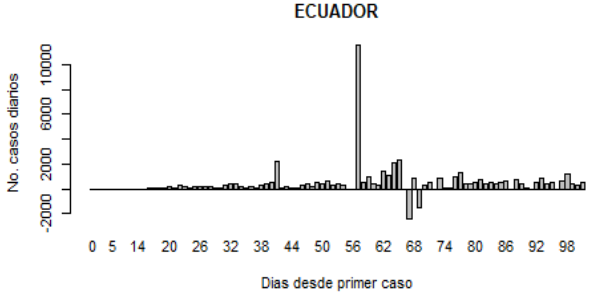


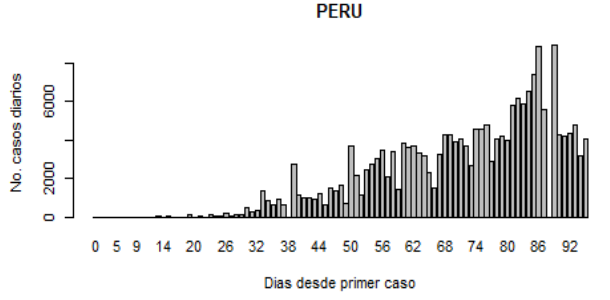


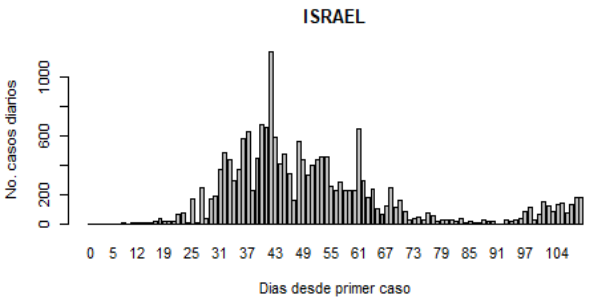


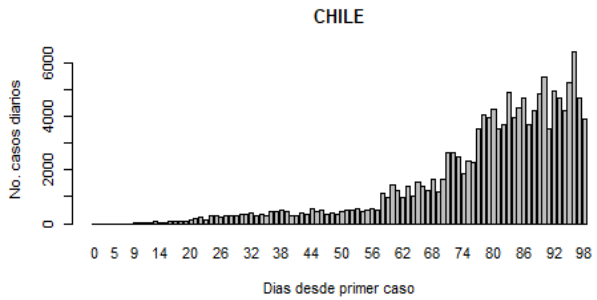


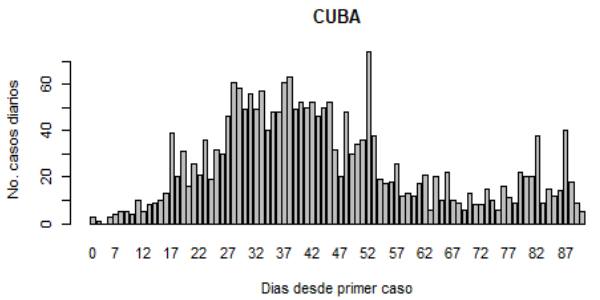


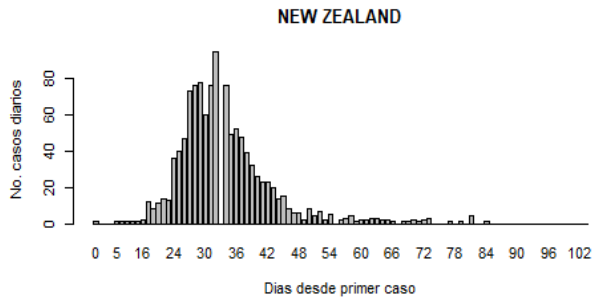




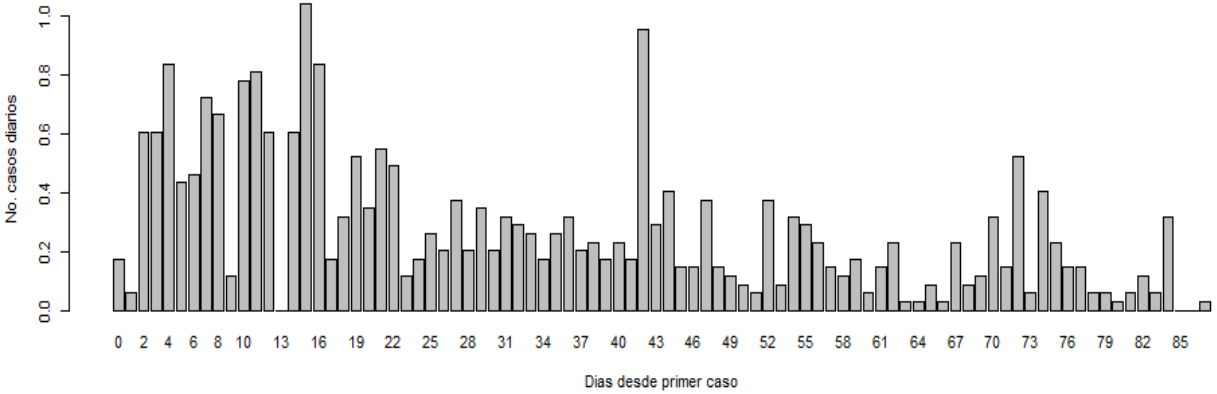




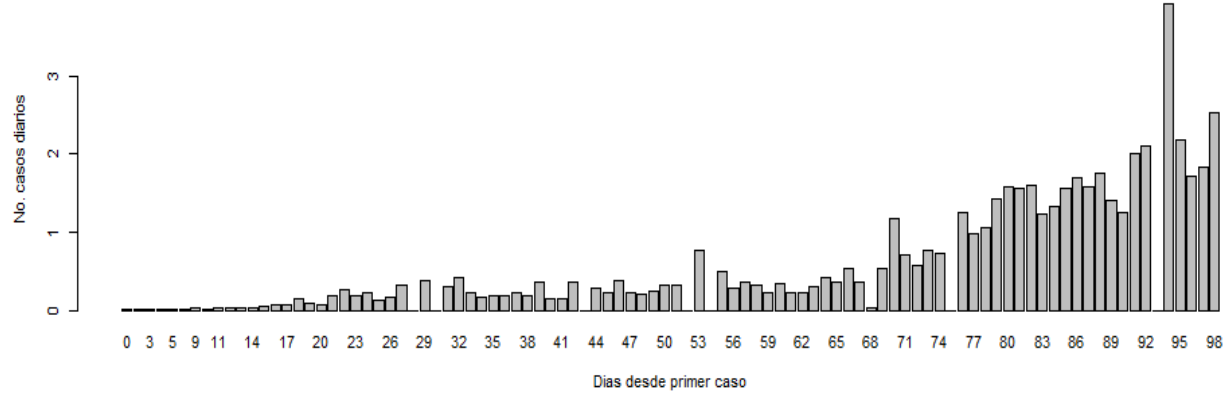




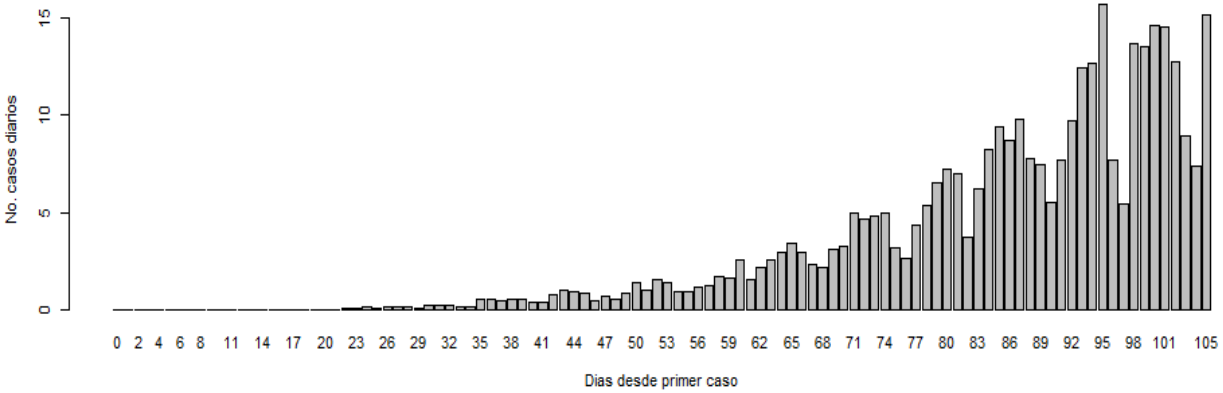
URUGUAY JUNIO 10
Casos diarios por 100 mil habitantes



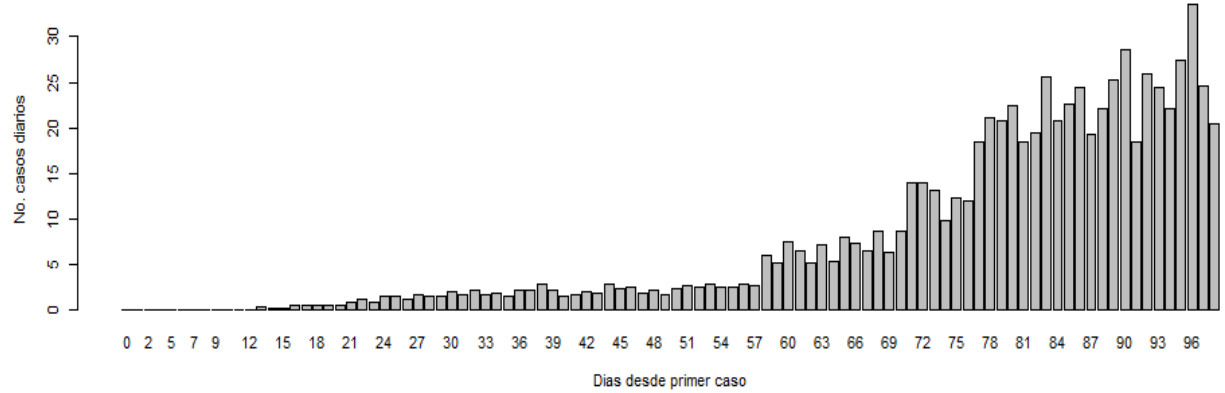
ARGENTINA JUNIO 10
Casos diarios por 100 mil habitantes



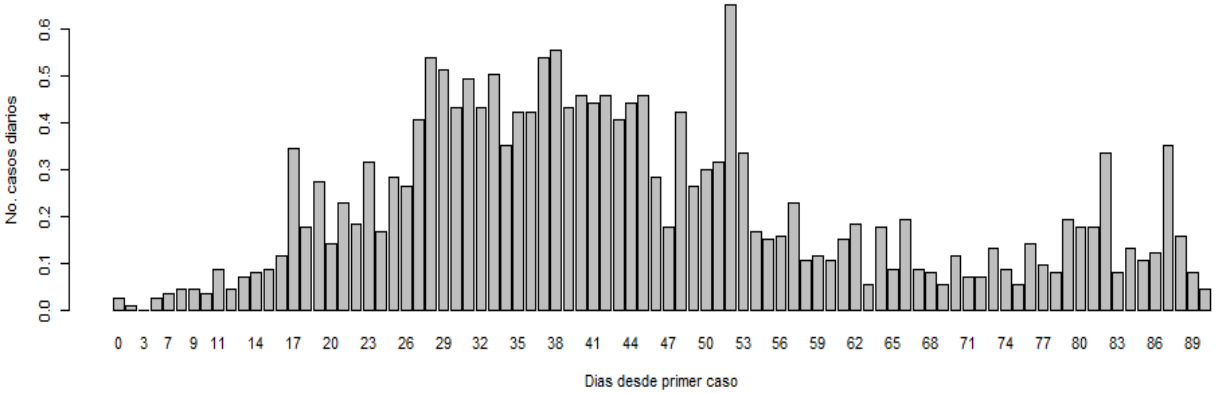
BRASIL JUNIO 10
Casos diarios por 100 mil habitantes



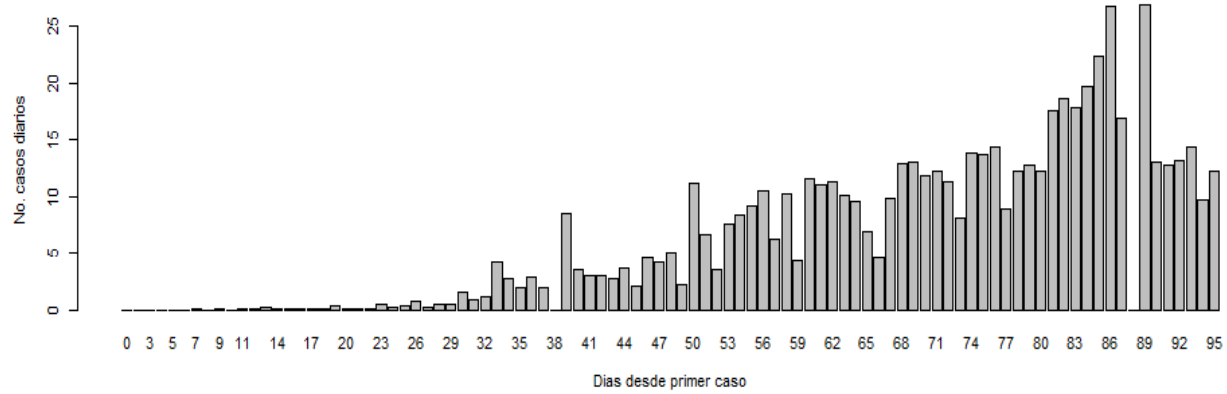
CHILE JUNIO 10
Casos diarios por 100 mil habitantes



