Outline:

Prof. Simone Cialdi, Physics Dept., Università degli Studi di Milano (Unimi), in collaboration with Prof. Carlo La Vecchia, Clinical Sciences and Community Health Dept. (Unimi).

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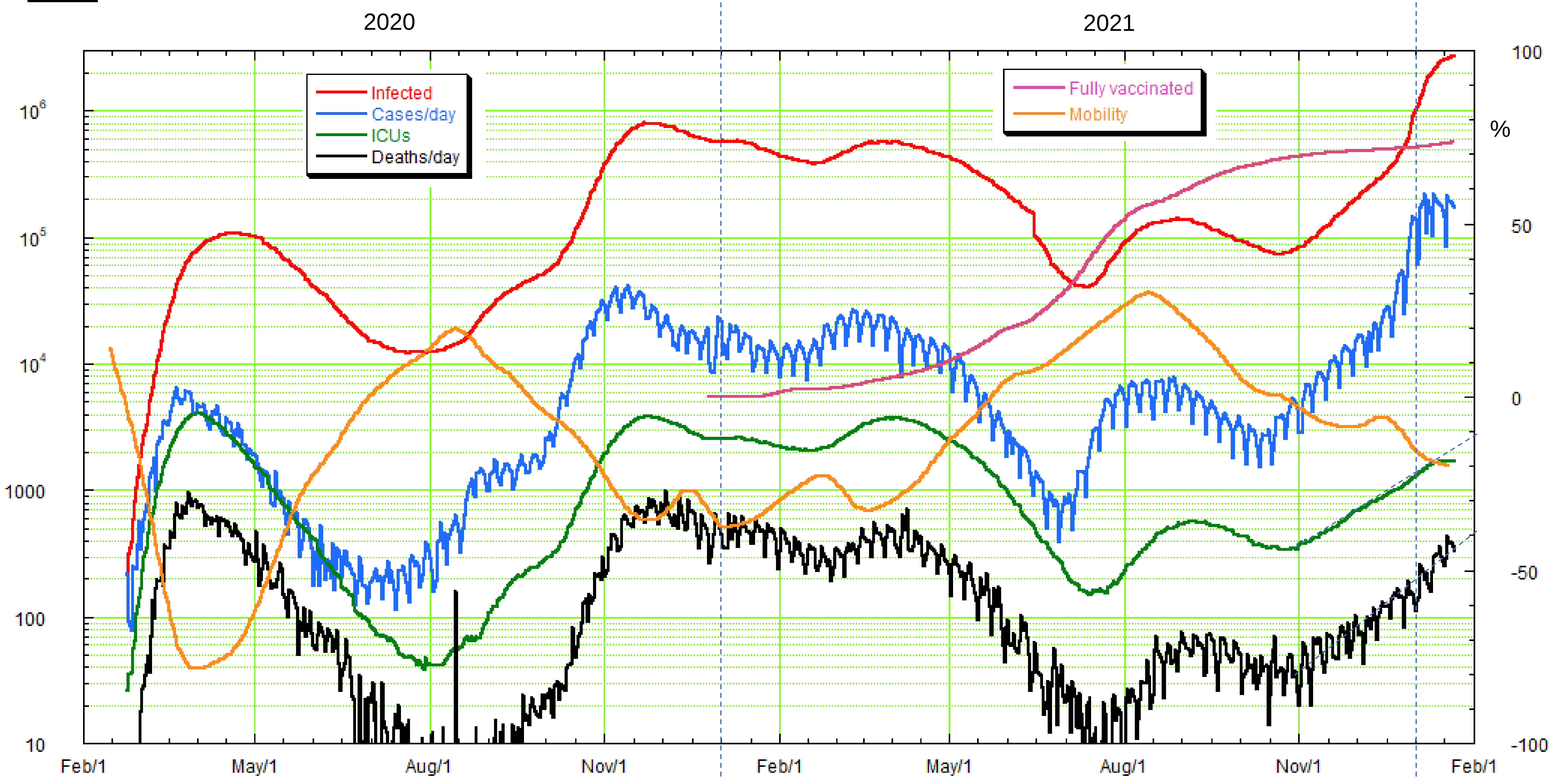
(Italy)

Monitoring of the covid19 disease in Italy

Data from Ministero della Salute and ISS



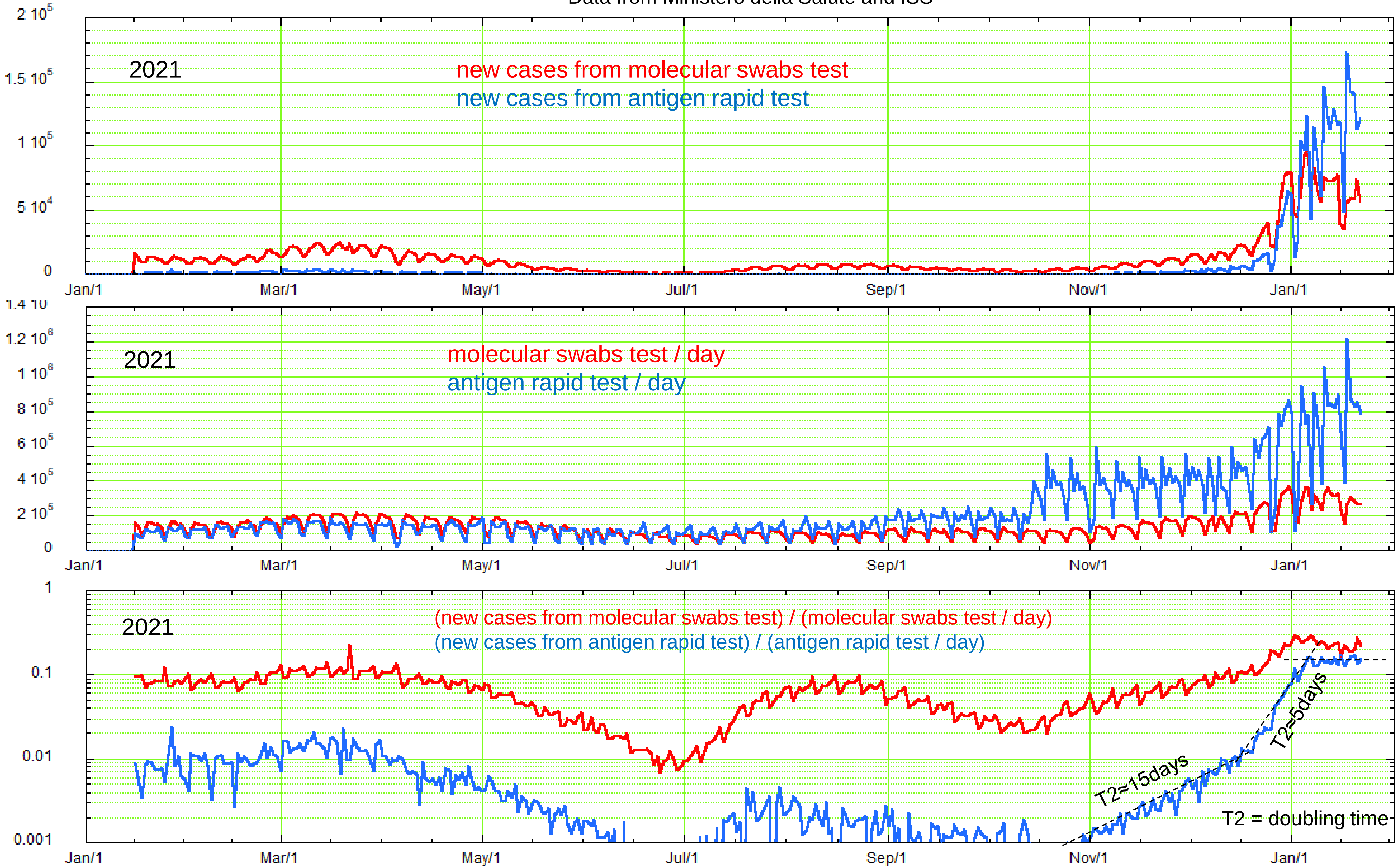
Mobility= (Retail&recreation+Parks+Transit stations+Workplaces)/4

Data about mobility from Google mobility reports (the baseline is the median value, for the corresponding day of the week, during the 5-week period Jan 3-Feb 6, 2020)

