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Incidence and outcomes of eating disorders during the COVID-19 pandemic

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16 **Abstract**

17 There are concerns that eating disorders have become commoner during the COVID-19 pandemic.

18 Using the electronic health records of 5.2 million people aged under 30, mostly in the USA, we show

19 that the diagnostic incidence was 15.3% higher in 2020 overall compared to previous years (relative

20 risk 1.15 [95% CI: 1.12-1.19). The relative risk increased steadily from March 2020 onwards,

21 exceeding 1.5 by the end of the year. The increase occurred solely in females, and primarily affected

22 teenagers and anorexia nervosa. A higher proportion of eating disorder patients in 2020 had suicidal

23 ideation (hazard ratio [HR]: 1.30 [1.16-1.47] or attempted suicide (HR: 1.69 [1.21-2.35]).

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25

26   An increased incidence of eating disorders during the COVID-19 pandemic has been reported but not

27   accurately or robustly quantified[1–3]. Referrals for eating disorders have doubled in the UK[4]. This study

28   used electronic health records (EHR) to assess the relative incidence and outcomes (in terms of

29   suicidal attempt, ideation, and death) of eating disorders during the COVID-19 pandemic compared to

30   previous years.

31   **Methods**

32   We used TriNetX Analytics, a federated EHR network with anonymized data from 81 million

33   patients, 93% of whom are in the USA. The participating health care organizations are a mixture of

34   hospitals, primary care, and specialist providers, and include insured and uninsured patients. For

35   further details about TriNetX see the Supplement, and ref. 5.

36

37   The incidence of a first diagnosis of eating disorder (ICD-10 code F50) was estimated for every 2-

38   month period between January 20, 2020 (the date of the first recorded COVID-19 case in the USA)

39   and January 19, 2021 in patients under 30 years-old who made at least one healthcare visit during this

40   time. The incidence was compared to those in corresponding periods in 2019 using χ^2 tests. Stratified

41   results by age, sex, and subcategories of eating disorder are provided. We also compared the 2020

42   data with 2017 and with 2018. In a sensitivity analysis, patients were only included if they also made

43   a healthcare visit between January 20, 2021 and April 28, 2021 (or the same period in 2020 for

44   comparison) thus guaranteeing that they were not lost to follow up.

45

46   We assessed whether a diagnosis of COVID-19 (ICD-10 U07.1) was associated with a higher risk of

47   subsequent eating disorders compared to a cohort of patients who had made a healthcare visit for

48   another reason (matched for timing of the visit [in 2-month strata], demographics, and risk factors for

49   COVID-19; see Supplementary Methods).

50

51   The risk of suicide ideation, attempt, and death within 6 months of an eating disorder diagnosis during

52   the pandemic was compared with the previous three years using Kaplan-Meier analysis. For further

53   details of analyses, see Supplementary Methods. STROBE reporting guidelines were followed.

54

55   **Results**

56   5,186,451 patients met the inclusion criteria (55.3% female, 44.4% male, 0.3% other; mean [SD] age:

57   15.4y [8.98]). 8,471 people were diagnosed with an eating disorder in the defined pandemic period

58   (78.1% female, mean [SD] age 16.2y [7.2], and 19,843 (75.4% female; mean [SD] age 16.3y [7.6])

59   during the prior three years. For details see Supplementary Table 1.

60

61   The incidence of a first diagnosis of an eating disorder has increased during the pandemic. An overall

62   excess of 15.3% was observed compared to the previous year (relative risk [RR]: 1.15, 95% CI: 1.12–

63   1.19, P<.001; Supplementary Table 2) with significant excesses observed in each 2-month period

64   during the pandemic except for March 20 - May 19, 2020 (Figure 1A). Similar results were found in

65   the sensitivity analysis (RR 1.34, 95% CI 1.29–1.40; significant excess observed for all but March 20-

66   May 19, 2021 periods; P<.001; Supplementary Figure 1). Results were also similar if 2020 was

67   compared to 2017 or 2018 (see Supplementary Table 2). The increased risk of eating disorders during

68   the pandemic period was limited to females (Figure 1B), was greatest for 10-19 year-olds (Figure 1C),

69   and mostly affected anorexia nervosa diagnoses (Figure 1D).

70

71   As shown in Supplementary Table 1 and Supplementary Figure 2, compared to patients diagnosed

72   with an eating disorder in the previous 3 years, those diagnosed during the pandemic were at a higher

73   risk of attempting suicide (0.89% [0.68-1.16] vs. 0.52% [0.43-0.64]; hazard ratio [HR]: 1.69 [1.21-

74   2.35], p=0.0015) and having suicidal ideation (6.3% [5.7-7.0] vs. 4.8% [4.5-5.1]; HR]: 1.30 [1.16-

75   1.47], p<0.001), but death did not differ.

76

77   Patients diagnosed with COVID-19 were not at an increased risk of an eating disorder compared to a

78   matched cohort of patients who made a visit to a healthcare organization for a different reason during

79   the pandemic (adequate matching was achieved for all covariates; Supplementary Tables 3-7; HR

80   0.86, 95% CI: 0.65–1.12, P=0.26, Supplementary Figure 3).

81

82   **Discussion**

83   These data show an increased incidence of eating disorders during the COVID-19 pandemic, and with

84   higher rates of suicidal behavior amongst those diagnosed. After a decrease in the early part of 2020

85   (which likely reflects the marked reduction in all diagnoses made in the EHR network during this

86   period[6]), the incidence of eating disorders increased steadily throughout the rest of 2020, such that the

87   relative risk compared to previous years had exceeded 1.5 by the end of the year (being 1.96 in the

88   primary analysis [Fig. 1A], and 1.59 in the sensitivity analysis [Suppl. Fig. 1]). The mechanisms

89   underlying these observations remain to be determined, though a range of plausible explanations have

90   been proferred.[2] The finding that the increase was seen only in females, and was greater in teenagers

91   and for anorexia nervosa, may help focus future investigations. No increased risk was observed

92   among people diagnosed with COVID-19 infection, unlike many other psychiatric disorders in this

93   EHR network.[5,6]

94

95   The main strength of the study is the use of a large EHR network which permits robust and up-to-date

96   estimates of incidence and relative risk. Limitations include those inherent to EHR studies (e.g., lack

97   of information about the accuracy or completeness of diagnoses; see the Supplement and ref. 5 for

98   discussion). Our findings relate to patients who made a healthcare visit and received a diagnosis, and

99   should not be generalized to the wider population, especially since many patients with eating

100   disorders do not seek treatment.[7] Since most patients were in the USA, findings may not apply in

101   other locations; it was not possible to analyze separately the 7% of patients from other countries.

102   Nationwide studies and prospective cohort studies in different settings are needed to complement

103   these findings, and to assess how the incidence trajectory changes as the pandemic progresses. It is

104   possible that the incidence may continue to rise further if there remains an excess of cases in the

105   community yet to present or receive a diagnosis; alternatively, the incidence might fall if some of the

106   recent excess reflects people whose diagnosis was made earlier than would have otherwise been the

107   case.

108

109   In summary, our findings support the view that the incidence and outcomes of eating disorders have

110   been adversely affected by the COVID-19 pandemic.[1-4,8-10] Services need to be resourced adequately

111   and urgently to deal with the increased demand.

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166   **Figure 1. Incidence of eating disorders during vs. before the COVID-19 pandemic**

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168   A: Incidence of eating disorders in 2-monthly periods during the pandemic (January 20, 2020 to

169   January 19, 2021) compared to previous years (January 20, 2017-2019 to January 19, 2018-2020).

170   The relative risks (RR) and their 95% confidence intervals are provided for each 2-monthly period

171   during the pandemic compared to the same period in 2019. B: Incidence stratified by sex. C:

172   Incidence stratified by age group. D: Incidence stratified by eating disorder subtype. RR in each

173   stratum compared to the corresponding stratum in the previous year. RR>1 indicates a risk that is

174   higher during the pandemic. AN=Anorexia Nervosa, BN=Bulimia nervosa, EDNOS=Eating disorder

175   not otherwise specified.

