

INTRODUCTION

- Real-world evidence (RWE) generated using real-world data (RWD) can be used to fill knowledge gaps in routine care and inform healthcare access decisions.¹
- The emergence of coronavirus disease 2019 (COVID-19) drastically shifted treatment seeking behavior and subsequent diagnosis, treatment, and healthcare utilization activity.²
- However, there are no accepted guidelines for adjustments in retrospective studies using RWD from the COVID-19 pandemic.
- The aim of this study was to assess and describe to what extent published retrospective database studies accounted for the COVID-19 pandemic.**

METHODS

- A targeted literature review (TLR) was conducted using OVID (Embase and MEDLINE) to identify studies published between January 2022 and June 2023.
- Search terms included:
 - Terms to identify utilization, persistence, prescribing patterns, adherence, burden, or economics in the title, AND
 - Terms to identify electronic medical records, electronic health records, or claims in the title, MeSH or Emtree.
- Two reviewers screened abstracts for relevance; a third reviewer was engaged in case of discordance.
 - Eligibility was determined by predefined population, intervention, comparison, outcome, and study design (PICOS) criteria (**Table 1**).
- Data were extracted for all eligible English-language publications with a study period that extended through the end of 2019 or later.
- Full-text articles were reviewed to identify methodological approaches used to account for potential confounding from the COVID-19 pandemic.

Table 1. PICOS criteria

Criteria	Inclusion Criteria
Population	Any population without restriction
Intervention	Any intervention without restriction
Comparator	Any comparison (independent or dependent) without restriction
Outcomes	Including economic outcomes, specifically healthcare resource utilization (HCRU) or costs
Study design	Primarily a retrospective design Analysis of real-world secondary data sources (electronic medical records [EMR], claims)
Other criteria	English language Non-missing abstract Full journal article Study data ending ~December 2019 or later

RESULTS

- Of 111 reviewed papers,
 - 53 publications excluded the COVID-19 pandemic period (**Figure 1**).
 - 5 studies stated a rationale of avoiding changes in healthcare activity and associated costs due to the pandemic (**Table 2**).
 - The remaining 48 publications did not provide a rationale or mention COVID-19.
- 58 publications had data periods that overlapped with the COVID-19 pandemic (**Figure 2**).
 - 11 publications acknowledged the impact of the pandemic on their findings (**Table 3**).
 - One publication (Mesa-Frias et al.) conducted specific analyses (i.e., a sensitivity analysis excluding the COVID-19 period) to assess the impact and account for the pandemic.
 - The remaining 46 publications made no mention of the pandemic, or any methods implemented to assess or address its potential impact on study results.
 - 34 studies used EMR data, 14 used claims data, 8 used data from a single institute and 2 used other data sources.
 - 35 studies reported data from 2020, 18 studies from 2020-2021, 4 studies from 2020-2022 and 1 study from 2020-2023.
 - There was a large range of therapy areas including chronic kidney disease, dermatologic conditions, mental health, multiple sclerosis and oncology.

DISCUSSION

- The impact of the significant shift in HCRU on short- and long-term outcomes in the RWD during the pandemic (2020 onwards) should be accounted for in retrospective database studies.
- Some methods to account for the potential confounding from the COVID-19 pandemic could include:¹⁹
 - Describing the study population at multiple time points relative to the pandemic.
 - Handling the data collected during the pandemic separately.
 - Adjusting for additional factors that may be impacted by the pandemic (e.g., type of care received, diagnosis or evidence of COVID-19, geographic location of patients).
 - Using alternative definitions of outcomes to address differences in pre- and post-pandemic data.

CONCLUSIONS

Overall, most retrospective studies of economic outcomes did not mention or account for the COVID-19 pandemic. In the limited studies that referenced COVID-19, only one study utilized specific methodology to mitigate potential confounding related to the pandemic.