CUBA JUNIO 10
Casos diarios por 100 mil habitantes

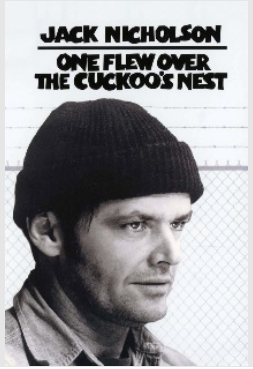


PERU JUNIO 10
Casos diarios por 100 mil habitantes



Marzo 15

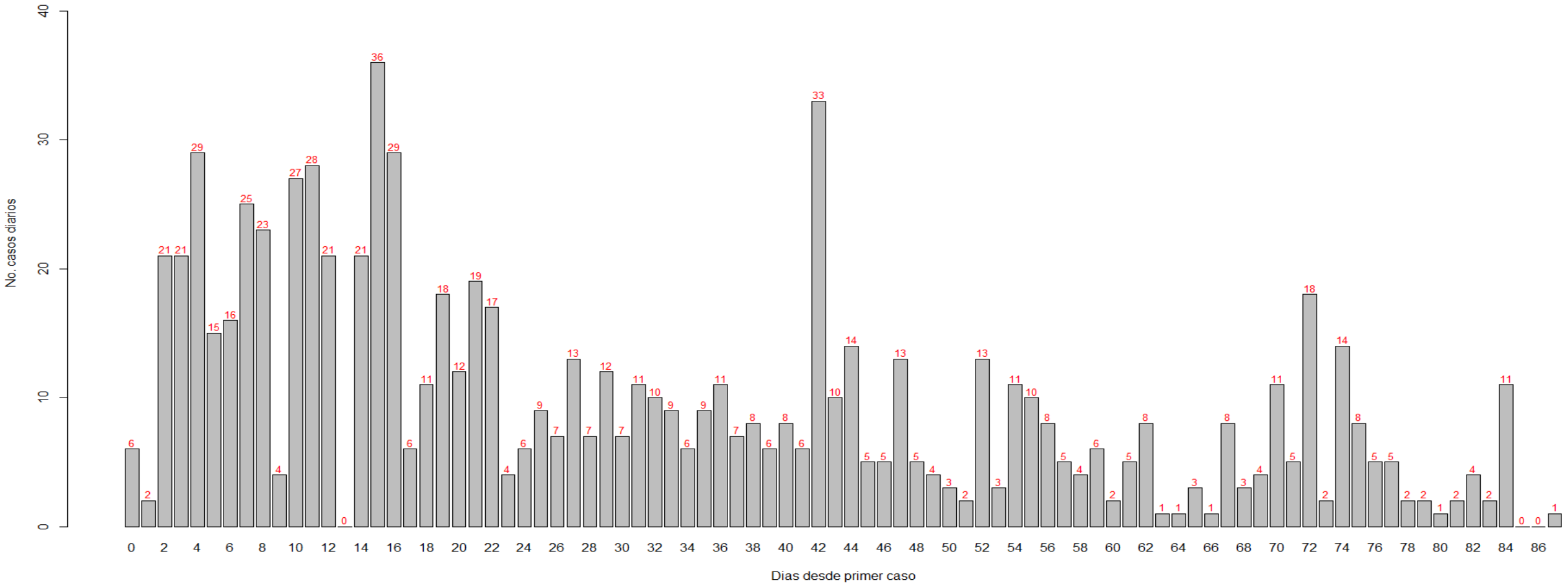
Marzo 30



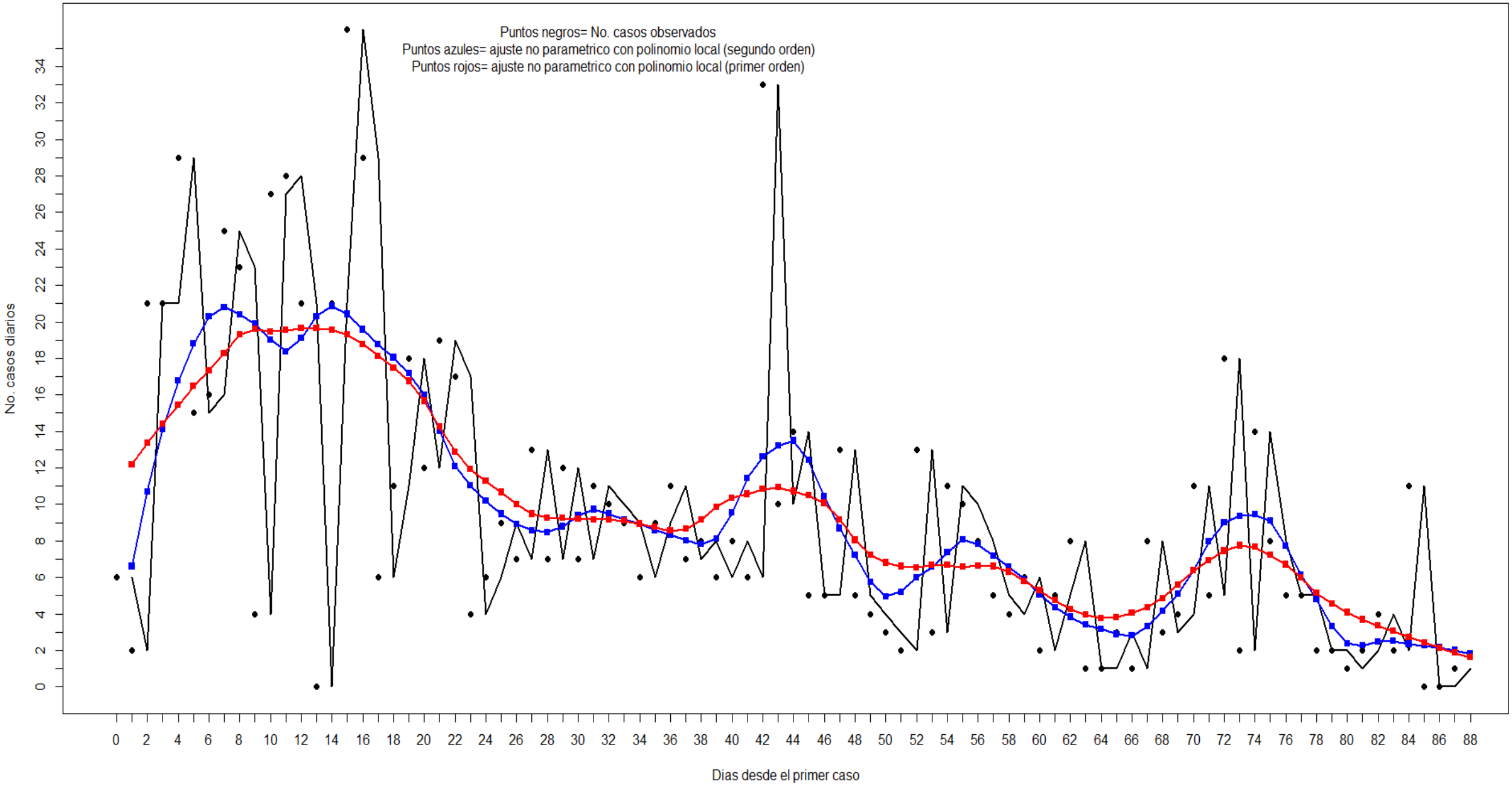
Abril 26

Mayo 26

EVOLUCION DE LA EPIDEMIA
URUGUAY-JUNIO 10
BASE DE DATOS: https://www.ecdc.europa.eu

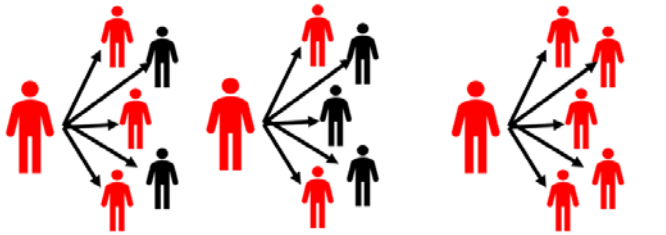


EPIDEMIA EN URUGUAY A JUNIO 9-DESCRIPCION ESTADISTICA
Base de datos: https://www.ecdc.europa.eu
Nota: curvas son descriptivas-no predictivas

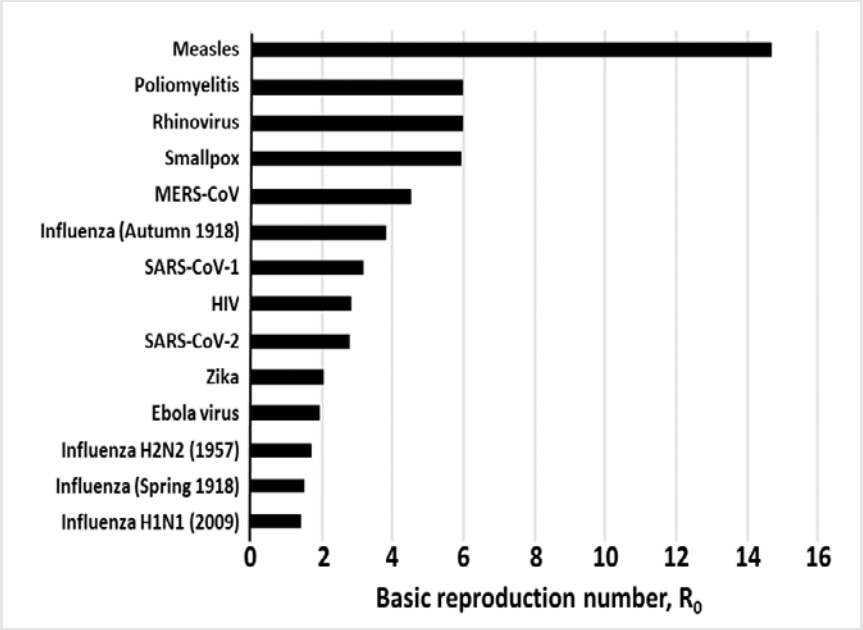


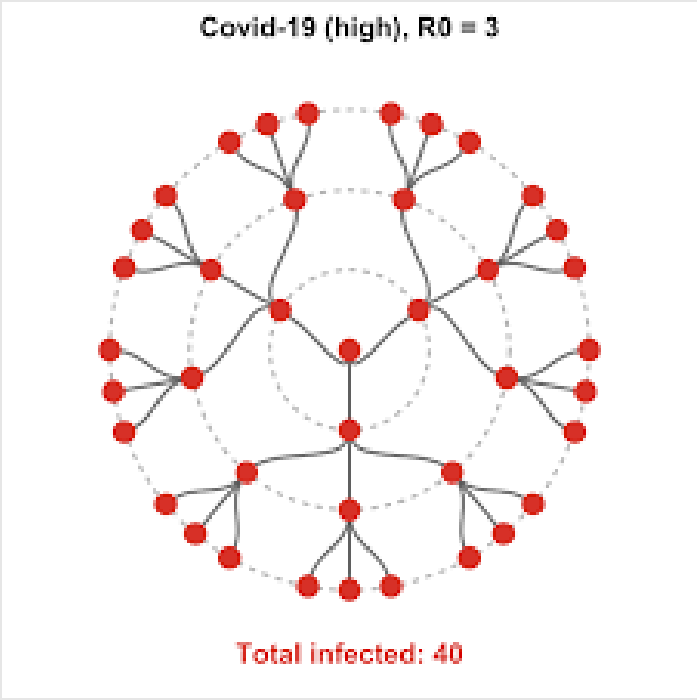
NUMERO DE REPRODUCCION DEL VIRUS:
R= numero promedio de infectados por infector

Basic Reproduction Number (R0) = Attack Rate * Contacts

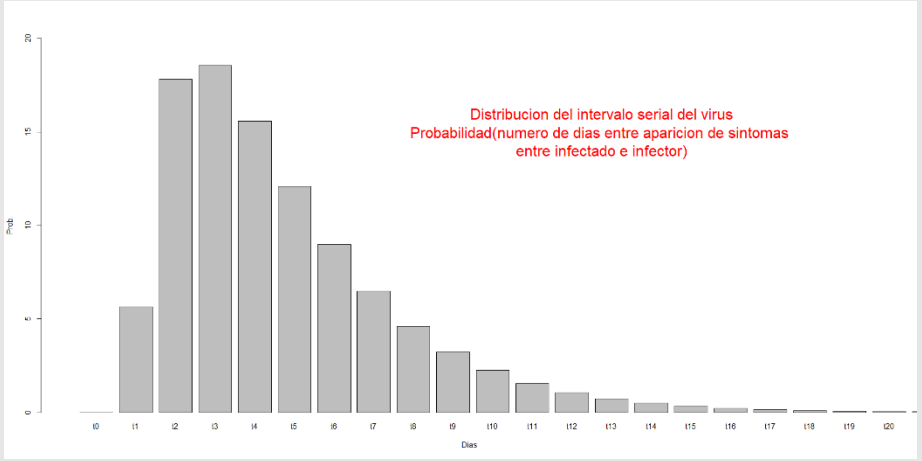


AR = 60% R0 = 3 | AR = 40% R0 = 2 | AR = 100% R0 = 5





$$
\begin{array}{lccccccc}
N_0 & . & . & . & . & . & . & . \\
N_1 = & X_{01} & . & . & . & . & . & . \\
N_2 = & X_{02} & X_{12} & . & . & . & . & . \\
N_3 = & X_{03} & X_{13} & X_{23} & . & . & . & . \\
N_4 = & . & X_{14} & X_{24} & X_{34} & . & . & . \\
N_5 = & . & . & X_{25} & X_{35} & X_{45} & . & . \\
N_6 = & . & . & . & X_{36} & X_{46} & X_{56} & . \\
 & . & . & . & . & X_{47} & X_{57} & X_{67}
\end{array}
$$



ESTIMACION DE R Y PREDICCION DE NUMERO DE CASOS

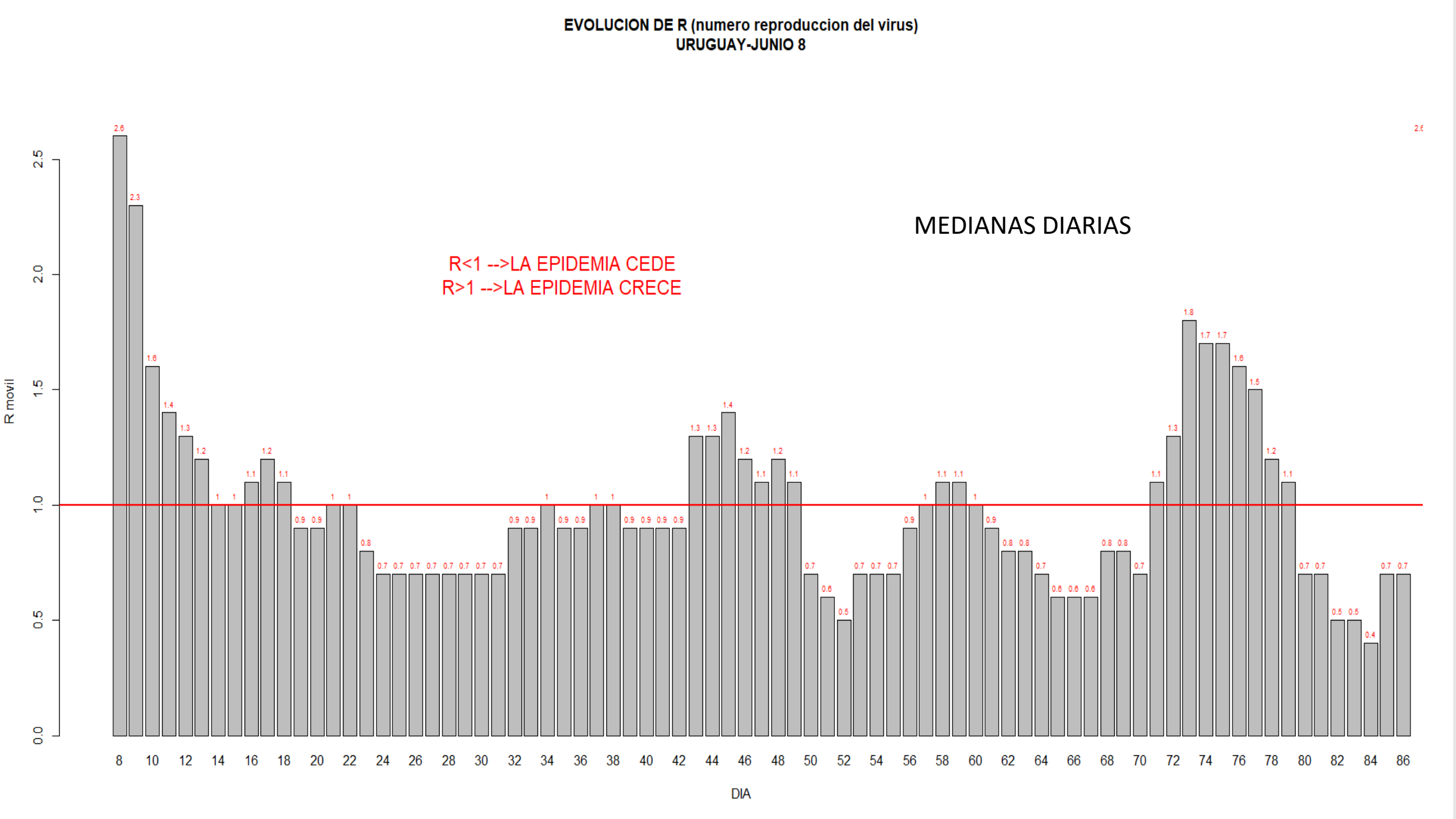
Inferencia
Teorema de Bayes

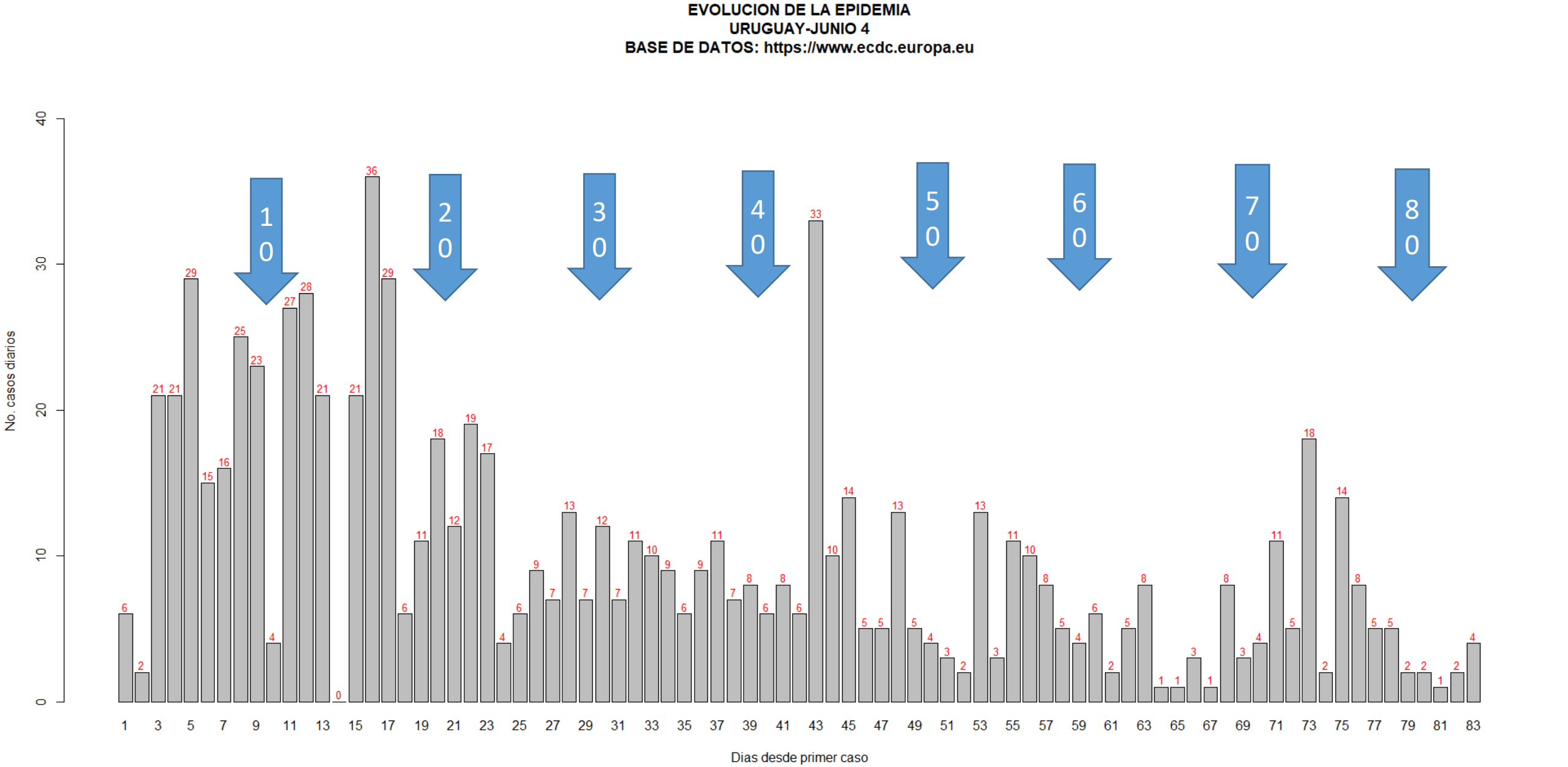
$$= \frac{p(R_t|\text{Casos "nuevos", Casos "viejos", supuestos iniciales})}{\int \Pr(\text{Casos "nuevos"}|R_t, \text{Casos viejos,supuestos}) p(R_t|\text{Casos "viejos", supuestos}) dR_t} \Pr(\text{Casos "nuevos"}|R_t, \text{Casos viejos,supuestos}) p(R_t|\text{Casos "viejos", supuestos})$$

