



Covid-19 follow-up

Clinical newsflow + graphics

Research team

14.07.2020



Treatment approach

Treatment approach / research	
Dexamethasone (low-cost steroid treatment) * First drug shown to reduce mortality *	June 16: The UK RECOVERY trial (11'500 patients - Randomised Evaluation of Covid-19 multiple therapies) demonstrated that dexamethasone reduces death by up to one third in hospitalised patients with severe respiratory complications of Covid-19
Remdesivir - antiviral (Gilead) * The drug shortens time to recovery by 4 days *	<ul style="list-style-type: none"> - June 29: Remdesivir will be priced at \$390 per vial (\$2'340 for a 5-day treatment) for governments in developed countries - June 13: Dr Reddy's has entered into a non-exclusive Licensing Agreement with Gilead that will grant Dr Reddy's the right to register, manufacture and sell remdesivir in 127 countries (in developing countries) - Gilead has donated the 1st wave of production (more than 280'000 treatment assuming a 5-day treatment duration) - Gilead has set a goal of producing at least 500'000 treatment by October and 1mio by December (assuming a 10-day treatment duration) - NIAID trial: patients who received remdesivir had 31% faster time to recovery vs placebo - The median time to recovery was 11 days (vs 15 days for placebo) - Mortality rate was 8% (vs 11.6% for placebo) - Evidence of lower respiratory tract infection - Findings highlight the need to identify cases and start treatment before the pulmonary disease progresses to require mechanical ventilation - Gilead's SIMPLE trial (5-day vs 10-day dosing durations) demonstrated that a 5-day dosing duration is the optimal treatment - Antivirals should work best in recently infected patients (with viral load) and not in very late-stage of the disease caused by cytokine release syndrome (hyperinflammation)
Actemra - rheumatoid arthritis - immunosuppressant (Roche)	<ul style="list-style-type: none"> - Roche initiated a phase III trial on March 19th to treat patients with severe Covid-19 pneumonia - data expected early summer - Anti-IL6 drug - should work in severe form of the disease caused by cytokine release syndrome (hyperinflammation)
Hydroxychloroquine (anti-malaria) + azithromycin (antibiotique)	<ul style="list-style-type: none"> - June 15: FDA revoked the Emergency Use Authorization for emergency use of chloroquine and hydroxychloroquine to treat Covid-19 - Based on recent clinical trial data, FDA concluded that this treatment may not be effective and that it's potential benefits for such use do not outweigh its known and potential risks - June 5: The investigators of the UK RECOVERY trial (11'500 patients) decided to stop enrolling participants to the hydroxychloroquine arm due to no beneficial effect - A trial of hydroxychloroquine as postexposure prophylaxis for Covid 19 in the US and Canada was published in NEJM. Treatment initiated within 4 days after a high-risk or moderate-risk exposure - The randomized trial did not demonstrate a significant benefit of hydroxychloroquine as postexposure prophylaxis for Covid-19 - NB: because of the lack of availability of diagnostic testing at the time of the trial, an a priori symptomatic case definition was used during the trial - Two retrospective studies didn't show statistically significant benefit from used of hydroxychloroquine, azithromycin or both in the management of critically ill patients (published in JAMA and NEJM)
Convalescent Plasma	<ul style="list-style-type: none"> - Plasma transfusion from recovered patients for critically ill patients - Clinical studies ongoing in France, Italy - Already used in US via FDA emergency autorisation - This therapy was successfully used in the treatment of SARS, MERS and 2009 H1N1 - Two studies with 10 severe patients and 5 critically ill patients with Covid-19 and acute respiratory syndrome in China recovered after administration of convalescent plasma
Lopinavir+ritonavir - HIV treatment (AbbVie)	Only little benefit
Favipiravir (generic)- Flu treatment (Fujifilm)	Study on 80 patients in China - showing a week earlier recovery vs HIV treatment Past pre-clinical studies showed side-effect suggesting risk for pregnant women