176

A Incidence by years

B Incidence and relative risk (compared to 2019) by sex

C Incidence and relative risk (compared to 2019) by age

D Incidence and relative risk (compared to 2019) by disorder
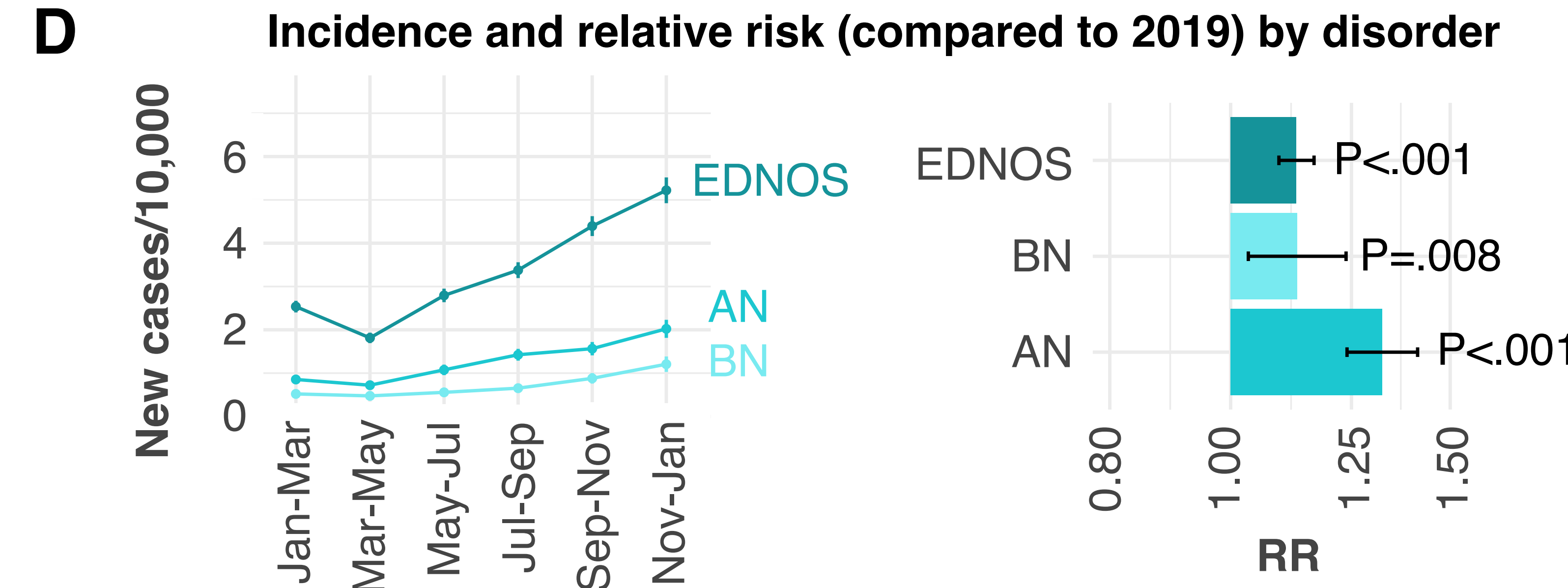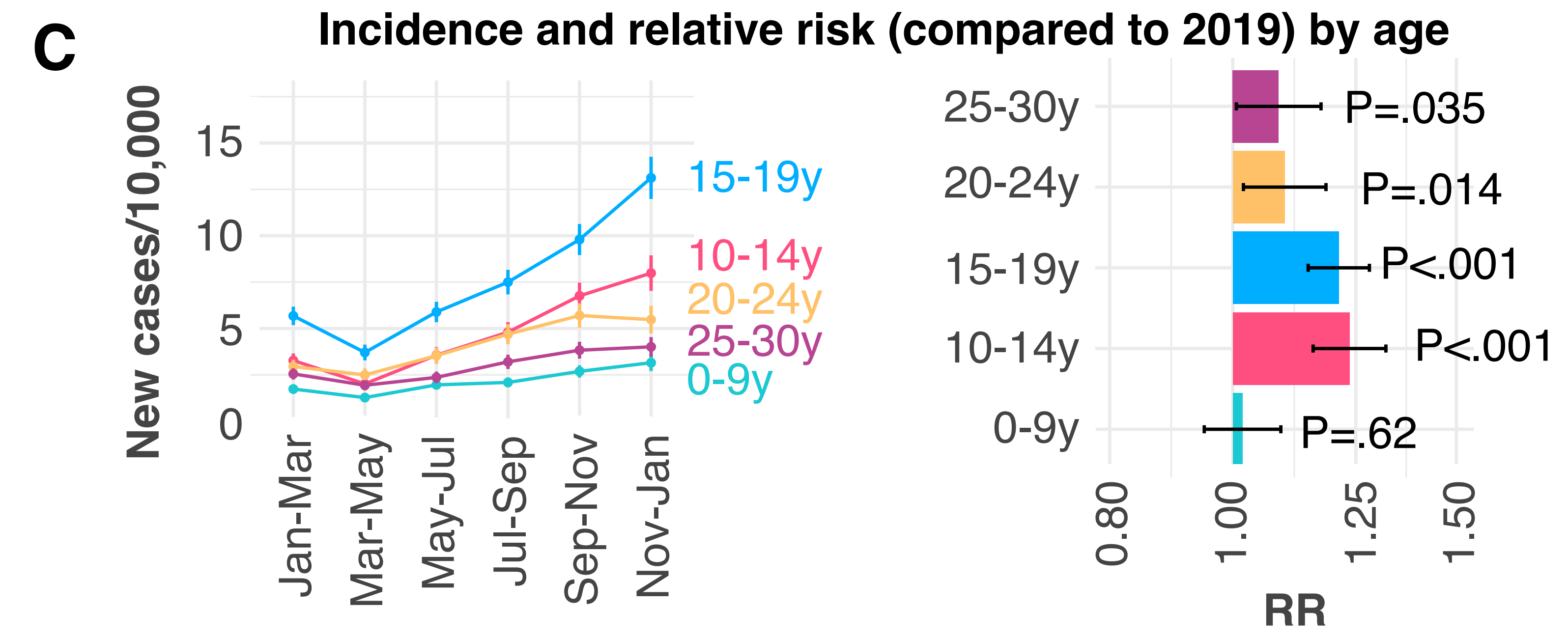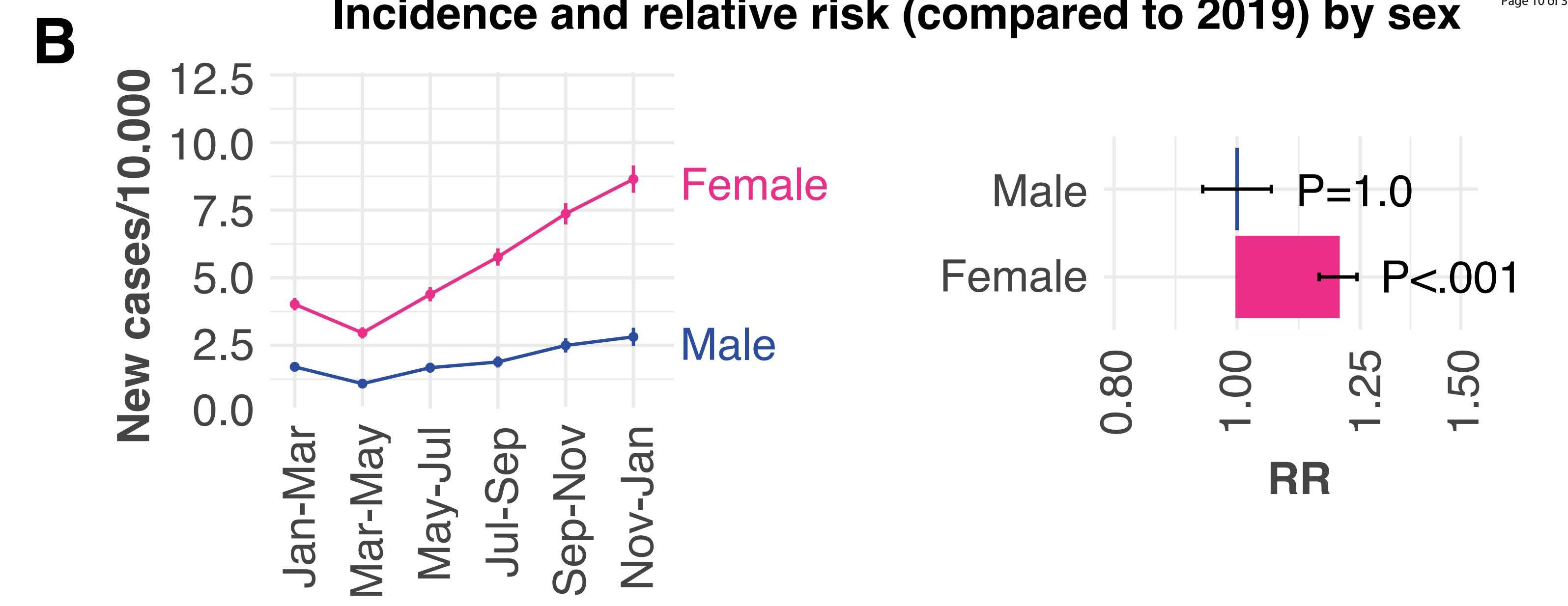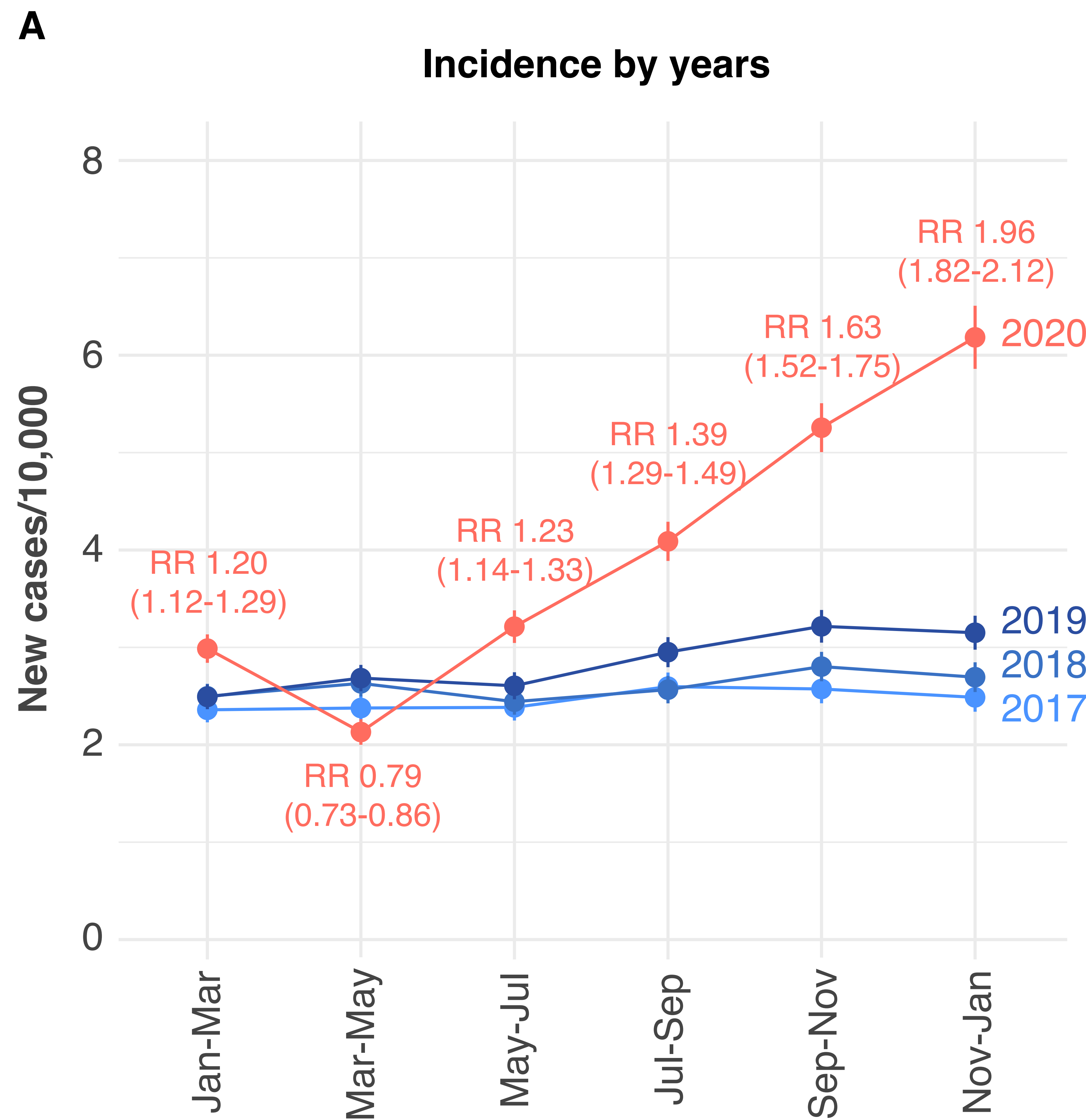
Supplementary material