Data about vaccinations from:https://github.com/italia/covid19-opendata-vaccini

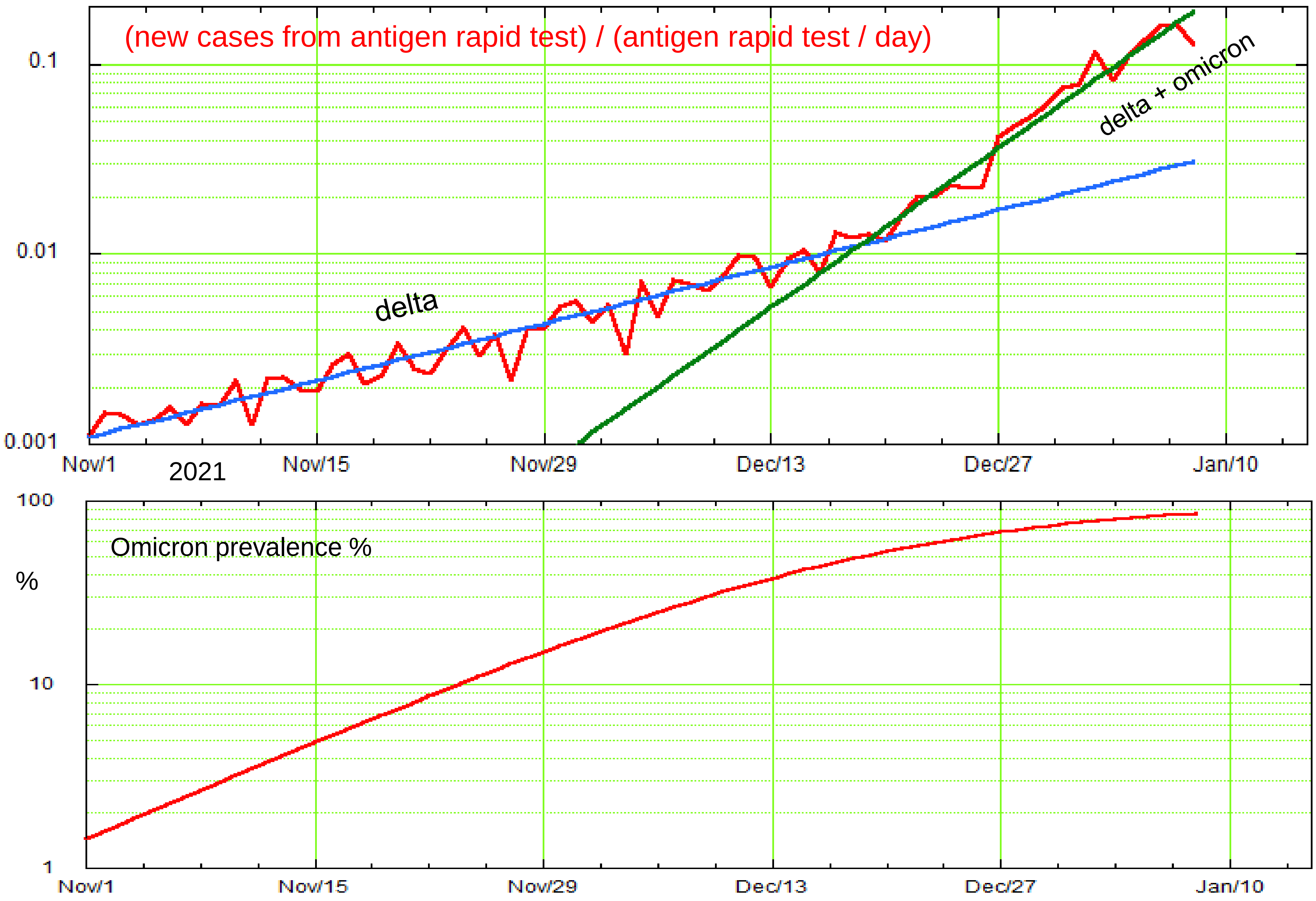
Covid-19 molecular and rapid tests (Italy)

Data from Ministero della Salute and ISS



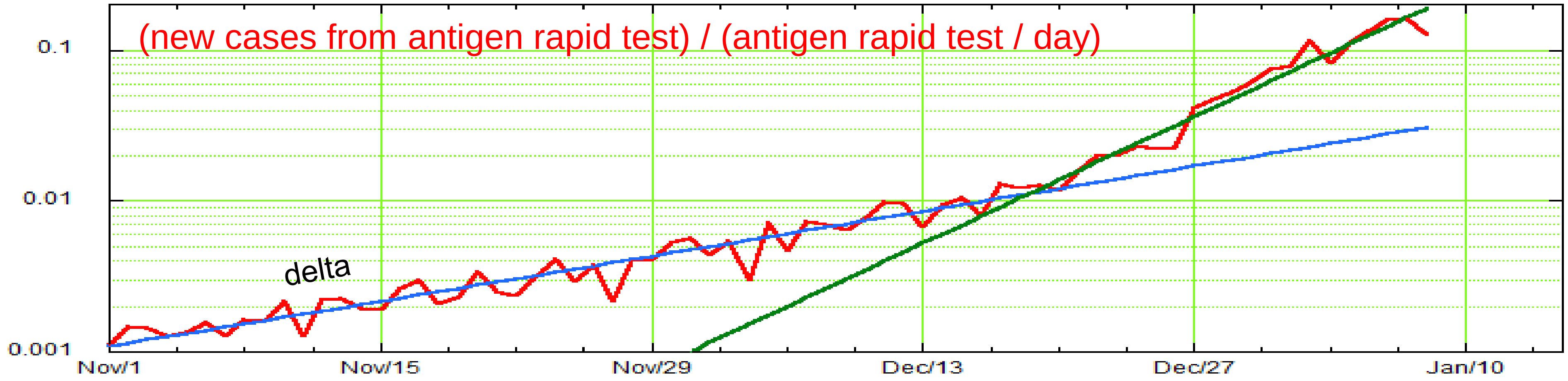
Omicron (prevalence estimation)

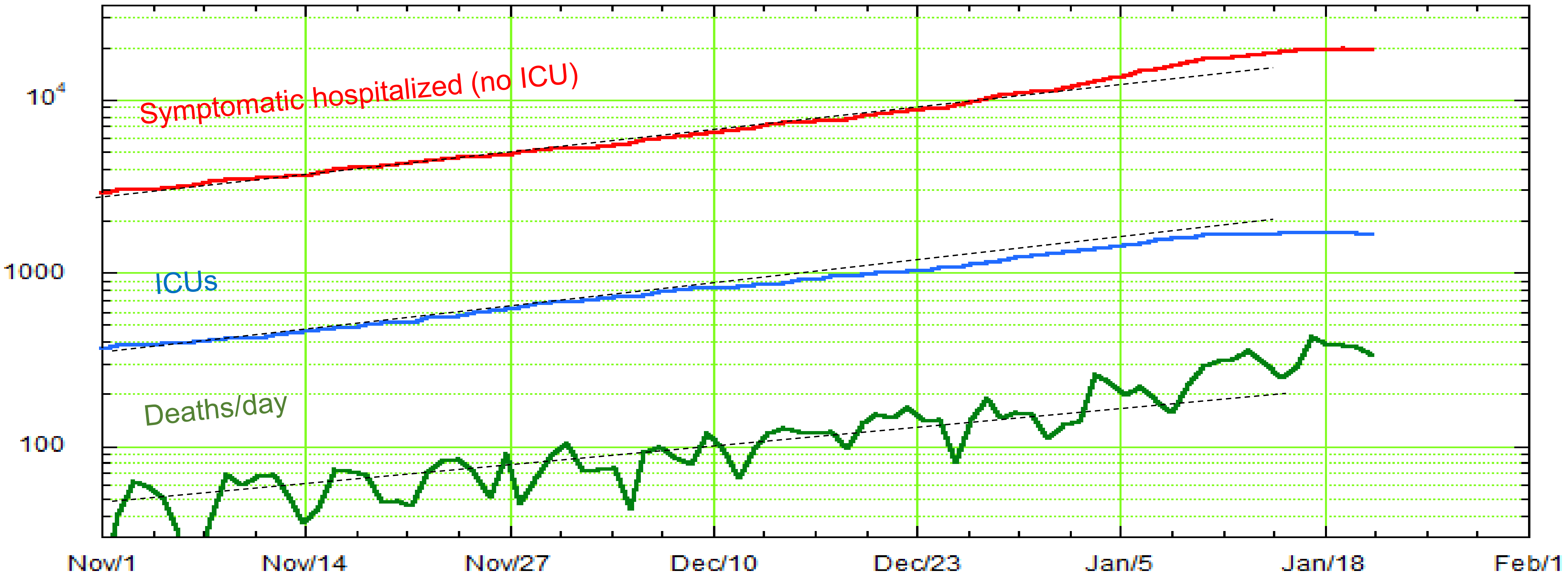
Data from Ministero della Salute and ISS



Cases / Symptomatic hospitalized / ICUs / Deaths/day comparison (ITALY)

