

Breakthrough COVID-19 Cases on the Rise: Still Rare for Vaccinated People

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Abstract: In patients known to be fully vaccinated for COVID-19, breakthrough infections and hospitalizations remain rare; highest in the most vulnerable.

On June 29, 2021, we reported that 0.049% of patients fully vaccinated for COVID-19 developed a breakthrough COVID infection.¹ This data included 8,662,367 fully vaccinated patients, of which 4,260 had a breakthrough COVID case. Patients were considered “fully vaccinated” 14 days after completing a manufacturer-recommend COVID-19 vaccination series (i.e., 14 days after the second dose of Pfizer-BioNTech, the second dose of Moderna, or the first dose of J&J/Janssen). Breakthrough cases were defined as those with a positive PCR-based SARS-CoV-2 test result and/or a COVID-19 diagnosis at least 14 days following the final dose in the series. The initial data included patients who were fully vaccinated on or before May 9, 2021.

As of October 13, 2021, the rate of breakthrough cases has risen to 1.15%. Out of the 19,514,682 patients who are fully vaccinated, 223,965 had a breakthrough case (1.15%), 22,822 were hospitalized (0.12%), and 2,752 died (0.014%). This is a similar rate of breakthrough hospitalizations and deaths as we reported in June—about 10% of breakthrough cases are hospitalized, and about 10% of those hospitalized die in the hospital.

Figure 1: COVID-19 Breakthrough Cases, Hospitalizations, Deaths

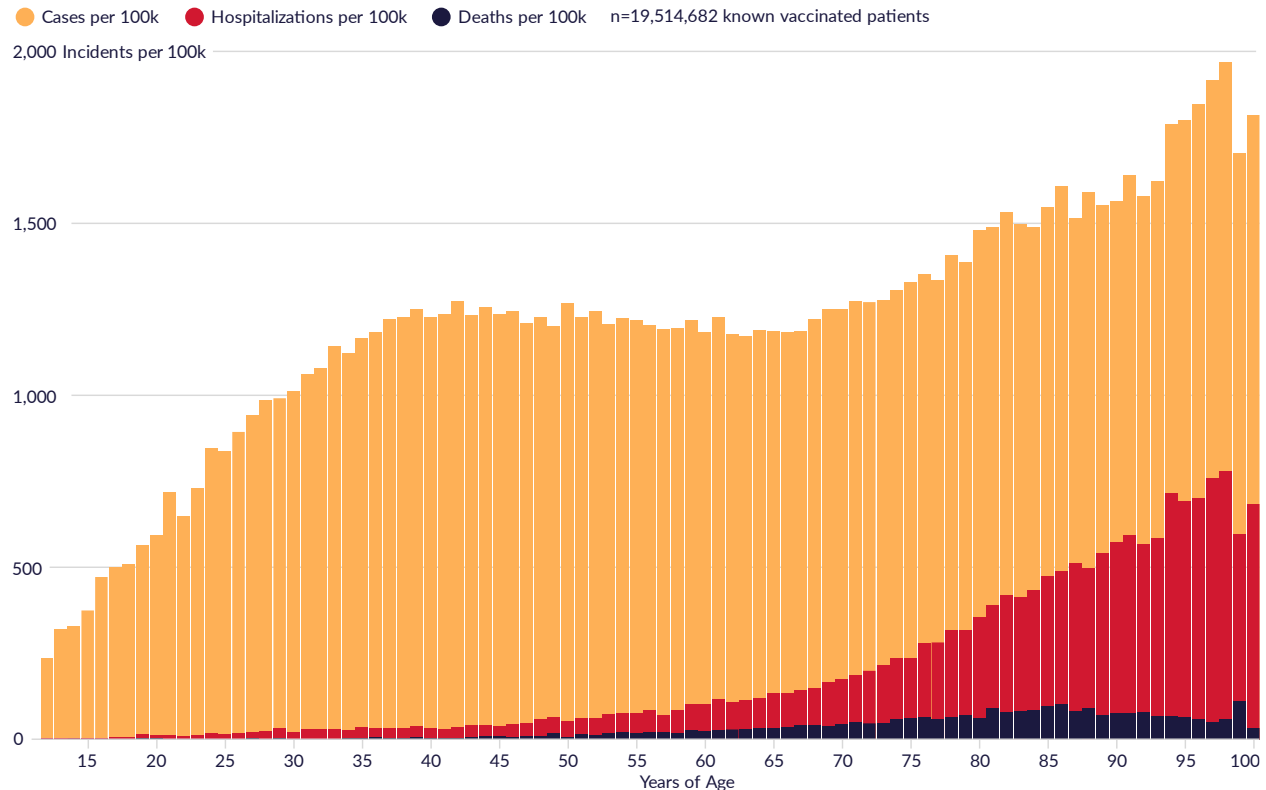
Vaccinated Individuals	Breakthrough Cases	Breakthrough Hospitalizations	Breakthrough Deaths
19,514,682	223,965 (1.15%)	22,822 (0.12%)	2,752 (0.014%)