Supplementary methods

1   TriNetX network

This section provides an expanded version of our previous description of the network[1].

Legal and ethical status

TriNetX's Analytics network is compliant with the Health Insurance Portability and Accountability Act (HIPAA), the US federal law which protects the privacy and security of healthcare data. TriNetX is certified to the ISO 27001:2013 standard and maintains an Information Security Management System (ISMS) to ensure the protection of the healthcare data it has access to and to meet the requirements of the HIPAA Security Rule. Any data displayed on the TriNetX Platform in aggregate form, or any patient level data provided in a data set generated by the TriNetX Platform, only contains de-identified data as per the de-identification standard defined in Section §164.514(a) of the HIPAA Privacy Rule. The process by which the data is de-identified is attested to through a formal determination by a qualified expert as defined in Section §164.514(b)(1) of the HIPAA Privacy Rule. This formal determination by a qualified expert, refreshed in December 2020, supersedes the need for TriNetX's previous waiver from the Western Institutional Review Board (IRB). The network contains data that are provided by participating Health Care Organizations (HCOs), each of which represents and warrants that it has all necessary rights, consents, approvals and authority to provide the data to TriNetX under a Business Associate Agreement (BAA), so long as their name remains anonymous as a data source and their data are utilized for research purposes. The data shared through the TriNetX Platform are attenuated to ensure that they do not include sufficient information to facilitate the determination of which HCO contributed which specific information about a patient.

Acquisition of data, quality control, and other procedures

The data are stored onboard a TriNetX appliance – a physical server residing at the institution's data centre or a virtual hosted appliance. The TriNetX platform is a fleet of these appliances connected into a federated network able to broadcast queries to each appliance. Results are subsequently collected and aggregated.

Once the data are sent to the network, they are mapped to a standard and controlled set of clinical terminologies and undergo a data quality assessment including 'data cleaning' that rejects records which do not meet the TriNetX quality standards. HIPAA compliance of the clinical patient data is achieved using de-identification. Different data modalities are available in the network. They include demographics (coded to HL7 version 3 administrative standards), diagnoses (represented by ICD-10-CM codes), procedures (coded in ICD-10-PCS or CPT), measurements (coded to LOINC), and medications (coded with the VA Formulary). While extensive information is provided about patients' diagnoses and procedures, other variables (such as socioeconomic and lifetime factors are not comprehensively represented).

The data from a typical HCO generally go back around 7 years, with some going back 13 years. The data are continuously updated. HCOs update their data at various times, with most refreshing every 1, 2, or 4 weeks.

The data come primarily (>93% of patients) from HCOs in the USA, with the remainder coming from India, Australia, Malaysia, Taiwan, Spain, UK, and Bulgaria. As noted above, to comply with legal frameworks and ethical guidelines guarding against data re-identification, the identity of participating HCOs and their individual contribution to each dataset are not disclosed to researchers.

Data quality assessment followed a standardised strategy wherein the data are reviewed for conformance (adherence to specified standards and formats), completeness (quantifying data presence or absence) and plausibility (believability of the data from a clinical perspective). There are pre-defined metrics for each of the above assessment categories. Results for these metrics are visualised and reviewed for each new site that joins the network as well as on an ongoing basis. Any identified issue is communicated to the data provider and resolved before continuing data collection.