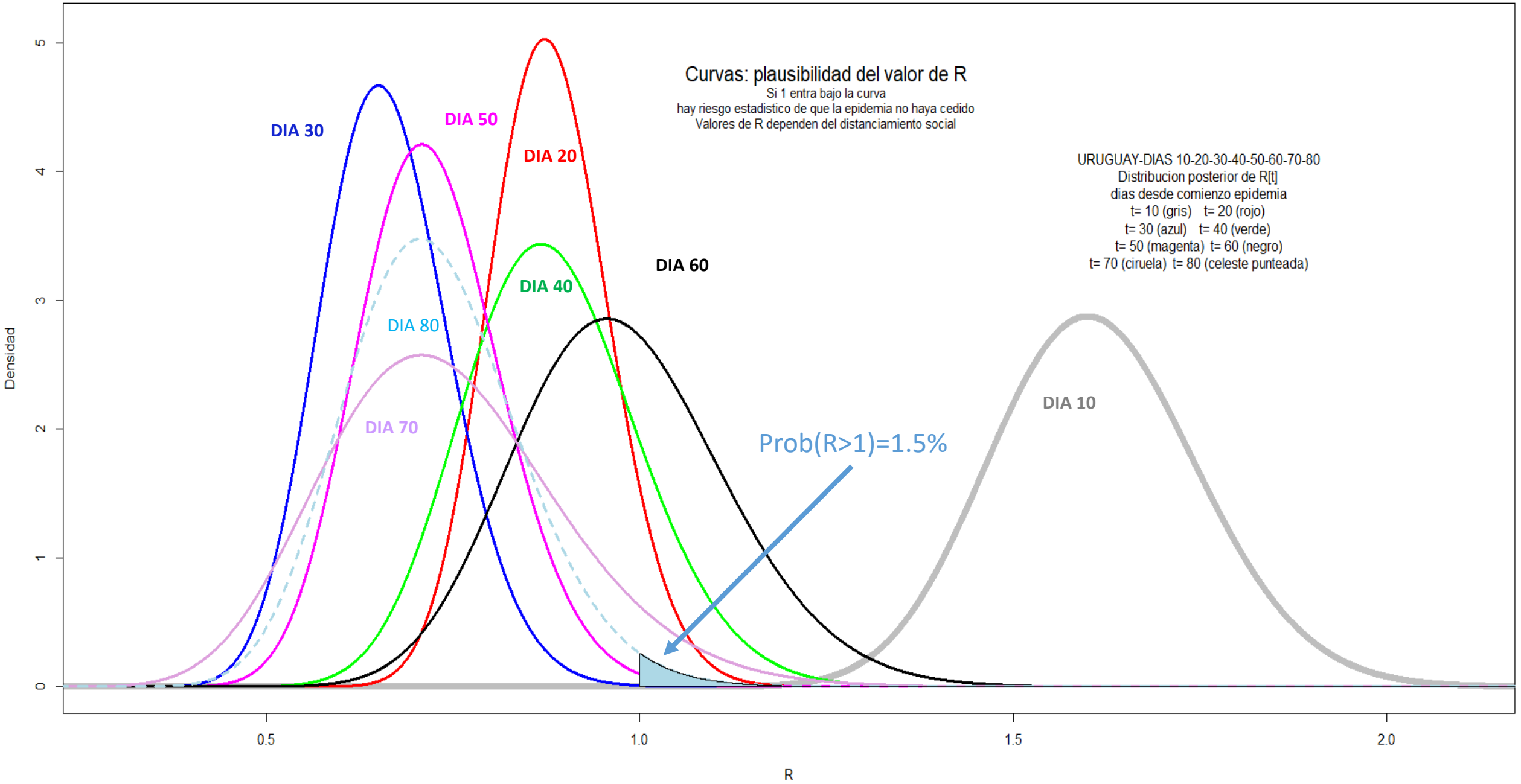
Prediccion
Distribucion Predictiva

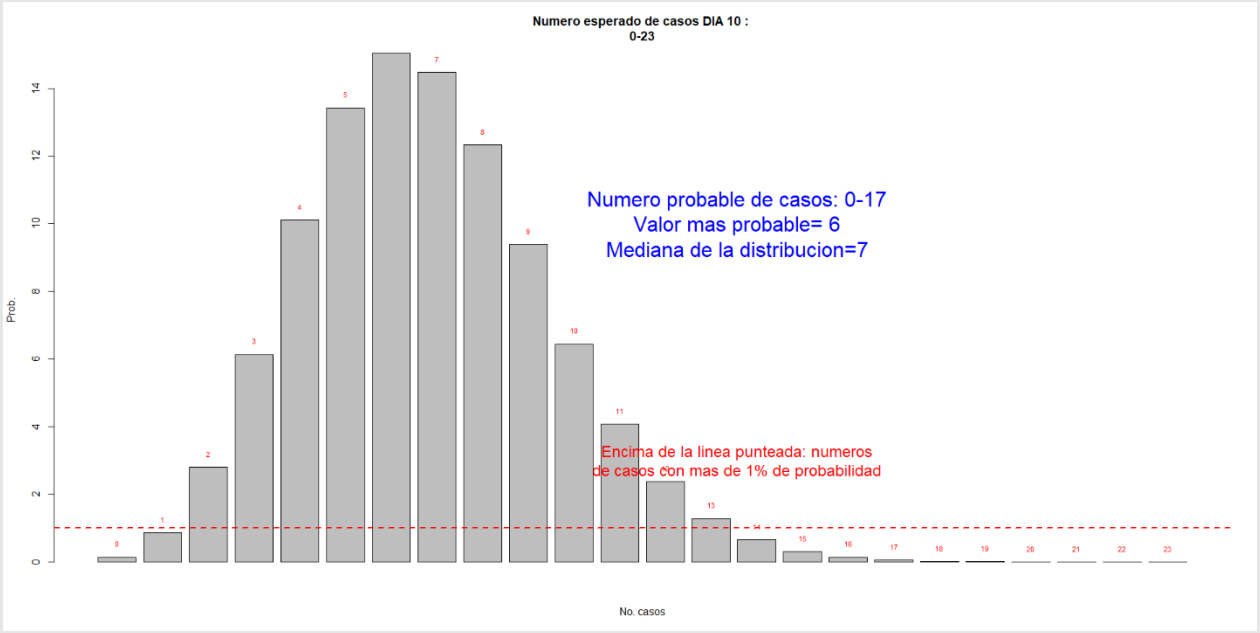
$$\Pr(\text{Casos futuros}|\text{Casos "N",Casos "V",supuestos})$$

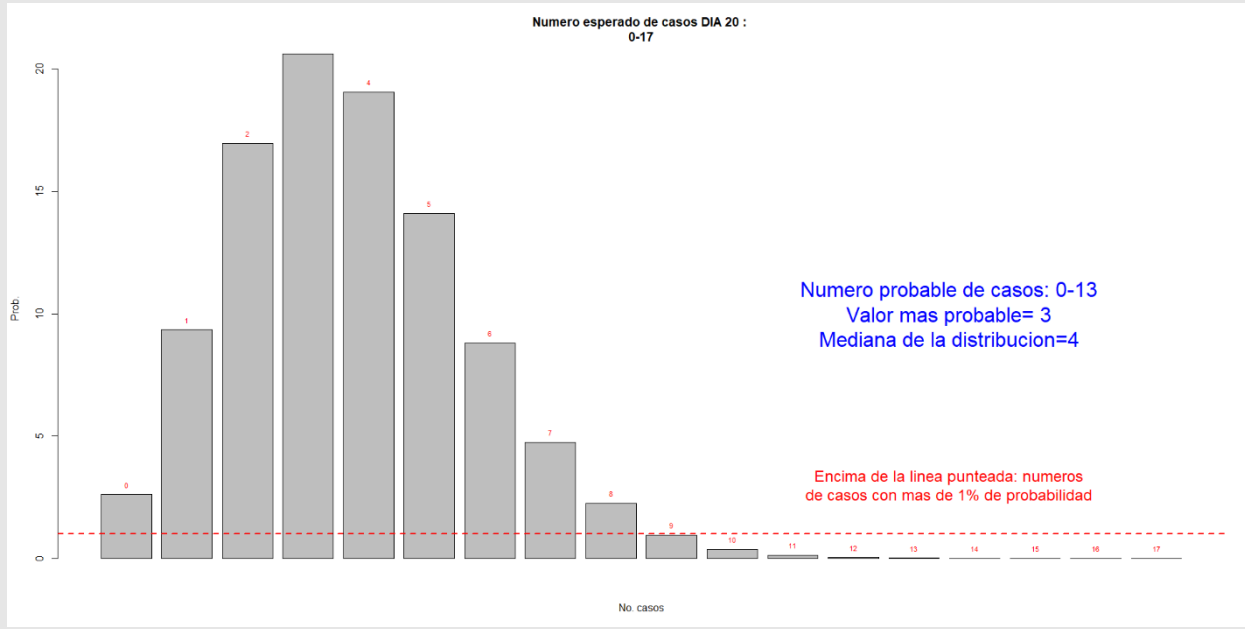
$$= \int \Pr(\text{Casos futuros}|R_t, \text{Casos "N" y "V",supuestos}) p(R_t|\text{Casos "N"y "V", supuestos iniciales}) dR_t$$

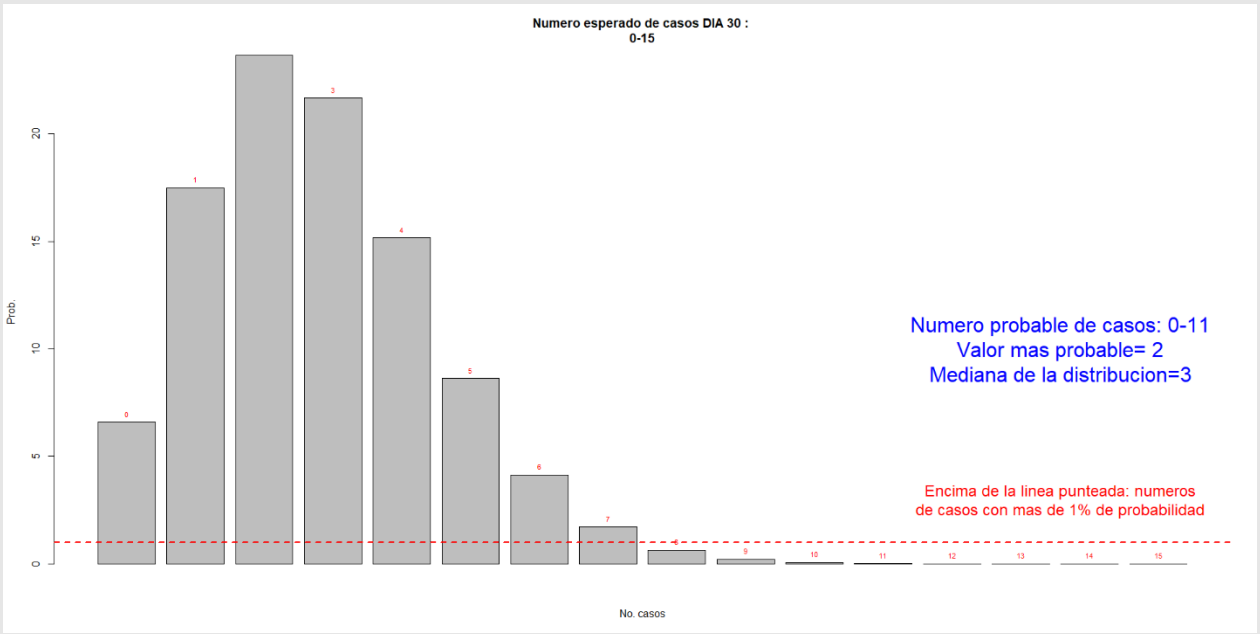

EVOLUCION DE R (numero reproduccion del virus)
URUGUAY-JUNIO 8
MEDIANAS DIARIAS
R<1 -->LA EPIDEMIA CEDE
R>1 -->LA EPIDEMIA CRECE
R movil
DIA
0.0
0.5
1.0
1.5
2.0
2.5
8 10 12 14 16 18 20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54 56 58 60 62 64 66 68 70 72 74 76 78 80 82 84 86
2.6 2.3 1.6 1.4 1.3 1.2 1 1 1.1 1.2 1.1 0.9 0.9 1 1 0.8 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.7 0.9 0.9 1 0.9 0.9 1 1 0.9 0.9 0.9 0.9 1.3 1.3 1.4 1.2 1.1 1.2 1.1 0.7 0.6 0.5 0.7 0.7 0.7 0.9 1 1.1 1.1 1 0.9 0.8 0.8 0.7 0.6 0.6 0.6 0.8 0.8 0.7 1.1 1.3 1.8 1.7 1.7 1.6 1.5 1.2 1.1 0.7 0.7 0.5 0.5 0.4 0.7 0.7

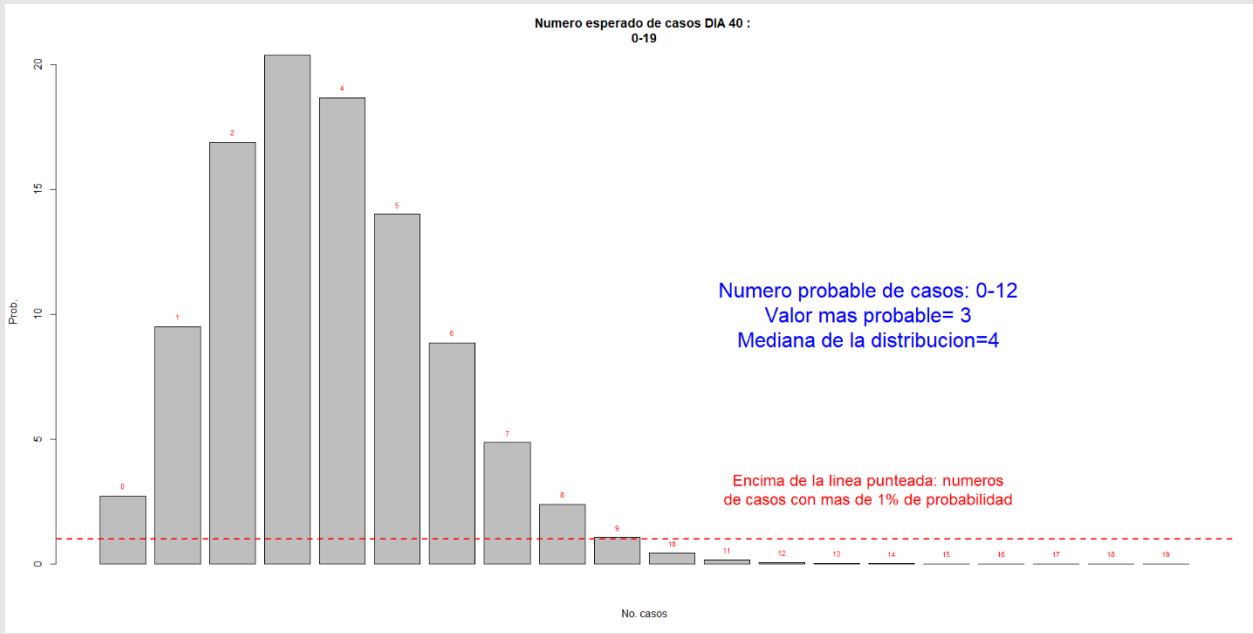

EVOLUCION DE LA EPIDEMIA
URUGUAY-JUNIO 4
BASE DE DATOS: https://www.ecdc.europa.eu
No. casos diarios
Dias desde primer caso
10
20
30
40
50
60
70
80

