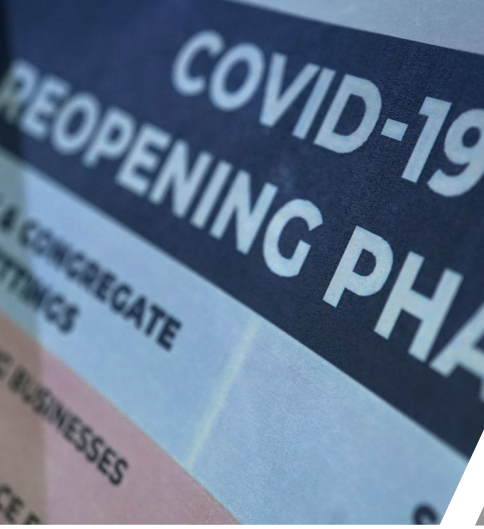

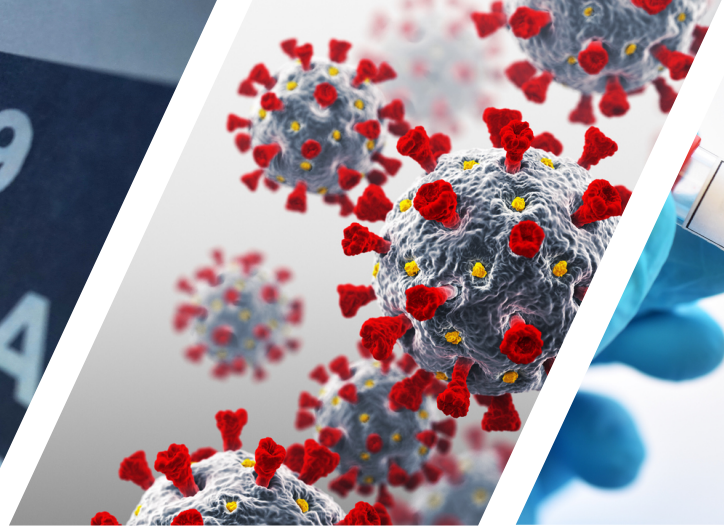

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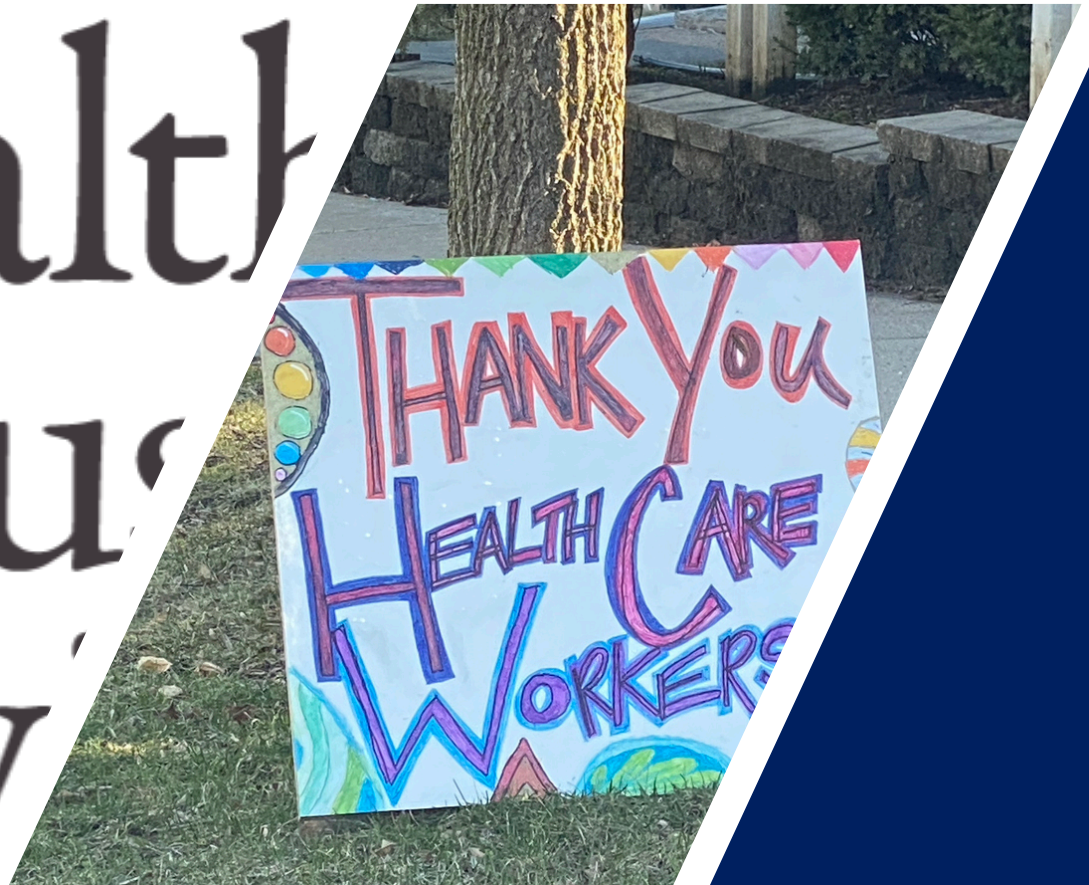

Issue # 207

Monday, November 9, 2020

COVID-19 Report

Highlights

Vaccine development

- First, the most significant news: **BioNTech and Pfizer announced this morning that its Covid-19 vaccine was exceeding expectations of its Phase 3 clinical trial. With a goal of 60% efficacy, preliminary results indicate a 90% effectiveness of the vaccine in preventing infections.** No serious side effects have been reported. Within a week or so, Pfizer should have sufficient safety data to enable it to apply for Emergency Use Authorization (EUA).

- Pfizer's vaccine is one of four in Phase 3 clinical trials in the U.S. and six worldwide. **The massive vaccine development effort, which includes more than 138 potential vaccines, appears to be on-track to deliver 1 or more viable vaccines within 12-18 months of discovery - that is, widespread distribution by Q2-Q4, 2021 (earlier availability for at-risk populations and healthcare workers). Typically, vaccine development takes 10+ years.**

- Due to the significance of this development, we have updated our vaccine development overview in today's report. We believe you will find it quite informative.

Strain on the healthcare system

- In the Spring, during the outset of the virus spread in the U.S., major concerns were being raised about the strain it was causing on the U.S. healthcare system. At the time, valid concerns were being raised that this strain could overwhelm the system and cause even more dire consequences. The mantra of "flattening the curve" through mandated economic shutdowns was arguably the right answer to avoid a calamity.

- New cases are currently being detected in the U.S. at an ever-increasing rate - and far greater in number than at any time since the pandemic began. Fortunately, **this case surge is not impacting the healthcare system any where near the degree that it had during previous surges in March/April and June/July**:

- **Covid-19 hospital census per 100 new cases fell yesterday to its lowest point since the pandemic began**. This rate is 1/2 what it was in mid-September and only 1/4 of what it was in May

- **In March/April and in June/July, several states experienced Covid-19 census per case at rates 3-5x higher than being experienced by any state at this point**

- **In April, Covid-19 patients exceeded inpatient bed capacity in Connecticut, New Jersey and New York, and came close to capacity in Massachusetts. As of yesterday, only four states - Illinois, Nevada, South Dakota and Wisconsin - are using 30-35% of their beds for Covid-19 patients. For the U.S. overall, Covid-19 patients are occupying 18% of available beds**

- ER and Outpatient visits for Covid-19-like illnesses remain lower than there were during their peaks in July and April, which coincided with their prior cases surges - by 20% and 50%, respectively

- **The likelihood of a Covid-19 patient would require ICU care is 20% lower than it was in mid-September and 30% lower than in early-April.** The improvement in ventilator use is even more-pronounced: the likelihood of a Covid-19 patient being on a ventilator has been cut in 1/2 since mid-May and by 2/3 since mid-March

Tests, Cases and Deaths

- Average daily test volume has now increased by 70% since mid-September; test-positive rates, however, continue to climb and are as high as they have been since early-May

- **New cases are being detected at an ever-increasing rate in the U.S., while the rate of increase has been declining worldwide for two weeks**

- Deaths reported with coronavirus are increasing since mid-October; **the case facility rate - that is deaths per newly-detected case with a 4-week lag - has been stable for two-and-a-half weeks**

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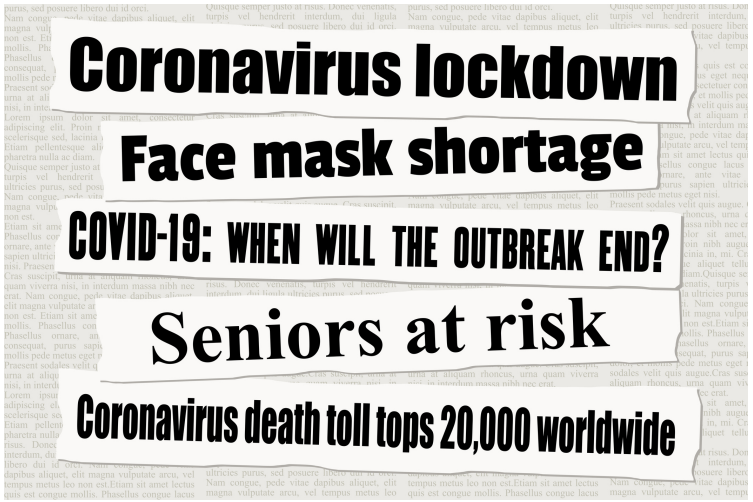

Vaccine Update

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Covid-19 Vaccine Development Process

- BioNTech and Pfizer announced this morning that its Covid-19 vaccine may be more effective than anticipated
  - In the initial results from it Phase 3 clinical trial, the vaccine proved to be more than 90% effective in the first 94 participants that developed symptoms (i.e., the vaccine reduced the incidence of contracting the virus by 90% in those receiving the vaccine versus those receiving the placebo)
  - The goal for the trial is 60% efficacy
  - Based on the initial trial protocol, the study will be complete once 164 participants develop symptoms
  - There have been no serious side effects from the vaccine; short-term effects include fatigue, headaches and chills
  - The protocol also calls for tests of safety, which may be completed by the third week of November
  - BioNTech/Pfizer could apply for Emergency Use Authorization (EUA) shortly after the safety tests are complete
  - This vaccine requires administration of two shots; it must be deep-frozen during transportation and storage
- The BioNTech/Pfizer vaccine is one of twelve potential vaccines in Phase 3 clinical trials, four of which are being conducted in the U.S. (AstraZeneca, JNJ, Moderna and BioNTech/Pfizer). The twelve clinical trials anticipate > 432k volunteers
- There are at least 138 vaccines worldwide at under development
- The typical vaccine development process takes 10 years and $500M; Based on current expectations, Covid-19 vaccine development could be accomplished in 12-18 months (Q2-Q4 2021 availability)
- Operation Warp Speed (OWS) is a multi-agency effort by the U.S. government to accelerate the vaccine development process, by de-risking the investment required and funding manufacturing efforts in advance of vaccine approval