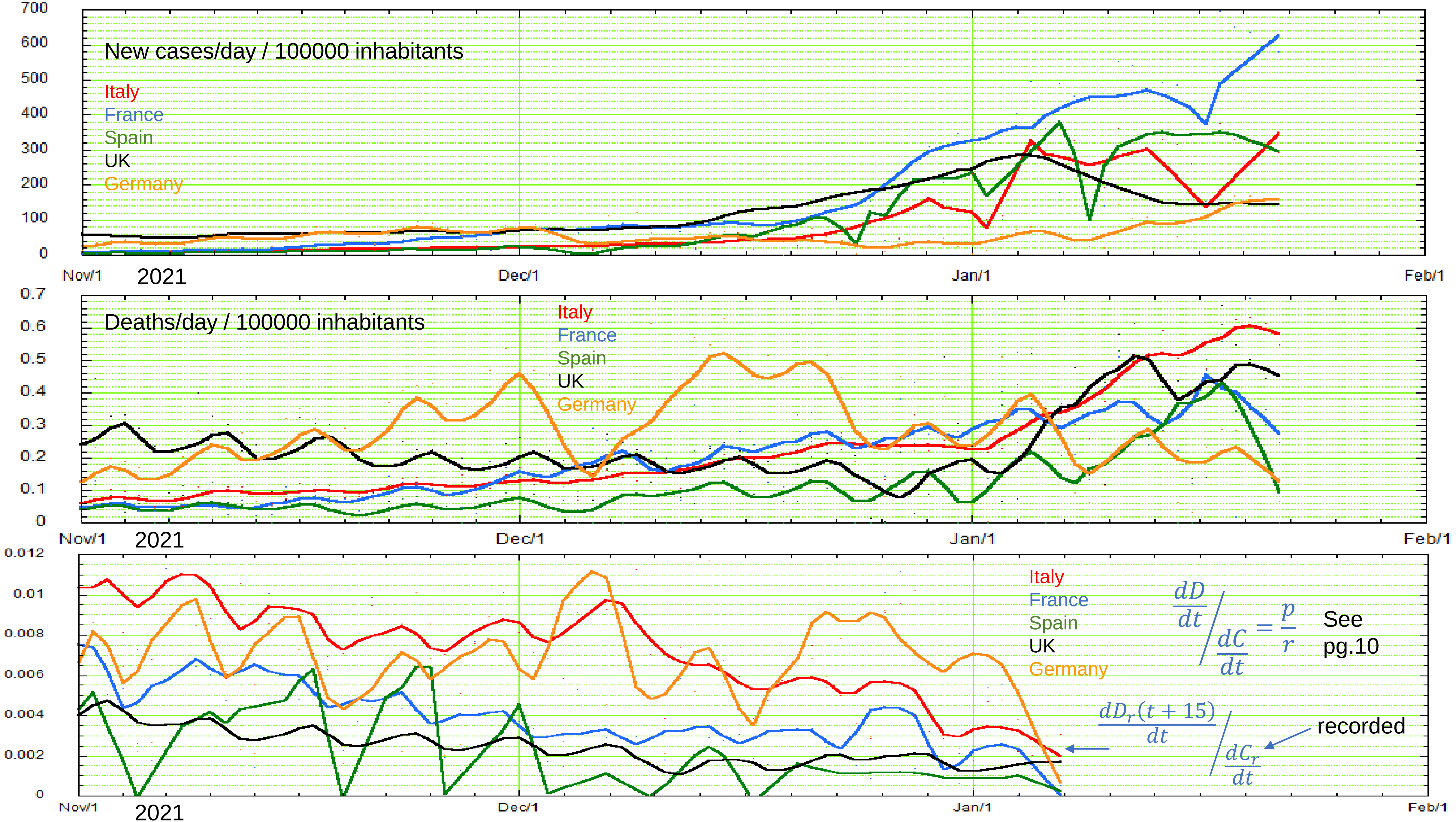
Data from Ministero della Salute and ISS





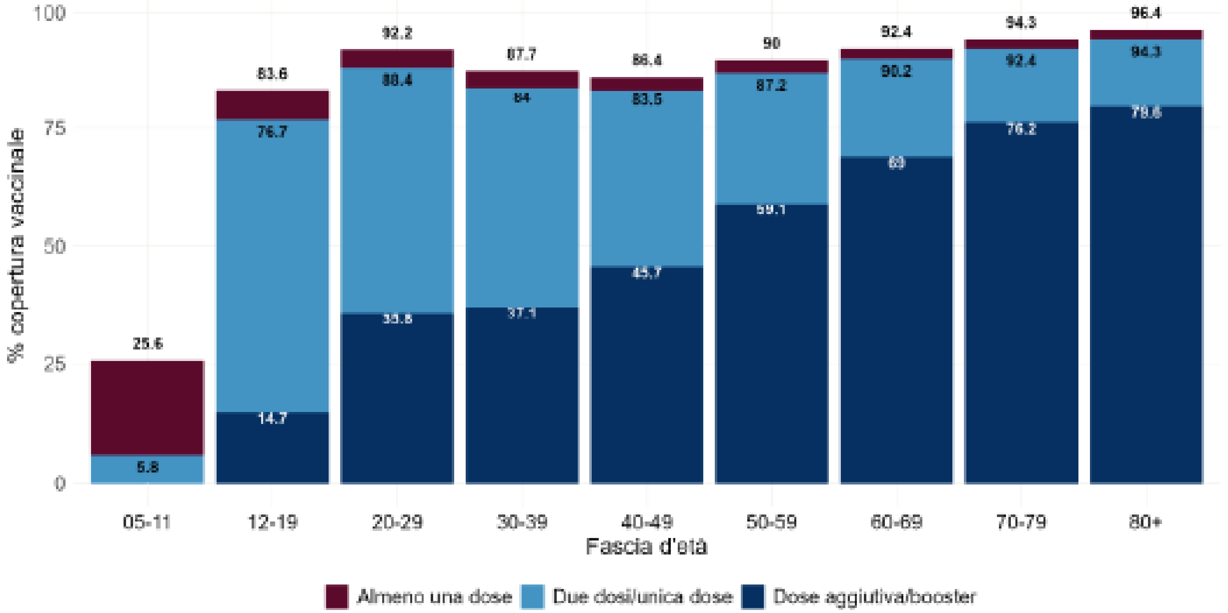
Cases & Deaths/day (Europe)

Data from John Hopkins Univ.



Covid19 Vaccinations in Italy

From ISS report (21 Jan 2021)



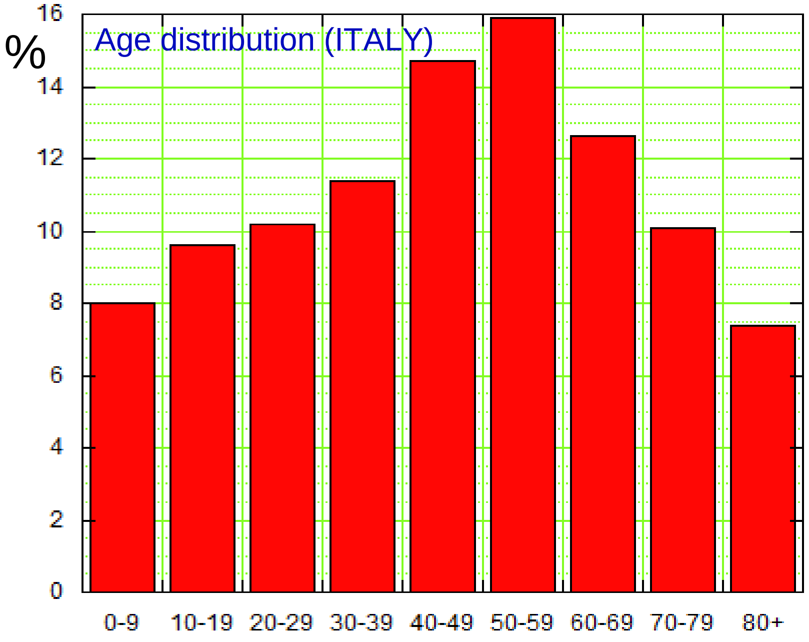


FIGURA 22 - COPERTURA VACCINALE PERCENTUALE PER FASCIA DI ETÀ, POPOLAZIONE ≥5 ANNI

Fonte Dati: https://raw.githubusercontent.com/italia/covid19-opendata-vaccini/master/dati/somministrazioni-vaccini-latest.csv

TABELLA 7 - STIMA EFFICACIA VACCINALE [IC 95%] PER FASCIA DI ETÀ DAL 2021-11-01

Gruppo	Fascia di età	Vaccinati con ciclo completo entro 90 giorni	Vaccinati con ciclo completo da 91-120 giorni	Vaccinati con ciclo completo da >120 giorni	Vaccinati con ciclo completo + dose aggiuntiva/booster
Diagnosi (2021-11-01/2022-01-16)	12-39	64,0 [63,5-64,5]	45,8 [45,2-46,5]	28,0 [27,3-28,7]	60,6 [59,8-61,3]
	40-59	65,5 [64,9-66,2]	61,2 [60,5-61,9]	37,0 [36,3-37,7]	65,2 [64,6-65,7]
	60-79	71,9 [70,6-73,2]	68,2 [67,0-69,4]	45,4 [44,4-46,4]	75,0 [74,4-75,6]
	80+	79,6 [76,8-82,1]	85,2 [82,2-87,6]	77,8 [76,7-78,9]	86,7 [86,1-87,4]
	Totale	**66,1 [65,8-66,5]**	**53,2 [52,7-53,6]**	**34,7 [34,3-35,1]**	**66,7 [66,4-67,1]**
Malattia severa (2021-11-01/2022-01-02)	12-39	94,1 [90,9-96,2]	91,1 [86,2-94,3]	84,5 [78,8-88,6]	-*
	40-59	97,8 [96,5-98,7]	95,1 [93,3-96,5]	90,9 [89,4-92,2]	94,8 [91,0-97,0]
	60-79	95,4 [93,4-96,8]	92,4 [90,6-93,8]	87,4 [86,2-88,6]	95,8 [94,4-96,9]
	80+	87,3 [82,1-91,0]	93,2 [88,2-96,1]	90,5 [89,2-91,7]	98,5 [98,1-98,8]
	Totale	**94,9 [93,8-95,8]**	**93,1 [91,9-94,1]**	**88,6 [87,8-89,3]**	**97,5 [97,1-97,9]**

Covid19 Vaccinations in Italy

From ISS report (21 Jan 2021)

TABELLA 5B - POPOLAZIONE ITALIANA DI ETÀ ≥ 12 ANNI E NUMERO DI CASI DI COVID-19 OSPEDALIZZATI E RICOVERATI IN TERAPIA INTENSIVA PER STATO VACCINALE E CLASSE D'ETÀ