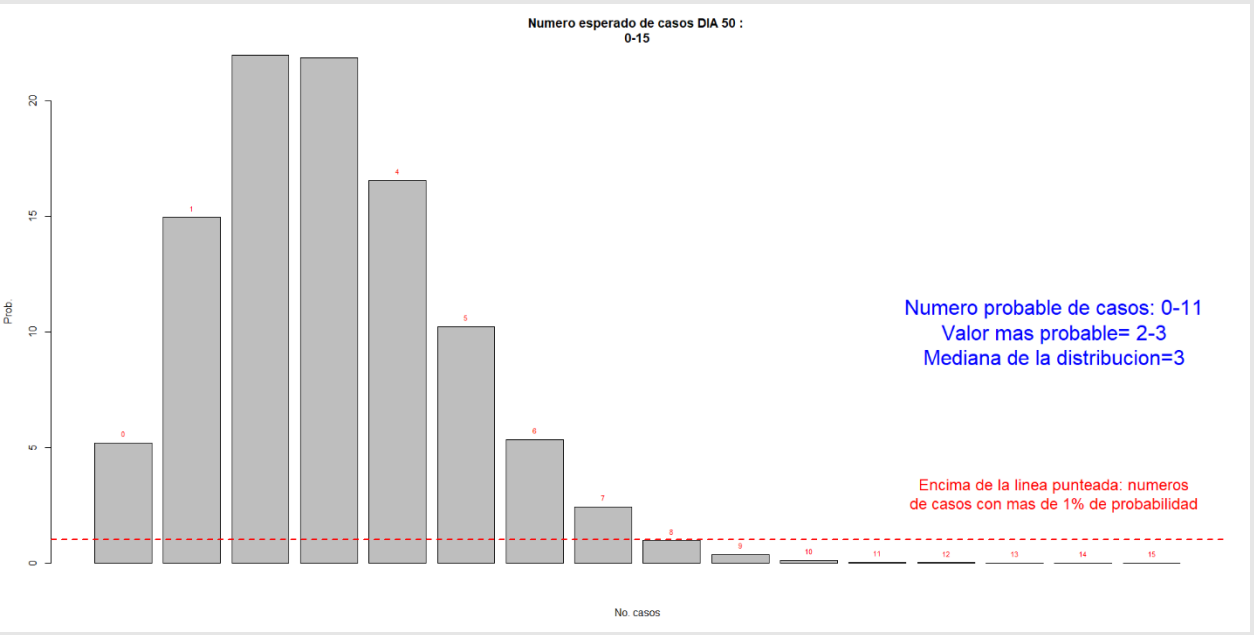

Curvas: plausibilidad del valor de R
Si 1 entra bajo la curva
hay riesgo estadistico de que la epidemia no haya cedido
Valores de R dependen del distanciamiento social
URUGUAY-DIAS 10-20-30-40-50-60-70-80
Distribucion posterior de R[t]
dias desde comienzo epidemia
t= 10 (gris) t= 20 (rojo)
t= 30 (azul) t= 40 (verde)
t= 50 (magenta) t= 60 (negro)
t= 70 (ciruela) t= 80 (celeste punteada)
DIA 30
DIA 50
DIA 20
DIA 60
DIA 40
DIA 80
DIA 70
DIA 10
Prob(R>1)=1.5%
Densidad
R
0
1
2
3
4
5
0.5
1.0
1.5
2.0

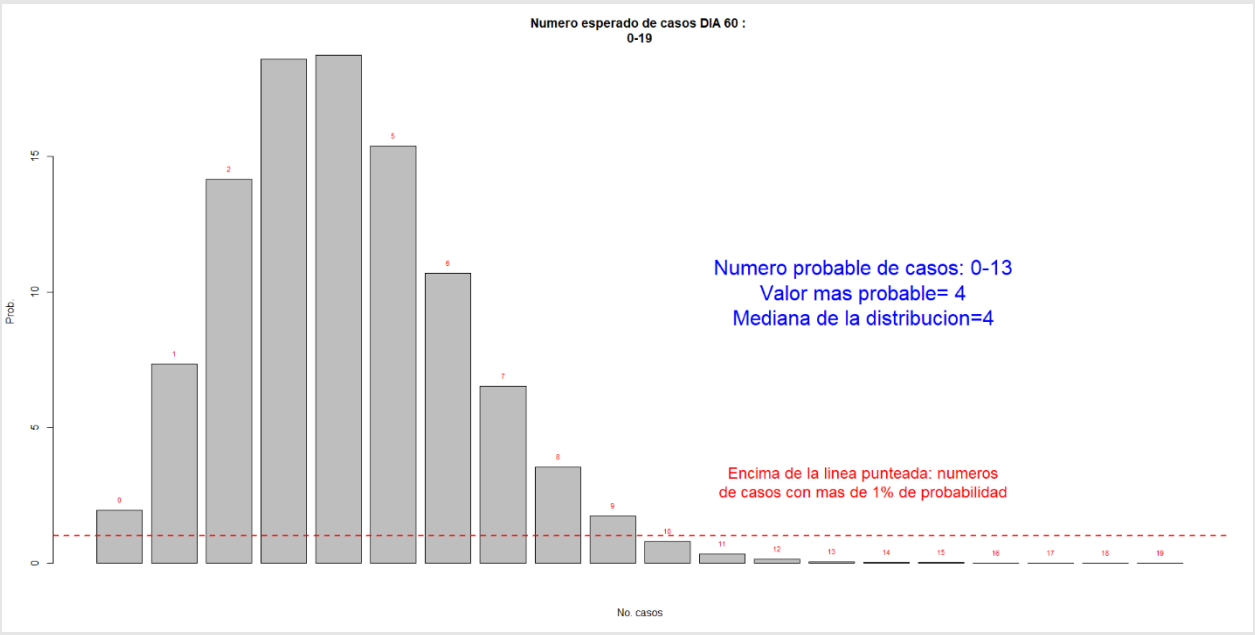

Numero esperado de casos DIA 10 :
0-23
Numero probable de casos: 0-17
Valor mas probable= 6
Mediana de la distribucion=7
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad
Prob.
No. casos

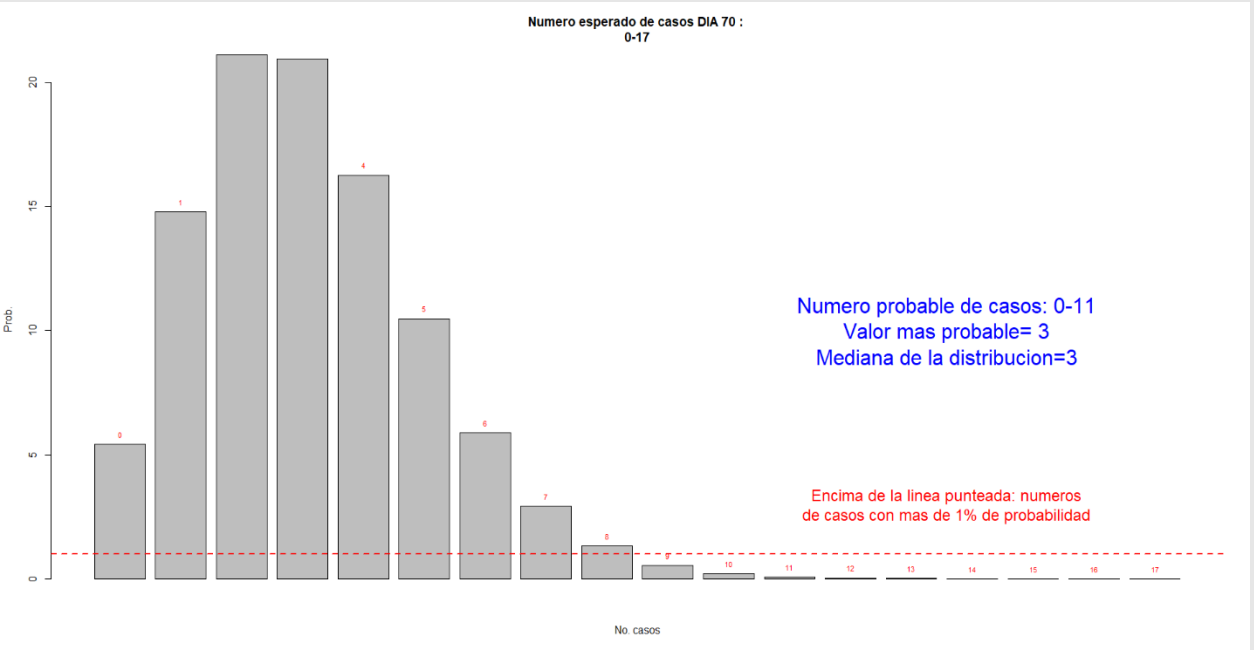

Numero esperado de casos DIA 20 :
0-17
Numero probable de casos: 0-13
Valor mas probable= 3
Mediana de la distribucion=4
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad
Prob.
No. casos

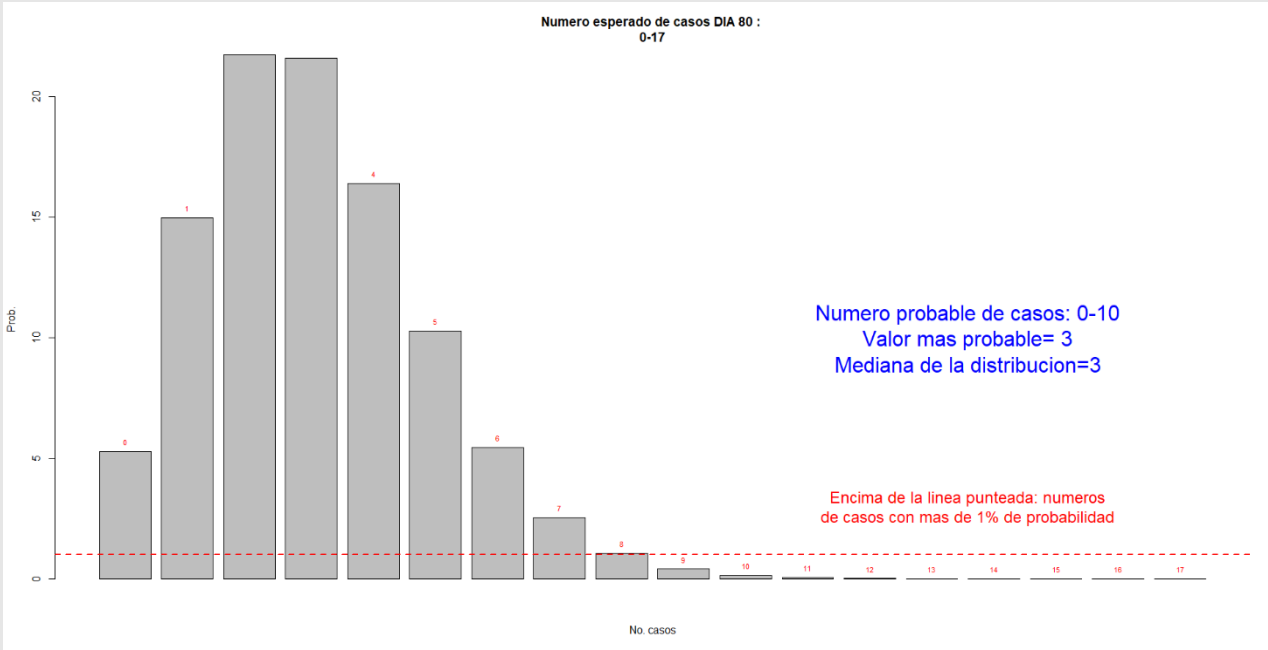

Numero esperado de casos DIA 30 :
0-15
Numero probable de casos: 0-11
Valor mas probable= 2
Mediana de la distribucion=3
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad
Prob.
No. casos


Numero esperado de casos DIA 40 :
0-19
Numero probable de casos: 0-12
Valor mas probable= 3
Mediana de la distribucion=4
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad
Prob.
No. casos


Numero esperado de casos DIA 50 :
0-15
Prob.
No. casos
Numero probable de casos: 0-11
Valor mas probable= 2-3
Mediana de la distribucion=3
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad


Numero esperado de casos DIA 60 :
0-19
Prob.
No. casos
Numero probable de casos: 0-13
Valor mas probable= 4
Mediana de la distribucion=4
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad


Numero esperado de casos DIA 70 :
0-17
Prob.
No. casos
Numero probable de casos: 0-11
Valor mas probable= 3
Mediana de la distribucion=3
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad


Numero esperado de casos DIA 80 :
0-17
Prob.
No. casos
Numero probable de casos: 0-10
Valor mas probable= 3
Mediana de la distribucion=3
Encima de la linea punteada: numeros
de casos con mas de 1% de probabilidad

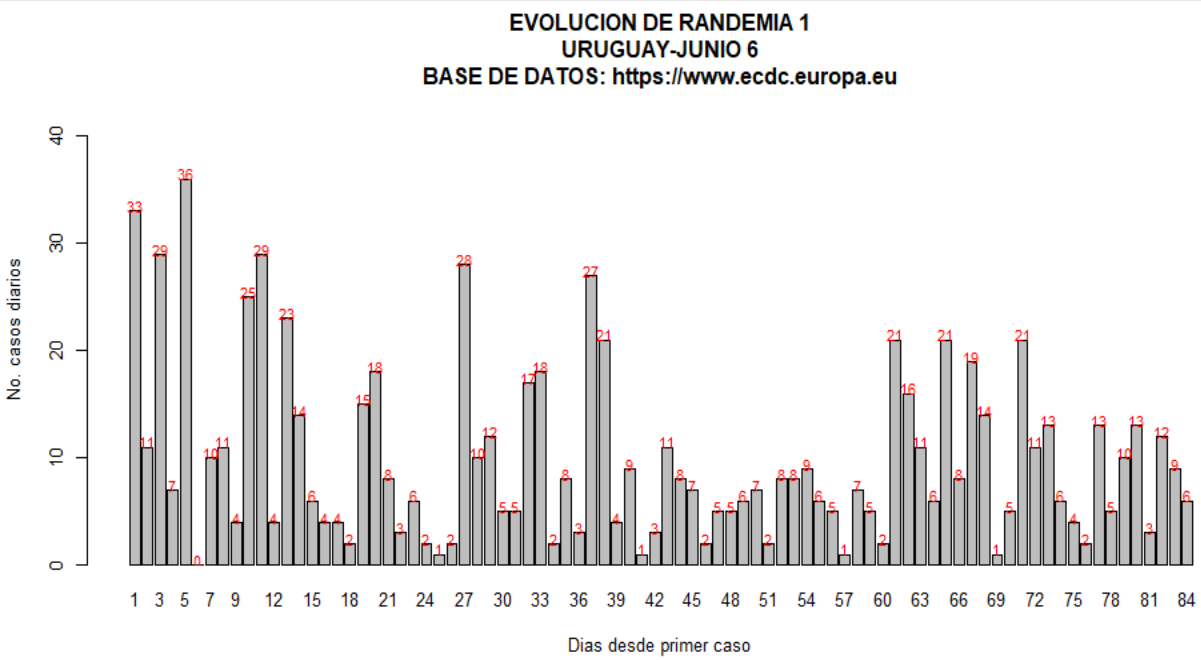
COMO EVALUAR SI LAS PREDICCIONES SON BUENAS O MALAS?