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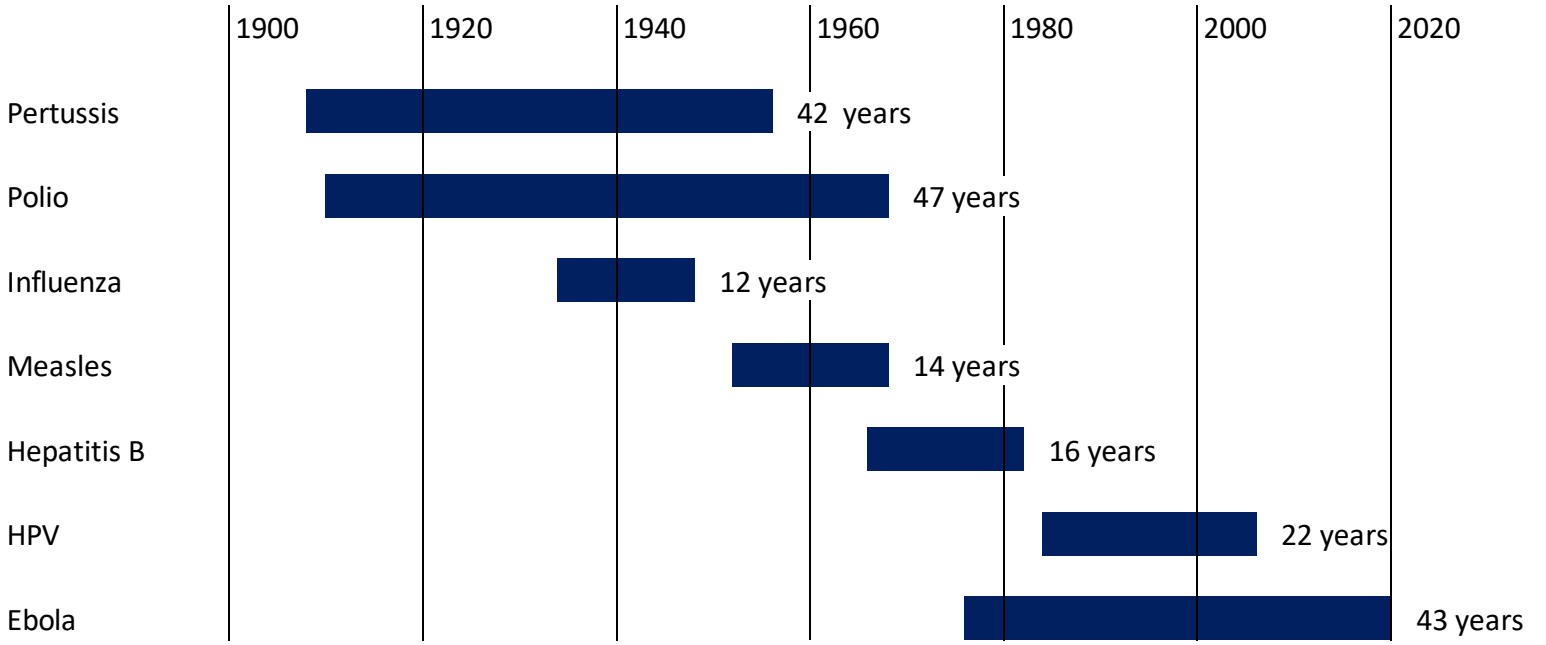
Vaccine Development timelines have improved over time

Nevertheless, vaccines for many well-known viruses are far longer that what is hoped for with the Covid-19 vaccine

Vaccine Development Time
Discovery of Cause to Vaccine Development



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There is a well-structured process for developing potential vaccines

This process typically involves 10+ years and >$500M in investment

Often, for each vaccine that ultimately receives approval, 100+ potential vaccines are researched

	Discovery	Pre-Clinical	Phase 1	Phase 2	Phase 3	Regulatory Approval
Description	Identify proper antigens	Animal tests of antigen formulation	Test on a small group of people (<100)	Test on a larger group: safety and formulation	Evaluate protection & safety on larger group (0000s)	
Time	2-5 years	2 years	1-2 years	2-3 years	2-4 years	1-2 years
Illustrative # of potential vaccines	100	20	10	5	1	1
Investment	$10-20M		$50-100M		$500M-$1B	

Covid-19 Vaccine Development:

# in Pipeline		89	33	14	12	0

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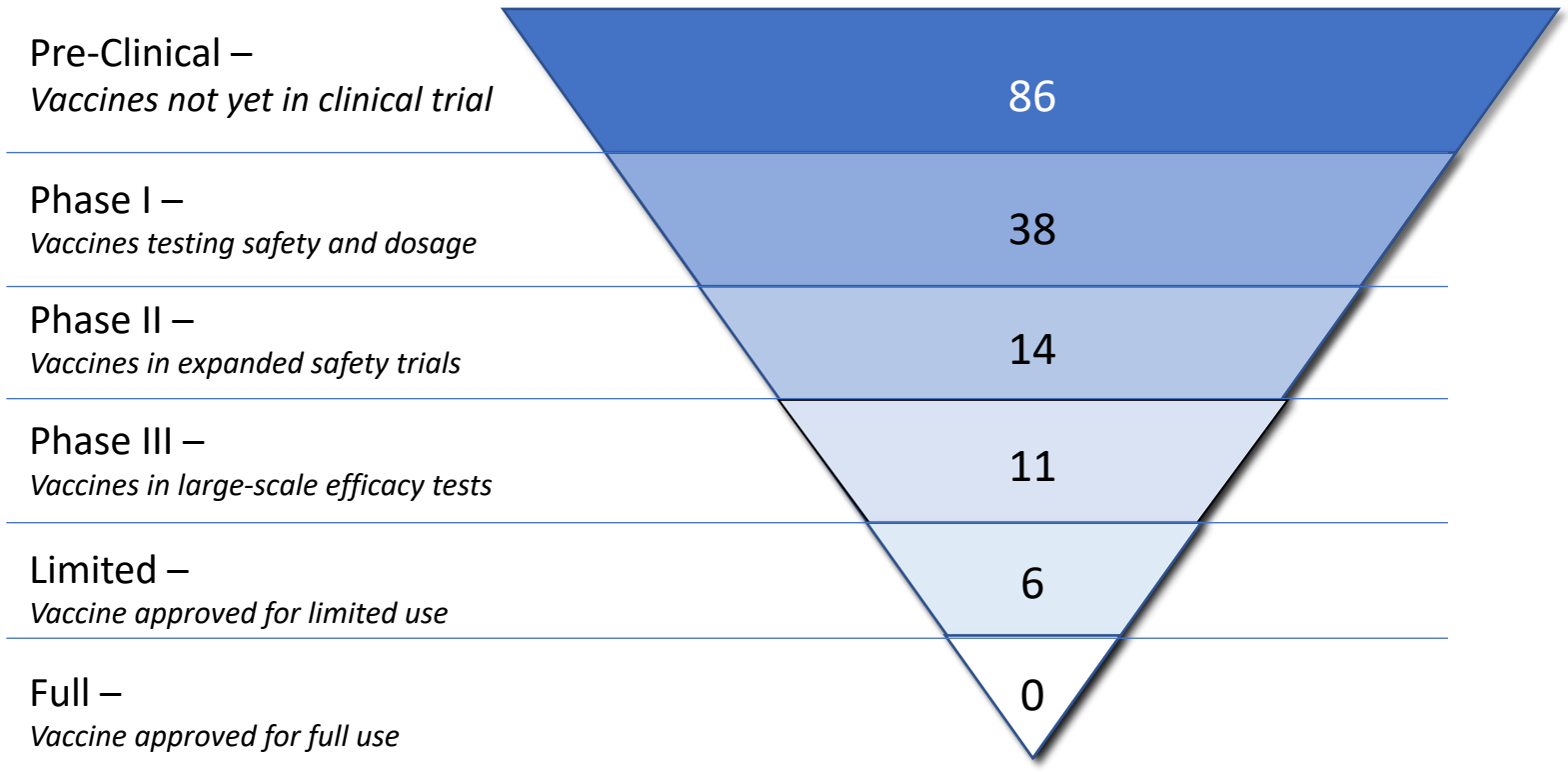
As of yesterday, there were at least 138 potential vaccines in the pipeline:

- 86 under active investigation in animals
- 52 in safety trials
- 11 in large-scale efficacy tests
- 6 approved for limited use (none in the U.S.)



* - Source: "Coronavirus Vaccine Tracker", New York Times, Updated October 12, 2020
https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

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There are now four Phase III clinical trials of a COVID-19 vaccine underway in the United States. JNJ is now the largest

Pfizer, JNJ and Moderna are targeting a 60% "efficacy" (i.e., reduction in infection risk); Astra-Zeneca is targeting 50% (WHO standard: 50%)

All four have established a threshold of a 30% risk reduction (95% confidence interval; consistent with FDA guidance)

Interim checkpoints are used to judge whether sufficient evidence ("events", infections) is available to end a trial early. Astra-Zeneca has established a single interim checkpoint; Moderna, 2; and Pfzier, 4

COVID-19 Phase III Clinical Trial Protocols - United States

	Pfizer	Moderna	AstraZeneca	JNJ
Sample Size	44,000	30,000	30,000	60,000
Participants getting vaccine	15,000	15,000	20,000	30,000
Type of vaccine	mRNA	mRNA	Adeno v	Adeno v
Efficacy target	60%	60%	50%	60%
Lower 95% CI efficacy	30%	30%	30%	30%
Number of events at completion	164	151	150	154
Number of interim analyses	4	2	1	N/A
Number of events 1st look	32	53	75	20
Number of shots	2	2	2	1
Deep freezing required	Yes	Yes	Yes	No

Table: Eric Topol, MD • Created with Datawrapper

Interpretation: Pfizer's "first look", can occur after 32 infections among its participants. Using the FDA's proposed evaluation criteria, the trial may be considered successful, if there is at least a 50% lower infection rate among participants receiving the vaccine versus those receiving the placebo. At that point, the company could apply for Emergency Use Authorization (EUA)

Pfizer's trial would be complete after 164 infections among its participants. The trial may be considered successful, if there is at least a 30% lower infection rate among participants receiving the vaccine versus those receiving the placebo. At that point, the company could apply for full approval

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There are reportedly twelve potential vaccines that have reached the Phase 3 clinical trial stage (ten are listed here)

A few of these, including BioNTech and Moderna are at or near full volunteer participation

Source: PLOS Blogs

Company	Vaccine	Target size	Countries	Single or similar trials	Reaching recruitment target
Johnson & Johnson	Ad26.COV2-S	60,000	Argentina, Brazil, Chile, Columbia, Mexico, Peru, South Africa, USA	Single trial	Months away
CanSino	Ad5-nCoV	45,500	40,000-Pakistan 500 – Russia Other sites unconfirmed	Mostly single trial	Months away
BioNTech/Pfizer	BNT162b1-b3	43,998	Argentina, Brail, South Africa, Turkey, USA (cleared to start in Germany)	Single trial	Less than a month away: 90% recruited
AstraZeneca (Oxford University)	ChAdx1 nCov-19/azd1222 (Covidshield)	54,190	12,390-UK 30,000-USA 10,000-Brazil 1,700-India 100-Russia	3 very different large trials & some small	Largest trial months away: 1 in 10,000 healthcare workers (60% recruited after 4 months)
Moderna	mRNA-1273	30,000	USA	Single trial	Fully recruited
Novavax	NVX-CoV2373	39,000	9,000-UK 30,000-USA	Two trials (one not yet underway	Months away
Sputnik V	Gam-COVID-Vac	43,600	40,000-Russia 100-Belarus 2,000-Venezuela ?-UAE 1,500-India	Mostly single trial	Months away (30% recruited)
Sinopharm	2 BBIBP-CoV	60,300	45,000-Bahrain, Egypt, Jordan, UAE 3,000-Beijing, Argentina 200-Morocco 12,000-Peru ?-Morocco, Serbia ?-Pakistan	Two large trials, several small	Close to 90% recruited
Sinovac	CoronaVac	27,980	13,060-Brazil 13,300-Turkey 1,620-Indonesia ?-Philippines	Two large trials, two small	Trial with 13,060 healthcare workers close (90% recruited) 1 small trial fully recruited; others: months away
Bharat Biotech, Indian Medical Research Council	Covaxin	28,500	India	Single trial	Months away