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The basic formatting of contributed data is also checked (e.g. to ensure that dates are properly represented). Records are checked against a list of required fields (e.g., patient identifier) and rejects those records for which the required information is missing. Referential integrity checking is done to ensure that data spanning multiple database tables can be successfully joined together. As the data are refreshed, changes in volume of data over time is monitored to ensure data validity. At least one non-demographic fact for each patient is required for them to be counted in the dataset. Patient records with only demographics information are discarded.

The software also undergoes quality control. The engineers testing the software are independent from the engineers developing it. Each test code is checked by two independent testing engineers. Each piece of software is tested extensively against a range of synthetic data (i.e. generated for the purpose of testing) for which the expected output is established independently. If the software fails to return this output, then the software is deemed to have failed the test and is examined and modified accordingly. For statistical software (including that used for propensity score matching, for Kaplan-Meier analysis, etc), an additional quality control step is implemented. Two independent codes are written in two different programming languages (typically R and python) and the statistical results are compared. If discrepancies are identified, then the codes are deemed to have failed the test and are examined and modified accordingly. All the code is reviewed independently by another engineer.

The test strategy follows three levels of granularity:

1. Unit tests: These test specific blocks, or units, of code that perform specific actions (e.g. querying the database).
2. Integration tests: These ensure that different components are working together correctly.
3. End-to-end tests: These tests run the entire system and check the final output.

Some comments on advantages and disadvantages of EHR data

The advantage of EHR data, like those in TriNetX, over insurance claim data is that both insured and uninsured patients are included. An advantage of EHR data over survey data is that they represent the diagnostic rates in the population presenting to healthcare facilities. This provides an accurate account of the burden of specific diagnoses on healthcare systems. The downside of relying on diagnoses is that they obviously do not account for undiagnosed patients who might be suffering from the illness but did not seek medical attention (or in whom the diagnosis was missed). A general limitation of EHR data is that a patient may be seen in different HCOs for different parts of their care and if one HCO is not part of the federated network then part of their medical records may not be available. Using a network of HCOs (rather than a single HCO) limits this possibility but does not fully remove it. Finally, historical data before the start of EHRs (or the addition of an HCO to the network) may be incomplete.

2   Cohorts definition

2.1   Assessing the relative incidence of eating disorder during the pandemic vs. before

To assess the relative incidence of eating disorders during the pandemic compared to previous years, 4 cohorts were defined: one cohort of interest and 3 comparison cohorts.

The cohort of interest consisted of all patients who met all the following criteria:
1. Patients made at least one healthcare visit between January 20, 2020 and January 19, 2021 (the start date was used as this was the date of the first case of COVID-19 recorded in the USA)
2. Patients were 30 years old or younger at the time of the visit. If multiple visits were made, the age at the first visit was used to include/exclude patients.
3. Patients made at least one healthcare visit before January 20, 2020 (to ensure that baseline information was available for each patient).
4. Patients did not have an eating disorder recorded in their health record on or before January 19, 2020.

The comparison cohorts were defined using the same criteria above shifted by 1, 2, and 3 years. For instance, the cohort which we refer to as the '2019 cohort', used for the primary analysis, include all patients who met each of the following criteria:
1. Patients made at least one healthcare visit between January 20, 2019 and January 19, 2020

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2. Patients were 30 years old or younger at the time of the visit. If multiple visits were made, the age at the first visit was used to include/exclude patients.
3. Patients made at least one healthcare visit before January 20, 2019 (to ensure that baseline information was available for each patient).
4. Patients did not have an eating disorder recorded in their health record on or before January 19, 2019.

The same approach was taken for the 2017 and 2018 cohorts, used in the sensitivity analysis.

The three cohorts cannot be merged as a single comparison cohort because patients may be part of several of them.

2.2   Assessing the relative risk of eating disorder among patients diagnosed with COVID-19 vs. not

To assess whether patients diagnosed with COVID-19 were at an increased risk of being subsequently diagnosed with an eating disorder, we defined and compared two cohorts.

The first cohort was defined as all patients who met each of the following criteria:
1. Patients had a confirmed diagnosis of COVID-19 (ICD-10 code U07.1) or a positive PCR test for SARS-CoV-2 between January 20, 2020 and November 19, 2021. The choice of the end date (10 months rather than 12 months after the beginning of the time window) guarantees that even the patients diagnosed at the later stages of that window, will have had the opportunity for sufficient follow-up at the time of the analysis (April 28, 2021).
2. Patients were 30 years old or younger at the time of diagnosis.
3. Patients had not died at the time of the analysis (April 28, 2021)

The comparison cohort was defined as all patients who met each of the following criteria:
1. Patients had made a healthcare visit between January 20, 2020 and November 19, 2021.
2. Patients were 30 years old or younger at the time of the visit.
3. Patients had not died at the time of the analysis (April 28, 2021).
4. Patients had not had a confirmed diagnosis of COVID-19 (ICD-19 code U07.1) nor a positive PCR test for SARS-CoV-2 between January 20, 2020 and the time of the analysis (April 28, 2021).

A positive PCR test for SARS-CoV-2 was defined as a positive entry for any of the following tests:
- Positive SARS-CoV-2 RNA in Respiratory specimen
- Positive SARS-CoV-2 RNA in Unspecified specimen
- Positive SARS-CoV-2 N gene in Respiratory specimen
- Positive SARS-CoV-2 N gene in Unspecified specimen
- Positive SARS-CoV-2 RdRp gene in Respiratory specimen
- Positive SARS-CoV-2 E gene in Respiratory specimen
- Positive SARS-CoV-2 E gene in Unspecified specimen
- Positive SARS-CoV-2 RNA panel in Respiratory specimen
- Positive SARS-CoV-2 RNA panel in Unspecified specimen
- Positive SARS-CoV-2 RNA in Nasopharynx
- Positive SARS coronavirus 2 and related RNA
- Positive SARS-related coronavirus RNA in Respiratory specimen
- Positive SARS coronavirus 2 ORF1ab in Respiratory specimen

Because these two cohorts likely differ significantly on many characteristics at baseline due to differential risks for COVID-19, they were matched for risk factors of COVID-19 and for more severe COVID-19 illness (see eMethods 3 for the covariates used in matching and eMethods 5.2 for the statistical analysis). In addition, because the rate of healthcare visits and diagnoses have varied during the pandemic, the two cohorts were stratified by the time of the visits in five 2-monthly periods: January 20 – March 19, 2020, March 20 – May 19, 2020, May 20 – July 19, 2020, July 20 – September 19, 2020, and September 20 – November 19, 2020. Matching for baseline characteristics was achieved separately in each stratum.

The index event from which follow-up started was the first time a diagnosis of COVID-19 was recorded (for the first cohort) or the first visit to a healthcare organization (for the second cohort) within the corresponding time window.

3

2.3   Assessing the outcomes of patients diagnosed with an eating disorder during vs. before the pandemic

To assess the outcomes of patients diagnosed with an eating disorder during vs. before the pandemic, the following two cohorts were defined.

The cohort of interest was defined as all patients who met all the following criteria:
1. Patients had a recorded diagnosis of an eating disorder (ICD-10 code F50) between January 20, 2020 and January 19, 2021.
2. Patients were 30 years old or younger at the time of the diagnosis.
3. Patients made at least one visit to a healthcare organization on or before January 19, 2020 (to guarantee that baseline information was available for each patient).
4. Patients did not have a diagnosis of an eating disorder on or before January 19, 2020.

The control cohort was defined as all patients who met all the following criteria:
1. Patients had a recorded diagnosis of an eating disorder (ICD-10 code F50) between January 20, 2017 and January 19, 2020.
2. Patients were 30 years old or younger at the time of the diagnosis.
3. Patients made at least one visit to a healthcare organization on or before January 19, 2017 (to guarantee that baseline information was available before the study window).
4. Patients did not have a diagnosis of an eating disorder on or before January 19, 2017.

The index event from which follow-up started was the first recorded diagnosis of an eating disorder within the corresponding time window.