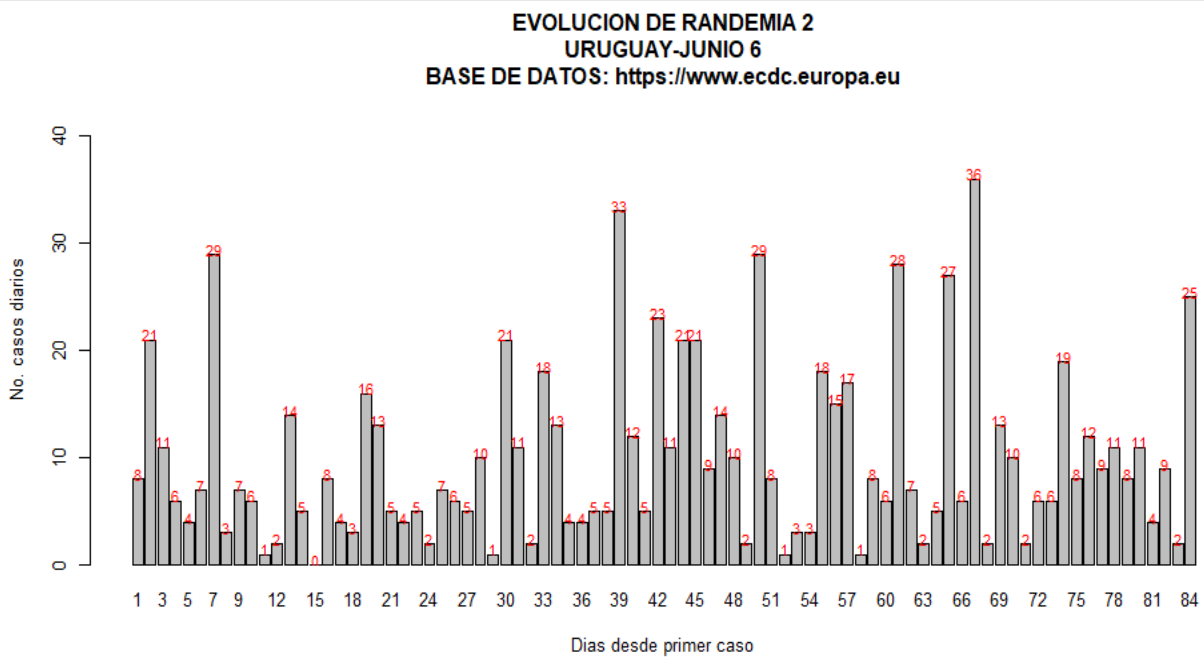
- SE NECESITARIA COMPARAR CON OTRA “MAQUINA” PREDICTIVA, QUE NO DISPONEMOS
- ENTONCES, COMPARAMOS CON LA PEOR MAQUINA PREDICTIVA: ENTROPIA, CAOS

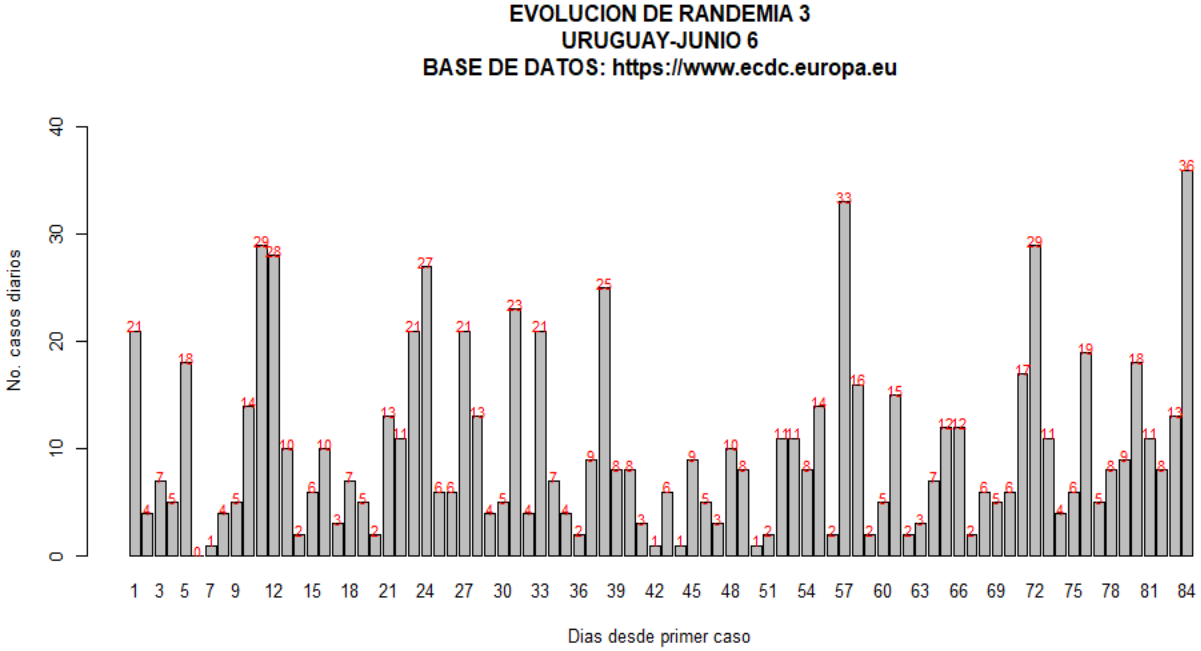
RANDEMIAS
(R:“RANDOM”,”ALEATORIO”)

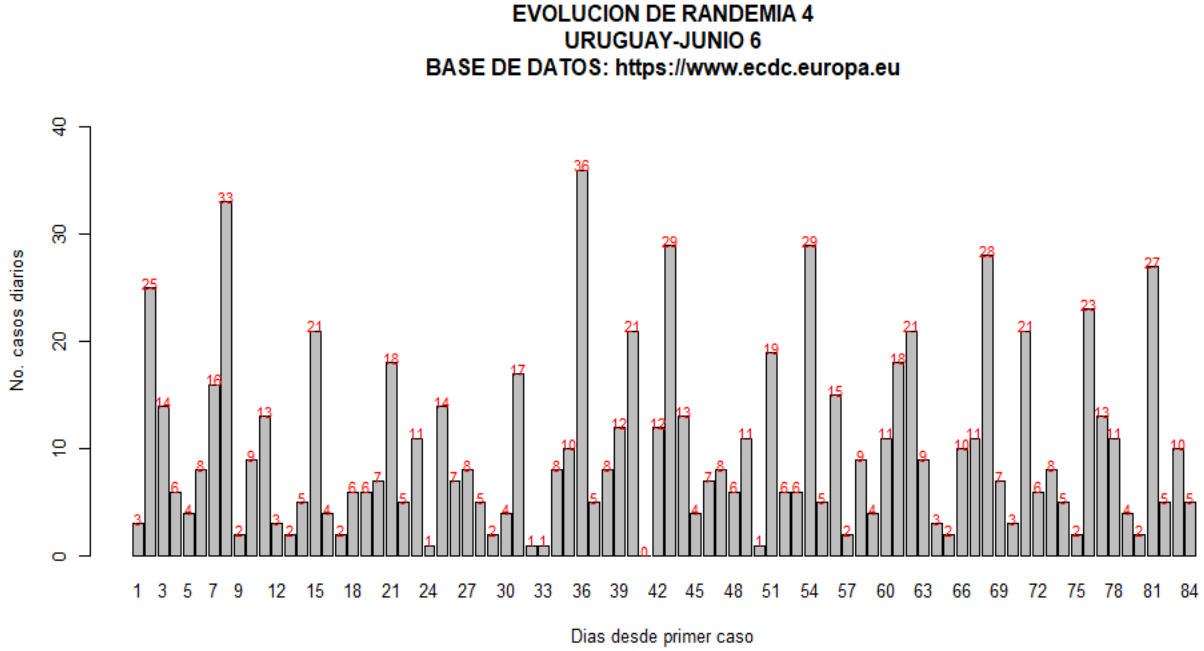
2.11×10^{132} *RANDEMIAS*

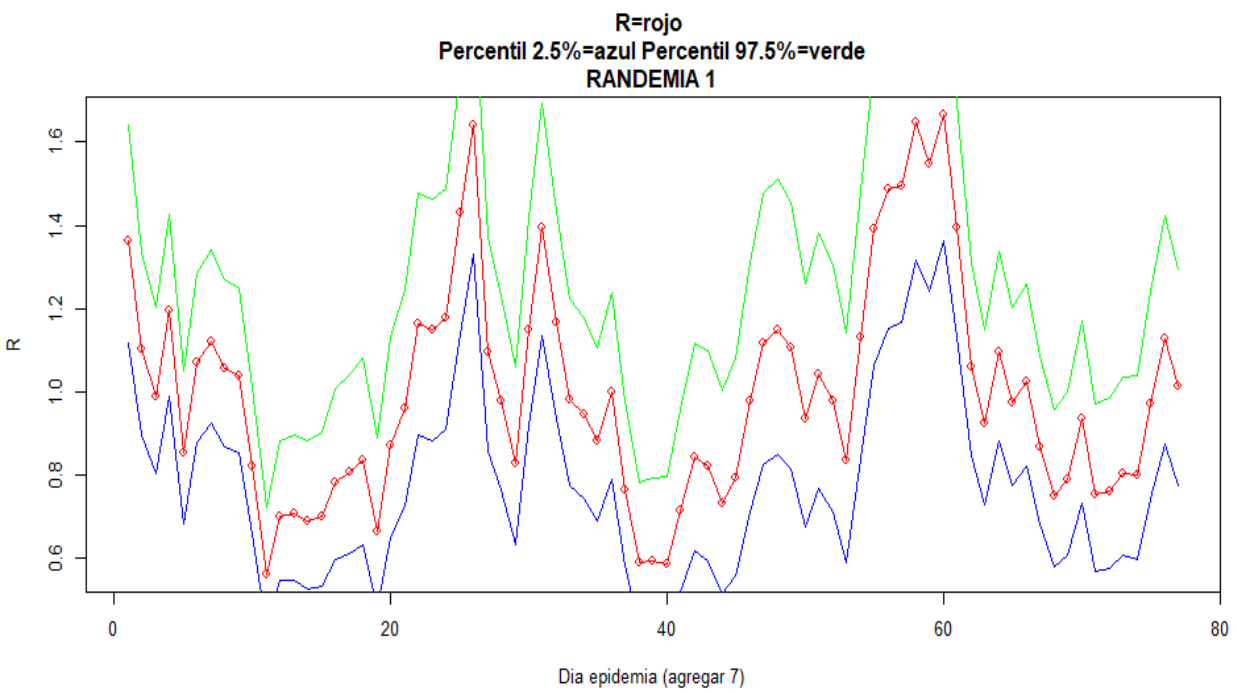
SARS-cov-2
Gusano Loco

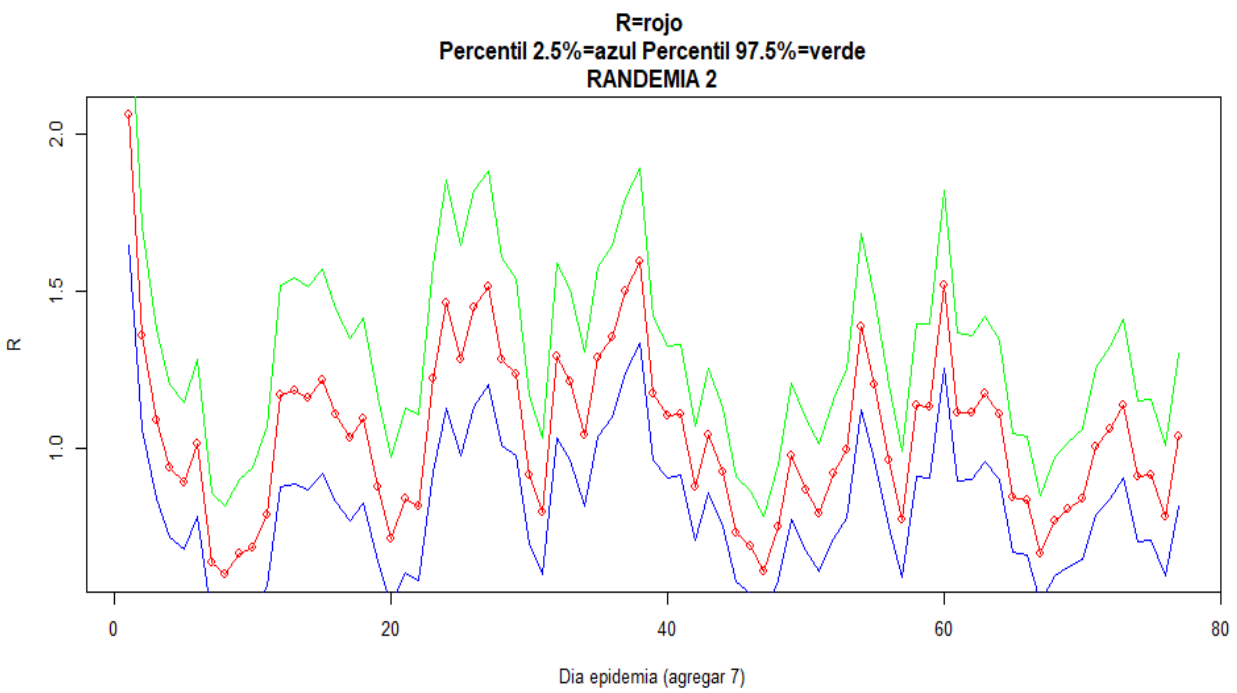

EVOLUCION DE RANDEMIA 1
URUGUAY-JUNIO 6
BASE DE DATOS: https://www.ecdc.europa.eu
No. casos diarios
Dias desde primer caso

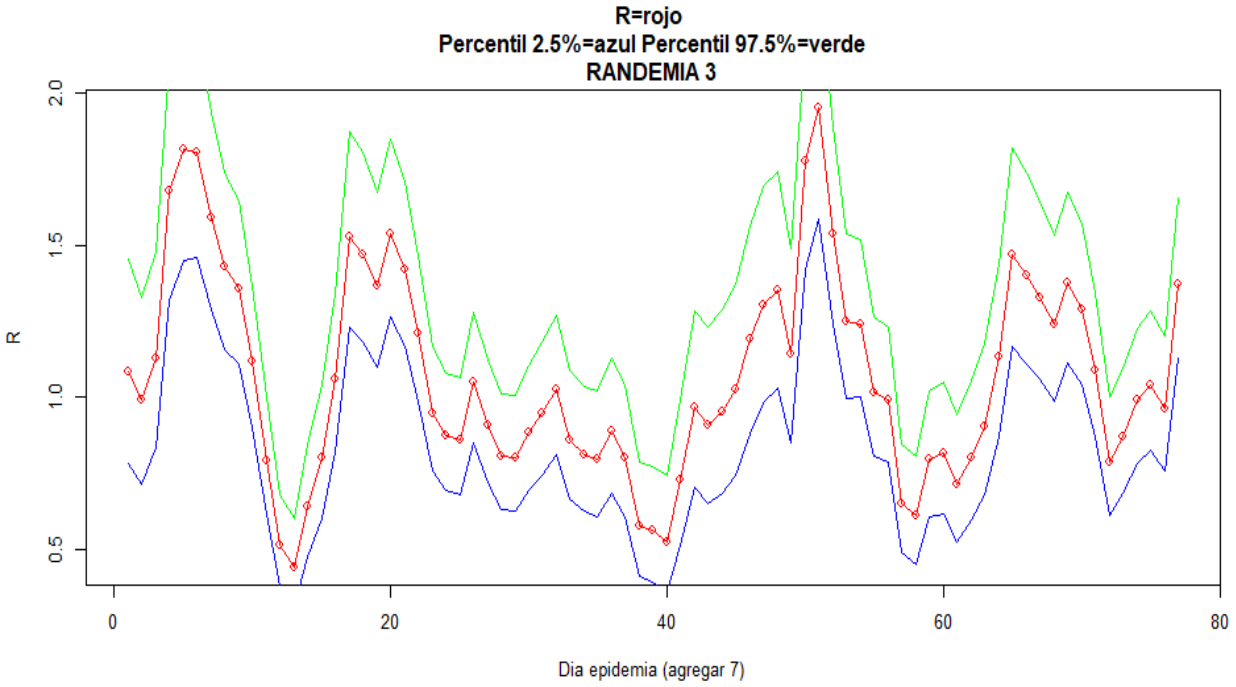

EVOLUCION DE RANDEMIA 2
URUGUAY-JUNIO 6
BASE DE DATOS: https://www.ecdc.europa.eu
No. casos diarios
Dias desde primer caso

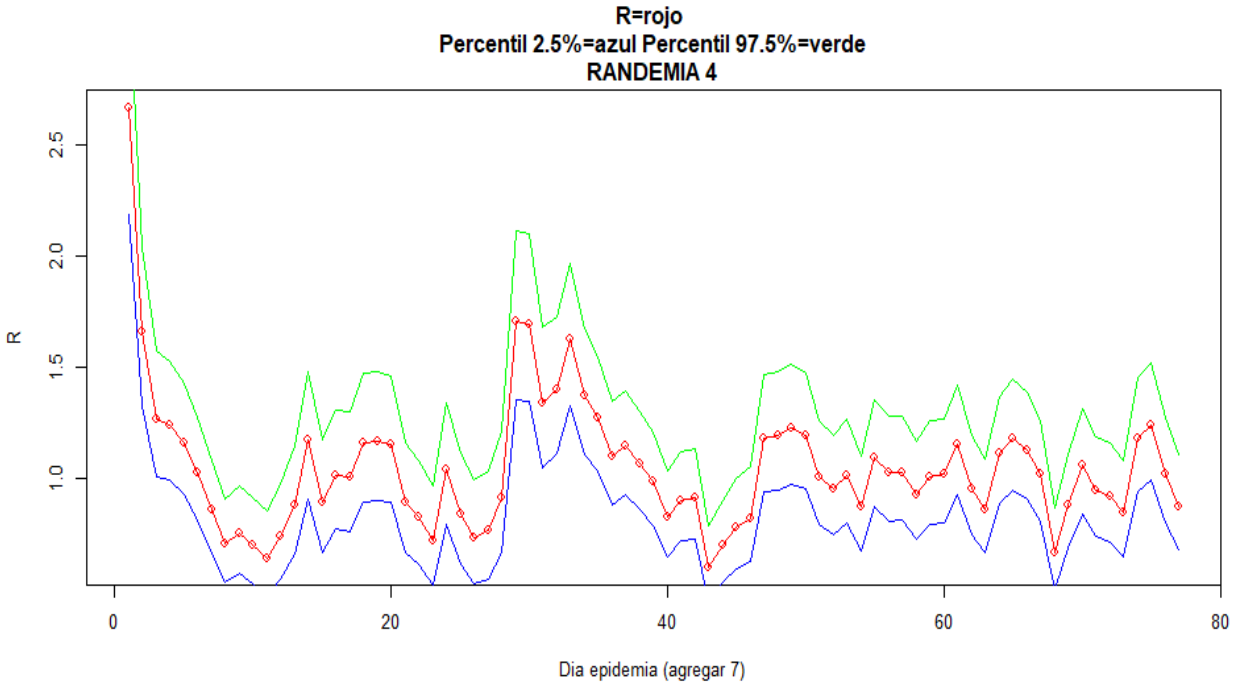

EVOLUCION DE RANDEMIA 3
URUGUAY-JUNIO 6
BASE DE DATOS: https://www.ecdc.europa.eu
No. casos diarios
Dias desde primer caso