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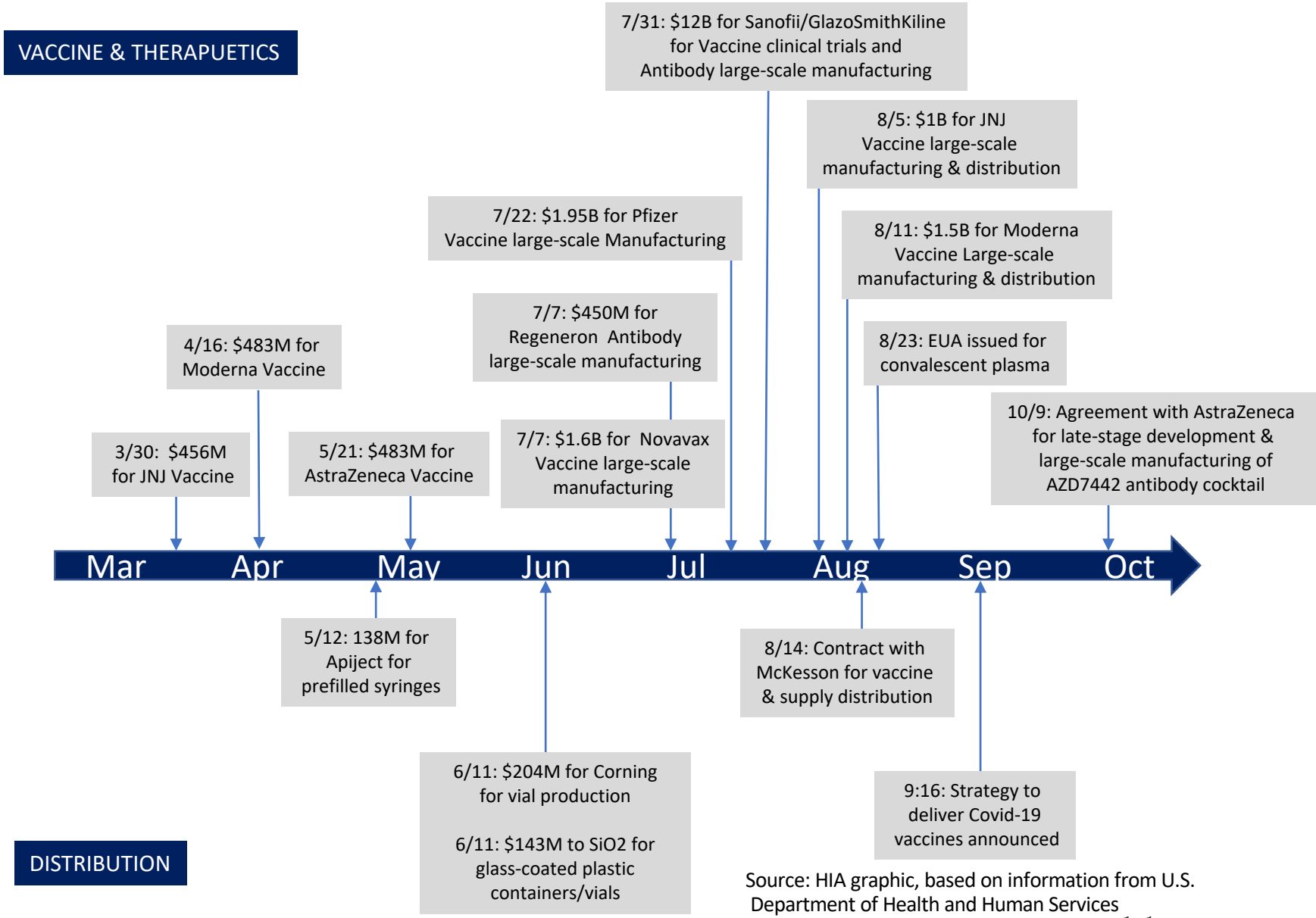
Operation Warp Speed (OWS) is a multi-agency effort of the U.S. government to accelerate the vaccine development and distribution effort

OWS is funding multiple companies, in both vaccine development and manufacturing/ distribution efforts

By de-risking the investment required of the companies, OWS is compressing the timeframe typically required of this process



Source: HIA graphic, based on information from U.S. Department of Health and Human Services

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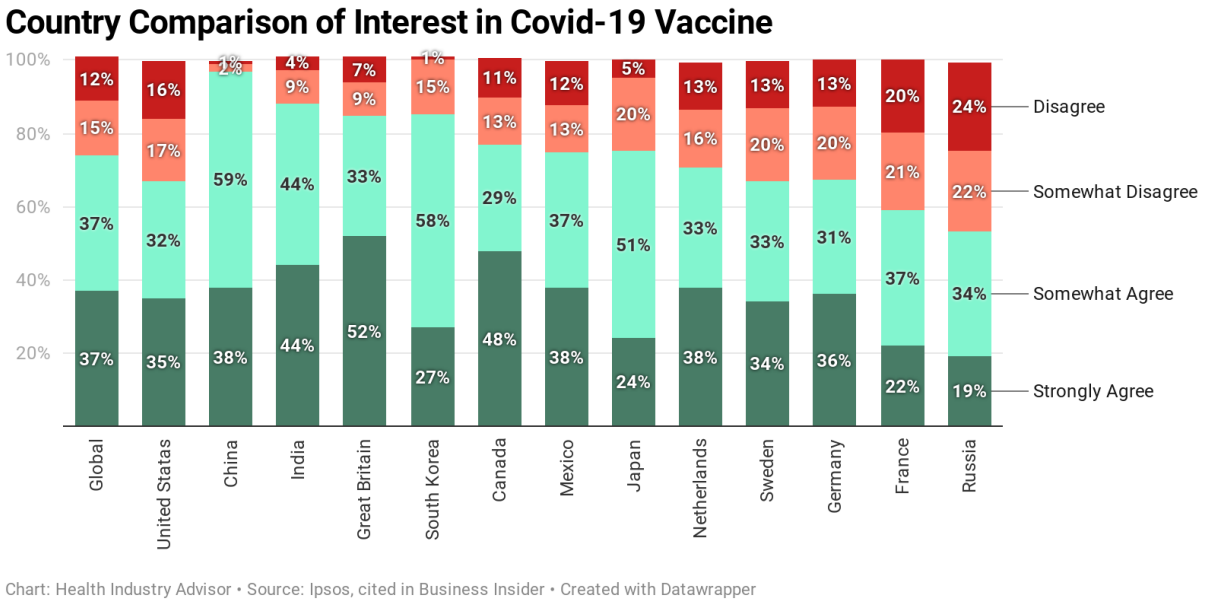
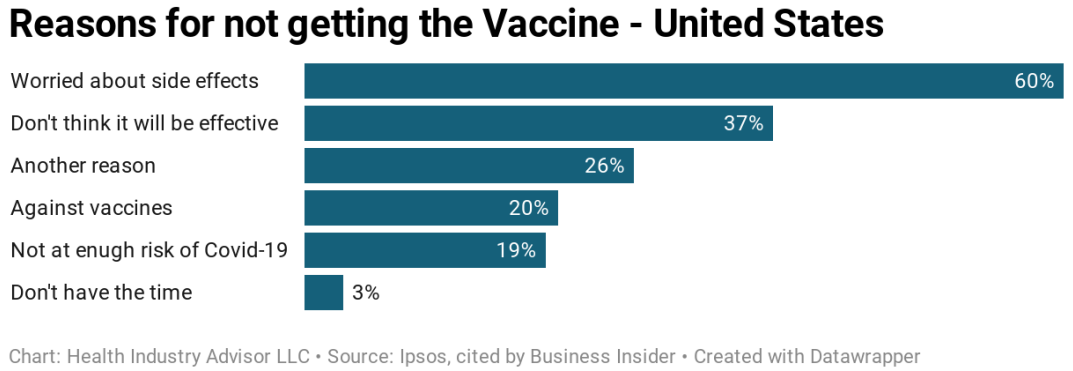
Consumer acceptance of a potential vaccine could be a major impediment to success in reaching herd immunity

In the U.S. 33% of Ipsos survey respondents disagreed or somewhat disagreed with having interest in obtaining the vaccine

Worries about side efforts and vaccine effectiveness drove this resistance; anti-vax concerns, as well as lack of perceived risk from contracting coronavirus were also high on the list





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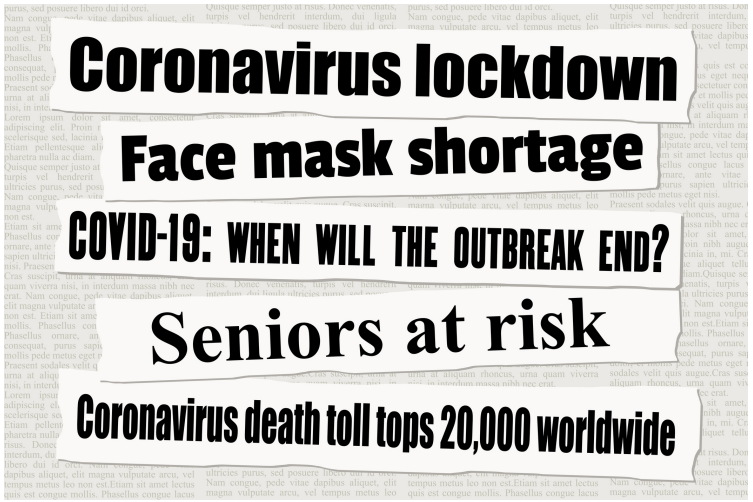

Healthcare Resource Usage Update

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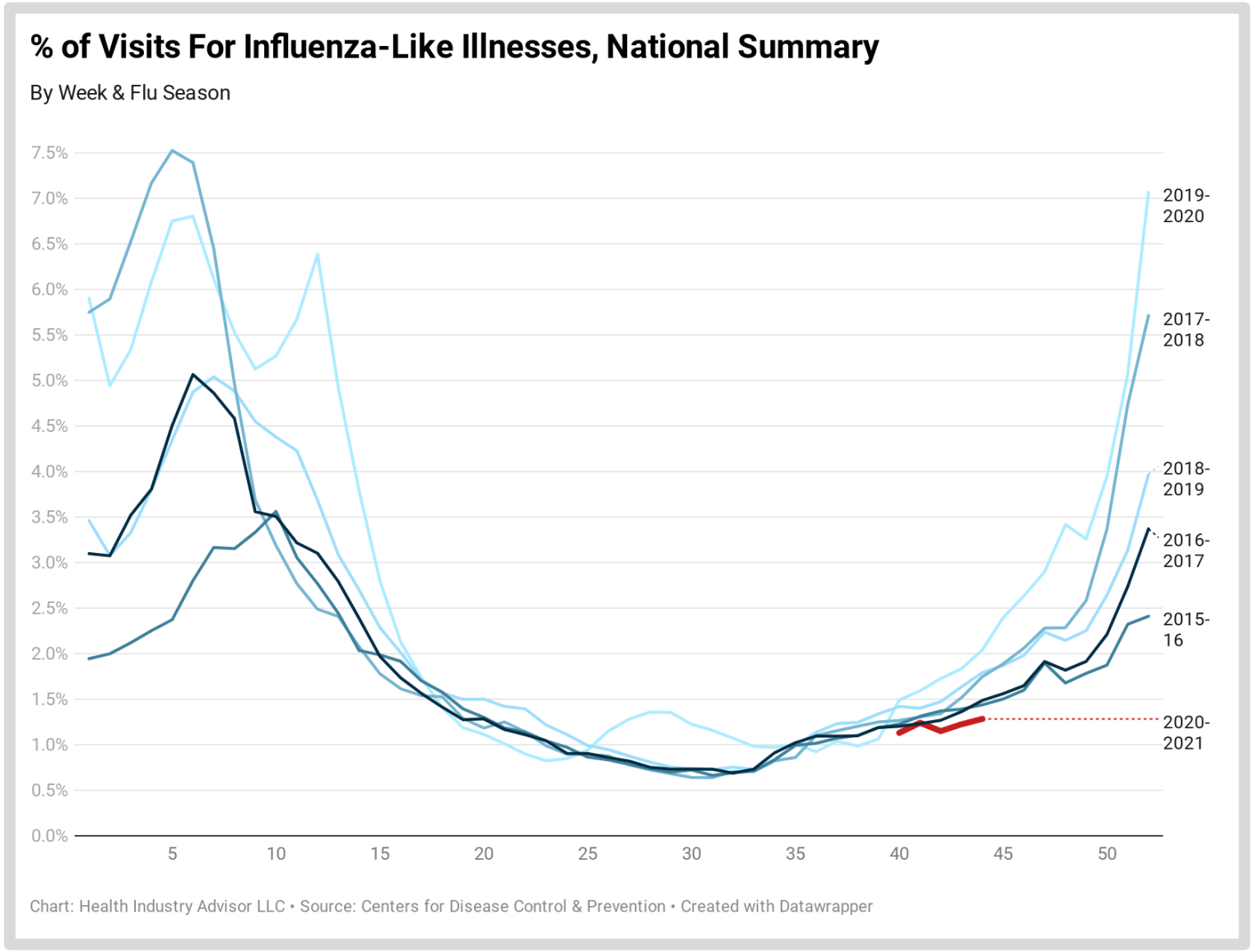
Now five weeks into the 2020-21 flu season, flu visits are trending lower than each of the past five years - and, markedly lower (40%) than last year