“COVID-19 Breakthrough Cases, Hospitalizations, Deaths,” 2021. Epic Health Research Network (EHRN.org)

Figure 1: Breakthrough cases, hospitalizations, and in-hospital deaths out of 19,514,682 patients known to be fully vaccinate.

Patients over age 65 were more likely to have breakthrough cases and more likely to require hospitalization, as shown in Figure 2. The median age of patients with breakthrough cases was 57 years, whereas the median age for patients with breakthrough hospitalizations or in-hospital death was 72 years and 76 years, respectively.

Figure 2: COVID-19 Breakthrough Age Distribution



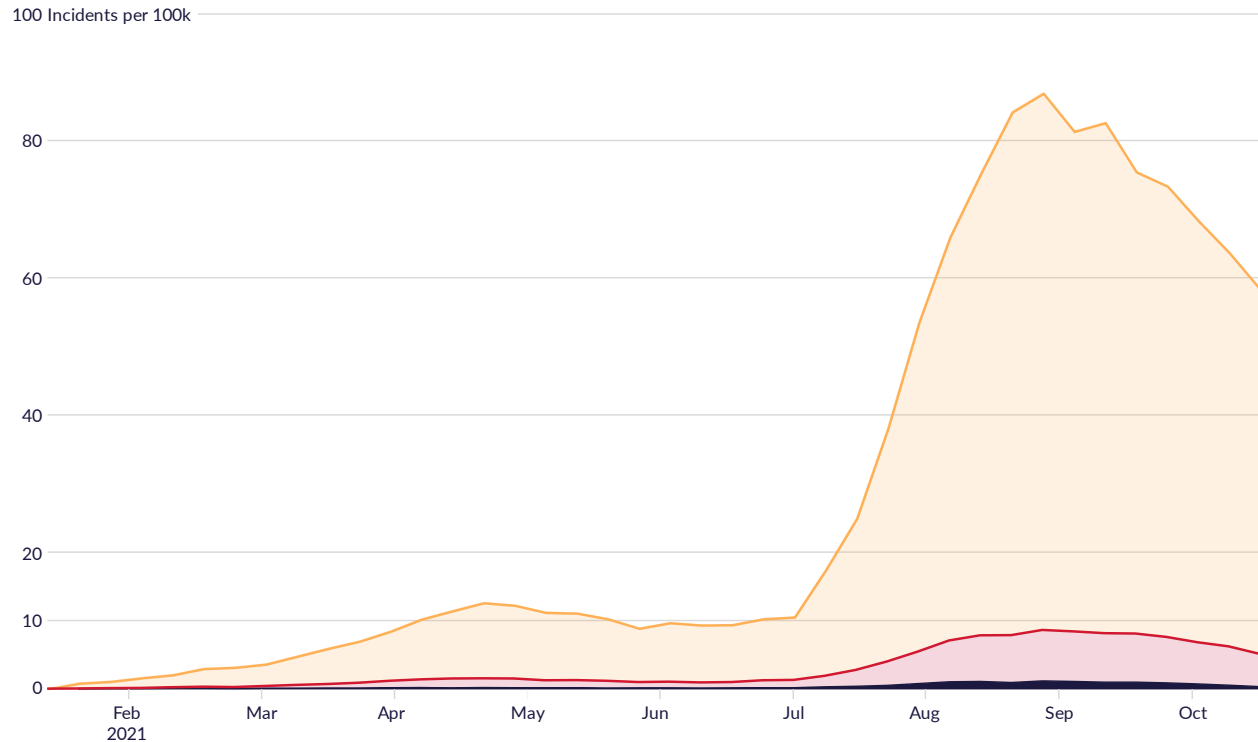
"COVID-19 Breakthrough Age Distribution," 2021. Epic Health Research Network (EHRN.org)

Figure 2: Rate of COVID-19 breakthrough cases, hospitalization, and in-hospital deaths per 100,000 fully vaccinated patients, by age distribution. Older patients who experienced breakthrough cases were more likely to require hospitalization or to die in the hospital.