Vaccine developments

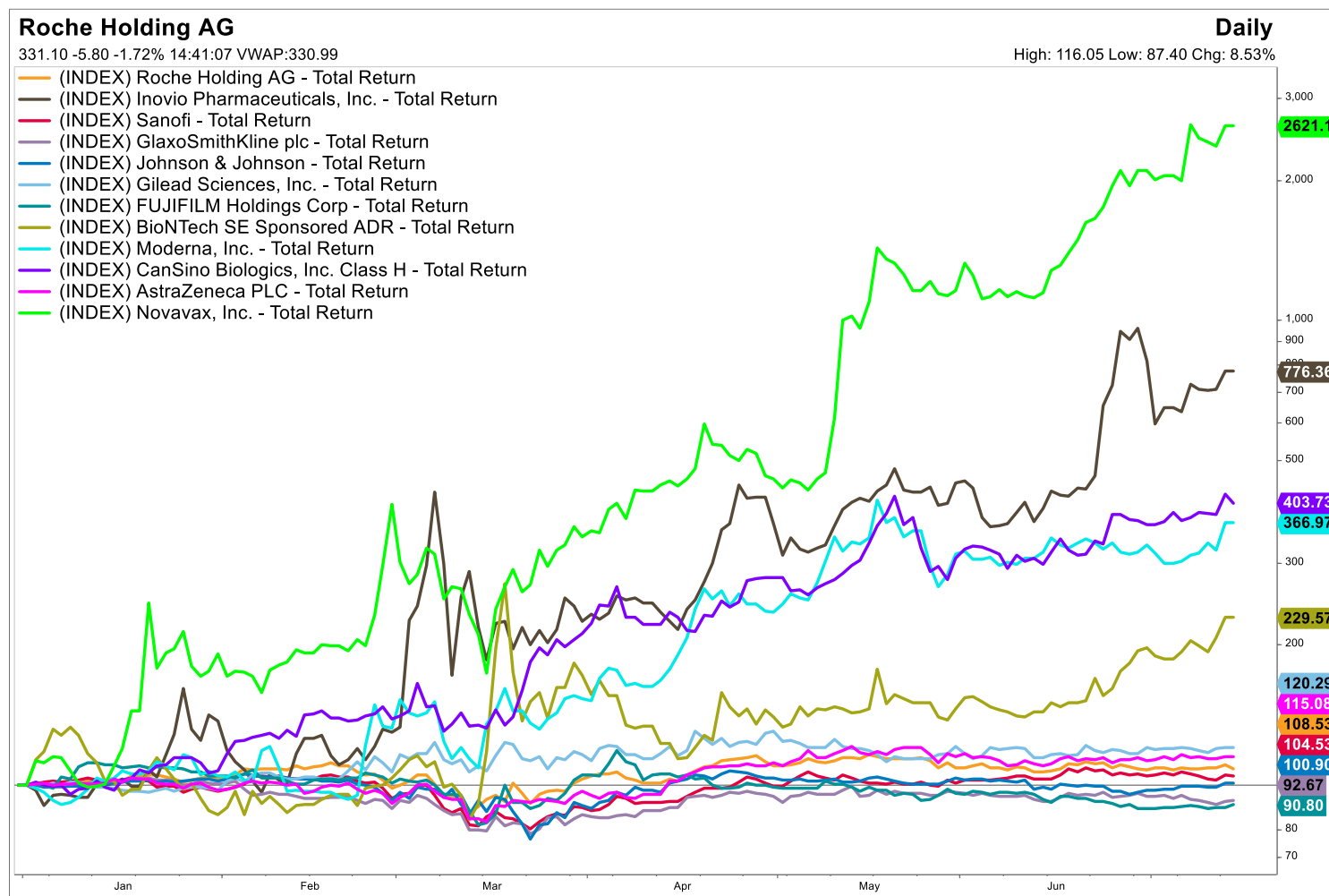
Vaccines: we have to wait at least 12 months before having a vaccine available for a public use --> potential approval for a public use H1 2021/mid-2021

Company	Phase/Timing
Moderna * mRNA based vaccine *	- Positive phase I update (45 participants / 3 dosing regimens) - interim data - signs of immune response - binding antibody levels in all 45 participants - The 8 initial participants developed neutralizing antibodies at the time of the update - Phase II study (600 participants) is evaluating two doses with the target to select one dose for Phase III (plan to start in July) - The Vaccine was generally safe and well tolerated - all adverse events observed were transient and self-resolving - If the virus mutates, they can modify and produce the new vaccine in 40 days without redoing clinical studies - The vaccine could be available in fall for healthcare workers - CEO expects an approval for summer 2021 for a public use - mRNA based vaccine --> shorter development than traditional vaccine but unproven technology at this stage
University of Oxford - Co-development deal with AstraZeneca * Non-Replicating Viral Vector (Adenovirus vaccine vector) *	- Phase III in Brazil and Phase II/III ongoing in UK (10'000 participants - of which a children group) - Other late-stage trials are due to begin in other countries with plan to initiate a paediatric trial AstraZeneca's CEO said the vaccine is expected to provide protection for 1 year - The vaccine will be distributed at cost during the pandemic phase - 2bn doses expected in 2021
CanSino Biologics * Non-Replicating Viral Vector (Adenovirus vaccine vector) *	Clinical development in China only - no timeline Phase II ongoing (based on preliminary safety data) - The vaccine has been approved for limited military use in China
JNJ * Non-Replicating Viral Vector (Adenovirus vaccine vector) *	- JNJ has accelerated the initiation of the Phase I/IIa trial, now expected to start in the 2nd half of July (vs September before) In April, CEO mentioned he expects the vaccine to be available for emergency use authorization in early 2021 - Proven technology - Supply target of more than 1 bn doses capacity - JNJ is committed to bringing an affordable vaccine to public on a not-profit-basis for emergency pandemic use
Inovio * DNA based vaccine *	Phase I (40 participants) - Analyses to date have shown that 94% demonstrated overall immune response rates based on preliminary data assessing humoral (binding and neutralizing) and T cell immune responses - Safe and well-tolerated with no serious adverse events Phase II/III efficacy study is expected to begin this summer DNA vaccine --> shorter development than traditional vaccine - unproven technology at this stage
BioNTech/Pfizer/Shanghai Fosun - * mRNA based vaccine *	Early phase I/II positive data (45 participants) - At day 28 all subjects had SARS-CoV-2 neutralizing antibodies - No serious events reported Phase II/III safety and efficacy study may begin in July Supply target of 100mio doses by the end of 2020 and more than 1.2bn doses by the end of 2021
Sinovac - * Inactivated Covid-19 vaccine *	Clinical development in China only - Phase I/II ongoing - Plan to start phase III in July
Novavax - * Protein Subunit vaccine *	Phase I/II clinical trial ongoing - preliminary immunogenicity and safety data expected in July
Sinopharm * Inactivated Covid-19 vaccine *	Clinical development in China - Phase I/II ongoing - 1'120 participants have received 2 injections - At the middle dose, all participants developed neutralizing antibodies that can defend a cell from infection
CureVac (private company) - * mRNA based vaccine *	Phase I clinical trial is starting
GSK/Clover/Dynavax - * Protein Subunit vaccine *	Phase I clinical trial is starting
Genexine - * DNA based vaccine *	Phase I clinical trial is starting
Medicago Inc - * Virus-Like Particle vaccine *	Phase I clinical trial is starting
Sanofi/GSK * Protein Subunit vaccine *	Clinical trial expected to start in September with a potential approval by H1 2021 (earlier than previously expected) Capacity to manufacture up to 1bn doses a year
Sanofi/Translate Bio - * mRNA based vaccine *	Clinical trial expected to start end-2020 with a potential approval by H2 2021