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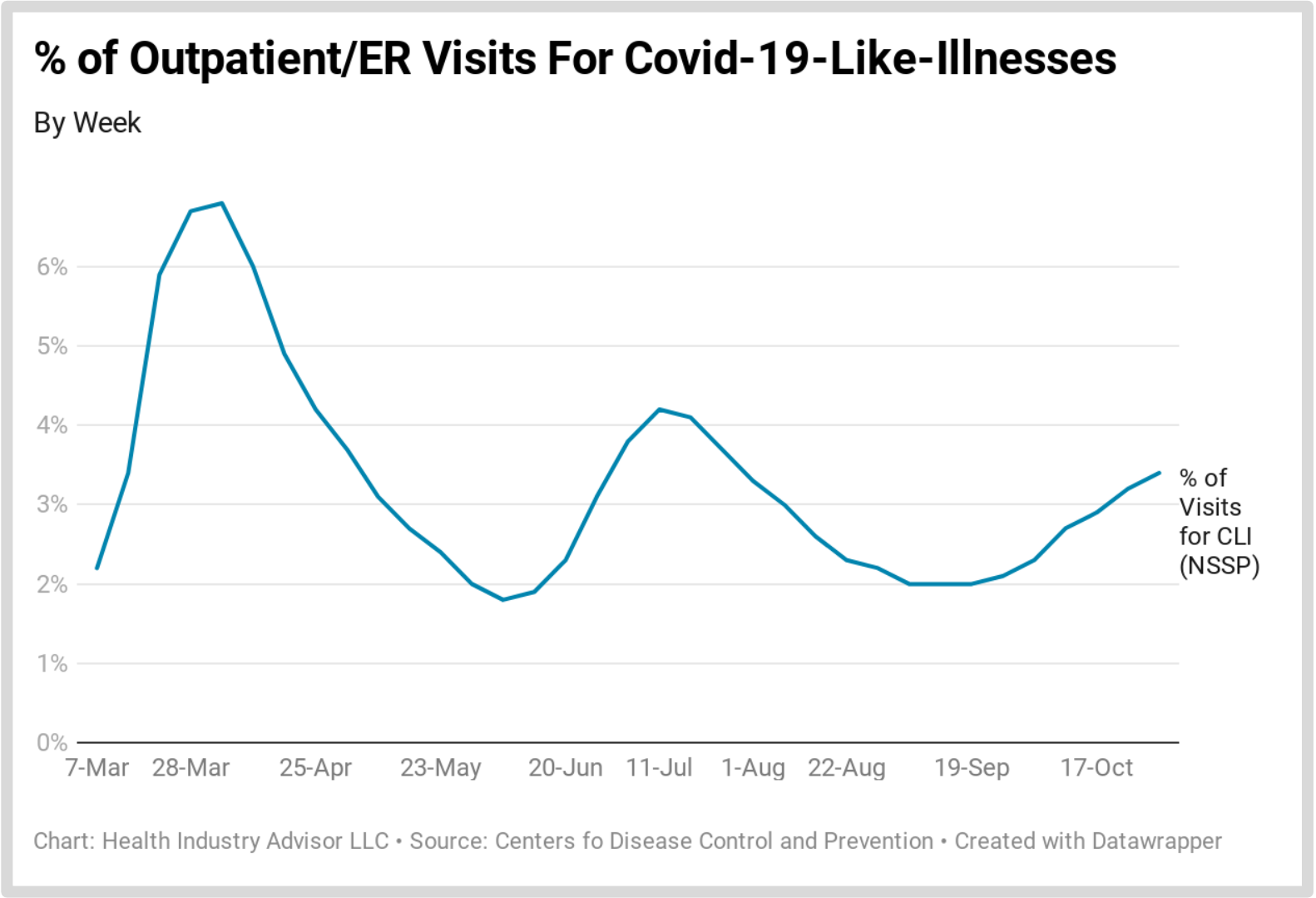
Visits to the ER and outpatient clinics for Covid-19-like illnesses have been rising since mid-September

Still, they peaked higher during the July case surge and even-higher during the March surge



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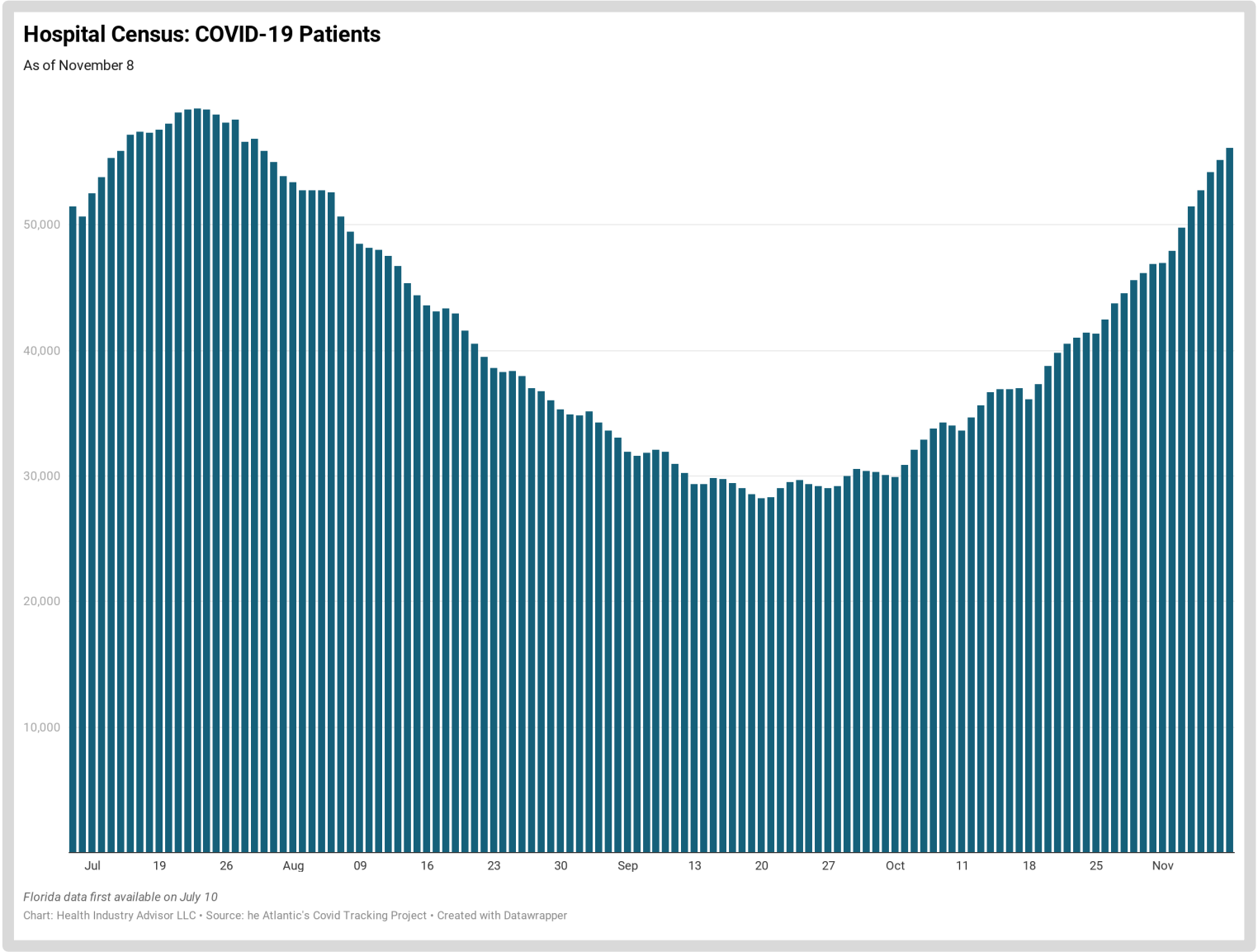
On a same-day, prior-week basis, inpatient Covid-19 census increased every day since September 23



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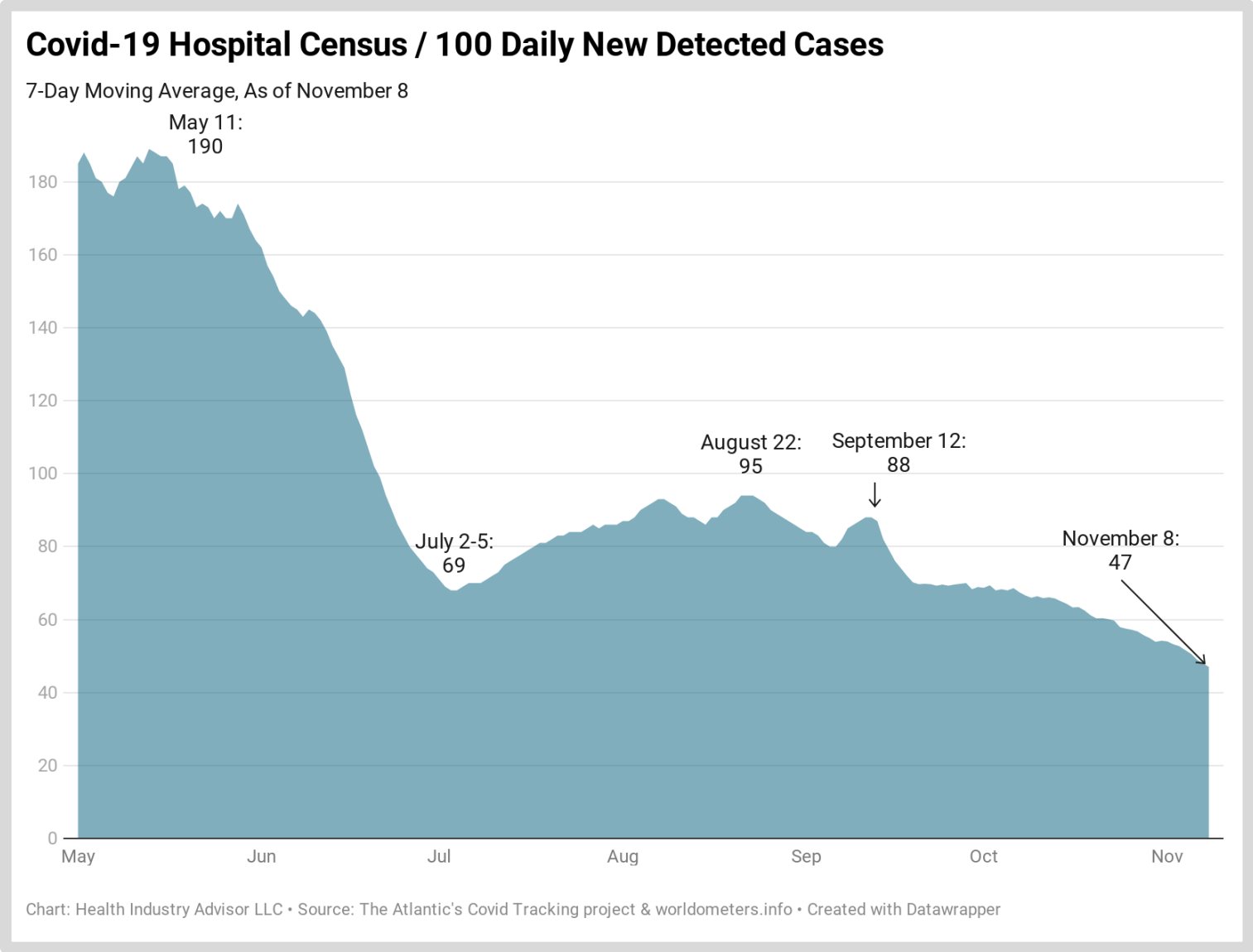
Covid-19 Hospitalizations, while increasing, have not kept pace with the increase in newly-detected cases:

The average Covid-19 census per 100 new cases has declined on twenty-four of the past twenty-six days