	Fascia di età	Non vaccinati	Vaccinati con ciclo incompleto	Vaccinati con ciclo completo >120 giorni	Vaccinati con ciclo completo ≤120 giorni	Vaccinati con ciclo completo + dose aggiuntiva/booster
Popolazione 18/12/2021	12-39	2.762.771	771.189	6.159.858	7.075.550	666.570
	40-59	2.544.977	490.146	10.073.734	3.399.998	1.919.425
	60-79	1.132.177	223.232	8.156.898	1.067.993	2.991.115
	80+	208.045	81.612	1.637.817	116.560	2.530.278
	Totale	**6.647.970**	**1.566.179**	**26.028.307**	**11.660.101**	**8.107.388**
Diagnosi tra 03/12/2021-02/01/2022 con ospedalizzazione	12-39	1.305	134	830	653	147
	40-59	3.520	136	1.369	340	282
	60-79	4.547	252	4.318	361	638
	80+	2.115	159	2.918	145	999
	Totale	**11.487**	**681**	**9.435**	**1.499**	**2.066**
Diagnosi tra 03/12/2021-02/01/2022 con ricovero in TI	12-39	58	1	13	12	1
	40-59	490	13	77	23	12
	60-79	914	30	448	37	49
	80+	95	7	96	5	36
	Totale	**1.557**	**51**	**634**	**77**	**98**

Nota: Per maggiori dettagli vedere Nota metodologica paragrafo 3

Rapporto sulla Sorveglianza dei vaccini COVID-19

9

27/12/2020 - 26/09/2021

AGENZIA ITALIANA DEL FARMACO

Decessi e nesso di causalità

Complessivamente, dopo aver verificato la presenza di duplicati, ovvero di casi per cui è stata inserita più di una segnalazione, 608 segnalazioni gravi riportano l'esito "decesso" al momento della segnalazione o come informazione acquisita successivamente al follow up. Il tasso di segnalazione è di 0,72/100.000 dosi somministrate, indipendentemente dalla tipologia di vaccino, dal numero di dose e dal nesso di causalità, simile a quello riportato nel Rapporto precedente. La distribuzione di questi casi a esito fatale per tipologia di vaccino è riportata in tabella 3.

Il 48,2% (293) dei casi riguarda donne, il 50,8% (309) uomini mentre l'1% (6 schede) non riporta questo dato. L'età media è di 76 anni. Il tempo intercorrente tra la somministrazione e il decesso varia da poche ore fino a un massimo di 189 giorni, ove riportato. In 397 casi il decesso è registrato dopo la prima dose e in 211 dopo la seconda.

Continuano a non essere segnalati decessi a seguito di shock anafilattico o reazioni allergiche importanti, mentre è frequente che il decesso si verifichi a seguito di complicanze di malattie o condizioni già presenti prima della vaccinazione.

Tabella 3 *- Distribuzione delle segnalazioni con esito decesso per tipologia di vaccino*

VACCINO	Casi fatali	Tassi per 100.000 dosi somministrate
Comirnaty	391	0,65
Spikevax	96	0,91
Vaxzevria	98	0,81
Janssen	23	1,56
Totale	**608**	**0,72**

Il 71,5% (435/608) delle segnalazioni con esito decesso presenta una valutazione del nesso di causalità con l'algoritmo dell'OMS, in base al quale il 59,5% dei casi (259/435) è non correlabile, il 30,6% (133/435) indeterminato e il 6,2% (27/435) inclassificabile per mancanza di informazioni sufficienti. Complessivamente, 16 casi (3,7%) sui 435 valutati sono risultati correlabili (circa 0,2 casi ogni milione di dosi somministrate), di cui 14 già descritti nei Rapporti precedenti. Le rimanenti 2 segnalazioni si riferiscono a 2 pazienti di 76 e 80 anni con condizione di fragilità per pluripatologie, deceduti per COVID-19 dopo aver completato il ciclo vaccinale.

SIR model

1 $$\frac{dS}{dt} = -\frac{r}{\tau}\frac{I}{N}S$$

r = reproduction number,

2 $$\frac{dI}{dt} = \frac{r}{\tau}\frac{S}{N}I - \frac{1}{\tau}I = \frac{r_{eff} - 1}{\tau}I$$

$$\Rightarrow \quad r_{eff} = 1 + \tau\frac{d}{dt}ln(I)$$

3 $$\frac{dC}{dt} = \frac{r}{\tau}I$$

C = cases, I = infected

4 $$\frac{dD}{dt} = \frac{p}{\tau}I$$

where p is the case fatality

5 $$\frac{dT}{dt} = \frac{q}{\tau}I - \frac{1}{\tau_T}T = \frac{dT^+}{dt} - \frac{1}{\tau_T}T$$

Where T is the number of ICUs, q is the ICU probability for an infected, τ_T is the ICU mean time and $\frac{dT^+}{dt}$ are the new accesses to the ICUs

τ, r, p, q, τ_T estimations from data:

$$\tau = \frac{I}{\frac{dC}{dt} - \frac{dI}{dt}} \qquad r = \tau\frac{\frac{dC}{dt}}{I} \qquad p = \tau\frac{\frac{dD}{dt}}{I} \qquad q = \tau\frac{\frac{dT^+}{dt}}{I} \qquad \tau_T = \frac{T}{\frac{dT^+}{dt} - \frac{dT}{dt}}$$

estimation of the reproduction number (r) from ICUs or hospitalizations

From SIR model: $$\frac{dI}{dt} = \frac{\tilde{r}}{\tau}\frac{I}{N}S - \frac{1}{\tau}I = \frac{r-1}{\tau}I$$ Where: $$r = \frac{S}{N}\tilde{r}$$

Note: r also depends on the reduction of the suscettibles due to the diffusion of the disease and the vaccination

$$\Rightarrow \quad r = 1 + \tau\frac{d}{dt}ln(I)$$

Note that: $$1 + \tau\frac{d}{dt}ln(I) = 1 + \tau\frac{d}{dt}ln(kI)$$ where k is a constant

For the ICUs: $$\frac{dT}{dt} = \frac{q}{\tau}I - \frac{1}{\tau_T}T$$

Where T is the number of ICUs, q is the ICU probability for an infected and τ_T is the ICU mean time

$$\Rightarrow \quad I = \frac{\tau}{q}\left(\frac{dT}{dt} + \frac{1}{\tau_T}T\right) \quad \Rightarrow \quad r = 1 + \tau\frac{d}{dt}ln\left(\frac{\tau}{q}\left(\frac{dT}{dt} + \frac{1}{\tau_T}T\right)\right) = 1 + \tau\frac{d}{dt}ln\left(\frac{dT}{dt} + \frac{1}{\tau_T}T\right)$$

Note: it is not necessary to know the value of q

τ_T estimation: $$\frac{dT}{dt} = \frac{q}{\tau}I - \frac{1}{\tau_T}T = \frac{dT^+}{dt} - \frac{1}{\tau_T}T \quad \Rightarrow \quad \tau_T = \frac{T}{\frac{dT^+}{dt} - \frac{dT}{dt}}$$

Where $\frac{dT^+}{dt}$ are the new accesses to the ICUs

Note that it is possible to write: $$r = 1 + \tau\frac{d}{dt}ln\left(\frac{dT^+}{dt}\right)$$

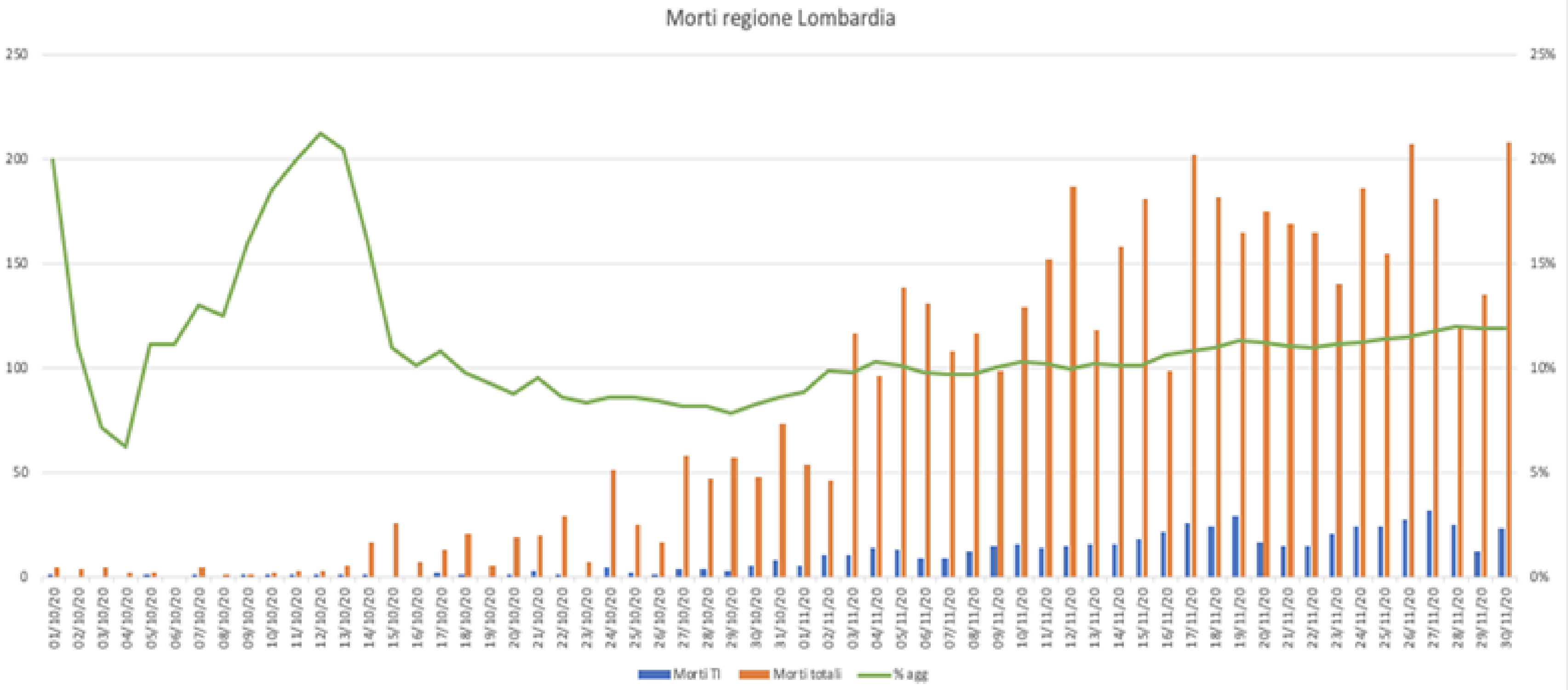
But the data about $\frac{dT^+}{dt}$ are only avaliable from 3 Dec 2020