Figure 1. Publications excluding COVID period

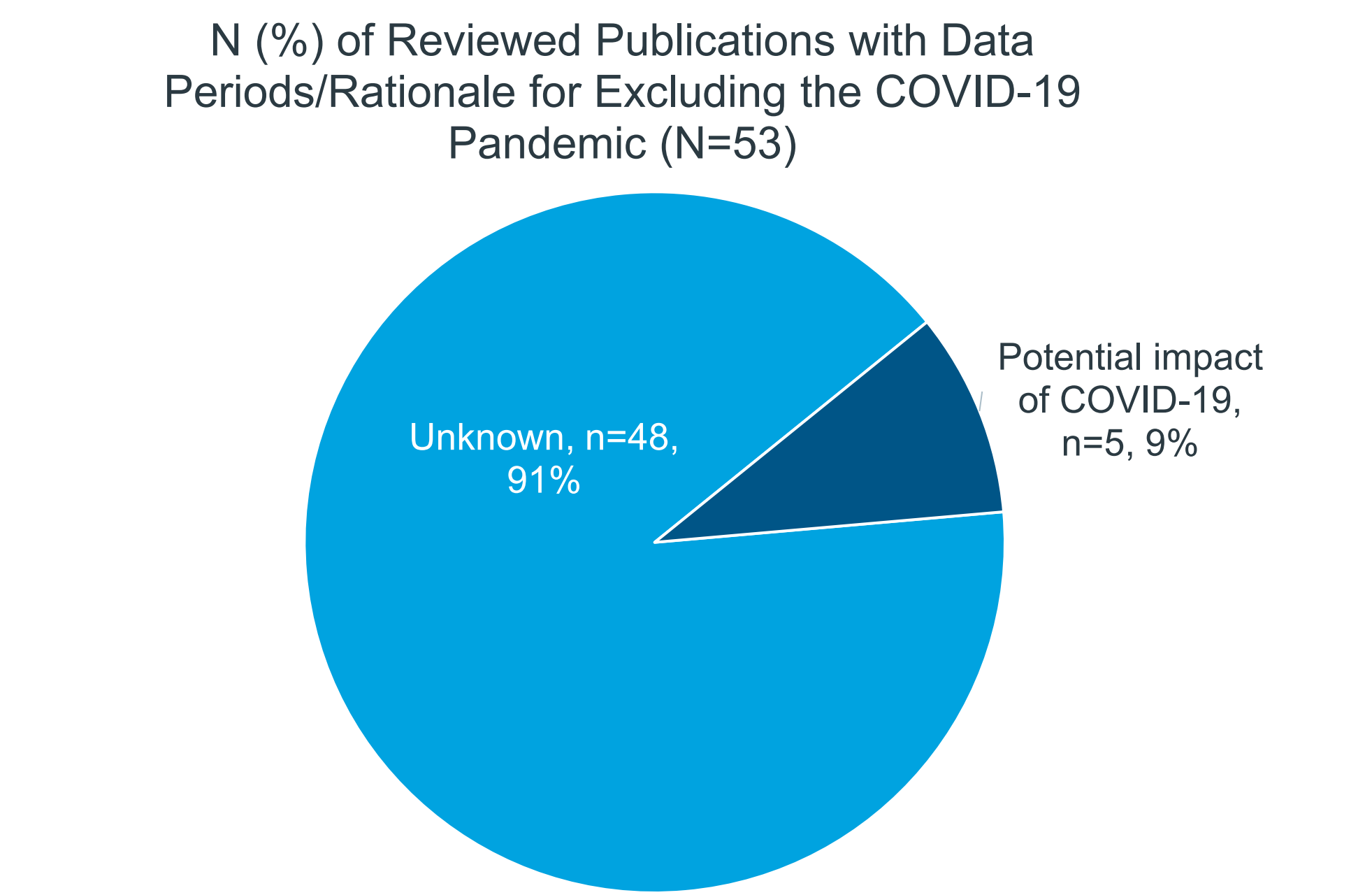


Figure 2. Publications overlapping with COVID period

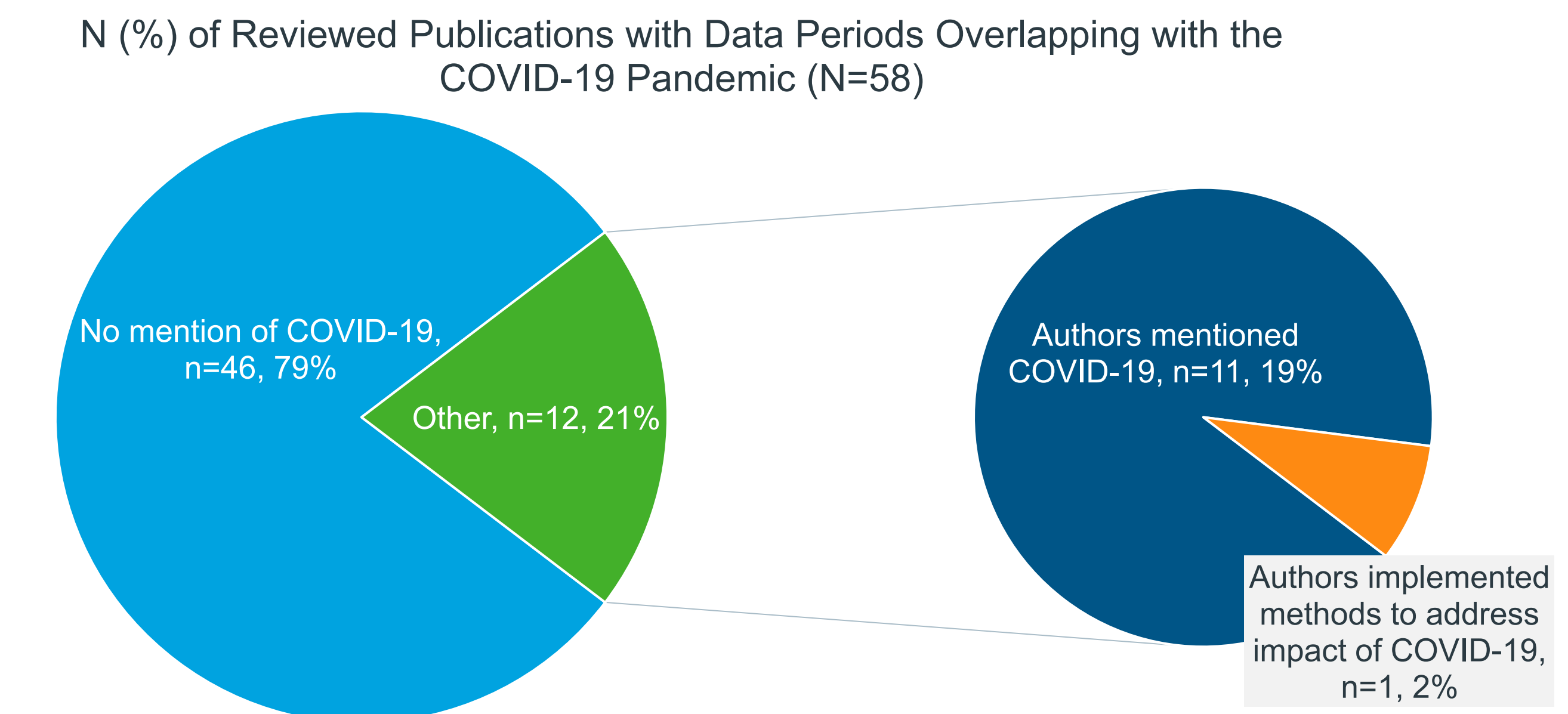


Table 2. Publications Ending Prior to COVID-19 period with Rationale

Citation	Rationale
[3] Mohan A et al	"The time course was chosen prior to Covid-19 pandemic and the current market to avoid the widespread and often unpredictable swings that have occurred over the past few years."
[4] Haun JN et al	"We enacted a COVID-19 crossover restriction to not examine cost data after March 1, 2020. This restriction was enacted to minimize the impact of reduced healthcare seeking behavior during height of the pandemic and government shutdowns. Specifically, in March 2020, in-person THRIVE groups were temporarily suspended, while THRIVE transitioned to a telehealth model. Non-emergency care went through a similar transition. While this could introduce bias, the inclusion of patients that potentially changed healthcare seeking behavior due to the pandemic may produce a false positive result of the intervention (healthcare savings)."
[5] Ehrlich AL et al	"Because the aim of this study was to examine cost outcomes, the year 2020 from our original study was excluded due to drastic and unpredictable changes in cost following the start of the COVID-19 pandemic."
[6] Halpin DMG et al	"Of note, the entire study period encompassing both baseline and follow-up was prior to the start of the COVID-19 pandemic, due to uncertainty in how patients were accessing healthcare during this period."
[7] Requeña G et al	"The follow-up period did not extend beyond the 31st December 2019 to exclude the COVID-19 pandemic and avoid any changes to the data expected due to that period."