- **For the landscape of Covid-19 candidate vaccines, please find below the NEW link to the draft of the World Health Organization:**
- <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>

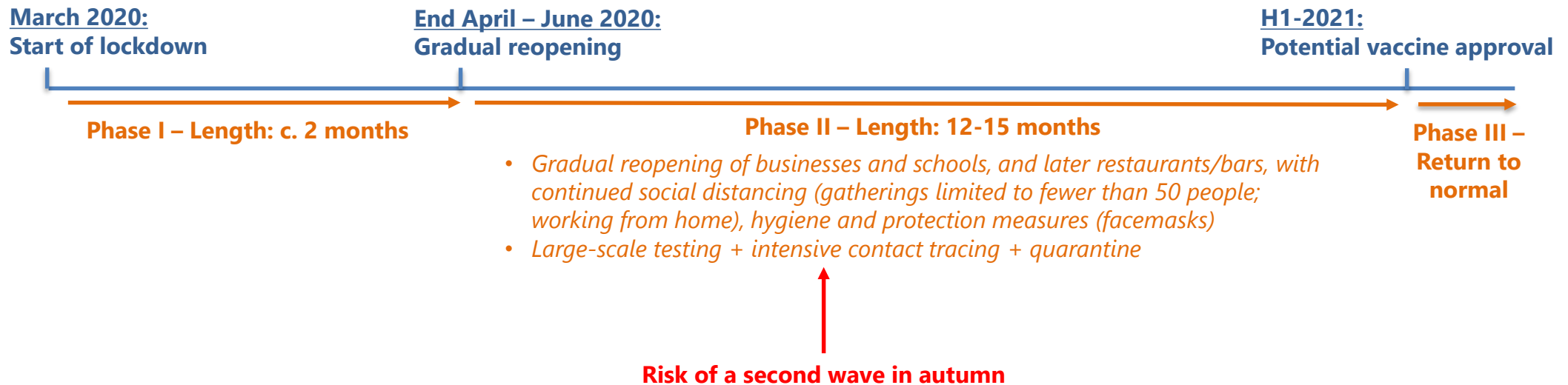
Share price performance of main players

Year to date – local currencies



No return to normal before H1-2021

Reopening – gradual process, with some measures remaining in place



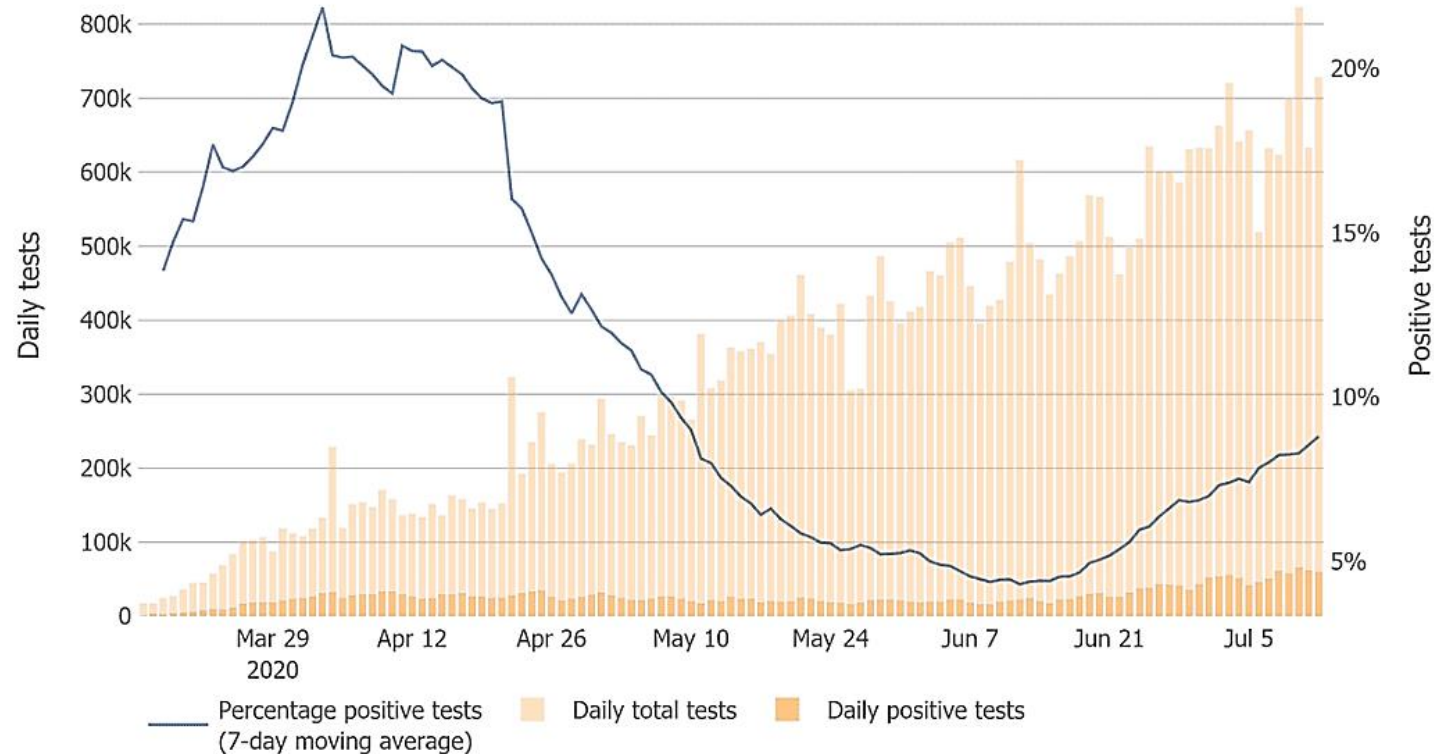
- The course of the epidemic will need to be closely monitored, with the risk of a second wave in the autumn