3   Definition of covariates

When comparing the cohort of patients diagnosed with COVID-19 to the cohort who were not, significant differences in baseline characteristics can be expected between the cohorts as a result of differential risks for COVID-19. To reduce the effect of confounding on associations between a diagnosis of COVID-19 and a subsequent diagnosis of eating disorder, cohorts were thus matched for established or suspected risk factors for COVID-19[2-6] and for established risk factors for COVID-19 death[7] (taken to be risk factors of a more severe COVID-19 illness). All the covariates used in our previous EHR-based studies of associations between psychiatric disorders and COVID-19[1,7] were included insofar as they were observed in at least 0.1% of the control cohort. In addition, previous use of antimicrobials were also included as it has been thought to be potentially associated with eating disorders[8] and might also capture risk factors for infection. Specifically, the following covariates were included (with ICD-19/CDC/VA Formulary codes in brackets):

1) Age at the time of diagnosis
2) Sex coded as female, male, or other
3) Race encoded as 6 separate dichotomous variables: White (2106-3), Black or African American (2054-5), American Indian or Alaska Native (1002-5), Asian (2028-9), Native Hawaiian or Other Pacific Islander (2076-8), or Unknown Race (2131-1)
4) Ethnicity encoded as Hispanic or Latino (2135-2), Not Hispanic or Latino (2186-5), or Unknown Ethnicity
5) Problems related to housing and economic circumstances encoded as the corresponding ICD-10 code (Z59)
6) Weight and BMI encoded as one dichotomous variable and one categorical variable: Overweight and obesity (E66) and body mass index (categorised into < 17 kg/m^2, 17-18.5 kg/m^2, 18.5-25 kg/m^2, 25-30 kg/m^2, and ≥ 30 kg/m^2)
7) Hypertensive diseases encoded as the corresponding ICD-10 code (I10-I16)
8) Diabetes mellitus encoded as 2 dichotomous variables: Type 1 diabetes mellitus (E10) and Type 2 diabetes mellitus (E11)
9) Bronchitis encoded as a dichotomous variable: Bronchitis, not specified as acute or chronic (J40)
10) Asthma encoded as the corresponding ICD-10 diagnosis (J45)
11) Nicotine dependence encoded as the corresponding ICD-10 diagnosis (F17.2)
12) Substance use disorders encoded as the ICD-10 code for mental and behavioural disorders due to psychoactive substance use (F10-F19)

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13) Psychotic disorders encoded as the ICD-10 code for schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders (F20-F29)
14) Mood disorders encoded as the corresponding ICD-10 code (F30-F39)
15) Anxiety disorders encoded as the ICD-10 code for anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (F40-F48)
16) Heart diseases encoded as 1 categorical variable: Other forms of heart disease (I30-I52)
17) Chronic kidney disease encoded as the corresponding ICD-10 code (N18)
18) Fatty liver disease encoded as the categorical variables: Fatty liver, not elsewhere classified (K76.0)
19) Neoplasm and haematological cancer in particular encoded as 2 dichotomous variables: Neoplasms (C00-D49) and Malignant neoplasms of lymphoid, hematopoietic and related tissue (C81-C96)
20) Lupus encoded as the corresponding ICD-10 code (M32)
21) Psoriasis encoded as the corresponding ICD-10 code (L40)
22) Certain disorders involving the immune mechanism encoded as the corresponding ICD-10 code (D80-D89)
23) Previous use of antimicrobial agents encoded as a dichotomous variable: Antimicrobials (VA Formulary code AM000)

Each individual code was considered a confounding factor in and of itself so that matching was achieved for each of them individually. For variables representing diagnoses and socioeconomic deprivation, an individual was considered positive if the ICD-10 code was recorded at least once in their health record before the index event. For BMI measurements, all available measurements for all individuals were used and propensity score matching sought to define cohorts with similar numbers of measurements falling into each category.

When comparing the outcomes of patients with an eating disorder diagnosed during vs. before January 20, 2020, there is no a priori reason to believe that the cohorts would differ significantly at baseline. We calculated the standardized mean difference (SMD) in age and sex between the two cohorts defined in eMethods 2.3. If cohorts were already well matched (SMD≤0.1) on these characteristics, then no further matching was applied. If they were not well matched for these characteristics, then propensity score matching was applied.

4   Definitions of outcomes

For the analysis of outcomes of patients diagnosed with an eating disorder during vs. before the COVID-19 pandemic, the primary outcome was a composite endpoint of any of the following events within 6 months of the index event:

- Death
- Suicide attempt (ICD-10 code T14.91)
- Suicidal ideations (ICD-10 code R45.851)

Each individual event was also analysed independently as secondary outcomes.

5   Details on statistical analyses

Unless otherwise stated, statistical analyses were conducted in R version 3.6.3. Statistical significance was set at two-sided P-values < .05.

5.1   Assessing the relative incidence of eating disorder during the pandemic vs. before

For the cohorts defined in eMethods 2.1, the incidence of an eating disorder (ICD-10 code F50) within a given time window was defined as a ratio (N/D). The denominator (D) was the number of patients from the cohort who met both the following criteria:

- their fact record (i.e. the period that starts with their earliest observation and ends with the most recent one) overlaps the time window by at least one day,
- their fact record does not include a diagnosis of eating disorders at any point before the time window.

The numerator (N) was the number of patients from the cohort who met the criteria for the denominator and whose fact record includes a diagnosis of eating disorders on a date within the time window.

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The incidence was calculated for the whole study window (January 20, 2020 to January, 19, 2021 for the cohort of interest, and January 20, 2019 to January 19, 2020 for the control cohort) as well as for every 2-month period within this time window.

The relative risk of an eating disorder being diagnosed during the COVID-19 pandemic (January 20, 2020 to January 19, 2021) vs. during the year before (January 20, 2019 to January 19, 2020) was calculated as the ratio of the corresponding incidences. The null hypothesis that the relative risk equals 1 was tested using a χ^2 test. Both the relative risk (RR) and the excess incidence (RR-1).

The analysis was repeated after stratifying cohorts by sex and age (in 5 categories: 0-9 years old, 10-14 years old, 15-19 years old, 20-24 years old, and 25-30 years old), and for specific subcategories of eating disorders: anorexia nervosa (ICD-10 code F50.0), bulimia nervosa (F50.2) and eating disorders not otherwise specified (F50.8 or F50.9).

5.2   Assessing the relative risk of eating disorder among patients diagnosed with COVID-19 vs. not

To assess the risk of being diagnosed with an eating disorder among patients diagnosed with COVID-19 vs. those making a visit to a healthcare organization for another reason, the cohorts defined in eMethods 2.2 (stratified by timing of the COVID-19 diagnosis/healthcare visit as explained above) were matched for the covariates defined in eMethods 3 using propensity score matching.

Propensity score matching was carried out within the TriNetX network. Propensity score 1:1 matching used a greedy nearest neighbour matching approach with a caliper distance of 0.1 pooled standard deviations of the logit of the propensity score. Any characteristic with a standardized mean difference (SMD) between cohorts lower than 0.1 was considered well matched.[9] In the matching process, the propensity score was calculated using a logistic regression (implemented by the function LogisticRegression of the scikit-learn package in Python 3.7) including each of the covariates mentioned above. To eliminate the influence of ordering of records, the order of the records in the covariate matrix were randomised before matching.

Kaplan-Meier analysis was used to estimate the risk of a first diagnosis of an eating disorder (i.e. excluding those who had a diagnosis before the follow-up window) within 6 months of either a diagnosis of COVID-19 or another healthcare visit. Cox proportional hazard model was used to calculate the hazard ratio and its confidence interval. The null hypothesis that the hazard ratio was equal to 1 was tested using a log-rank test.

5.3   Assessing the outcomes of patients diagnosed with an eating disorder during vs. before the pandemic

To assess the outcomes of patients diagnosed with an eating disorder during vs. in the year before the COVID-19 pandemic, Kaplan-Meier analysis was applied to the cohorts defined in eMethods 2.3 with the outcomes defined in eMethods 4. The Cox proportional hazard model was used to calculate the hazard ratio and its confidence interval. The null hypothesis that the hazard ratio was equal to 1 was tested using a log-rank test.

6   Details on the sensitivity analysis

In the primary analysis of the incidence of eating disorders, patients who did make further visits to a healthcare organization were assumed not to have an eating disorder. But it might be that they were lost to follow-up (e.g. because they moved to another area and started receiving their care from another healthcare organization that is not part of the network). In the primary analysis, we mitigated that risk by only including patients who made at least one visit during the study window. However, it might be that they were lost to follow-up after that visit.