Note:it is possible to write the same equation for the hospitalizations in place of the ICUs (with different parameters qH and τH). In particular, in the case of the small regions dT/dt is very small and the fluctuations on the retrived R are to much big.

See ref [1] for the results

[1] Stimare R(t) dalle terapie intensive, Simone Cialdi, Chiara Sabelli. https://www.scienzainrete.it/articolo/stimare-rt-dalle-terapie-intensive/simone-cialdi-chiara-sabelli/2021-01-24.

Proporzione Dei Decessi da TI Vs Totale, Ottobre-Novembre, Lombardia (Gerli-Centanni)



	Nuovi ricoveri	Deceduti	Dimessi
	TOT	TOT	TOT
dal 1° agosto	1575	244	485
dal 1° settembre	1537	242	464
dal 1° ottobre	1477	236	421
dal 1° novembre	883	186	264
ultima settimana	430	100	149
da ieri alle ore 00.00	52	14	15

(30/11/2020)

deceduti/(deceduti+dimessi), %	
dal 1° agosto	33.5
dal 1° settembre	34.3
dal 1° ottobre	35.9
dal 1° novembre	41.3
ultima settimana (30/11/2020)	40.2

From clinical data

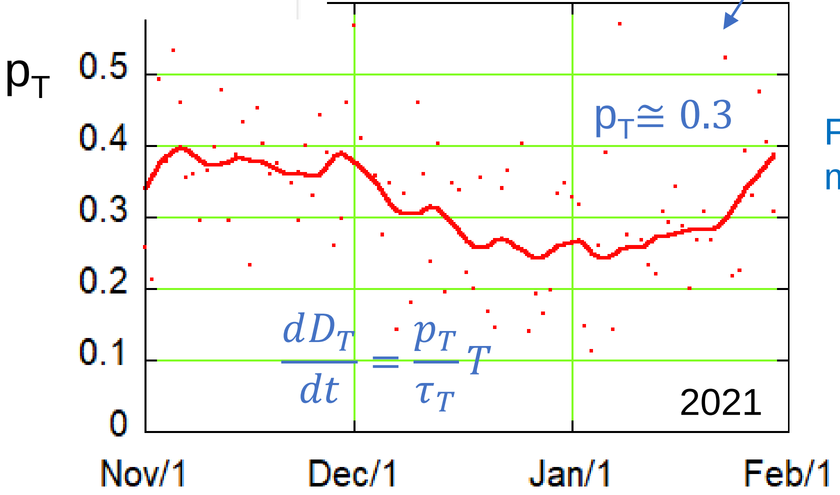
D_T = deaths from ICUs (D_T=0.1D), T = ICUs,
p_T=case fatality in the ICUs, τ_T = ICUs mean time

$$\tau_T = \frac{T}{\frac{dT^+}{dt} - \frac{dT}{dt}}$$

τ_T = 20 days

Lombardy

See pg. 8,9



From SIR model

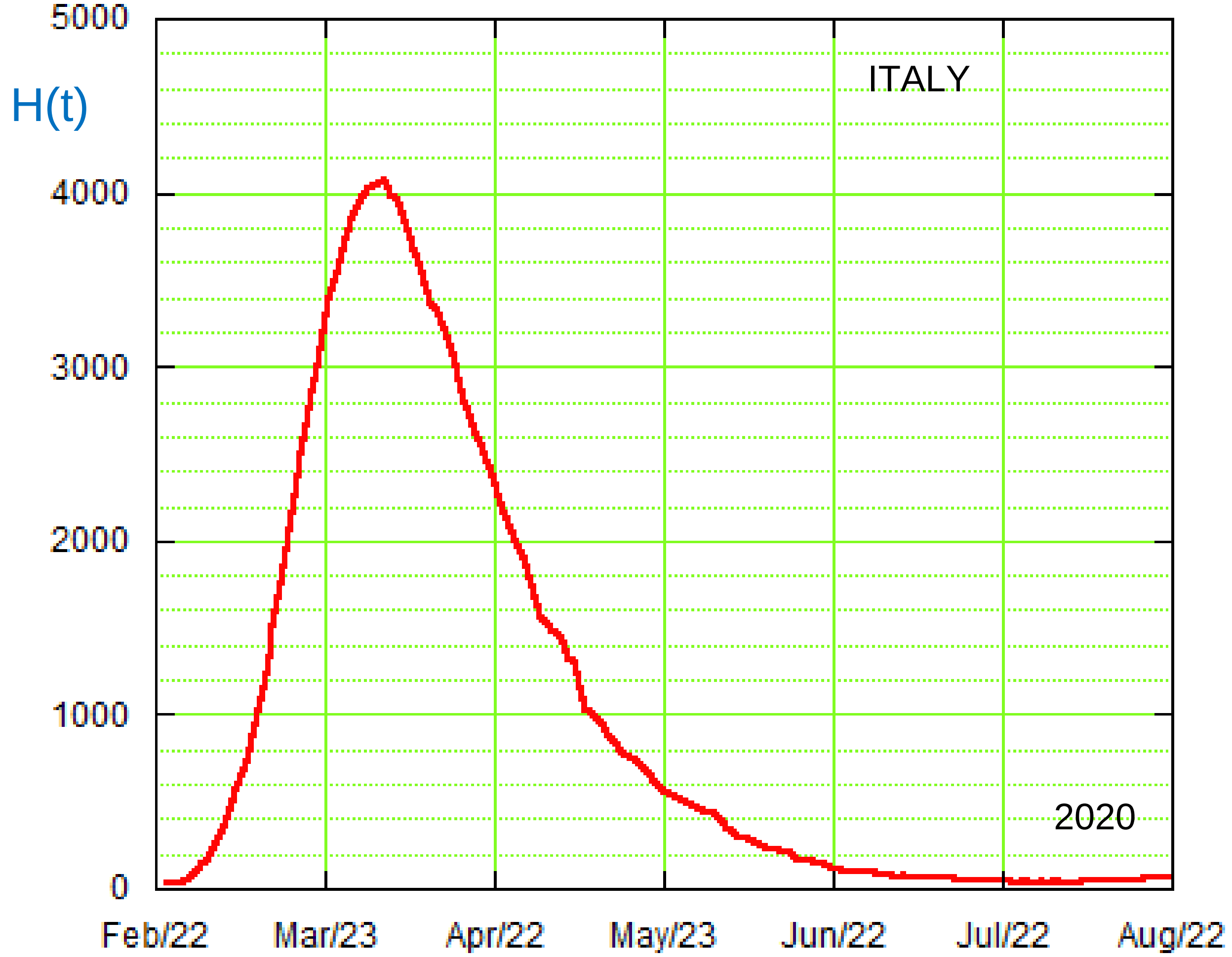
Deaths from ICUs in the first pandemic wave:

T=ICUs

$$\frac{dT}{dt} = \frac{dT^+}{dt} - \frac{1}{\tau_T} T \quad \Rightarrow \quad T^+ = \frac{1}{\tau_T}\int T dt = \frac{187660}{\tau_T}$$

$$\tau_T = \frac{T}{\frac{dT^+}{dt} - \frac{dT}{dt}}$$

See pg. 8,9



Considering τ_T=15days (Italy) and p_T=0.3 (see pg. 10):

$$T^+ = 12510 < D \ (where\ D = 35430\ deaths)$$

$D_T = p_T\, T^+ = 3753$

$D_T / D = 10.6\%$

Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: Insights from linking epidemiological and genetic data