This rate has been reduced by ~1/2 since mid-September and by ¾ since mid-May



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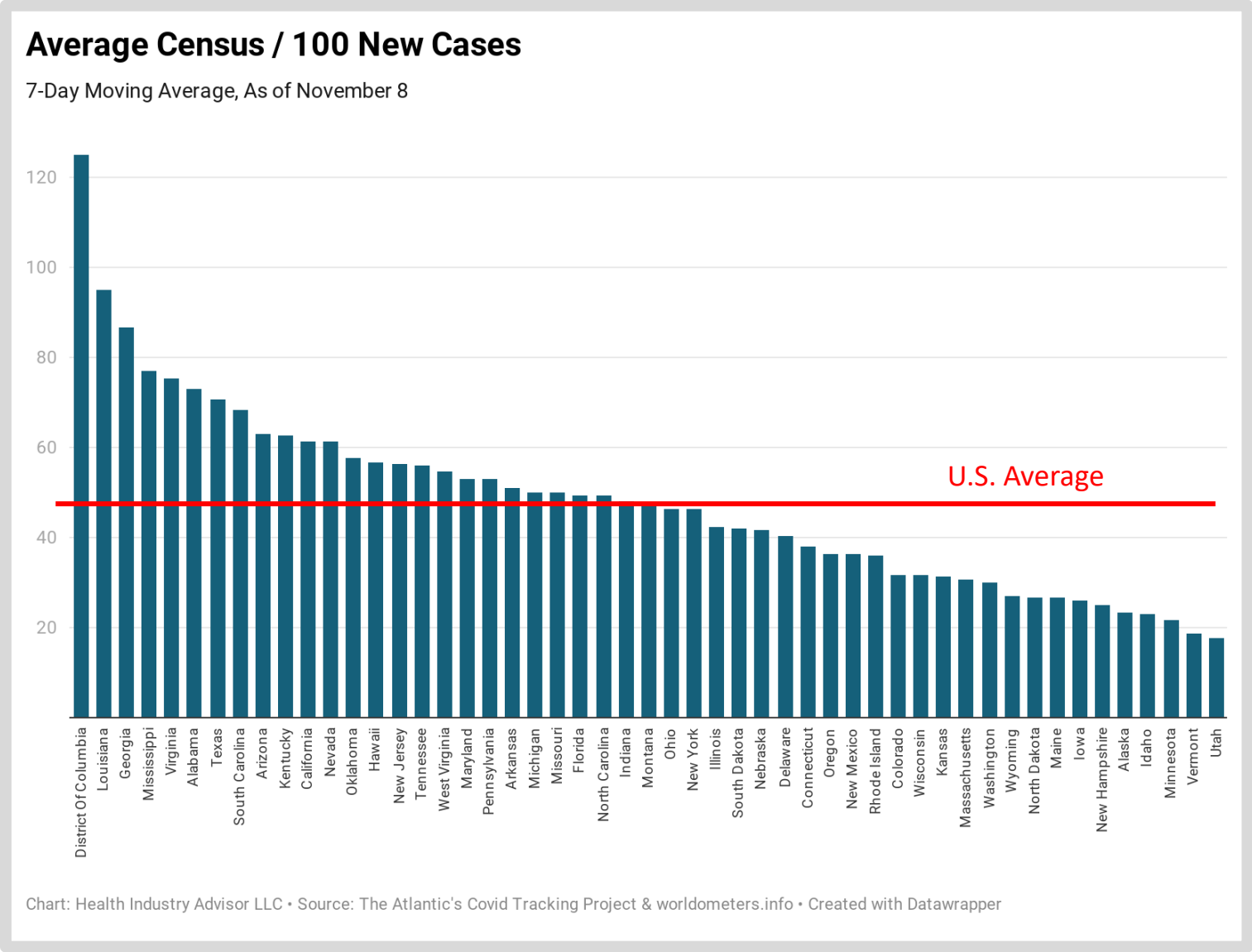
The highest average census per new case is currently experienced in D.C., followed by Louisiana and Georgia

The lowest rates are found in Utah, Vermont and Minnesota

Contrast these rates to those experienced in selected hard-hit states during earlier surges:

- Arizona: 305 (4/20)
- California: 416 (4/17)
- Connecticut: 293 (4/29)
- Massachusetts: 475 (6/21)
- Michigan: 422 (4/21)
- New York: 330 (5/22)



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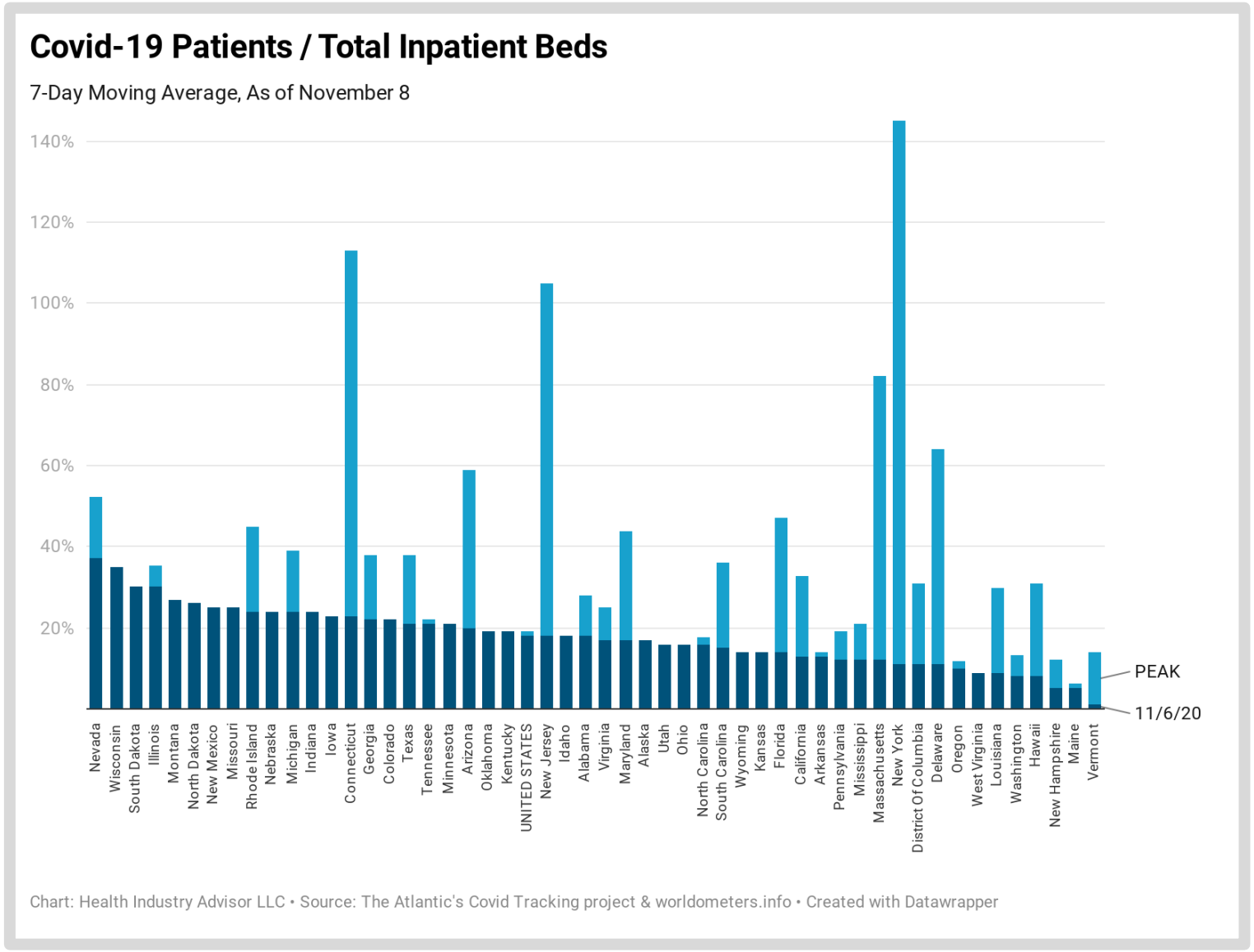
Despite the recent rise in new cases, Covid-19 is not straining the U.S. healthcare system as it had in April and, to a lesser degree in July:

In April, Covid-19 patients exceeded the normal inpatient bed capacity in three states: Connecticut, New Jersey and New York, and peaked at 82% of bed capacity in Massachusetts

In July, Covid-19 patients occupied >1/2 the available beds in Arizona and Nevada

As of yesterday, in only four states are Covid-19 patients occupying >30% of available inpatient beds – Nevada, Wisconsin, South Dakota and Illinois



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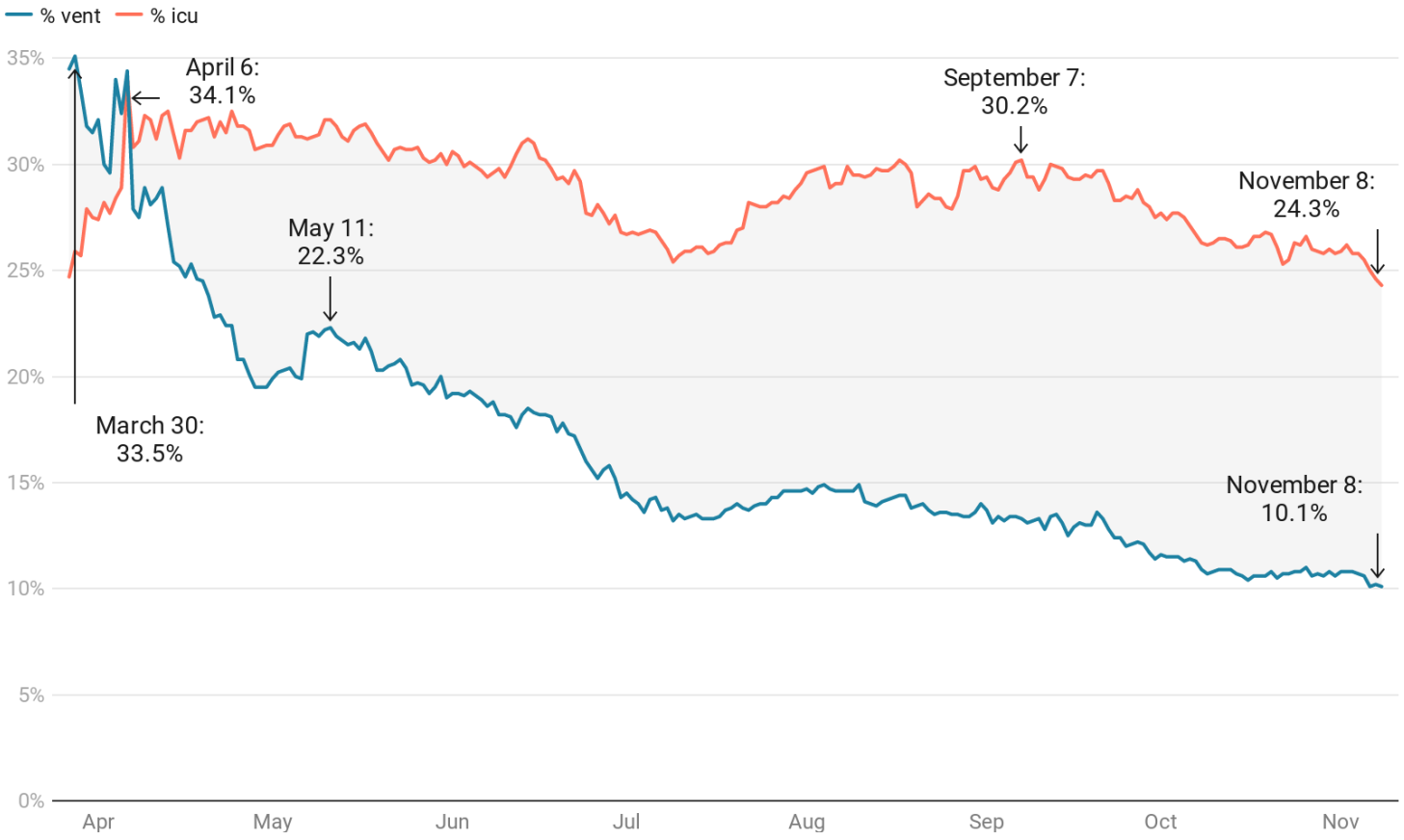
The likelihood of a hospitalized Covid-19 patient would require ICU care has declined 20% since early-September and nearly 30% since early-April

The likelihood of a hospitalized Covid-19 patients would be on a ventilator has reduced by>1/2 since mid-May and by >2/3 since March

Severity of Hospitalized Patients

% of patients on ventilators and in the ICU, As of November 8



Health Industry Advisor LLC analysis

Chart: Health Industry Advisor LLC • Source: The Atlantic's Covid Tracking Project • Created with Datawrapper