To assess whether differences in incidences of eating disorders during vs. before the COVID-19 could be explained by differences in patients lost to follow-up, a sensitivity analysis was conducted. In this sensitivity analysis, patients were only included if they not only made a healthcare visit during the follow-up window (as is the case in the primary analysis), but also made at least one healthcare visit in the months after the follow-up window (between January 20, 2021 and April 28, 2021 for the cohort of interest, or between January 20, 2020 and April 28, 2020 for the control cohort). This guarantees that they continued to visit healthcare organizations within the network after the study window so that the absence of further visits during the follow-up window more likely reflects the absence of a diagnosis. This is useful to confirm the relative risk of eating disorders during vs. before the pandemic. However, because these patients are by definition making more frequent visits

6

to healthcare organizations, they might be less representative of the general population and this is why we only report relative risks whereas the primary analysis is used to report incidences.

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Supplementary figure

Incidence by years
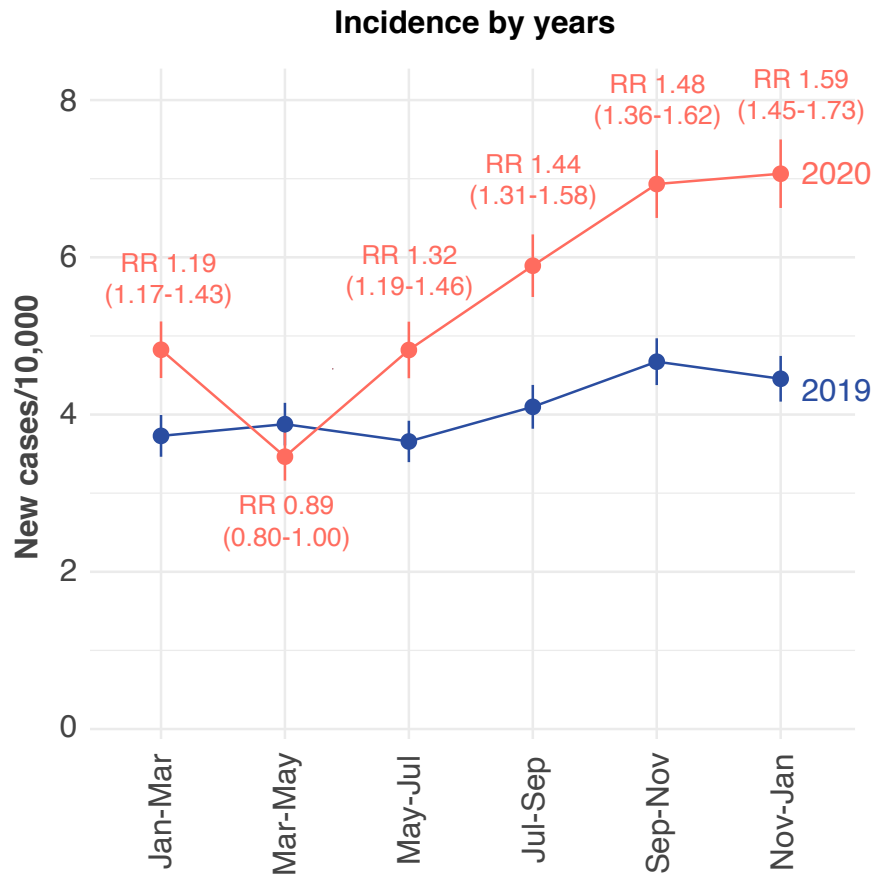
Supplementary Figure 1: Incidence of eating disorders in 2-monthly periods during the pandemic (January 20, 2020 to January 19, 2021) compared to the previous year (January 20, 2019 to January 19, 2020) when the cohort is restricted to those patients who also made a visit to a healthcare organization between January 20, 2021 and April 28, 2021 (or the same period in 2020 for comparison) thus guaranteeing that they were not lost to follow up. The relative risks (RR) and their 95% confidence intervals are provided for each 2-monthly period during the pandemic compared to the same period the previous year.

8
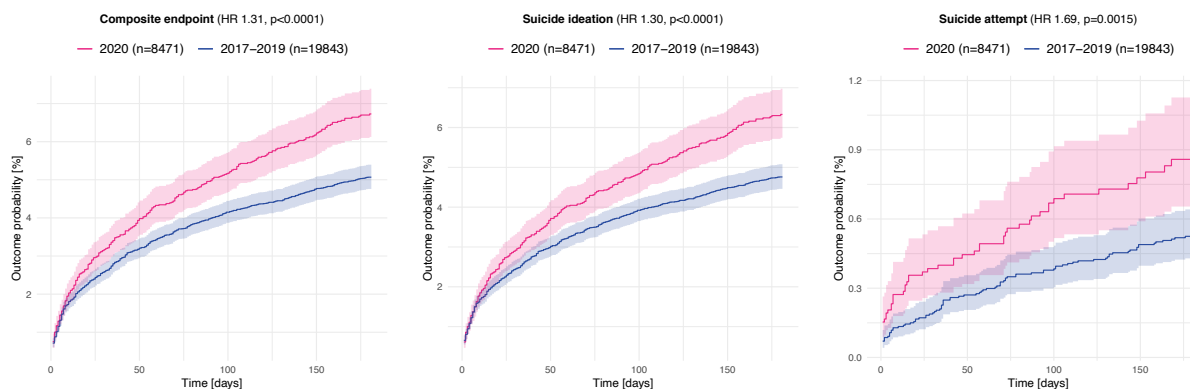
Supplementary Figure 2: Kaplan-Meier curves for the outcomes of patients diagnosed with an eating disorder during the pandemic (pink curves) compared to the three years before (blue curves). Curves are shown for the composite endpoint of suicide ideation, suicide attempt or death (left), as well as for suicide ideation (centre) and suicide attempt (right) separately. The curves for death are not shown because the rarity of the event meant that fewer than 10 events occurred in the 2020 cohort and the exact number of such rare events is not directly returned by TriNetX to protect patient's confidentiality.
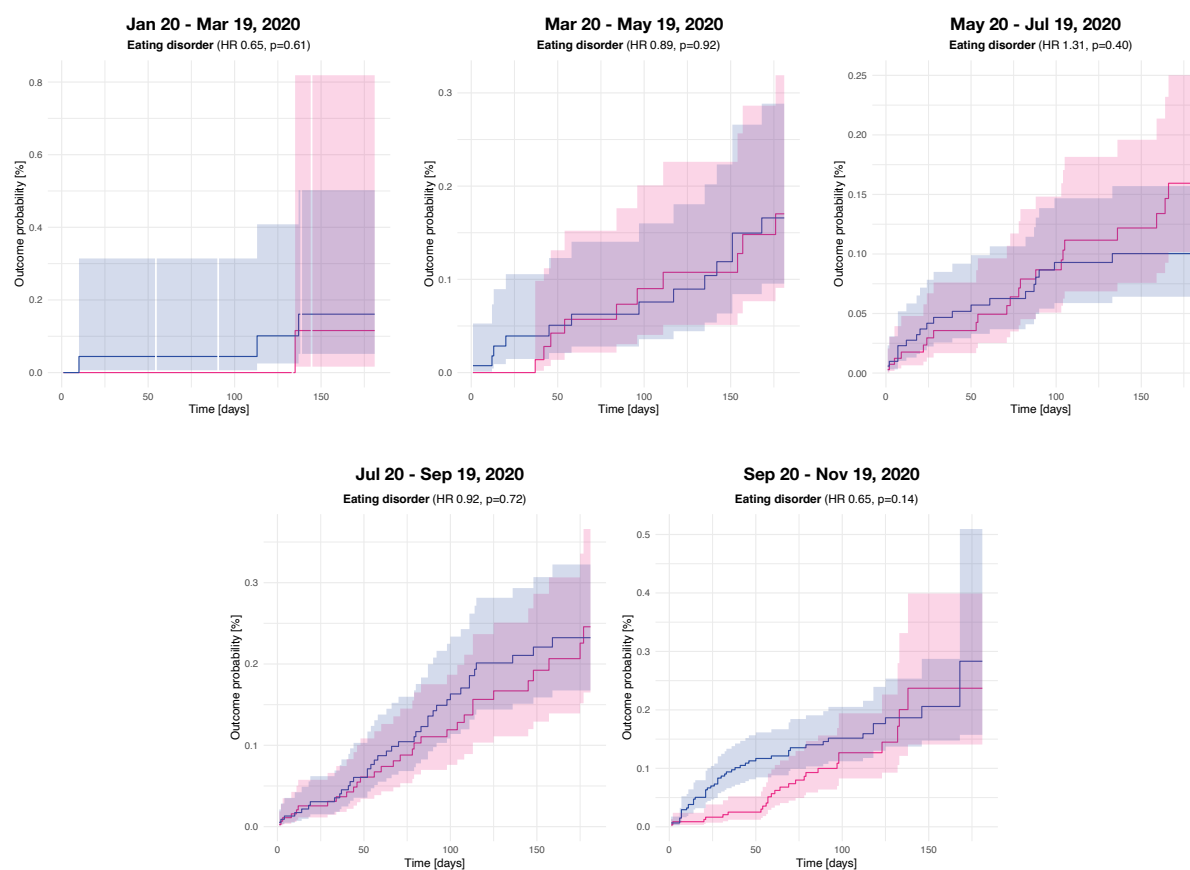
Supplementary Figure 3: Kaplan-Meier curves for incidence of eating disorders in the 6 months after a diagnosis of COVID (pink curve) compared to a matched control cohort making a healthcare visit for another reason (blue curve). The analysis was stratified by the timing of the diagnosis/visit in five 2-months periods.