Daily US testing tracker

Source: The COVID Tracking Project – 13.07.2020

Rate of Positive Tests in the US Over Time

HOW MUCH OF THE DISEASE ARE WE FINDING THROUGH TESTS?

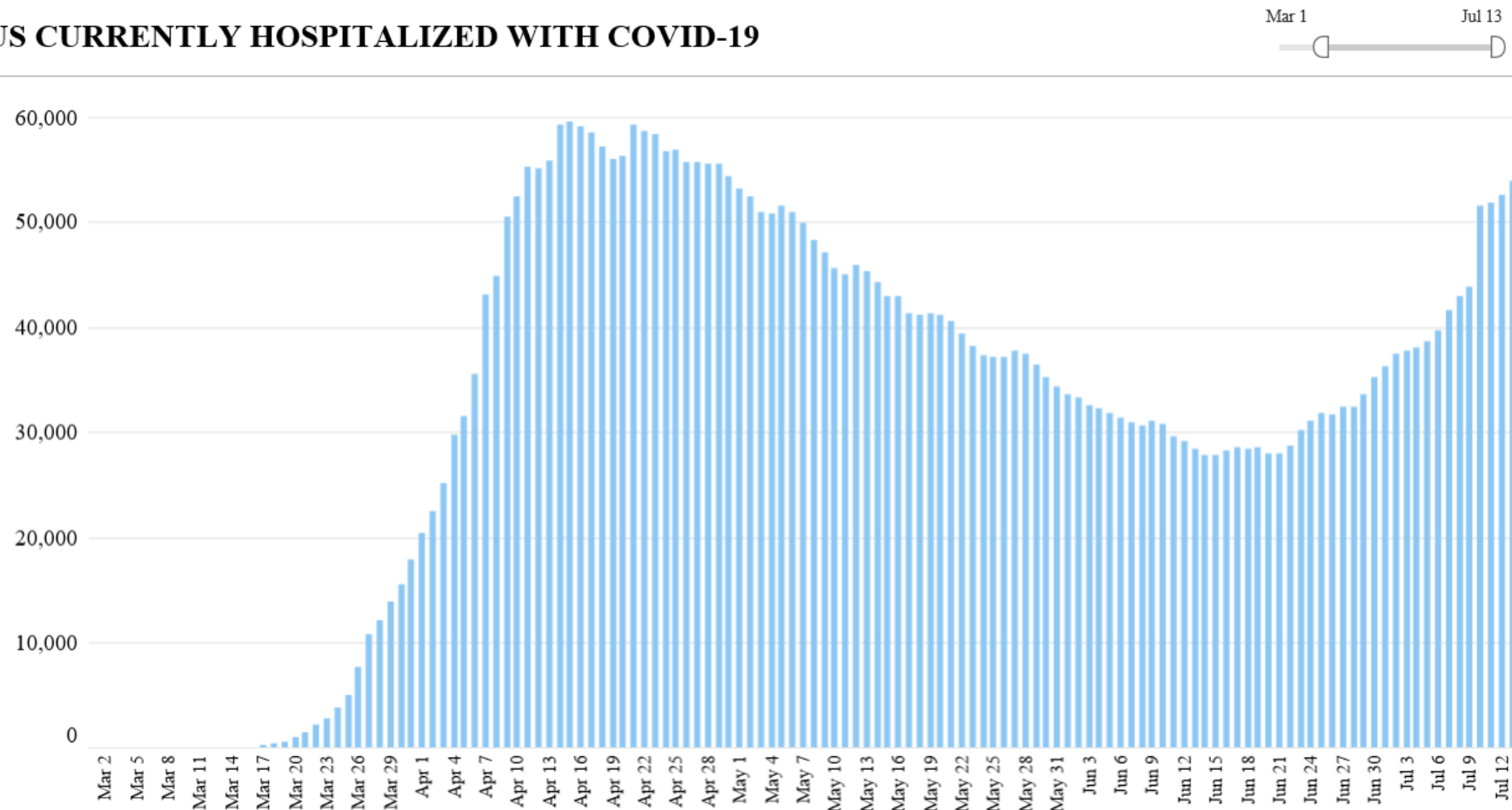


- Current number of tests per week (last 7 days): 4'868'500

US current hospitalization

Source: The COVID Tracking Project – 13.07.2020

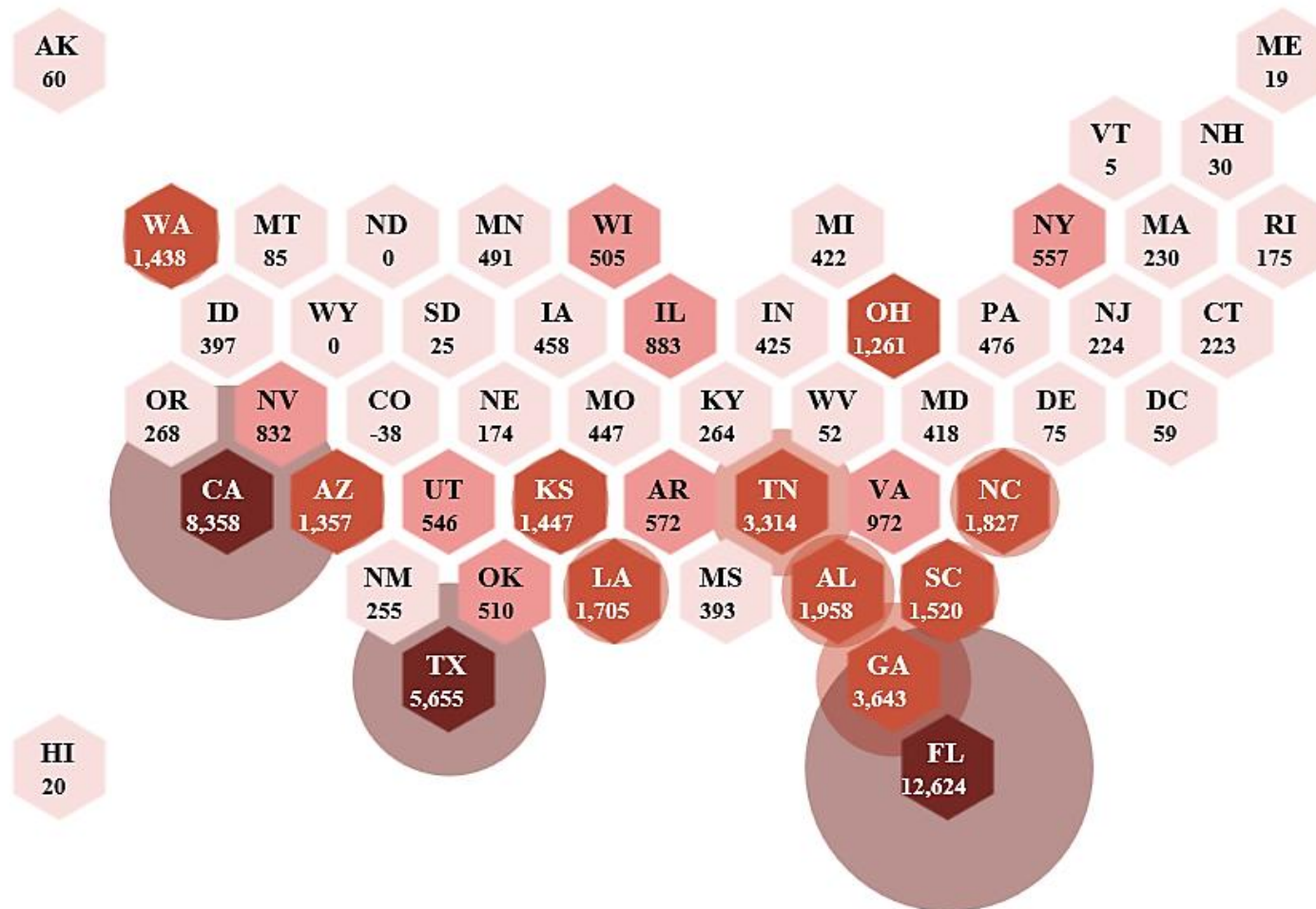