Erik Volz[1*+], Swapnil Mishra[1*], Meera Chand[4*], Jeffrey C. Barrett[5*], Robert Johnson[1*], Lily Geidelberg[1], Wes R Hinsley[1], Daniel J Laydon[1], Gavin Dabrera[4], Áine O'Toole[3], Roberto Amato[5], Manon Ragonnet-Cronin[1], Ian Harrison[4], Ben Jackson[3], Cristina V. Ariani[5], Olivia Boyd[1], Nicholas J Loman[4,6], John T McCrone[3], Sónia Gonçalves[5], David Jorgensen[1], Richard Myers[4], Verity Hill[3], David K. Jackson[5], Katy Gaythorpe[1], Natalie Groves[4], John Sillitoe[5], Dominic P. Kwiatkowski[5], The COVID-19 Genomics UK (COG-UK) consortium[7], Seth Flaxman[2], Oliver Ratmann[2], Samir Bhatt[1], Susan Hopkins[4], Axel Gandy[2*], Andrew Rambaut[3*], Neil M Ferguson[1*+]

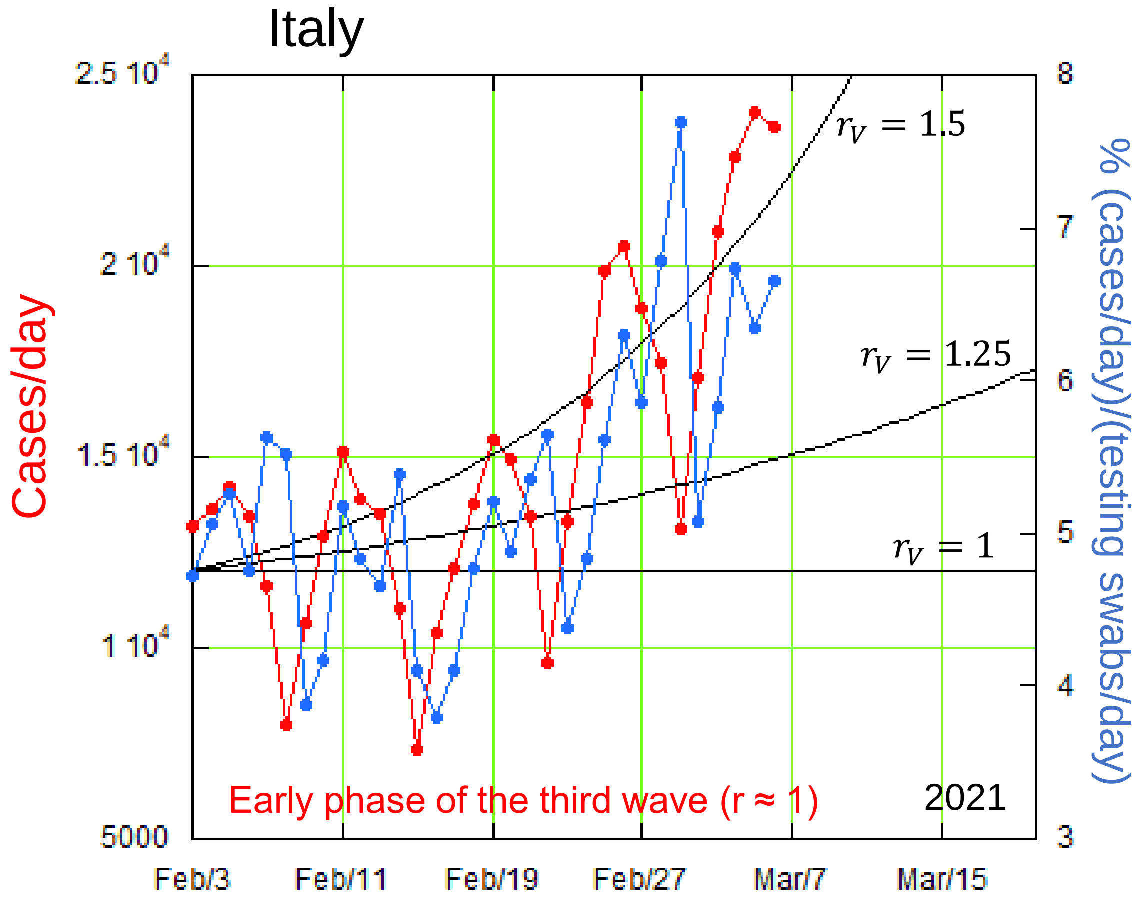
From pg. 11 of [3]

of 42x6 (STP x week) posteriors of R_t estimated for the VOC and non-VOC. The mean ratio of the estimated R_t for the VOC and non-VOC was 1.56 [95%CI: 0.92 - 2.28] for the same period, see Figure S5. Aggregating across all STPs we find that the mean R_t during the second English lockdown across all STPs was 1.45 [0.91-1.89] for the VOC and 0.92 [0.86-1.06] for non-VOC strains.

r is the reproduction number for the current lineage in Italy ($r \approx 1$)

r_V is the reproduction number for the B.1.1.7 lineage (UK variant)

$$\frac{r_V}{r} \approx 1.56 \quad \Rightarrow \quad r_V \approx 1.56$$



At 3 Feb 2021:

(12000 → $\frac{dC_{tot}(0)}{dt}$; 17.8% [4] → $\frac{dC_V(0)}{dt}$; 1.56 [3] → r_V; 1 → r; 9 days → τ)

$$\frac{\text{cases}}{\text{day}} = \frac{dC_{tot}(0)}{dt} = \frac{dC_V(0)}{dt} + \frac{dC(0)}{dt} = \frac{r_V}{\tau} I_V(0) + \frac{r}{\tau} I(0)$$

After 3 Feb 2021:

See pg. 8

$$\frac{\text{cases}}{\text{day}} = \frac{dC_{tot}(t)}{dt} = \frac{dC_V(t)}{dt} + \frac{dC(t)}{dt} = \frac{dC_V(0)}{dt} e^{\frac{r_V-1}{\tau} t} + \frac{dC(0)}{dt}$$

[3] Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: Insights from linking epidemiological and genetic data , medRxiv preprint doi: https://doi.org/10.1101/2020.12.30.20249034

[4] https://www.iss.it/primo-piano/-/asset_publisher/3f4alMwzN1Z7/content/comunicato-stampa-n%25C2%25B011-2021-covid-19-in-italia-il-17-8%2525-delle-infezioni-dovute-a-variante-inglese-
see also: https://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2021&codLeg=78758&parte=1%20&serie=null

[5] Prevalenza delle varianti VOC 202012/01 (lineage B.1.1.7), P.1, e 501.V2 (lineage B.1.351) in Italia Indagine del 18 febbraio 2021 (ISS). (18 Feb 2021: 54% lineage B.1.1.7 «Inglese»). 4.3% P1 «Brasiliana»

Case fatality estimation considering serological tests in Italy

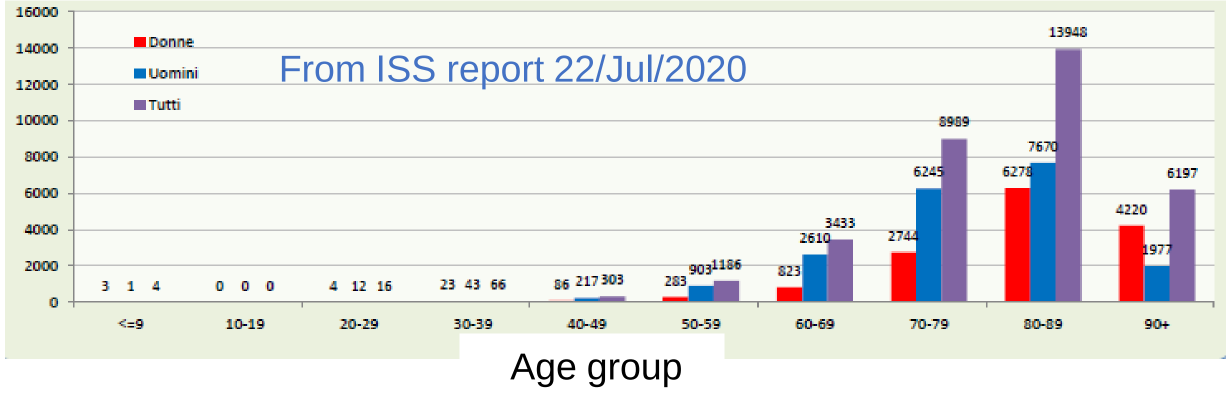
Data from ISTAT 3 Ago 2020 (people tested: 64660)