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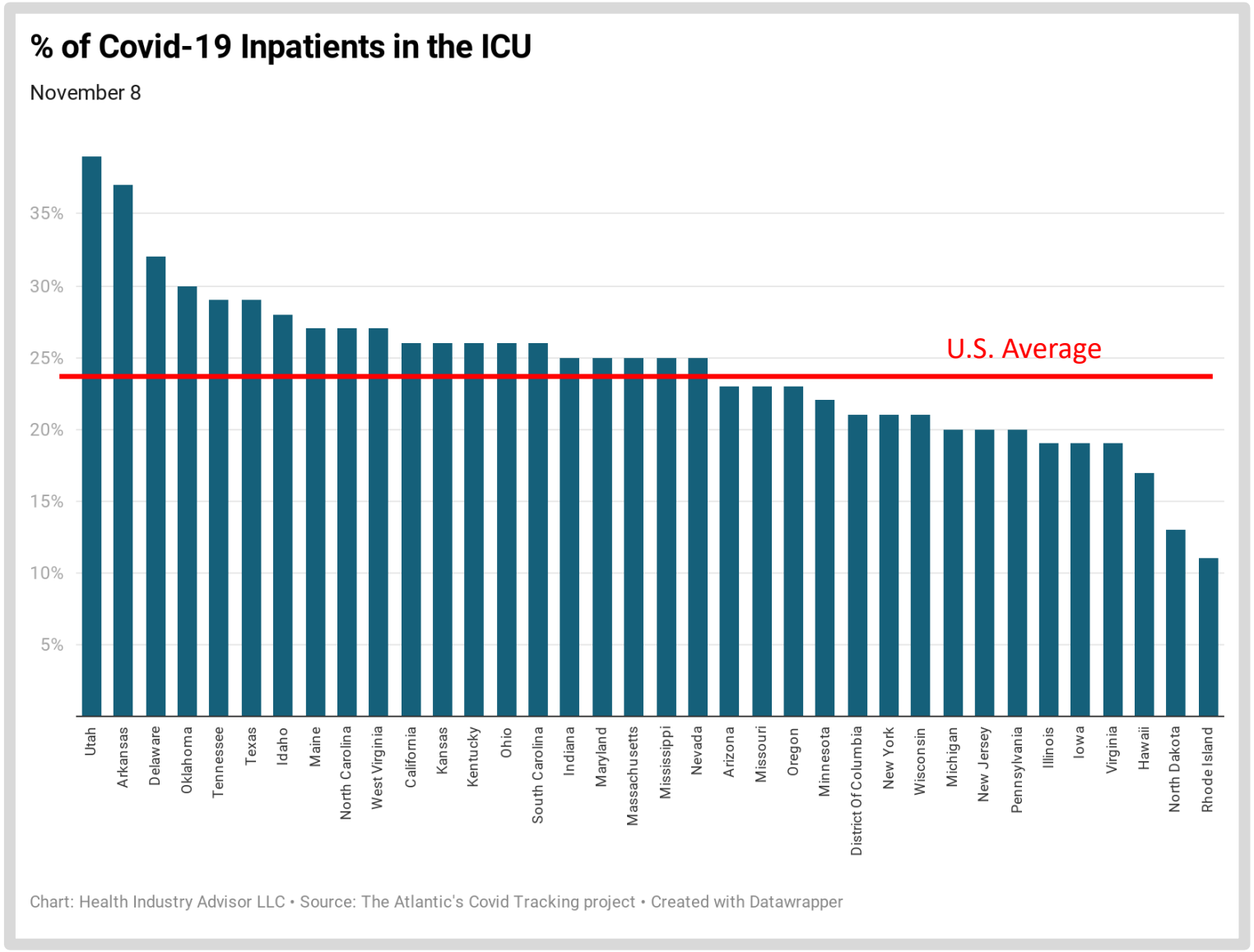
On average, less than 1-in-4 Covid-19 inpatients are in the ICU

Rates are highest in Utah, Arkansas and Delaware, where >1-in-3 are in the ICU



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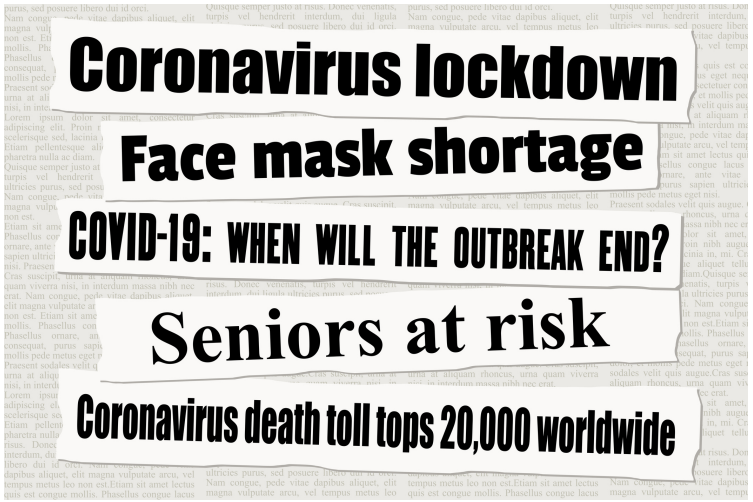

Tests, Cases and Deaths

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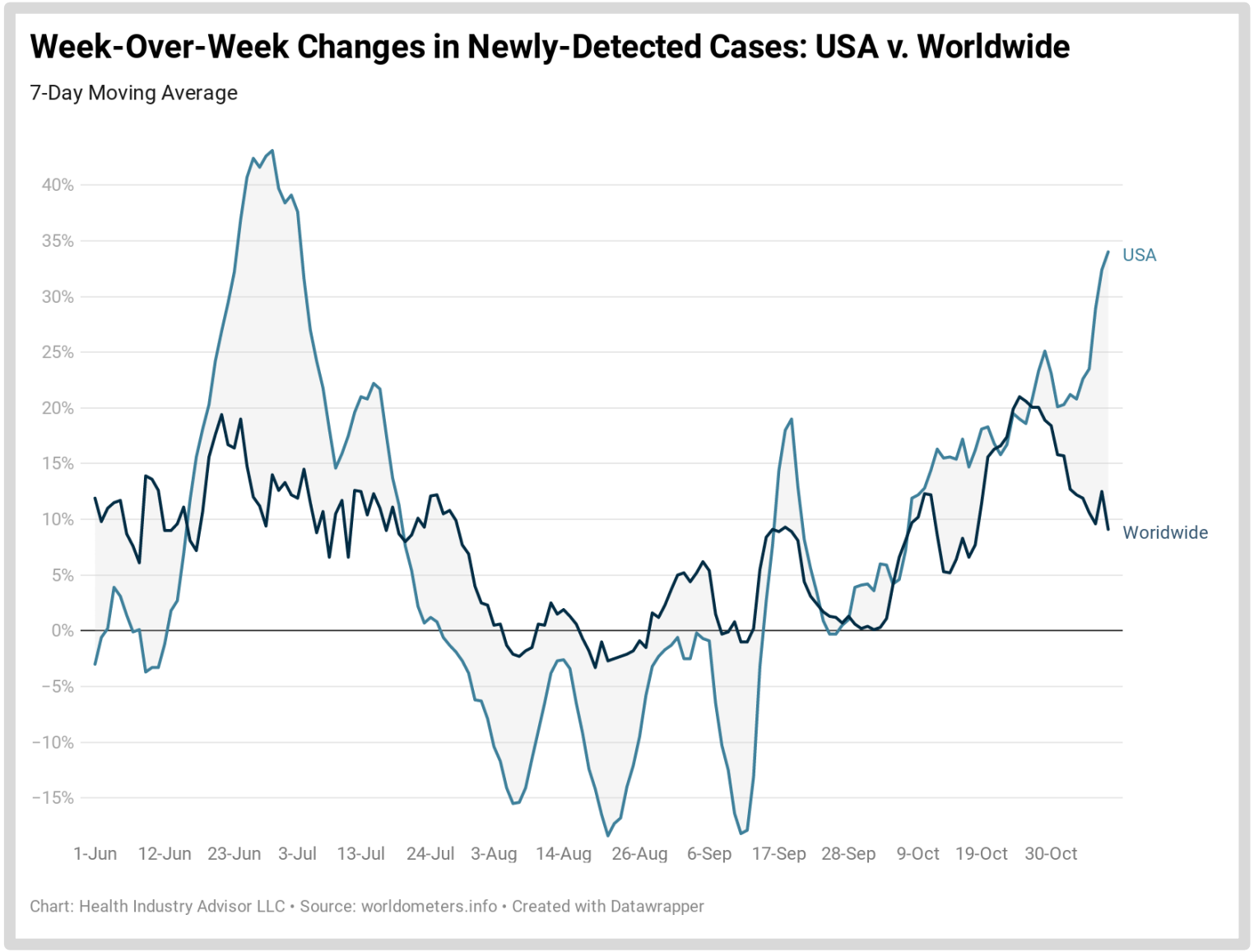
Worldwide, the rate of growth slowed over the past two weeks

The U.S. is moving in the opposite direction



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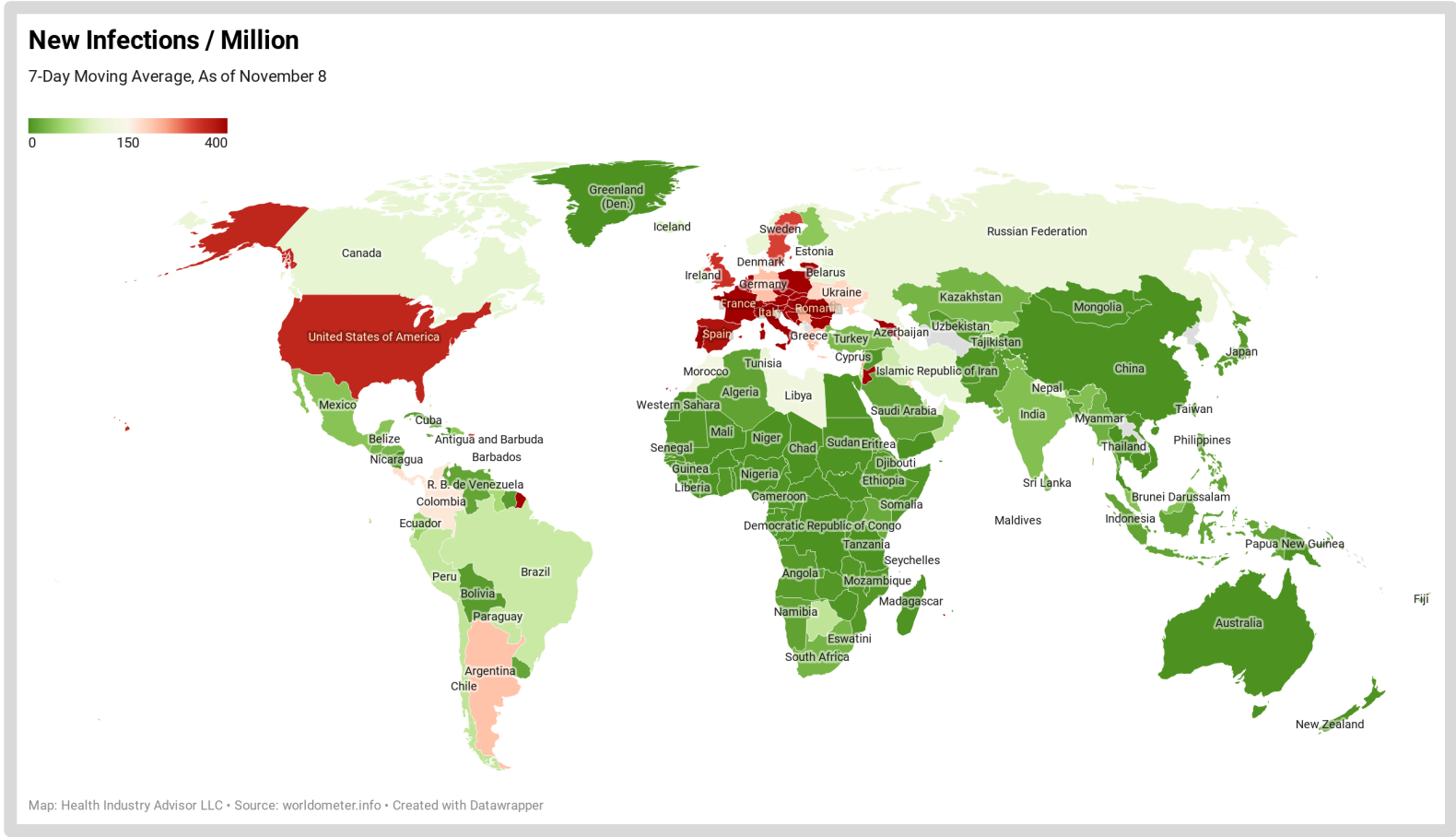
European countries continue to experience the highest infection rates per capita