US CURRENTLY HOSPITALIZED WITH COVID-19



US new cases map

Source: The COVID Tracking Project – 13.07.2020

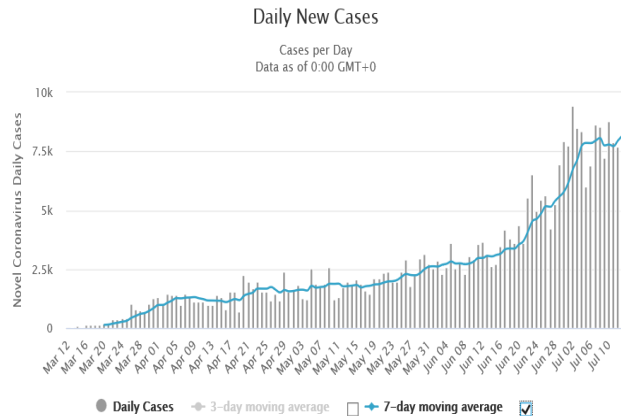
NEW CASES BY STATE



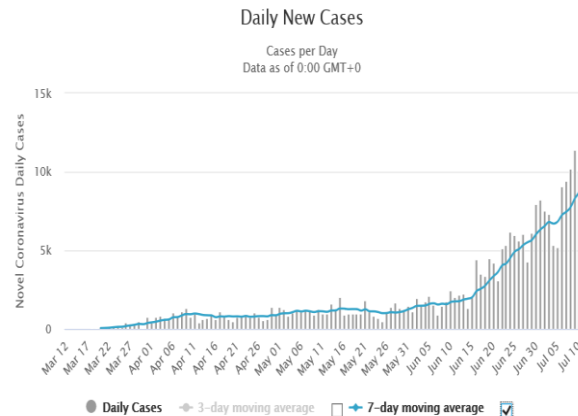
US states with concerning trend

Source: Worldometers – 14.07.2020

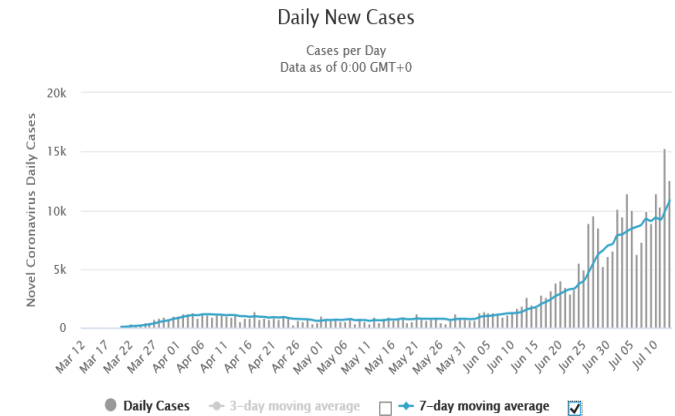
Daily New Cases in California



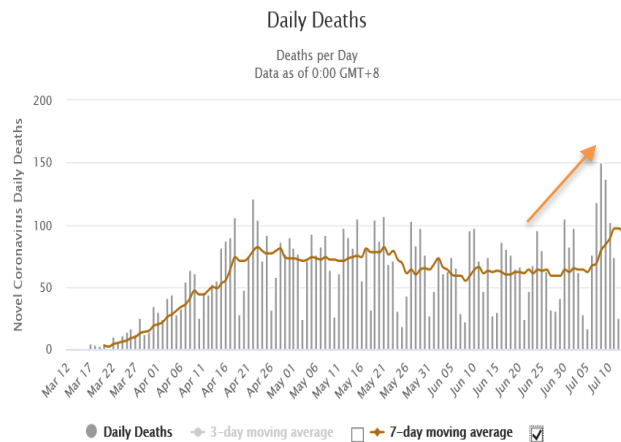