While the proportion of breakthrough cases is still very low, we are seeing an increasing rate of breakthrough cases since July 2021, as shown in Figure 3. One reason for the increased breakthrough rate is the current predominance of the delta variant, which is more contagious.² Another likely reason for the increase is waning vaccination immunity in our patient population.^{3,4} This study excludes patients who had a booster vaccine. We expect that as boosters become more prevalent, we will see fewer breakthrough cases.

Figure 3: COVID-19 Breakthroughs by Date

● Cases per 100k ● Hospitalizations per 100k ● Deaths per 100k n=19,514,682 known vaccinated patients



"COVID-19 Breakthroughs by Date," 2021. Epic Health Research Network (EHRN.org)

Figure 3: Rate of COVID-19 breakthrough cases, hospitalizations, and in-hospital deaths per 100,000 fully vaccinated patients, by week between January 17, 2021, and October 13, 2021. Cases significantly increased starting in July 2021, which correlates with the emergence of delta as the predominant variant.³ The dark line across the bottom of the graph represents the deaths per 100k.

We wondered whether the recent increase in breakthrough cases was primarily due to waning immunity or the changing patterns in viral spread starting around July 2021. Figure 4 shows the number of weeks after the last dose of vaccine that a breakthrough case, hospitalization, or death occurred. We see the greatest number of breakthroughs between 22 and 27 weeks (or about 5-6 months) after completing a COVID-19 vaccine series. The decline in number of breakthroughs greater than 30 weeks after vaccination can be attributed to the smaller number of vaccinated individuals that had their last vaccine dose prior to April 2021, as the vaccine was not yet widely available at that time.