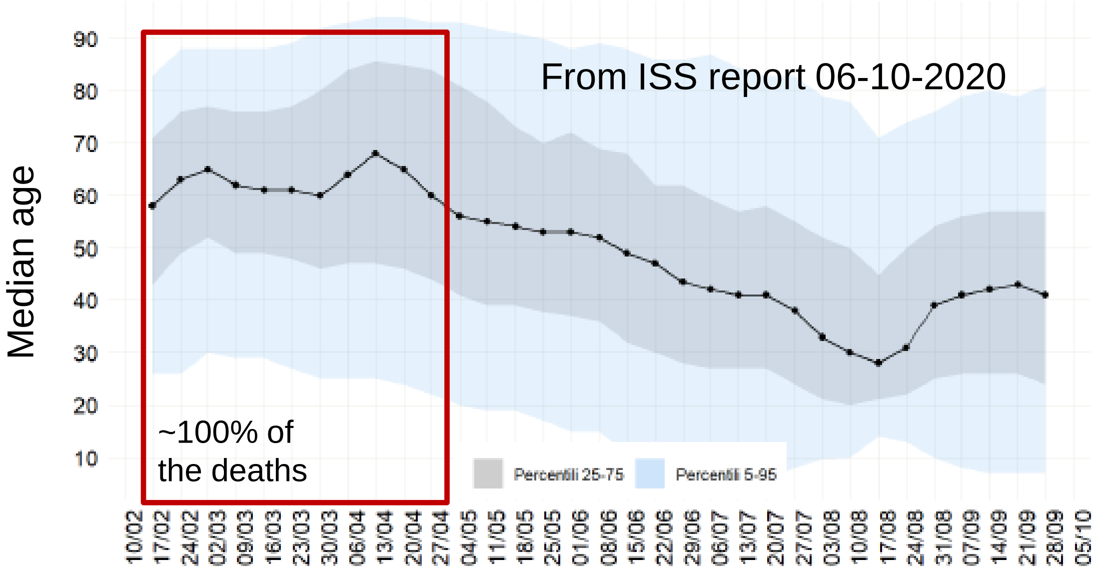
Regione	Inhabitants	% positive	Deaths (22Jul)	Lethality (%)
Piemonte	4325895	3	3114	2.4
Valle d'Aosta	125052	4	146	2.9
Liguria	1534594	3.1	1676	3.5
Lombardia	10017994	7.5	16776	2.2
Bolzano	523422	3.3	292	1.7
Trento	534843	3.1	405	2.4
Veneto	4872440	1.9	1990	2.1
Friuli	1204309	1	349	2.9
Emilia-Romagna	4426983	2.8	4266	3.4
Toscana	3707737	1	1132	3
Umbria	878270	0.9	80	1
Marche	1518186	2.7	984	2.4
Lazio	5843220	1	868	1.5
Abruzzo	1306856	1.5	470	2.4
Molise	302755	0.7	22	1
Campania	5793968	0.7	459	1.1
Puglia	4017306	0.9	548	1.5
Basilicata	559419	0.8	30	0.67
Calabria	1935010	0.6	97	0.83
Sicilia	4978732	0.3	304	2
Sardegna	1633210	0.3	134	2.7
ITALIA	**60030201**	**2.3**	**34142**	**2.5**

60030210 X 0.023 =
1381000 cases

Case fatality estimation by age group in Italy

Deaths by age group





A method to estimate the lethality by age group

$$p = \sum_i \Delta_i \frac{D_i}{C_i}$$

deaths (D_i); cases (C_i); Lethality (0.025. see pg. 14) (p); age group index (i)

$$C_i = \alpha \Delta_i$$

$$\alpha = \frac{\sum_i D_i}{p}$$

$$p_i = \frac{D_i}{C_i} = \frac{D_i}{\alpha \Delta_i}$$

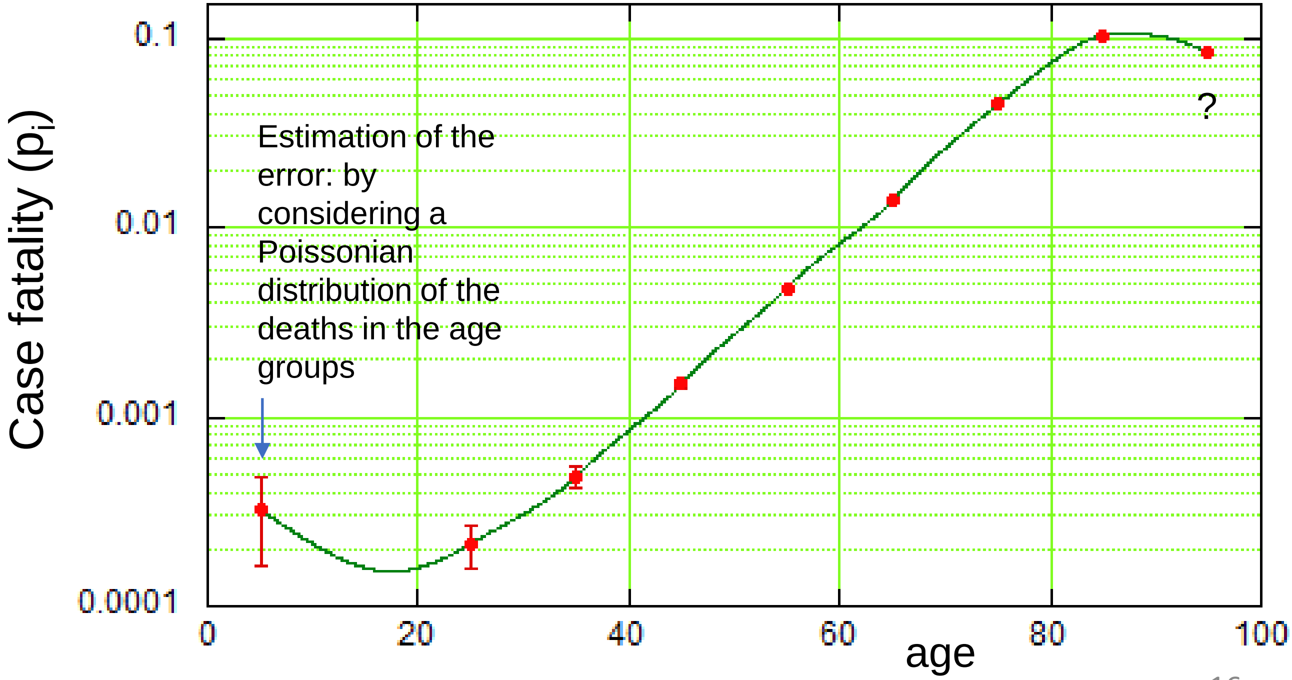
$$\Delta_i = N\, e^{-\frac{(x_i - m)^2}{2\sigma^2}}$$

$$m = 60$$

$$\sigma = \frac{15}{0.67}$$

$$x_i = mean\ age\ of\ the\ group$$

N = normalization factor consideging the avaliable age groups



Appendix: data about influenza (1)

Mortality : is a measure of the number of deaths in a particular population, scaled to the size of that population

from [A1], see also [A2]

Results: We estimated excess deaths of 7,027, 20,259, 15,801 and 24,981 attributable to influenza epidemics in the 2013/14, 2014/15, 2015/16 and 2016/17, respectively, using the Goldstein index. The average annual mortality excess rate per 100,000 ranged from 11.6 to 41.2 with most of the influenza-associated deaths per year registered among the elderly.

→ 0.01% – 0.04%

Attack Rate: in epidemiology, the attack rate is the percentage of the population that contracts the disease

from [A3], see also [A4,A5]

Results: We included 32 RCTs that had a total of 13,329 participants. The pooled estimates for symptomatic influenza were 12.7% (95%CI 8.5%, 18.6%) for children (<18 years), 4.4% (95%CI 3.0%, 6.3%) for adults, and 7.2% (95%CI 4.3%, 12.0%) for older people (65 years and above). The pooled estimates for symptomatic and asymptomatic influenza combined for all influenza were 22.5% (95%CI 9.0%, 46.0%) for children and 10.7% (95%CI 4.5%, 23.2%) for adults. Only one study was identified for symptomatic and asymptomatic combined in older people which had a rate of 8.8% (95%CI 7.0%, 10.8%). There was substantial heterogeneity between studies.

→ ~10%

[A1] Investigating the impact of influenza on excess mortality in all ages in Italy during recent seasons (2013/14–2016/17 seasons), https://doi.org/10.1016/j.ijid.
[A2] A comprehensive review of the epidemiology and disease burden of Influenza B in 9 European countries, http://dx.doi.org/10.1080/21645515.2015.1111494
[A3] Estimating the annual attack rate of seasonal influenza among unvaccinated individuals: A systematic review and meta-analysis, https://doi.org/10.1016/j.vaccine.2018.04.063
[A4] https://old.iss.it/site/RMI/influnet/pagine/stagioni.aspx
[A5] https://www.agi.it/fact-checking/news/2020-02-26/coronavirus-influenza-stagionale-7231278/