Daily New Cases in Texas



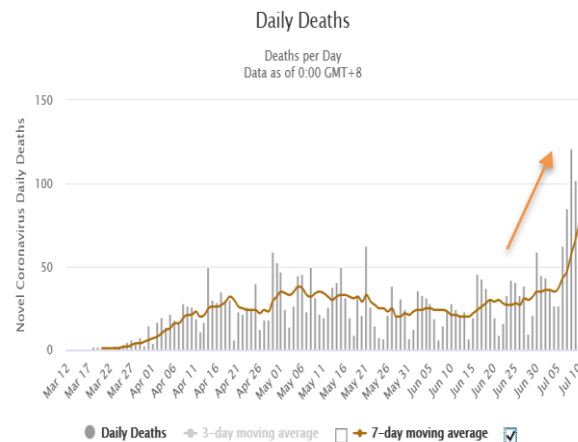
Daily New Cases in Florida



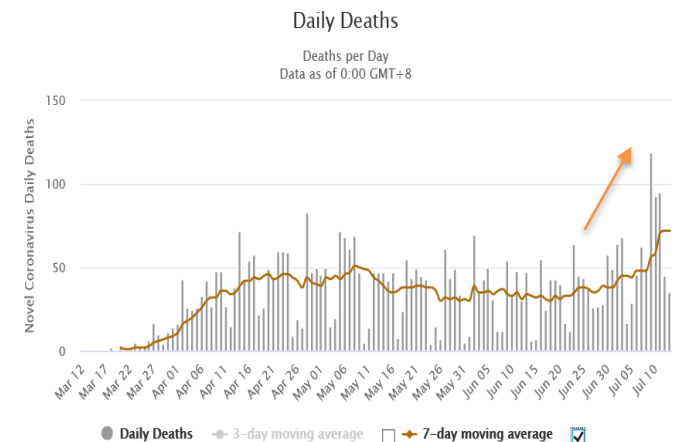
Daily New Deaths in California



Daily New Deaths in Texas



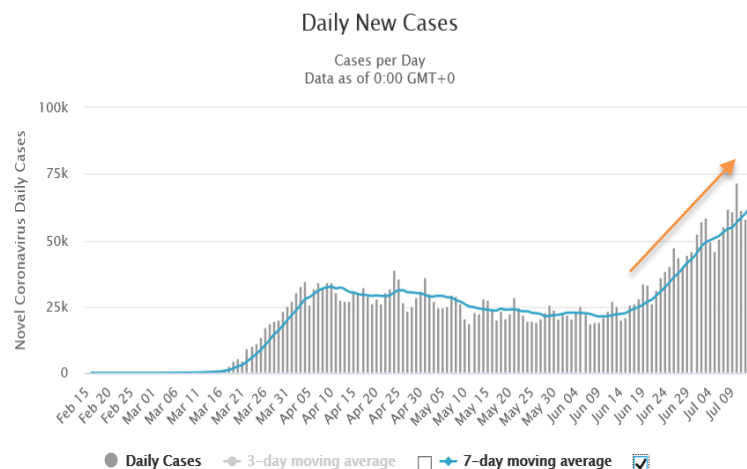
Daily New Deaths in Florida



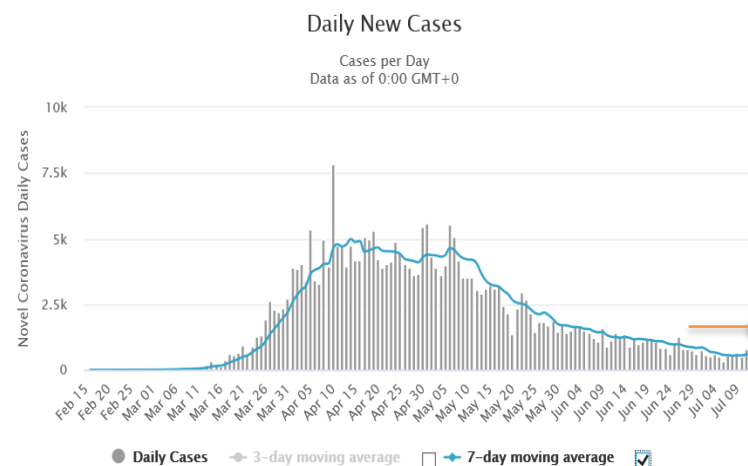
Countries under scrutiny

Source: Worldometers – 14.07.2020