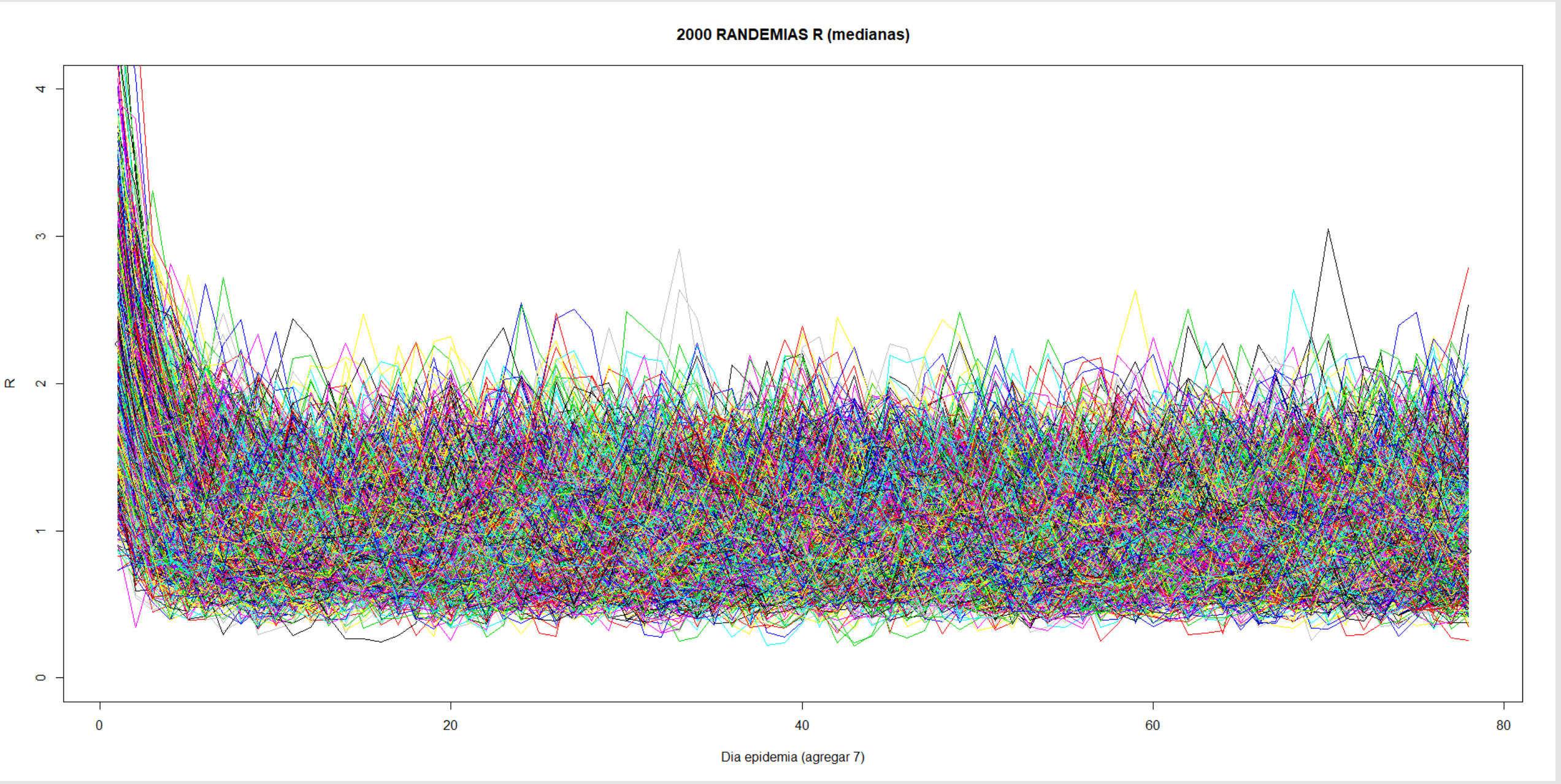

EVOLUCION DE RANDEMIA 4
URUGUAY-JUNIO 6
BASE DE DATOS: https://www.ecdc.europa.eu
No. casos diarios
Dias desde primer caso


R=rojo
Percentil 2.5%=azul Percentil 97.5%=verde
RANDEMIA 1
R
Dia epidemia (agregar 7)


R=rojo
Percentil 2.5%=azul Percentil 97.5%=verde
RANDEMIA 2
R
Dia epidemia (agregar 7)


R=rojo
Percentil 2.5%=azul Percentil 97.5%=verde
RANDEMIA 3
R
Dia epidemia (agregar 7)


R=rojo
Percentil 2.5%=azul Percentil 97.5%=verde
RANDEMIA 4
R
Dia epidemia (agregar 7)


2000 RANDEMIAS R (medianas)
R
0
1
2
3
4
0
20
40
60
80
Dia epidemia (agregar 7)

ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 10

Median=49 Min=0 Max=2704

ROU=841

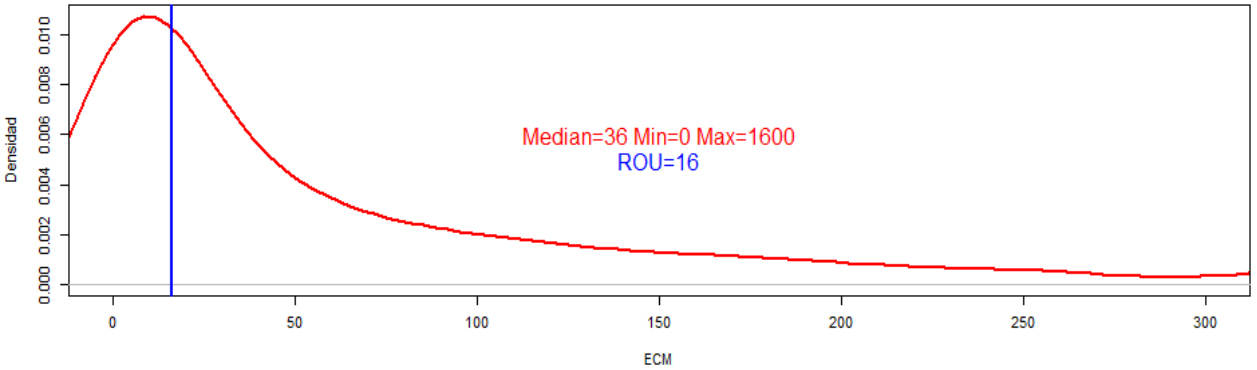
Densidad

0.000
0.001
0.002
0.003
0.004
0.005
0.006
0.007

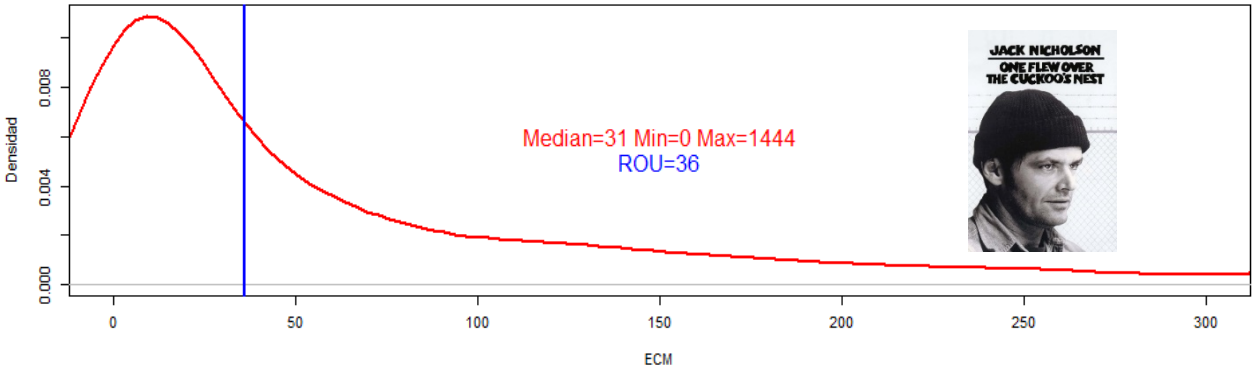
0
200
400
600
800
1000

ECM

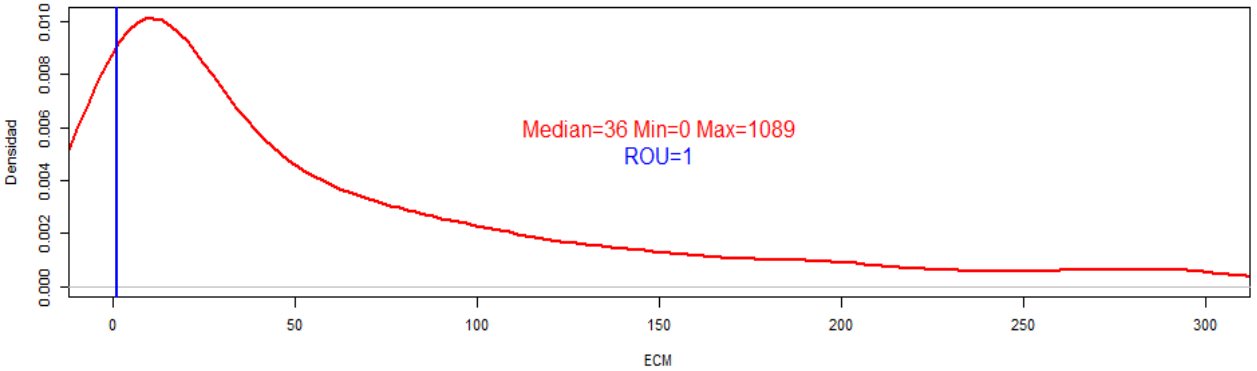
ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 20



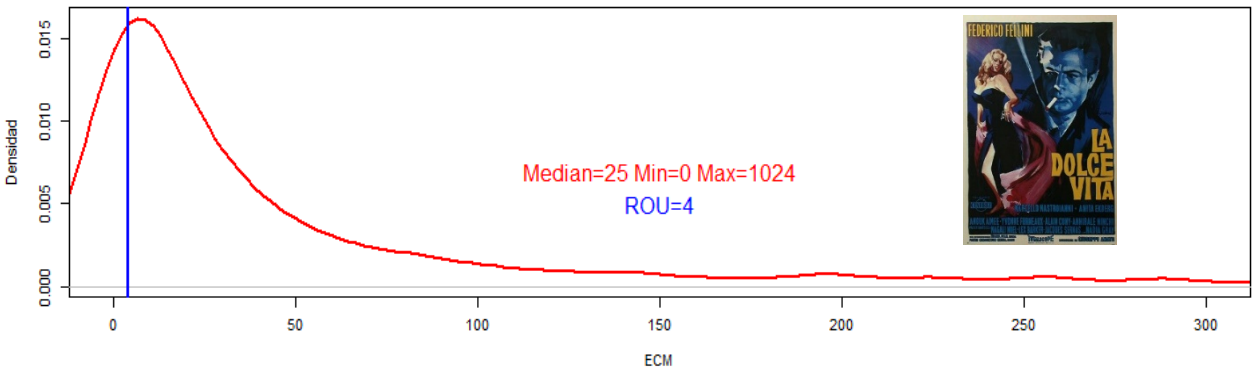
ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 30



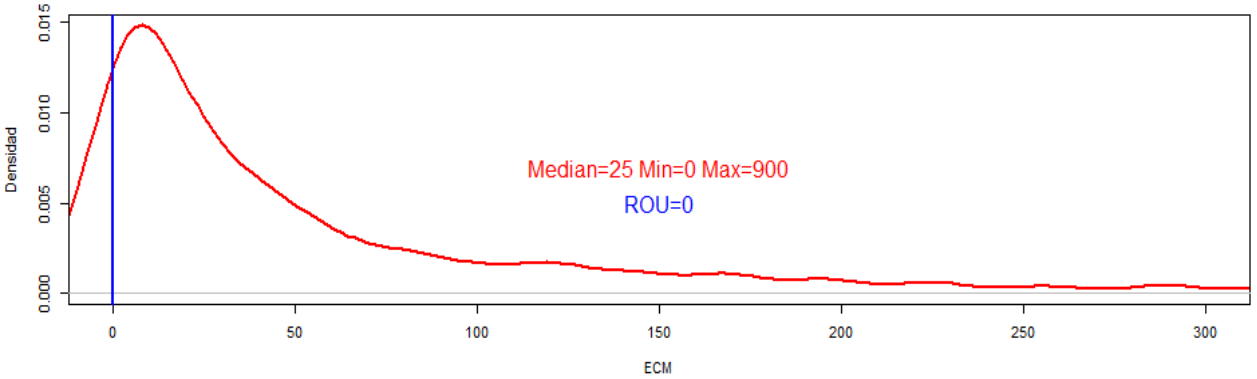
ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 40



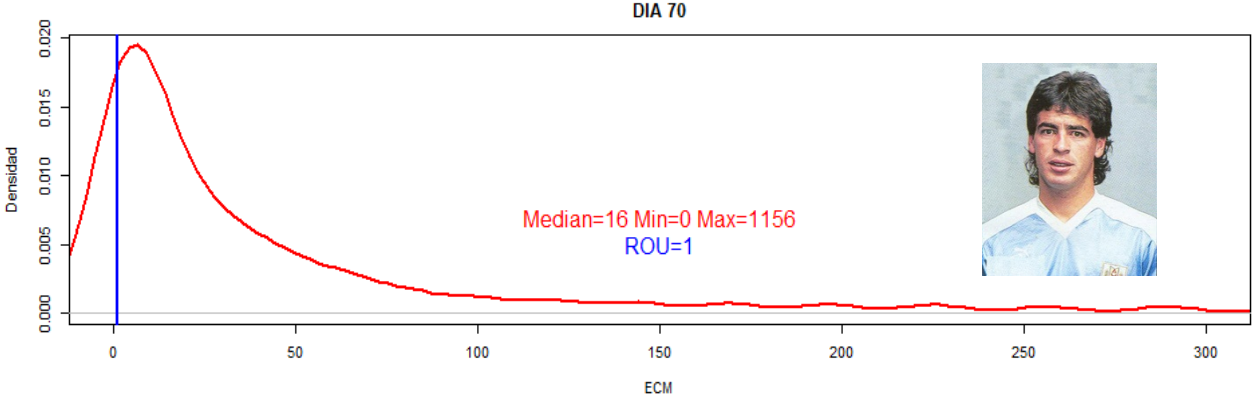
ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 50



ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 60

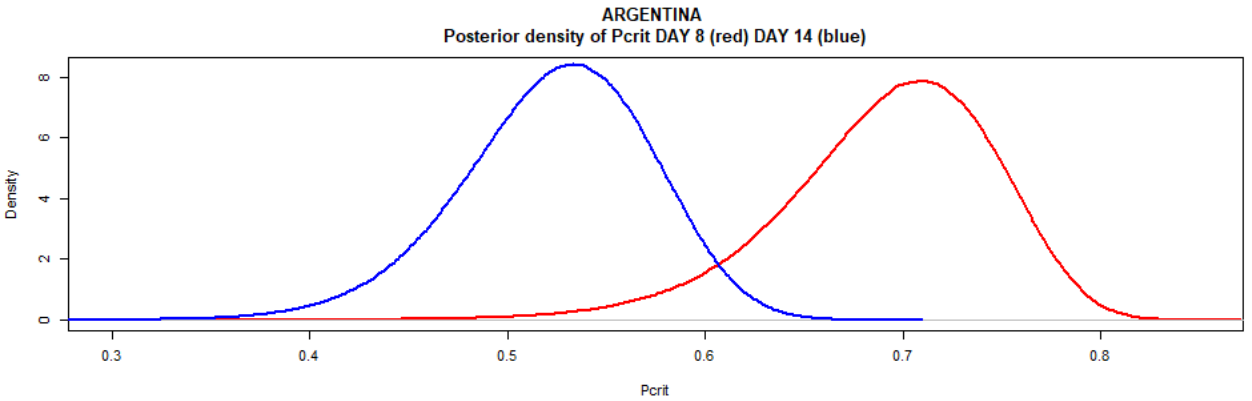


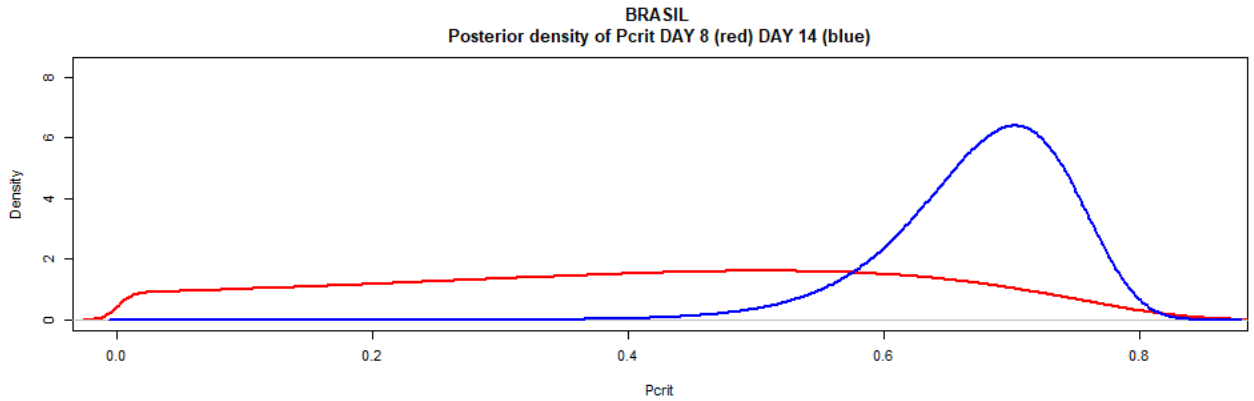
ERROR CUADRATICO MEDIO: 2000 RANDEMIAS
DIA 70

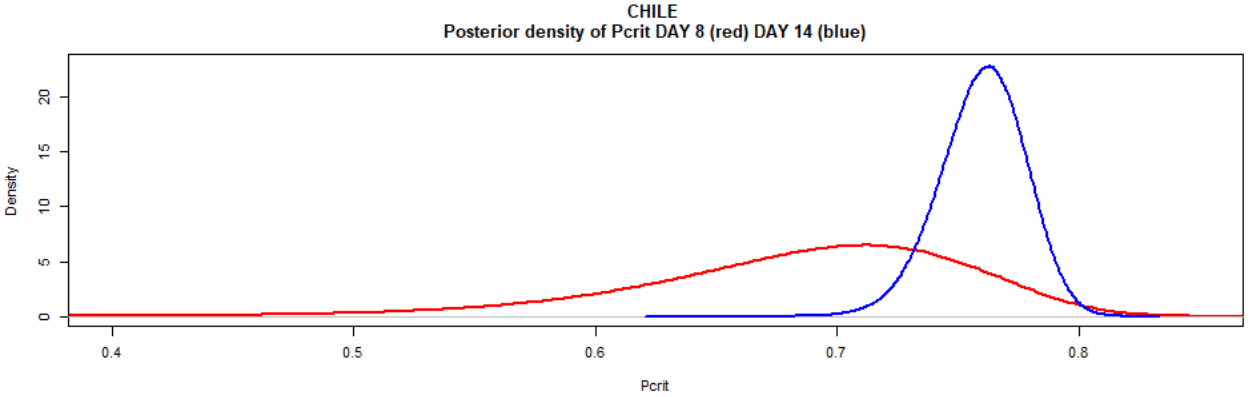


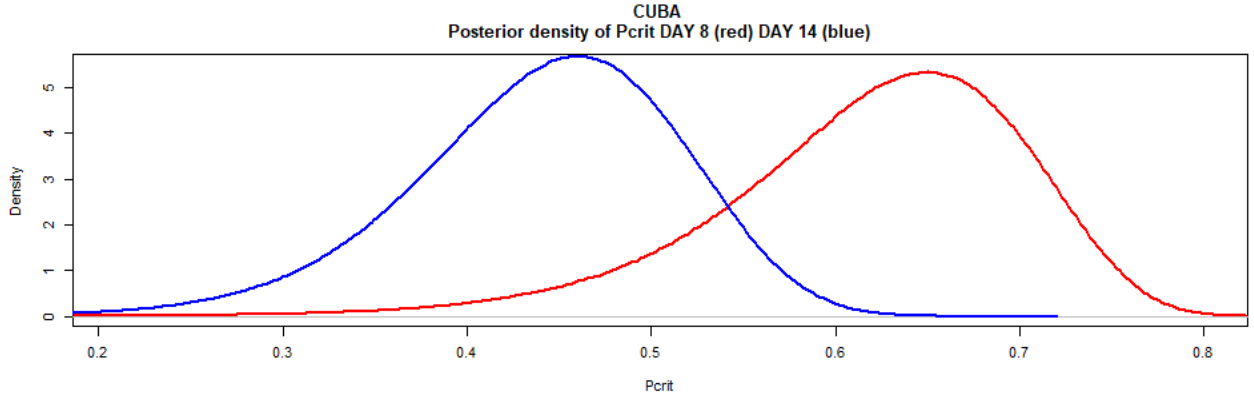
SI FUERAMOS COMO SUECIA…

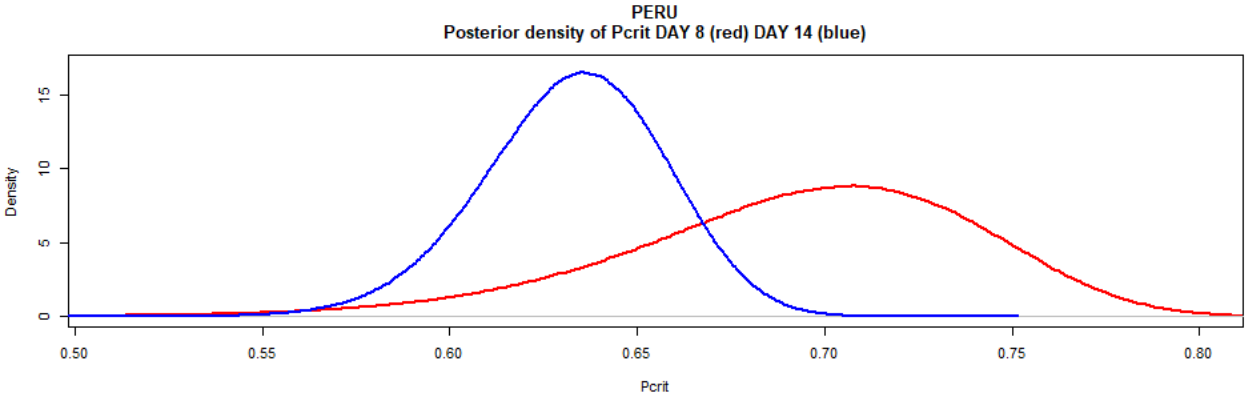
DENSIDAD POSTERIOR DE P_{crit} (porcentaje minimo infectados para “inmunidad rebaño)

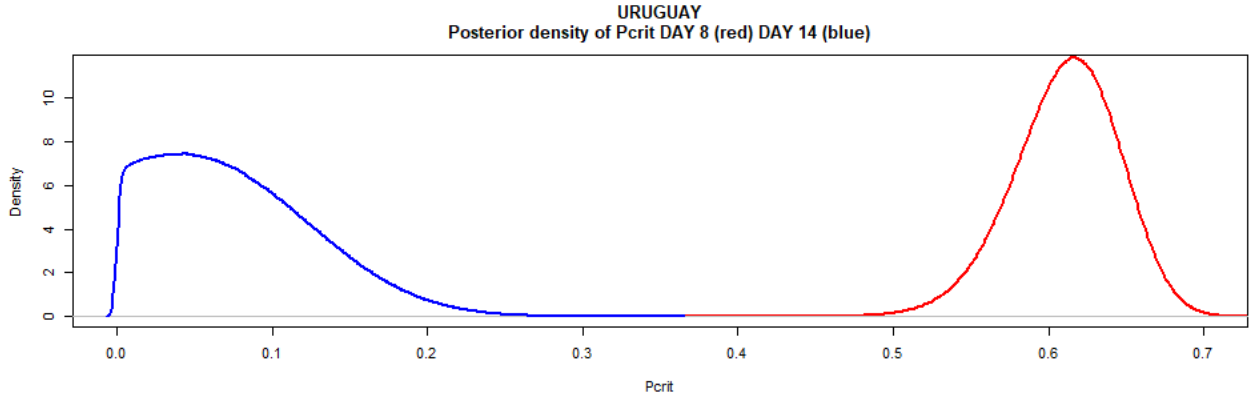




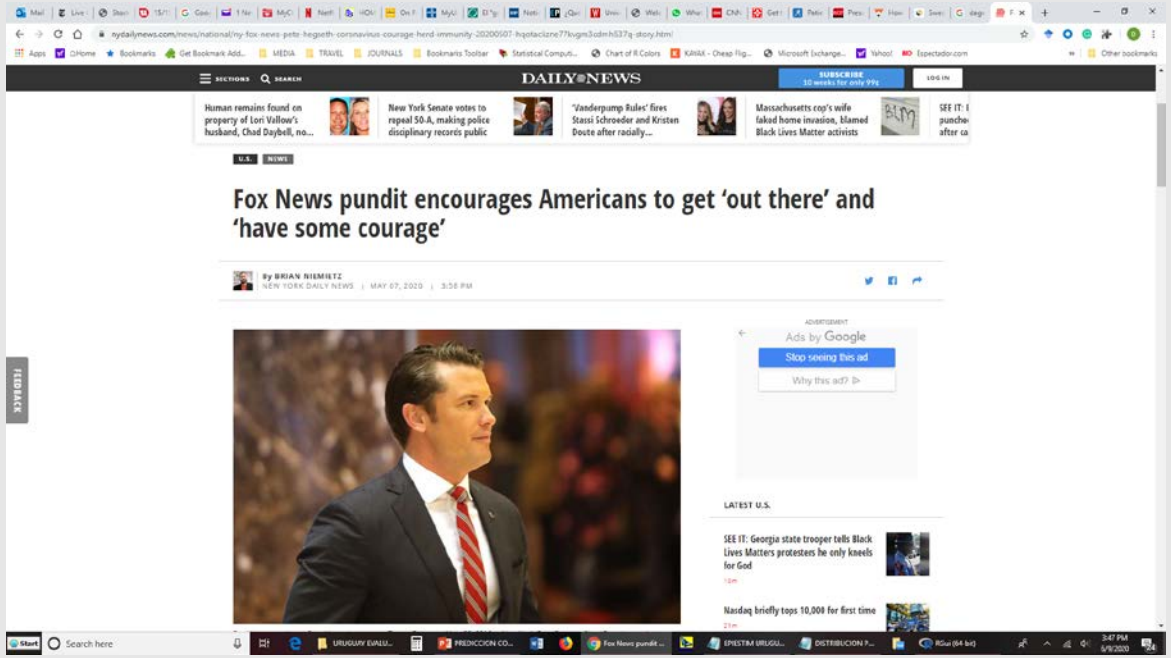








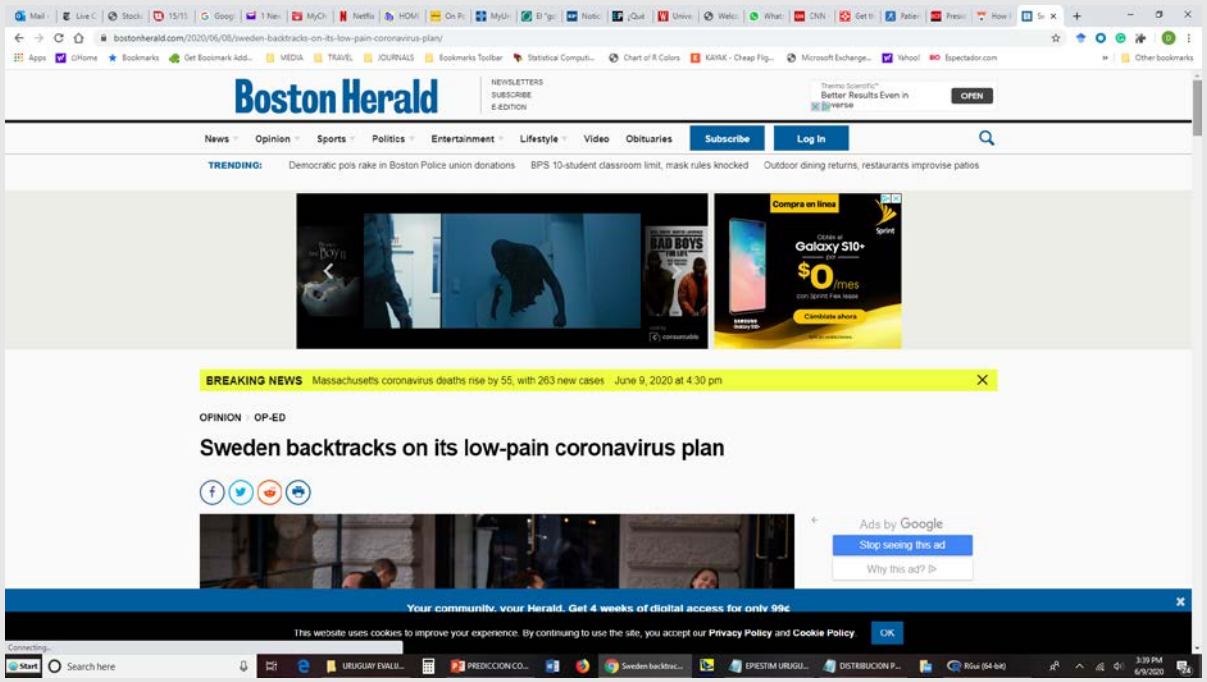
	PAIS	POBLACION (millones)	Tests/ millon	Casos/ millon	Muertes/ millon	PBI 2020(%)	
	SUECIA	10.1	27290	4431	462	-5.1	
	ALEMANIA	83.8	51917	2218	105	-6.1	
	DINAMARCA	5.8	121992	2063	102	-4.5	
	NORUEGA	5.4	47487	1577	44	-6.0	
	EEUU	330.9	63484	6038	339	-3.8	
	URUGUAY	3.5	13829	243	7	-----	
	REINO UNIDO	67.9	82241	4217	597	-8.7	