Argentina and the United States have lower, yet still concerning rates

* - 7-day moving average basis



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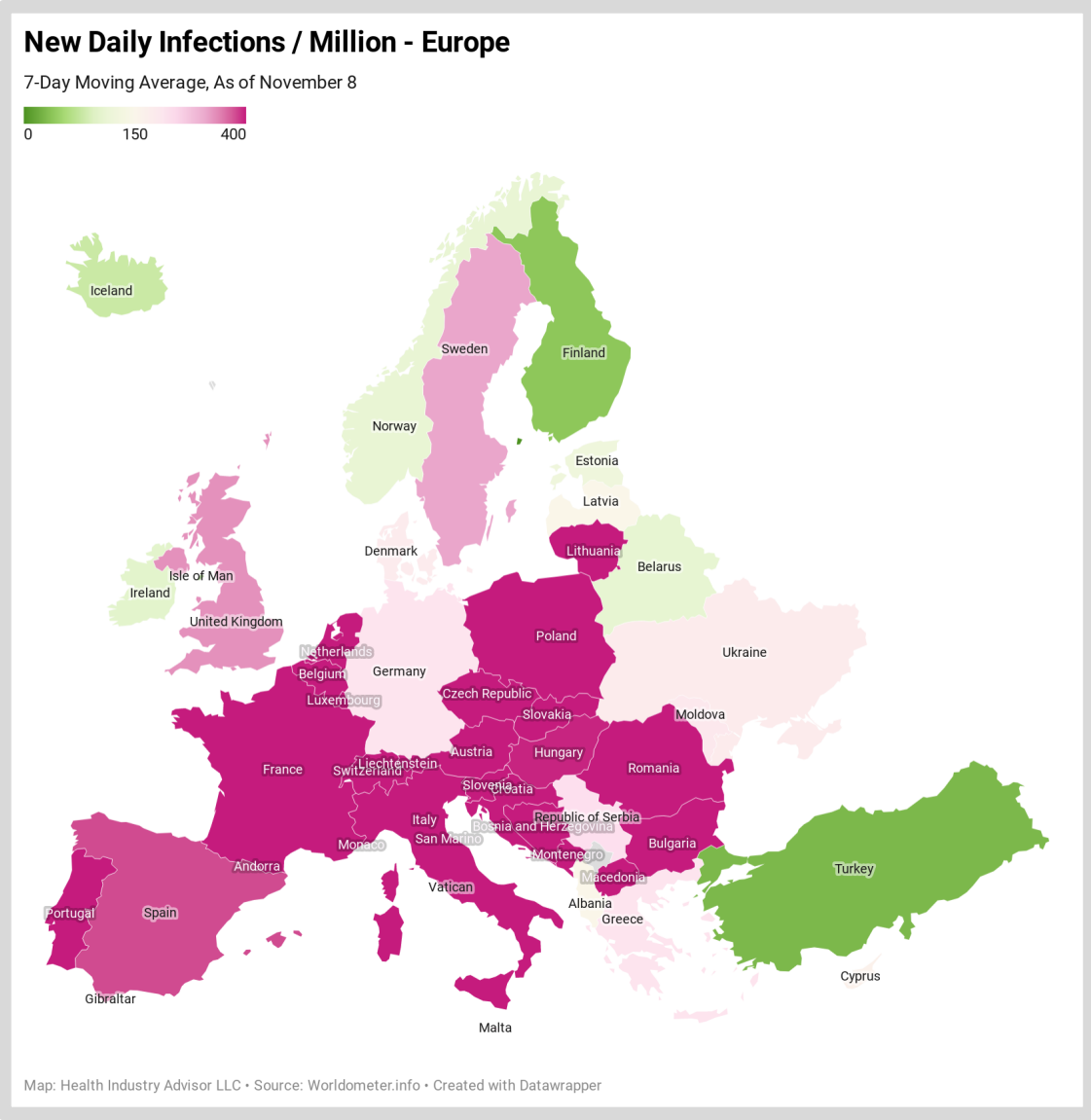
High rates of new infections are being reported across Europe – with exceptions in the north and eastern parts of the continent

* - 7-day moving average basis



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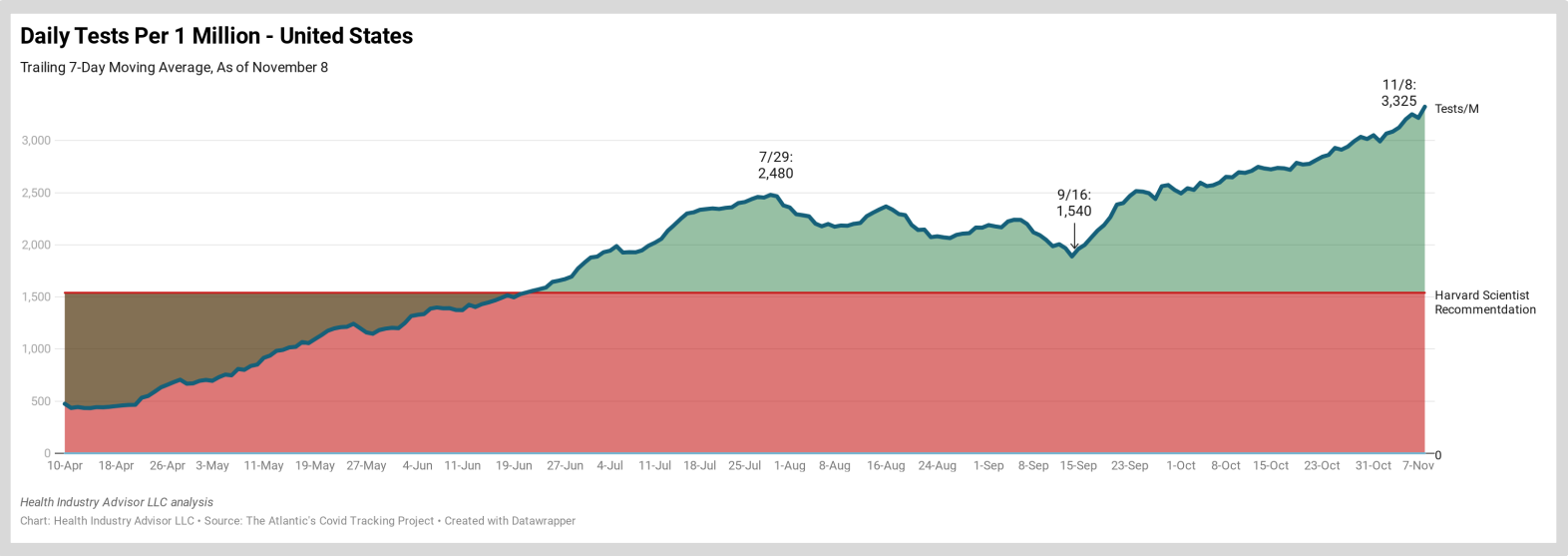
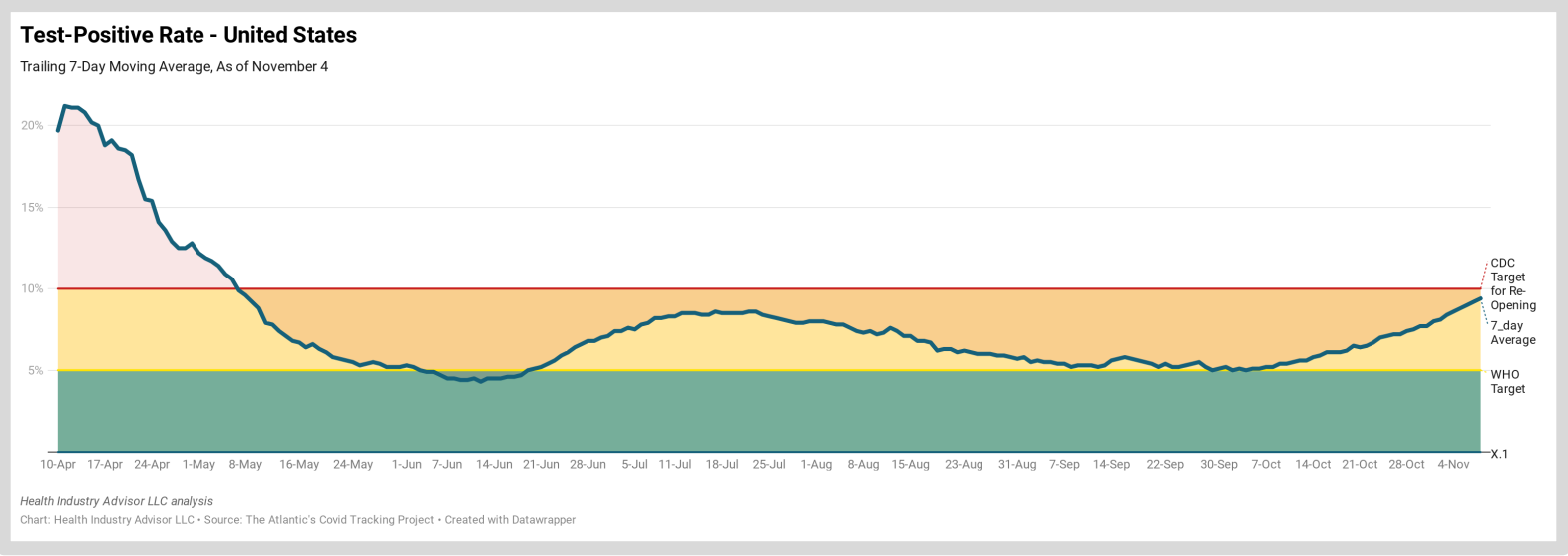
The 7-day average testing volume set another new high on Sunday; this rate has increased by 70% since mid-September

The 7-day test-positive rate, however, has been trending upward since the beginning of October





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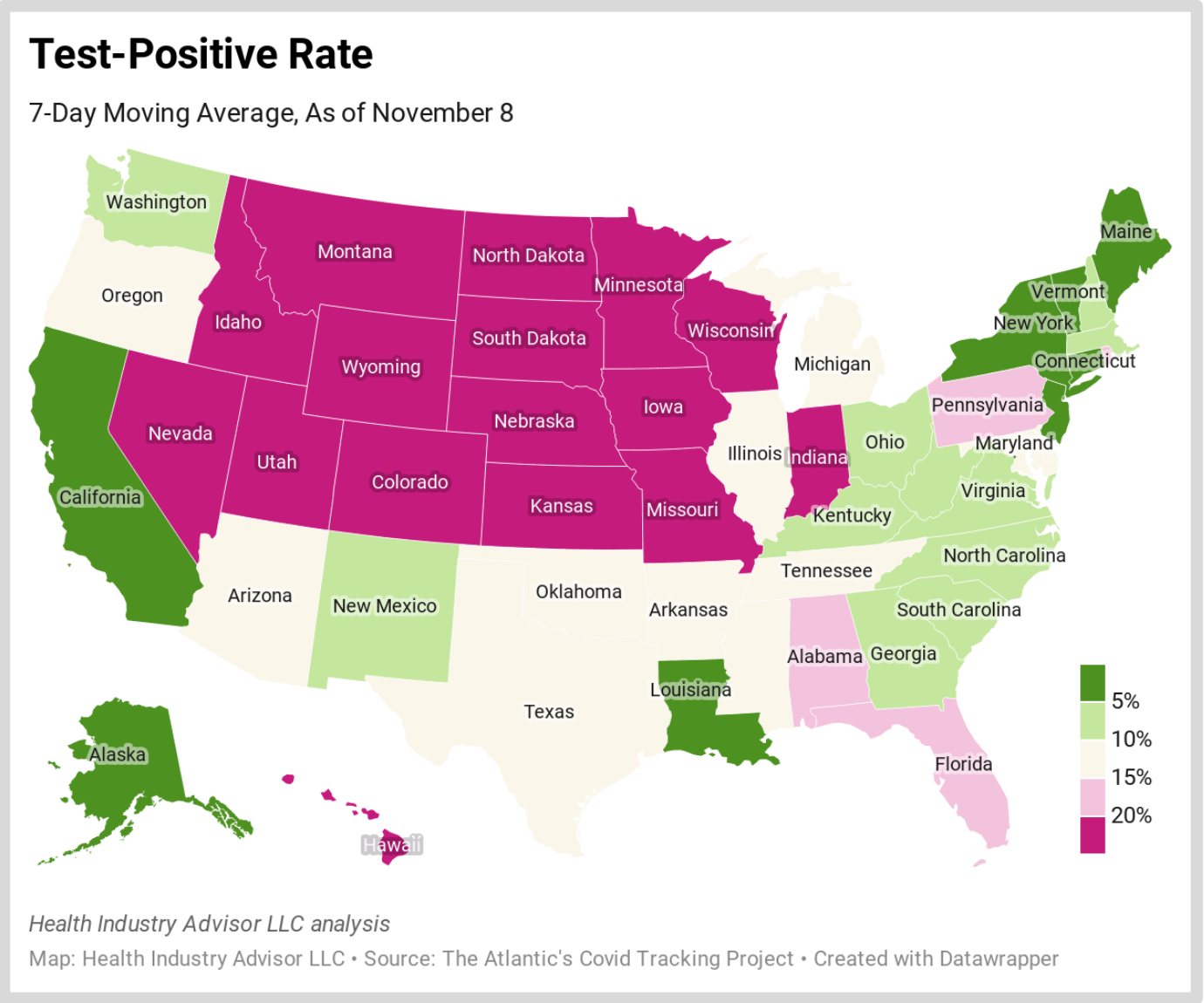
High test-positive rates continue to plague the Midwest and Mountain States