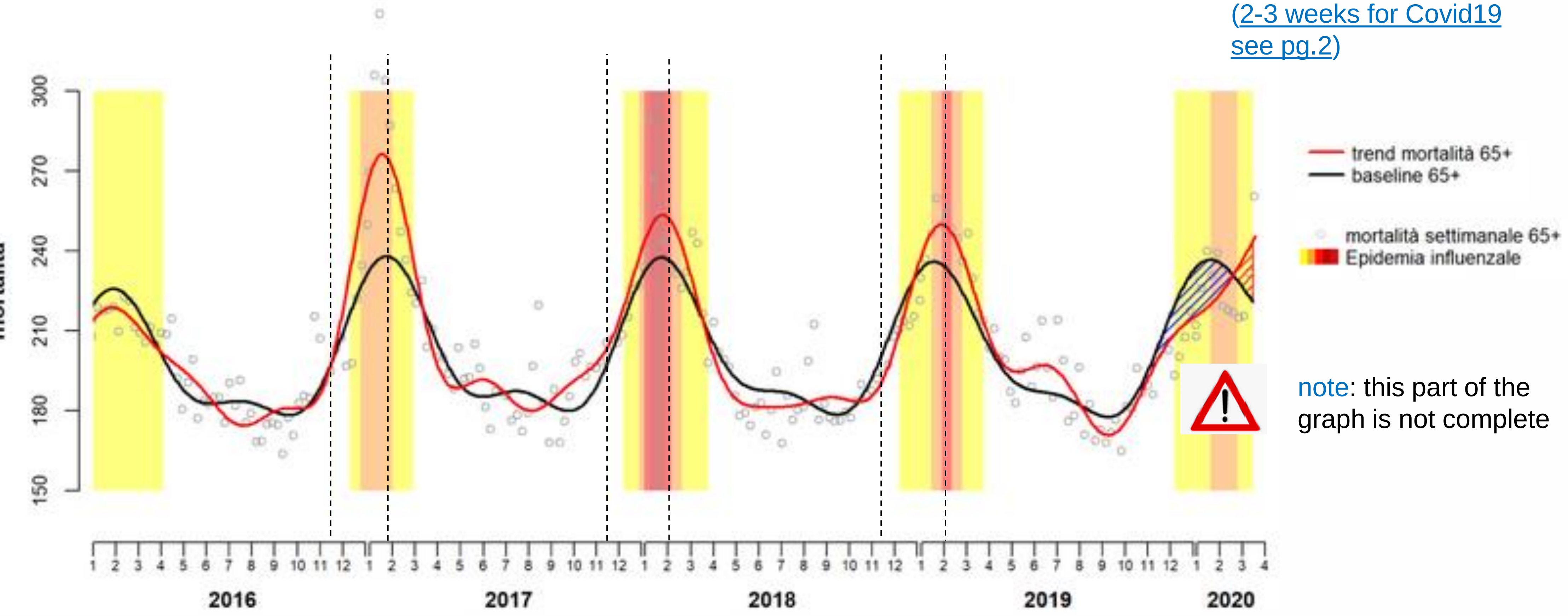
Appendix: data about influenza (2)

Lethality or Case fatality ratio/proportion: lethality is how capable something (disease) is of causing death

from [A6,A7 and the data at pg. 18] → 0.1%-0.4%

Rise time: is the time taken by a signal to change from a specified low value to a specified high value → 9-10 weeks (2-3 weeks for Covid19 see pg.2)

from [A8] see also [A1]



note: this part of the graph is not complete

[A6] https://www.virology.ws/2009/06/16/how-many-people-die-from-influenza/
[A7] https://en.wikipedia.org/wiki/Influenza
[A8] https://www.scienzainrete.it/articolo/confermato-eccesso-di-mortalit%C3%A0-molto-superiore-ai-casi-di-covid/luca-carra-roberto-satolli

Appendix: data about influenza (3)

Deaths/day:

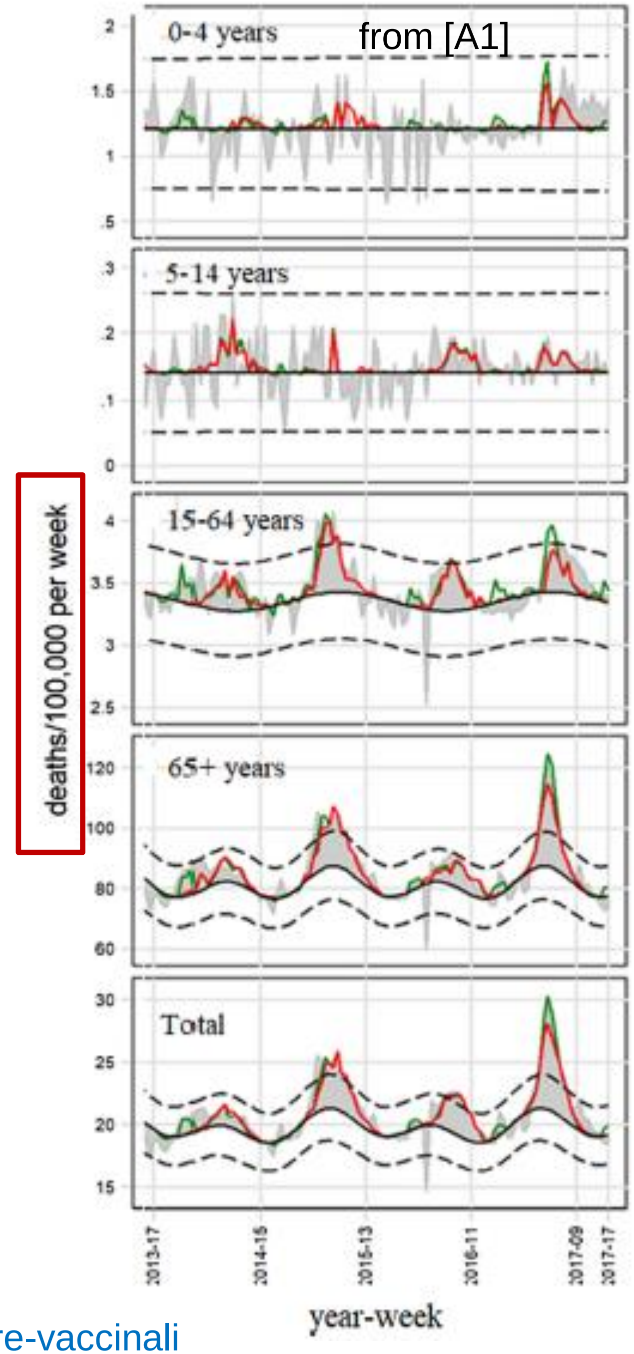
Considering the 65+ years population from [A1] we observe a peak of 5-20 deaths/100000 per week or 0.7-2.8 deaths/100000 per day.

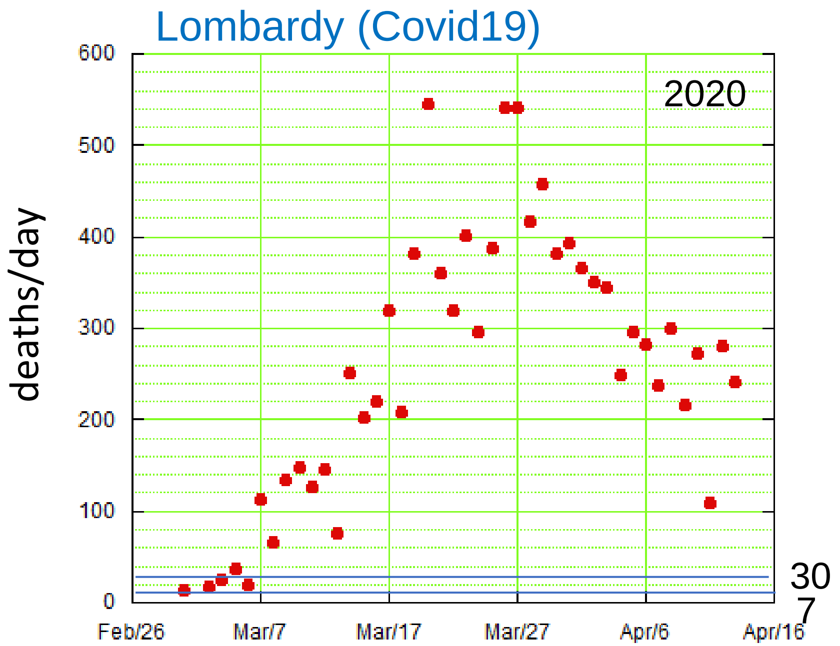
We have to consider that the 65+ years italian population is 20% of the total population and about 50% [A9] of the 65+ years pop. is vaccinated. So we obtain a peak of 40-170 deaths/day in Italy

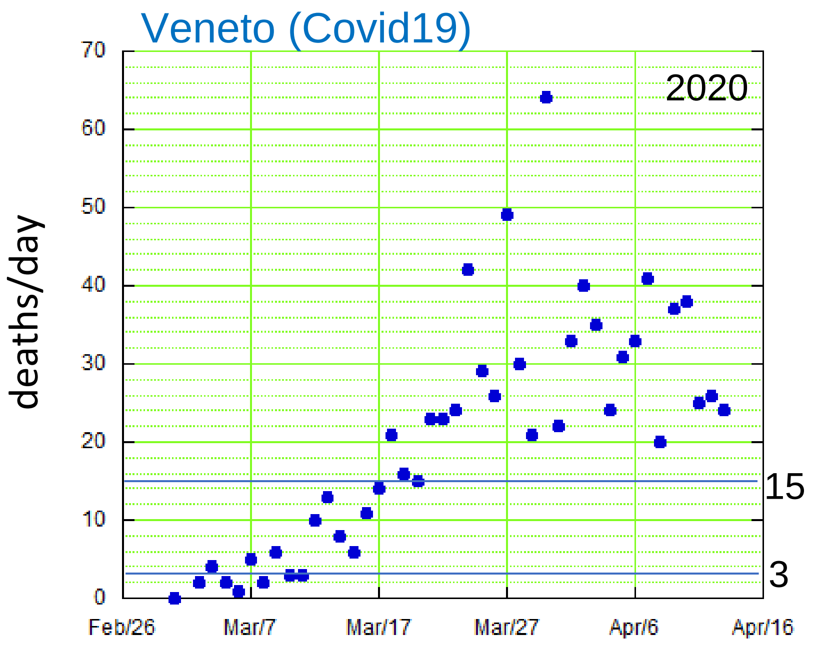
Considering an uniform distribution of the cases we obtain a peak of about 7-30 deaths/day for Lombardy and 3-15 deaths/day for Veneto.

currently the total number of real cases for the Covid19 is totally unknown

Influenza in Italy







[A9] https://www.epicentro.iss.it/influenza/coperture-vaccinali