Figure 4: COVID-19 Breakthroughs by Weeks Since Last Vaccine Dose

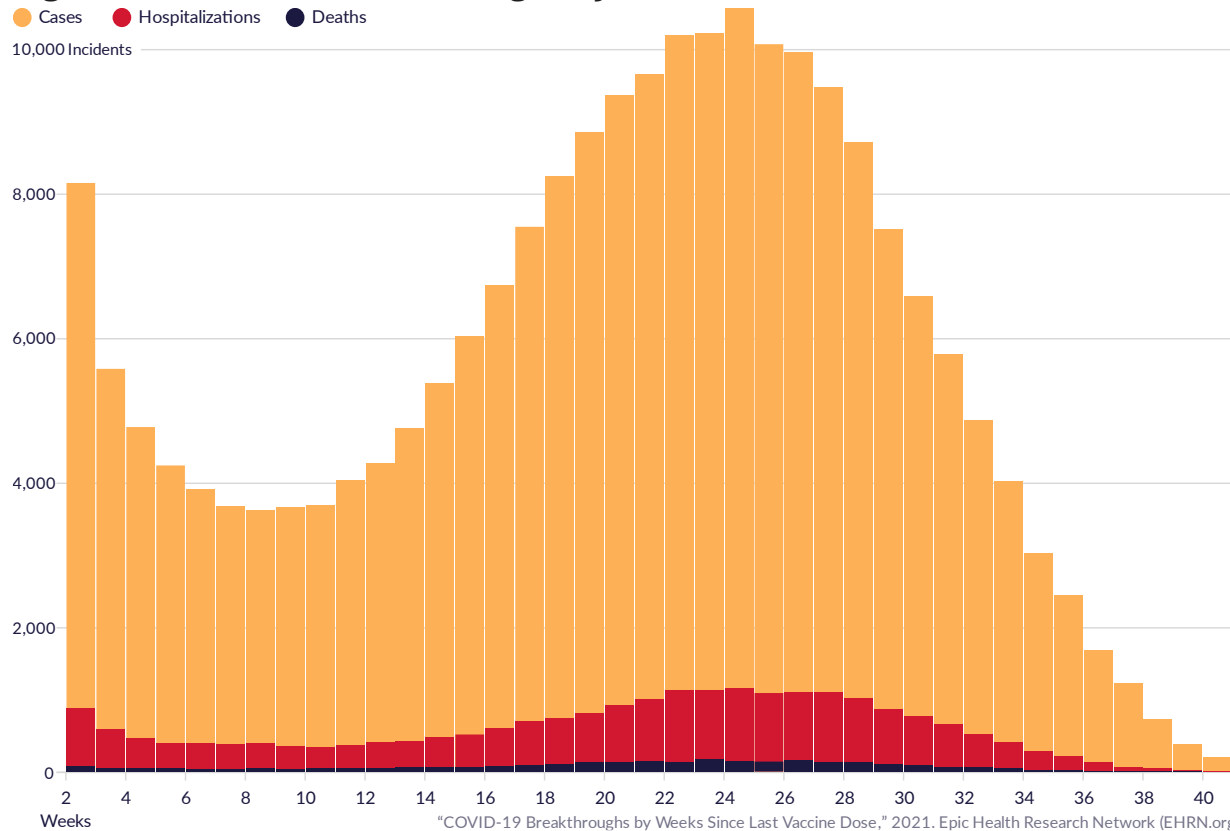


Figure 4: Weekly counts of COVID-19 breakthrough cases, hospitalizations, and in-hospital deaths by number of weeks since final vaccine dose. We start at 2 weeks past the last vaccine dose, as that is when an individual is considered fully vaccinated.

Taking figures 3 and 4 together, it appears that the rate of increase in breakthroughs is correlated both with the emergence of delta as the predominant variant and with waning vaccine immunity. Local rates of social distancing and masking also affect these numbers, as do variations in local vaccination rates and the number of COVID cases overall. The Wall Street Journal also published on these findings; read their article [here](#).

These data come from Cosmos, a HIPAA-Limited Data Set of more than 120 million patients from 141 Epic organizations including 832 hospitals and 13,421 clinics, serving patients in all 50 states.

References

1. Little D, Allen S. Vaccine Victory: Hospitalization for COVID-19 After Receiving a Vaccine Very Rare. Epic Health Research Network (EHRN). Published online Jun 29, 2021. <https://www.ehrn.org/articles/vaccine-victory-hospitalization-for-covid-19-after-receiving-a-vaccine-very-rare>
2. CDC COVID Data Tracker. Variant Proportions. Accessed Sept 21, 2021. <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>.

3. CDC ACIP Meeting, September 23, 2021. Evidence to Recommendation Framework Pfizer-BioNTech COVID-19 Booster Dose. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-9-23/03-COVID-Oliver.pdf>
4. CDC ACIP Meeting, October 20, 2021. COVID-19 Vaccine Effectiveness for Moderna and Janssen Vaccines. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/10-COVID-jones-508.pdf>

Data Definitions

Term	Definition
Study period	December 11, 2020 through October 13, 2021
Fully vaccinated patient	A patient who received manufacturer-recommend dosing for COVID-19 vaccination is considered fully vaccinated after 14 days have passed since the patient's last dose in the series. We have vaccination data for a patient if the vaccine was given at an organization that contributes to Cosmos or if the patient had an encounter with a healthcare system that prompted the automatic reconciliation of vaccination from outside sources, such as the state vaccination registry, into the EHR of an organization that contributes to Cosmos. We also capture data that a patient reports to their health system directly.
Manufacturer recommendations for timing	Moderna: Two doses, at least 28 days apart. Pfizer: Two doses, at least 21 days apart. Johnson & Johnson: 1 dose
COVID-19 breakthrough case	A PCR-based SARS-CoV2 test result of positive and/or a COVID-19 diagnosis after being fully vaccinated.
PCR-based SARS-CoV2 test	A final result for one of the lab tests for SARS-CoV-2, with a lab value that could be interpreted definitively as Positive or Negative. LOINC codes include: 943068, 943076, 943084, 943092, 943100, 943118, 943126, 943134, 943142, 943159, 943167, 945006, 945022, 945097, 945105, 945113, 945311, 945329, 945337, 945345, 945584, 945592, 945659, 946392, 946400, 946418, 946426, 946434, 946442, 946459, 946467, 946475, 946608, 947457, 947465, 947564, 947572, 947580, 947598, 947606, 947630, 947648, 947655, 947663, 947671, 948190, 948224, 948455, 952093, 954065, 954099, 954248, 954255, 955211, 955229, 956086, 956094, 958231, 958249, 958264, 959700, 959718, 959726, 959734, 959742, 960914, 960948, 961193, 961201, 961219, 961227, 961235, 964486, 967414, 967513, 967521. Test Date: Date when the sample was collected; the date the test was resulted is used when the collection date is not available.
COVID-19 diagnosis	ICD-10-CM: U07.1
Hospital admission	A hospital admission during which the patient had a COVID-19 diagnosis OR a hospital admission with any respiratory diagnosis that happened within 14 days following the patient's COVID-19 start date. Respiratory Diagnosis Codes: J00-J99 (ICD-10-CM)

**Emergency Use
Authorization dates**

Moderna: December 18, 2020
Pfizer: December 11, 2020
Johnson & Johnson: February 27, 2021