Table 3. Publications Overlapping with COVID-19 period with COVID-19 Acknowledgement

Citation	Text acknowledging the COVID-19 pandemic
[8] Abdelmeseh V et al	"Lastly, biosimilar uptake has been gradual due to more pressing priorities, namely the coronavirus disease 2019 (COVID-19) pandemic."
[9] Breda K et al	"The Geriatric Fracture Program, implemented in a mixed practice health system, resulted in sustained improved inpatient outcomes, reduced costs of care, and was shown to be sustainable through stressors, such as the Covid-19 pandemic. Of note, we found that although clinicians ordered DEXA scans for 42% of patients during or after the follow-up visit throughout the program, only 22% of patients had a completed scan within six months. There could be numerous reasons for these findings, including patient fears of the diagnosis of osteoporosis, fears of infection from Covid-19 during the pandemic surges in 2020 and 2021 leading to avoidance of in-person imaging visits, a lack of perceived urgency from the patient perspective of the need for a DEXA scan, transportation challenges for the appointment, or the patient may have a primary care physician outside of the health system and the scan was completed but not in the health system's electronic health records. We found that inpatient clinicians and outpatient geriatricians faced numerous challenges in providing care. Several years of the GFP overlapped with the Covid-19 pandemic."
[10] Carson JS et al	"The increased patient throughput is of particular interest in the context of the COVID-19 pandemic, given that severe labor shortages increase the value of reducing LOS, and in turn, the diminishing labor hours associated with a given healthcare encounter."
[11] Chen K et al	"This period represents when local COVID cases were past initial peak and telehealth visits were available to patients electively instead of preferentially."
[12] Ferris H et al	"A slight reduction in incidence was seen in 2020 during the COVID 19 pandemic."
[13] Kwon C et al	"In particular, the decrease in the number of patients in 2020 may be because of a decrease in the total number of patients visiting hospitals owing to social distancing and fear of infection due to COVID-19."
[14] Mesa-Frias M et al	"Sensitivity analyses were conducted to exclude the COVID-19 period (i.e., from March 1, 2020, to end of data availability)." ... "However, data for the last season available should be interpreted with caution, since this season overlapped with the onset of the COVID-19 pandemic in the United States (March 2020). This overlap in timing may have resulted in a decrease in RSV incidence after the pandemic started because of quarantine rules and increased awareness regarding protection against respiratory infections."
[15] Ngu NLY et al	"It is unclear the impact of the COVID-19 pandemic on both ours and international cohorts of patients reporting particularly in Melbourne, Victoria where the lockdown strategy was particularly prolonged FBI, however, the isolation, rise in mental health issues and substance use disorders may also contribute."
[16] O'Connor S et al	"The COVID-19 pandemic may have impacted the findings from 2020 in this analysis. All sport, including Ladies Gaelic football, was stopped for a period of time that year which may have impacted the injury rate and costs reported in 2020."
[17] Shilane D et al	"Since the onset of the COVID-19 pandemic, telehealth use has grown exponentially, both because of the circumstances of the pandemic and associated changes in policy. The circumstances of the COVID-19 pandemic have exacerbated disparities in telehealth utilization. Patients with a household income below the 25th percentile had a 40% reduced odds of utilizing telehealth during the COVID-19 pandemic. During the initial peak of the COVID-19 pandemic in March and April of 2020, significant racial and ethnic disparities in telehealth utilization were observed in New York City."
[18] Zhao Y et al	"Despite a considerable decrease in patients in 2020, there was less decline in the lower age group in this study, particularly among children younger than three. One of the explanations was that during the coronavirus disease 2019 (COVID-19) pandemic, parents spent more time with their children which led to earlier detection of symptoms of ASD and a higher incidence of ASD. Previous research found that the COVID-19 pandemic caused children with mental health needs to miss out on opportunities for basic skill development due to the cessation or suspension of therapy courses. We did find tentative evidence that the epidemic may have brought about an increase in early diagnoses. Along with the results mentioned above, we also found a strong relationship between physical/mental comorbidities and costs, which was consistent with the findings of previous studies. According to the recent research, the COVID-19 pandemic was associated with an increase in mental health hospitalizations, but we did not find a direct relationship between ASD hospitalization and the epidemic in this study."

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