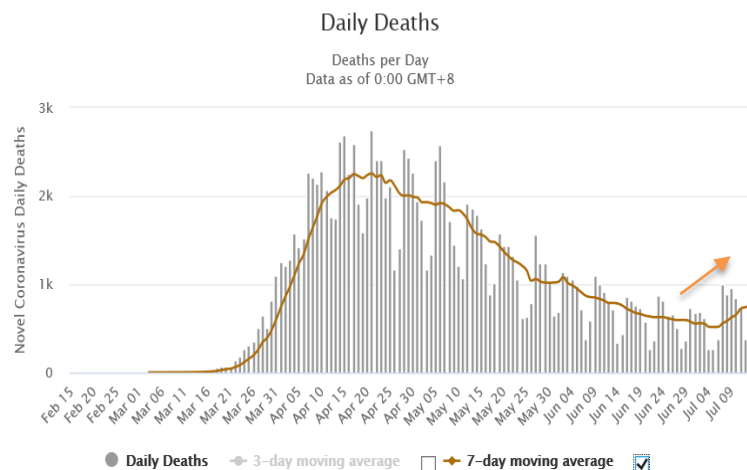
Daily New Cases in the United States



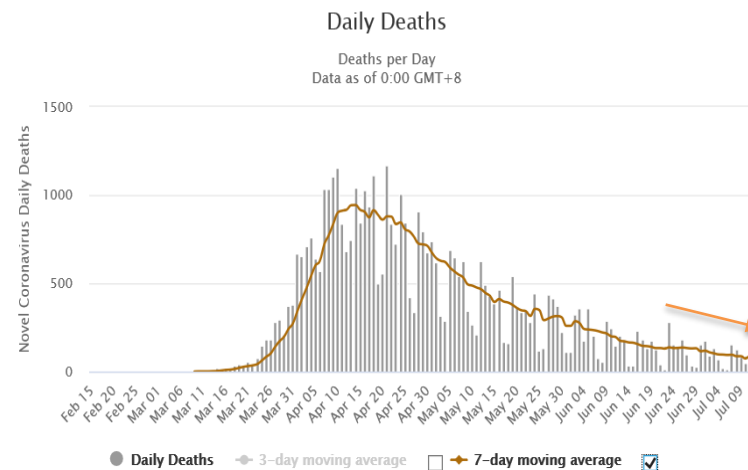
Daily New Cases in the United Kingdom



Daily New Deaths in the United States



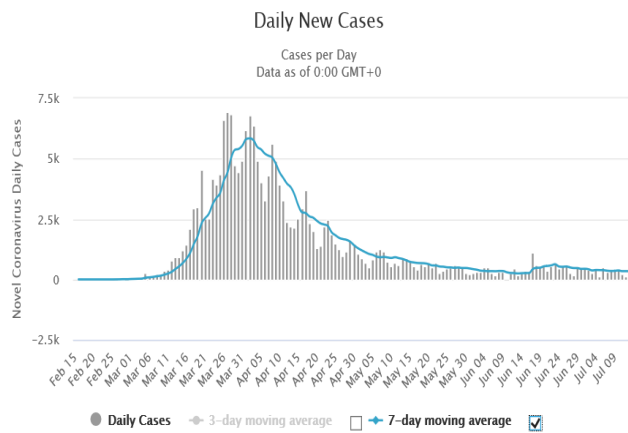
Daily New Deaths in the United Kingdom



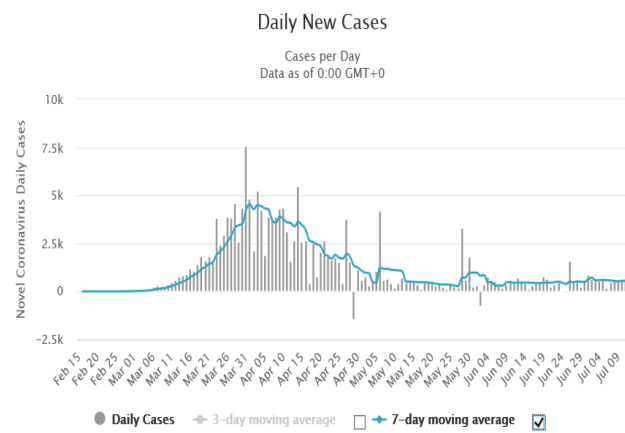
Countries with reassuring trend

Source: Worldometers – 14.07.2020