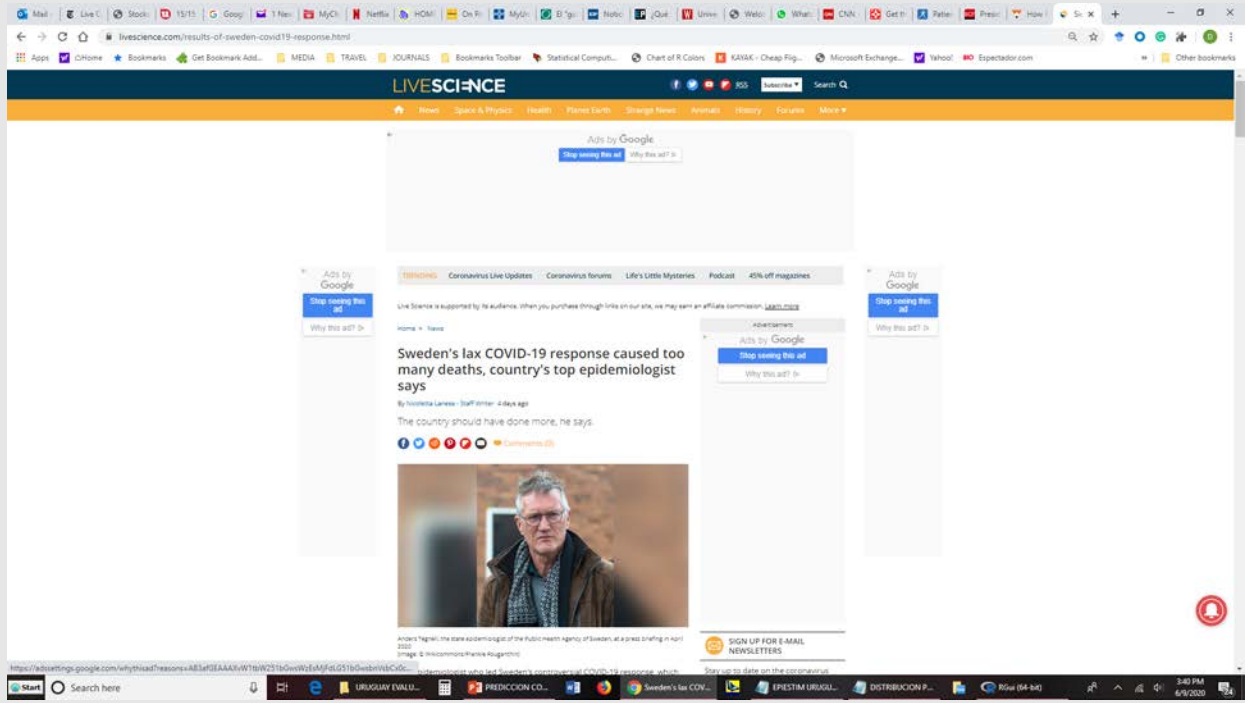


Strategin: Låt många smittas i lagom takt

CORONAVIRUSET | Artikeln publicerades 15 mars 2020

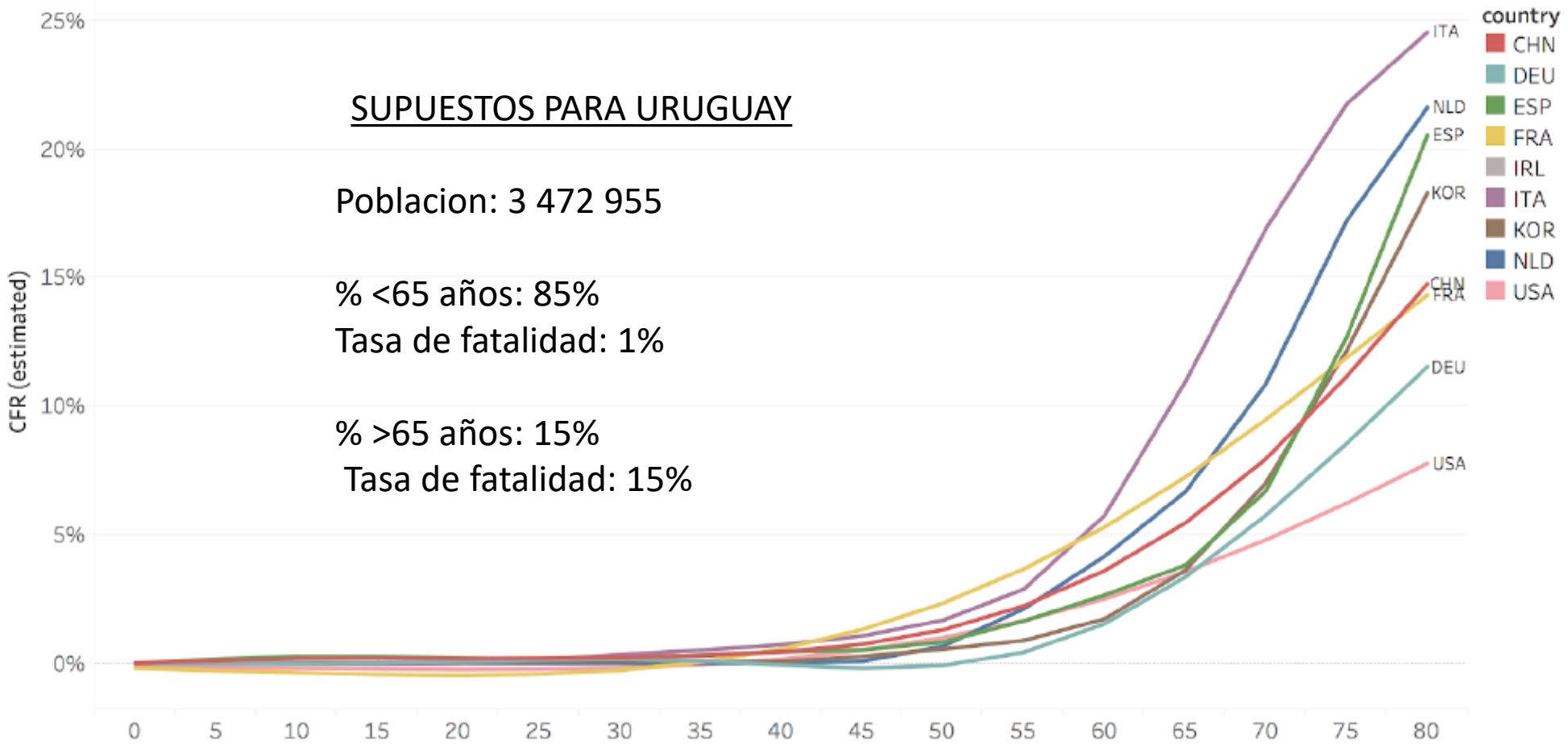
Dåvarande statsepidemiolog Annika Linde tillsammans med Anders Tegnell, som då var avdelningschef på Socialstyrelsen. Arkivbild från 2009.





“CASE FATALITY” RATES (%) POR EDAD (Natale et al. 2020)

https://ec.europa.eu/knowledge4policy/publication/covid-19-cases-case-fatality-rate-age_en



SUPUESTOS PARA URUGUAY

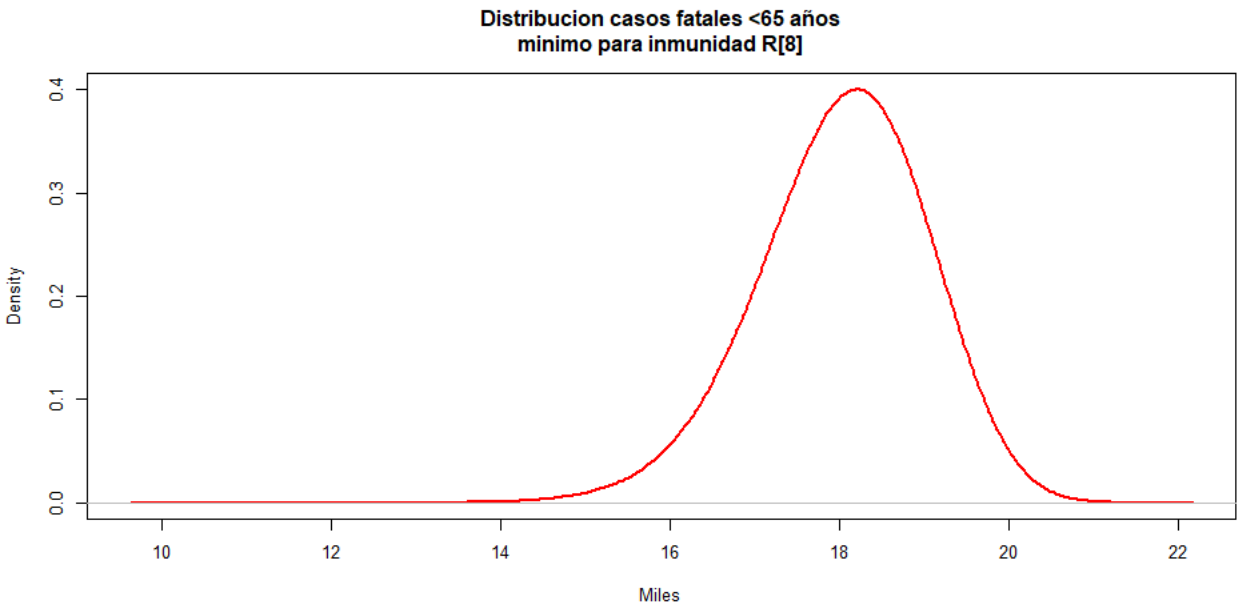
Poblacion: 3 472 955

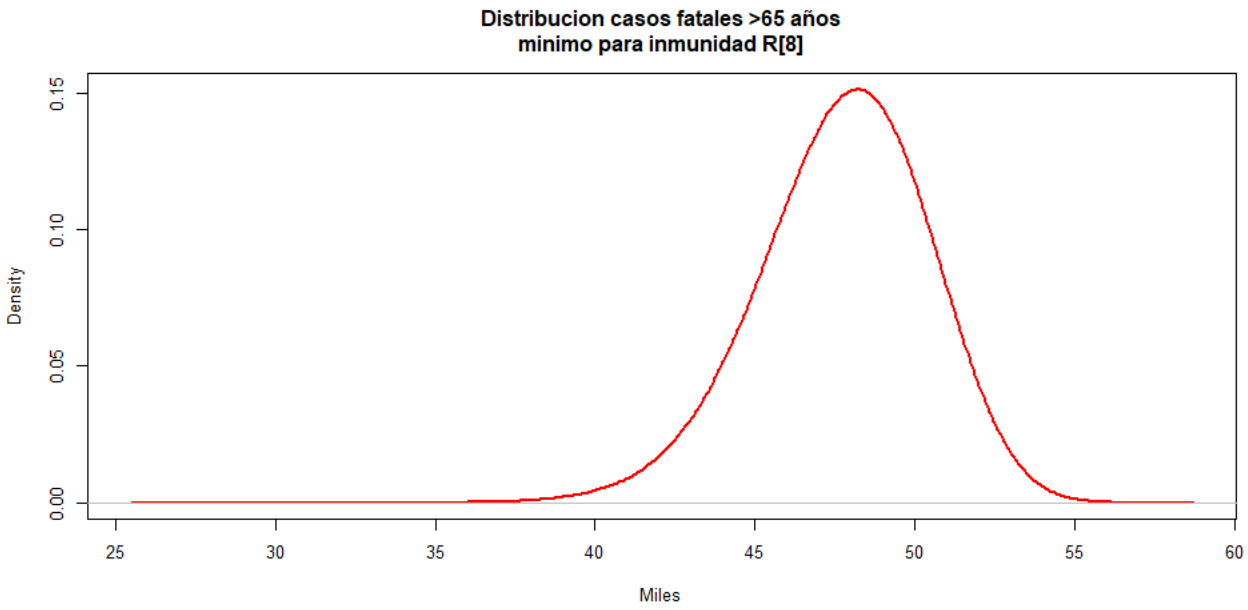
% <65 años: 85%
Tasa de fatalidad: 1%

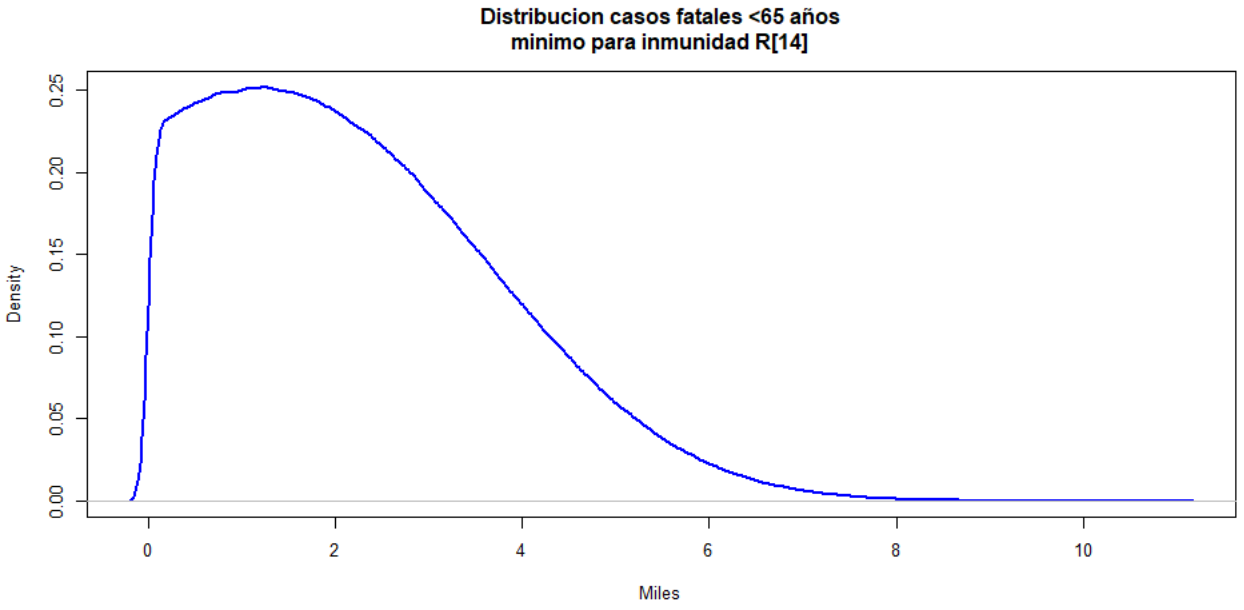
% >65 años: 15%
Tasa de fatalidad: 15%

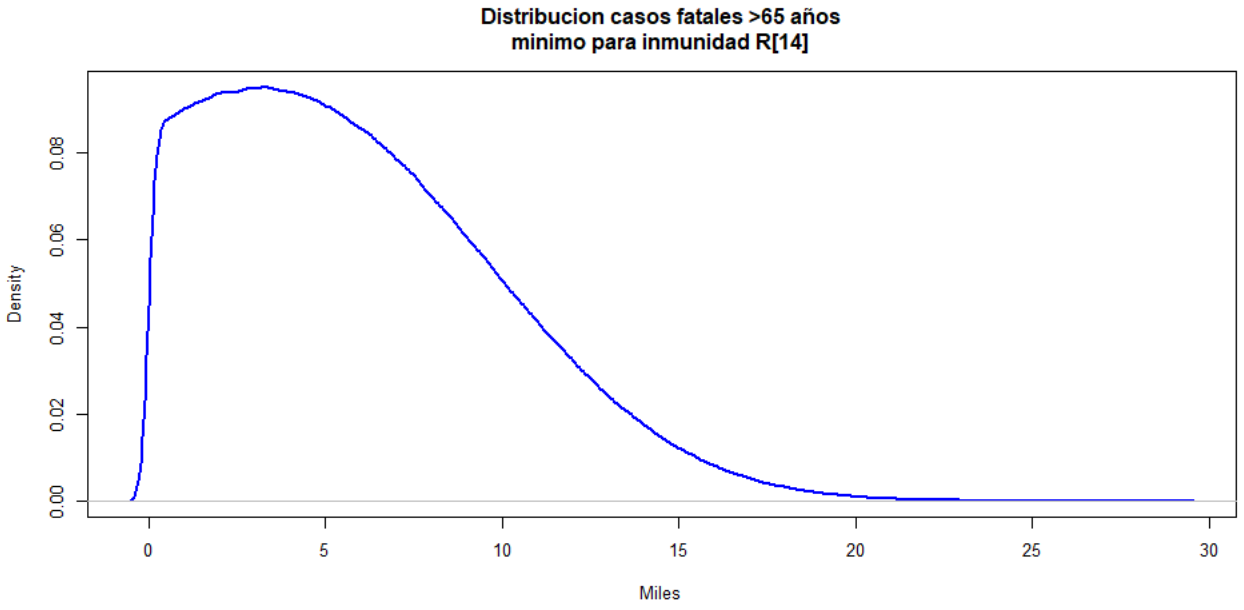
Figure 2 COVID-19 cases and CFR by harmonised 5-years age groups.

DISTRIBUCION DE MUERTES SEGUN EDAD PARA DOS POLITICAS HERD IMMUNITY









“PUTTING THE RISK OF COVID-19 IN PERSPECTIVE” (New York City)
David Roberts, New York Times

- “Micromorts” (Unidad, 1 en 1 millon chances de morirse en un dia)
- Dia comun y corriente (1 micromort)
- Anestesia general (5 micromorts por operacion)
- Paracaidismo (7 micromorts por salto)
- Andar 70km diarios en motocicleta (11 micromorts)
- Combatir en Afganistan en 2010 (25 micromorts)
- Parto (210 micromorts)
- Trepar mas de 8 mil metros en el Himalaya (10 mil micromorts)
- Vivir en Michigan durante la epidemia 11 micromorts
- Vivir en NY durante la epidemia 50 micromorts adicionales
- Vivir en NY, ser “mayorcito, contraer COVID:➔

ligeramente menos riesgoso que ser piloto de la RAF y bombardear Alemania en cuatro misiones durante la Segunda Guerra mundial

“Maracana de la pandemia”? (visto desde la distancia…)

- Se sabia que, tarde o temprano, SARS-COV-2 llegaria (equipamiento, camas CTI, etc.)
- Uruguay no es un “hub” (contrariamente a Milan, Frankfurt, NY City, etc.)
- Baja densidad demografica
- Decidida y rapida accion gubernamental. Alto nivel de testaje (regional). Control focos.
- Uso de evidencia y de asesoramento cientifico (“Triunvirato”, apoyado por un batallon de cientificos y medicos)
- Politica de switches, jugando el “partido en La Paz” (Radi et al.), sin demorar cambios (OWT)
- Consenso politico sobre las medidas (de “estado”)
- Sistema de salud estructurado
- Excelente cobertura de atencion primaria
- Uruguayos: respondieron ante la emergencia
- **NZ (islas) “erradico” el virus: 18 dias consecutivos sin ningun caso nuevo**
- **Jacinda Ardern no enfrenta el “riesgo Brasil”**