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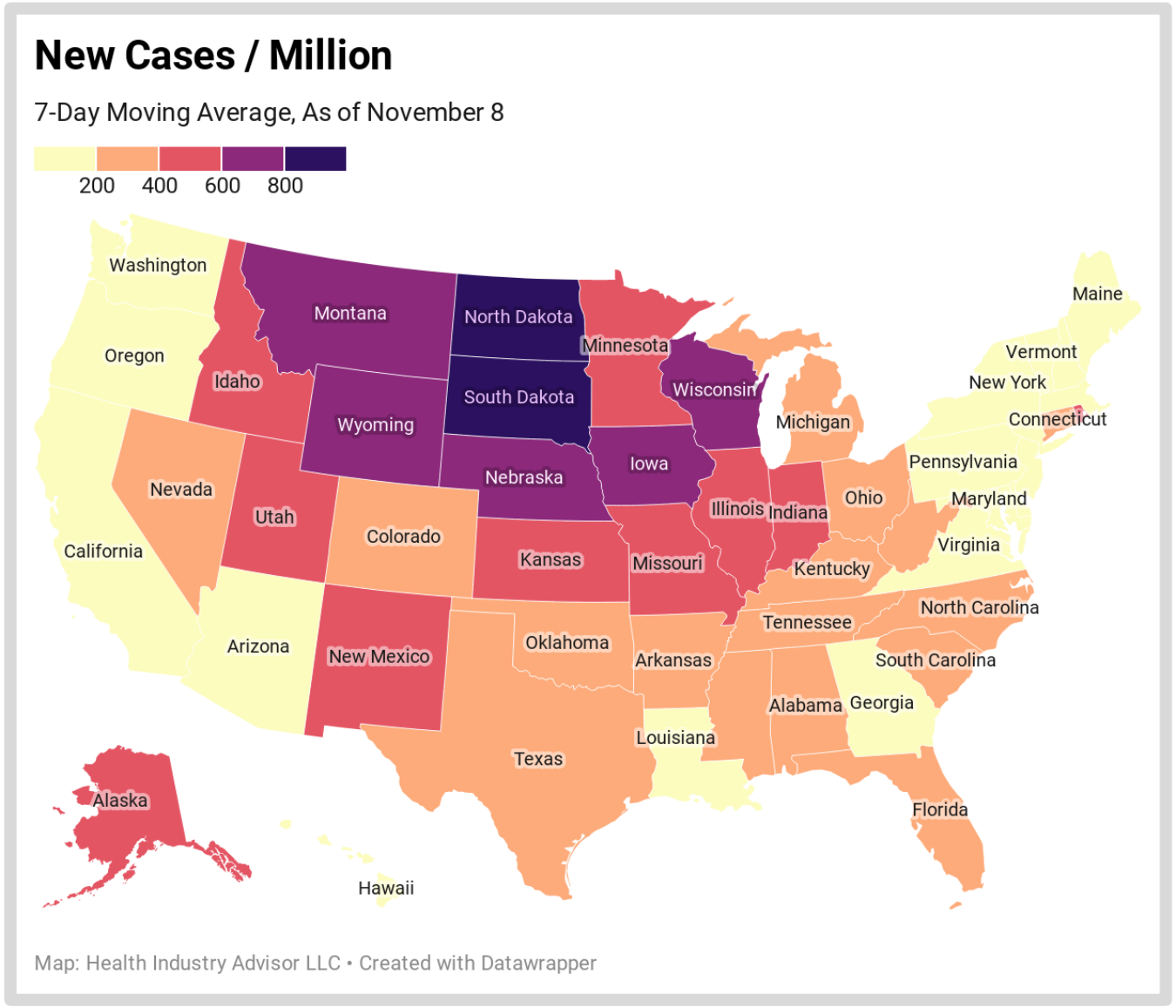
The highest current new infection rates per capita are found in the Upper Midwest and Mountain States

Coastal states and those in the South are seeing lower rates



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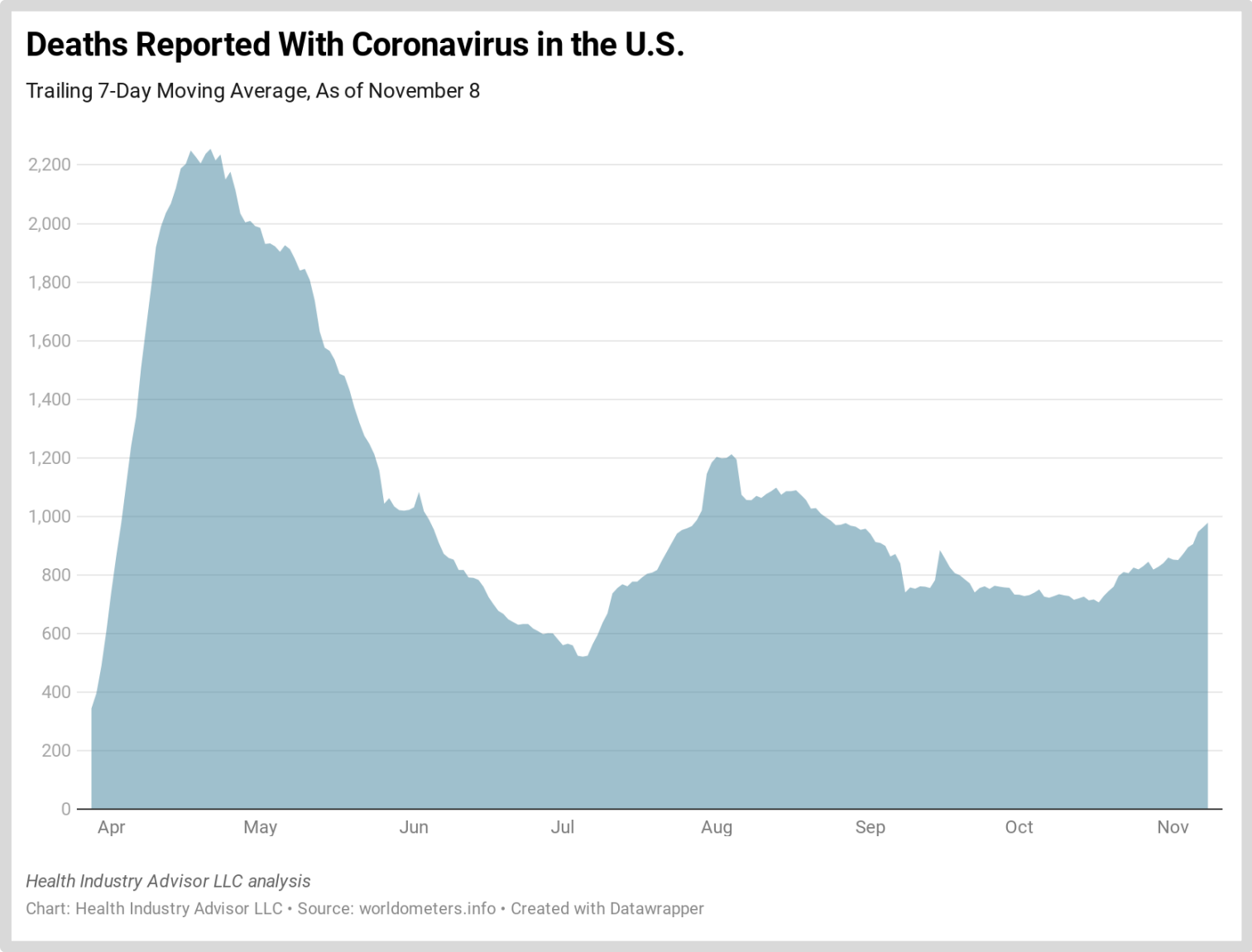
The recent uptick in newly-detected cases is is resulting in increased deaths:

The 7-day average deaths per day has generally been higher from mid-October to now than from early-September through early October



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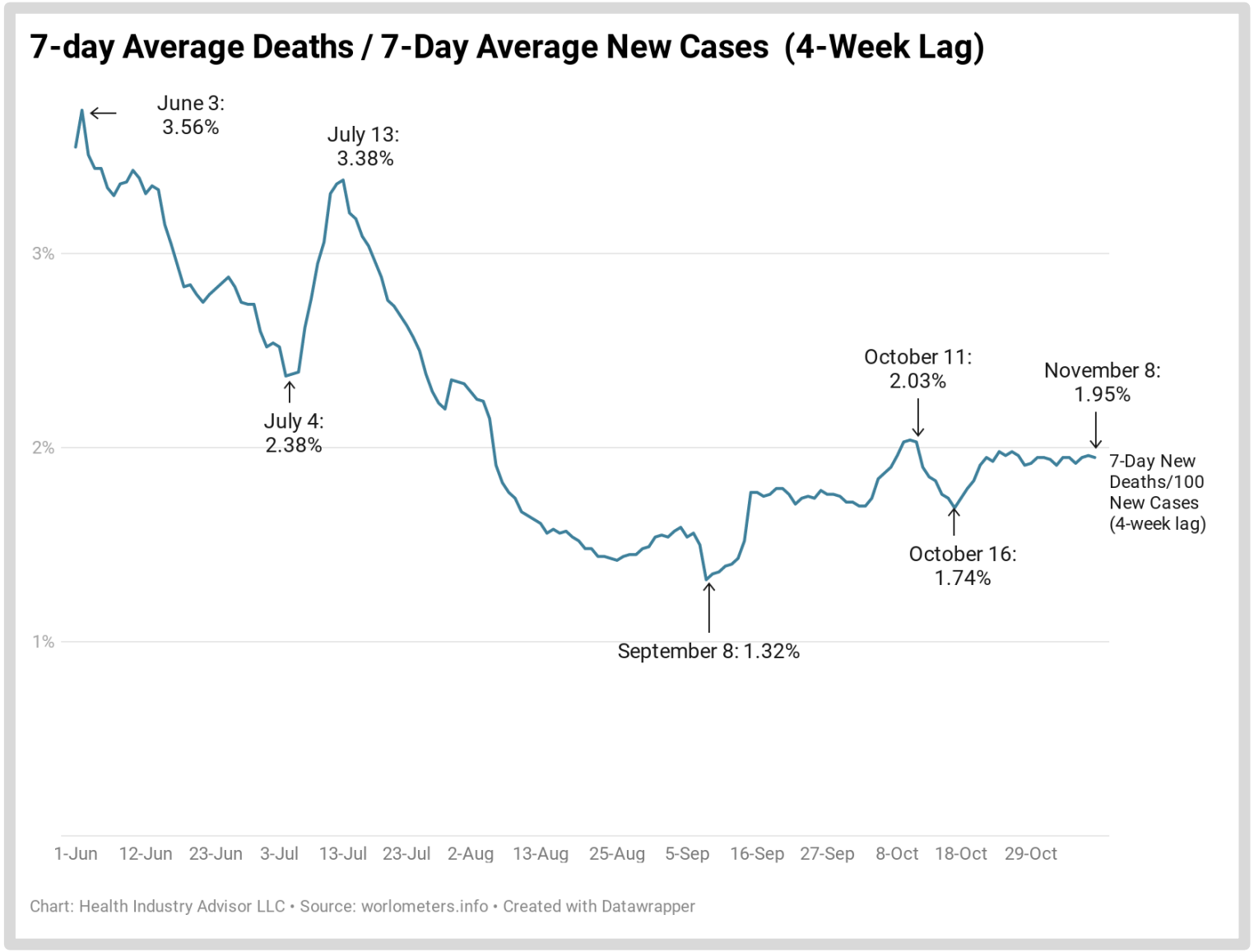
Deaths with coronavirus, relative to new cases (lagged 4 weeks) have moved within a narrow range for the past month

This rate declined rapidly in July and August



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Data Sources

The following data sources are accessed on a daily or weekly basis:

- The Atlantic's Covid Tracking Project: https://covidtracking.com
- Worldometers.info: https://www.worldometers.info/coronavirus/
- Centers for Disease Control, National, Regional, and State Level Outpatient Illness and Viral Surveillance https://gis.cdc.gov/grasp/fluview/fluportaldashboard.html
- Centers for Disease Control, COVID-19 Laboratory-Confirmed Hospitalizations https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html
- Centers for Disease Control, COVID Data Tracker https://www.cdc.gov/covid-data-tracker/index.html#mobility
- Institute for Health Metrics and Evaluation, COVID-19 estimate downloads http://www.healthdata.org/covid/data-downloads
- New York Times, Covid-19 data https://github.com/nytimes/covid-19-data
- COVID-19 Data Repository by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University https://github.com/CSSEGISandData/COVID-19
- COVID-19 Projections Using Machine Learning, https://covid19-projections.com

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