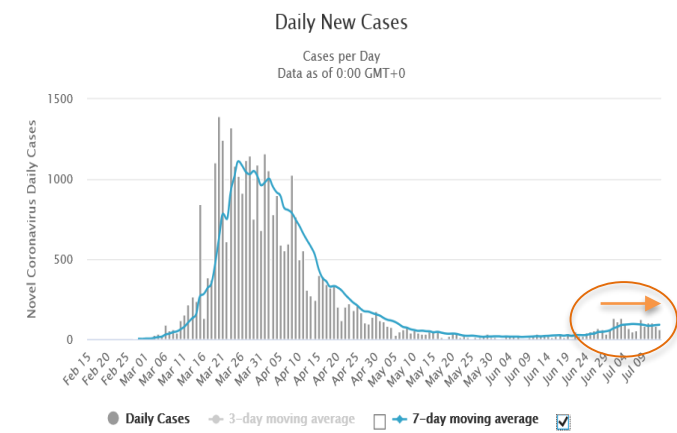
Daily New Cases in Germany



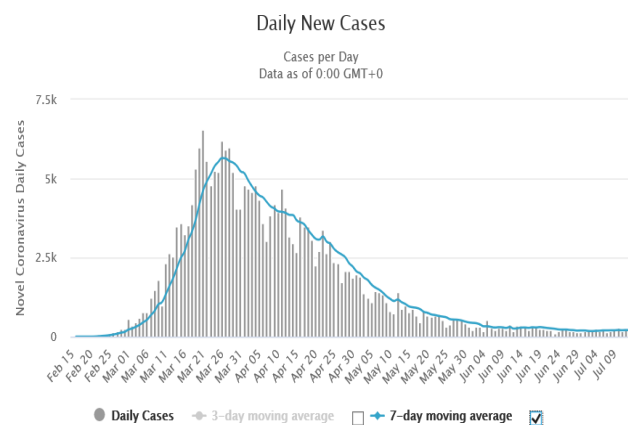
Daily New Cases in France



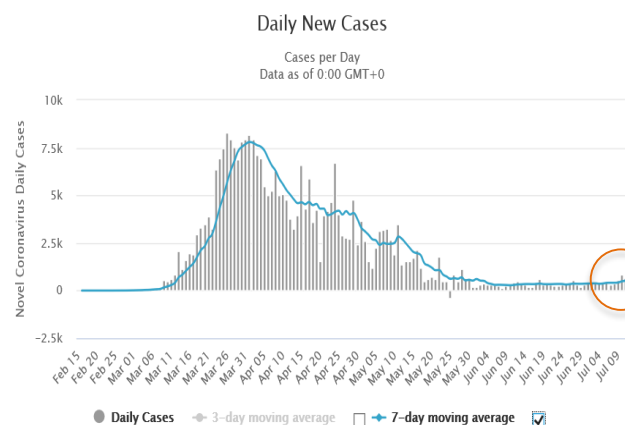
Daily New Cases in Switzerland



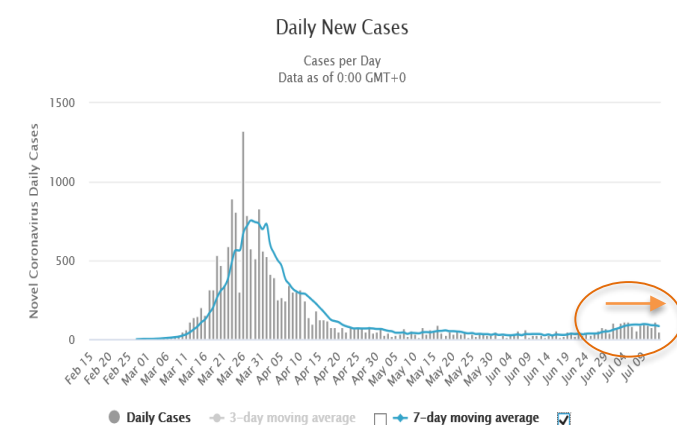
Daily New Cases in Italy



Daily New Cases in Spain



Daily New Cases in Austria



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