9

Supplementary Tables

Supplementary Table 1

Demographics, diagnostic subcategory, and outcomes of patients diagnosed with an eating disorder between January 20, 2020 and January 19, 2021, compared to patients diagnosed with an eating disorder in the previous three years. SMD=Standardized mean difference. EDNOS=Eating disorder not otherwise specified (ICD-10 codes F50.8 or F50.9).

	Patients diagnosed between Jan 20, 2020 and Jan 19, 2021	Patients diagnosed between Jan 20, 2017 and Jan 19, 2020	
Demographics			**SMD**
Sample size, n	8471	19843	-
Age, mean [SD], y	16.25 (7.19)	16.34 (7.60)	0.013
Sex, n (%)			
Female	6613 (78.07)	14954 (75.36)	0.064
Male	1855 (21.90)	4885 (24.62)	0.064
Other	3 (0.04)	4 (0.02)	0.0091
Diagnostic subcategory, n (%)			**SMD**
Anorexia nervosa	1334 (15.75)	2500 (12.60)	0.09
Bulimia nervosa	628 (7.41)	1638 (8.26)	0.031
EDNOS	6509 (76.84)	15705 (79.15)	0.056
Outcomes	**% at 6 months (95% CI)**	**% at 6 months (95% CI)**	**HR (95% CI), P**
Suicide attempt, ideation, or death	6.73 (6.13-7.39)	5.07 (4.76-5.40)	1.31 (1.17-1.47), P<.001
Suicide ideation	6.33 (5.74-6.97)	4.76 (4.46-5.08)	1.30 (1.16-1.47), P<.001
Suicide attempt	0.89 (0.68-1.16)	0.52 (0.43-0.64)	1.69 (1.21-2.35), P=0.0015
Death	0.047 (0.015-0.15)	0.096 (0.06-0.15)	0.48 (0.14-1.63), P=0.33

10

Supplementary Table 2: Relative risks (RR) and p-value (from χ^2 tests) comparing the incidence of eating disorders between the pandemic (January 20, 2020 to January 19, 2021) and each of the previous three years for the overall cohort as well as for each sex and age category, and for subcategories of eating disorders.

	2019		2018		2017	
	RR	p	RR	p	RR	p
Overall	1.15 (1.12 - 1.19)	<0.0001	1.18 (1.15 - 1.22)	<0.0001	1.22 (1.18 - 1.26)	<0.0001
Female	1.20 (1.16 - 1.24)	<0.0001	1.21 (1.17 - 1.26)	<0.0001	1.26 (1.22 - 1.31)	<0.0001
Male	1.00 (0.94 - 1.06)	1	1.08 (1.02 - 1.16)	0.013	1.06 (0.99 - 1.13)	0.1
0-9y	1.02 (0.95 - 1.09)	0.63	0.99 (0.92 - 1.06)	0.71	1.06 (0.98 - 1.13)	0.14
10-14y	1.24 (1.16 - 1.32)	<0.0001	1.33 (1.24 - 1.42)	<0.0001	1.37 (1.28 - 1.47)	<0.0001
15-19y	1.21 (1.15 - 1.28)	<0.0001	1.31 (1.23 - 1.38)	<0.0001	1.35 (1.27 - 1.43)	<0.0001
20-24y	1.10 (1.02 - 1.18)	0.014	1.11 (1.03 - 1.20)	0.0072	1.11 (1.03 - 1.20)	0.0091
25-30	1.09 (1.01 - 1.17)	0.035	1.05 (0.97 - 1.13)	0.25	1.02 (0.95 - 1.11)	0.55
AN	1.32 (1.24 - 1.41)	<0.0001	1.36 (1.27 - 1.45)	<0.0001	1.59 (1.48 - 1.71)	<0.0001
BN	1.13 (1.03 - 1.24)	0.0081	1.03 (0.94 - 1.12)	0.58	1.10 (1.01 - 1.21)	0.039
EDNOS	1.13 (1.09 - 1.17)	<0.0001	1.16 (1.12 - 1.20)	<0.0001	1.19 (1.15 - 1.23)	<0.0001

Supplementary Table 3: Baseline characteristics of the matched cohorts of patients who were diagnosed with COVID-19 or made a visit to a healthcare organisation for another reason between January 20, 2020, and March 19, 2020. To de-confound the effect of the timing of diagnosis/healthcare visit on subsequent diagnosis of eating disorder, matching was stratified by the time of diagnosis into 2-month strata, and propensity score matching was applied separately in each stratum. To avoid the possibility of patient identification, when a baseline characteristic is present in less than 10 patients, TriNetX returns 10 as a number. This only affected this 2-month period and not the other 4 (Supplementary Tables 4-7) which are all larger. SMD=Standardised mean difference

	COVID-19	Visit	SMD
Number	3215	3215	-
Demographics			
Age; mean (SD); y	18.8 (7.8)	18.8 (7.9)	0.002
Sex; n (%)			
Female	1688 (52.5)	1685 (52.4)	0.002
Male	1525 (47.4)	1527 (47.5)	0.001
Other	10 (0.3)	10 (0.3)	0
Race; n (%)			
White	2241 (69.7)	2232 (69.4)	0.006
Black or African American	413 (12.8)	420 (13.1)	0.006
Asian	69 (2.1)	72 (2.2)	0.006
American Indian or Alaska Native	19 (0.6)	17 (0.5)	0.008
Native Hawaiian or Other Pacific Islander	10 (0.3)	10 (0.3)	0
Unknown	469 (14.6)	464 (14.4)	0.004
Ethnicity; n (%)			
Hispanic or Latino	1426 (44.4)	1414 (44.0)	0.008
Not Hispanic of Latino	1596 (49.6)	1591 (49.5)	0.003
Unknown	193 (6.0)	210 (6.5)	0.02
Problems related to housing and economic circumstances; n (%) (Z59)	15 (0.5)	10 (0.3)	0.02
Comorbidities; n (%)			
Overweight and obesity (E66)	400 (12.4)	381 (11.9)	0.02
Hypertensive diseases (I10-I16)	75 (2.3)	57 (1.8)	0.04
Type 1 diabetes mellitus (E10)	20 (0.6)	28 (0.9)	0.03
Type 2 diabetes mellitus (E11)	44 (1.4)	43 (1.3)	0.003
Bronchitis (J40)	140 (4.4)	130 (4.0)	0.02
Asthma (J45)	345 (10.7)	340 (10.6)	0.005
Nicotine dependence (F17.2)	60 (1.9)	48 (1.5)	0.03
Substance use disorder (F10-F19)	105 (3.3)	92 (2.9)	0.02
Psychotic disorder (F20-F29)	15 (0.5)	10 (0.3)	0.02
Mood disorder (F30-F39)	237 (7.4)	206 (6.4)	0.04
Anxiety disorder (F40-F48)	354 (11.0)	315 (9.8)	0.04
Heart disease (I30-I52)	133 (4.1)	113 (3.5)	0.03
Chronic kidney disease (N18)	13 (0.4)	11 (0.3)	0.01
Fatty liver disease (K76.0)	26 (0.8)	14 (0.4)	0.05

12

Neoplasm (C00-D49)	153 (4.8)	132 (4.1)	0.03
Haematological cancer (C81-C96)	10 (0.3)	10 (0.3)	0
Lupus (M32)	10 (0.3)	10 (0.3)	0
Psoriasis (L40)	10 (0.3)	10 (0.3)	0
Certain disorders involving the immune mechanism (D80-D89)	17 (0.5)	15 (0.5)	0.009
Medications; n (%)			
Previous use of antimicrobial agents	1844 (57.4)	1826 (56.8)	0.01

13

Supplementary Table 4: Baseline characteristics of the matched cohorts of patients who were diagnosed with COVID-19 or made a visit to a healthcare organisation for another reason between March 20, 2020, and May 19, 2020. To de-confound the effect of the timing of diagnosis/healthcare visit on subsequent diagnosis of eating disorder, matching was stratified by the time of diagnosis into 2-month strata, and propensity score matching was applied separately in each stratum. SMD=Standardised mean difference.

	COVID-19	Visit	SMD
Number	13564	13564	-
Demographics			
Age; mean (SD); y	20.5 (7.7)	20.4 (7.8)	0.01
Sex; n (%)			
Female	7568 (55.8)	7417 (54.7)	0.02
Male	5921 (43.7)	6073 (44.8)	0.02
Other	75 (0.6)	74 (0.5)	0.001
Race; n (%)			
White	6496 (47.9)	6534 (48.2)	0.006
Black or African American	2670 (19.7)	2645 (19.5)	0.005
Asian	378 (2.8)	392 (2.9)	0.006
American Indian or Alaska Native	74 (0.5)	63 (0.5)	0.01
Native Hawaiian or Other Pacific Islander	37 (0.3)	29 (0.2)	0.01
Unknown	3909 (28.8)	3901 (28.8)	0.001
Ethnicity; n (%)			
Hispanic or Latino	3985 (29.4)	3975 (29.3)	0.002
Not Hispanic of Latino	6020 (44.4)	6093 (44.9)	0.01
Unknown	3559 (26.2)	3496 (25.8)	0.01
Problems related to housing and economic circumstances; n (%) (Z59)	104 (0.8)	83 (0.6)	0.02
Comorbidities; n (%)			
Overweight and obesity (E66)	1656 (12.2)	1540 (11.4)	0.03
Hypertensive diseases (I10-I16)	495 (3.6)	435 (3.2)	0.02
Type 1 diabetes mellitus (E10)	125 (0.9)	108 (0.8)	0.01
Type 2 diabetes mellitus (E11)	271 (2.0)	211 (1.6)	0.03
Bronchitis (J40)	378 (2.8)	322 (2.4)	0.03
Asthma (J45)	1530 (11.3)	1462 (10.8)	0.02
Nicotine dependence (F17.2)	497 (3.7)	462 (3.4)	0.01
Substance use disorder (F10-F19)	834 (6.1)	751 (5.5)	0.03
Psychotic disorder (F20-F29)	117 (0.9)	103 (0.8)	0.01
Mood disorder (F30-F39)	1248 (9.2)	1171 (8.6)	0.02
Anxiety disorder (F40-F48)	1725 (12.7)	1630 (12.0)	0.02
Heart disease (I30-I52)	606 (4.5)	511 (3.8)	0.04
Chronic kidney disease (N18)	85 (0.6)	62 (0.5)	0.02
Fatty liver disease (K76.0)	142 (1.0)	101 (0.7)	0.03
Neoplasm (C00-D49)	647 (4.8)	586 (4.3)	0.02

14

Haematological cancer (C81-C96)	50 (0.4)	38 (0.3)	0.02
Lupus (M32)	21 (0.2)	16 (0.1)	0.01
Psoriasis (L40)	46 (0.3)	42 (0.3)	0.005
Certain disorders involving the immune mechanism (D80-D89)	117 (0.9)	97 (0.7)	0.02
Medications; n (%)			
Previous use of antimicrobial agents	6718 (49.5)	6600 (48.7)	0.02

15

Supplementary Table 5: Baseline characteristics of the matched cohorts of patients who were diagnosed with COVID-19 or made a visit to a healthcare organisation for another reason between May 20, 2020, and July 19, 2020. To de-confound the effect of the timing of diagnosis/healthcare visit on subsequent diagnosis of eating disorder, matching was stratified by the time of diagnosis into 2-month strata, and propensity score matching was applied separately in each stratum. SMD=Standardised mean difference.

	COVID-19	Visit	SMD
Number	34533	34533	-
Demographics			
Age; mean (SD); y	19.9 (7.5)	19.8 (7.6)	0.01
Sex; n (%)			
Female	19309 (55.9)	19174 (55.5)	0.008
Male	15146 (43.9)	15278 (44.2)	0.008
Other	78 (0.2)	81 (0.2)	0.002
Race; n (%)			
White	17566 (50.9)	17700 (51.3)	0.008
Black or African American	7645 (22.1)	7574 (21.9)	0.005
Asian	756 (2.2)	761 (2.2)	0.001
American Indian or Alaska Native	154 (0.4)	152 (0.4)	9.00E-04
Native Hawaiian or Other Pacific Islander	93 (0.3)	83 (0.2)	0.006
Unknown	8319 (24.1)	8263 (23.9)	0.004
Ethnicity; n (%)			
Hispanic or Latino	7643 (22.1)	7432 (21.5)	0.01
Not Hispanic of Latino	16329 (47.3)	16361 (47.4)	0.002
Unknown	10561 (30.6)	10740 (31.1)	0.01
Problems related to housing and economic circumstances; n (%) (Z59)	130 (0.4)	104 (0.3)	0.01
Comorbidities; n (%)			
Overweight and obesity (E66)	2662 (7.7)	2394 (6.9)	0.03
Hypertensive diseases (I10-I16)	989 (2.9)	822 (2.4)	0.03
Type 1 diabetes mellitus (E10)	217 (0.6)	179 (0.5)	0.01
Type 2 diabetes mellitus (E11)	465 (1.3)	351 (1.0)	0.03
Bronchitis (J40)	728 (2.1)	655 (1.9)	0.02
Asthma (J45)	2782 (8.1)	2608 (7.6)	0.02
Nicotine dependence (F17.2)	1072 (3.1)	972 (2.8)	0.02
Substance use disorder (F10-F19)	1780 (5.2)	1573 (4.6)	0.03
Psychotic disorder (F20-F29)	154 (0.4)	134 (0.4)	0.009
Mood disorder (F30-F39)	2398 (6.9)	2216 (6.4)	0.02
Anxiety disorder (F40-F48)	3577 (10.4)	3369 (9.8)	0.02
Heart disease (I30-I52)	1381 (4.0)	1192 (3.5)	0.03
Chronic kidney disease (N18)	167 (0.5)	143 (0.4)	0.01
Fatty liver disease (K76.0)	232 (0.7)	174 (0.5)	0.02
Neoplasm (C00-D49)	1355 (3.9)	1238 (3.6)	0.02
Haematological cancer (C81-C96)	119 (0.3)	94 (0.3)	0.01

16

Lupus (M32)	67 (0.2)	43 (0.1)	0.02
Psoriasis (L40)	85 (0.2)	74 (0.2)	0.007
Certain disorders involving the immune mechanism (D80-D89)	233 (0.7)	182 (0.5)	0.02
Medications; n (%)			
Previous use of antimicrobial agents	15638 (45.3)	15318 (44.4)	0.02

17

Supplementary Table 6: Baseline characteristics of the matched cohorts of patients who were diagnosed with COVID-19 or made a visit to a healthcare organisation for another reason between July 20, 2020, and September 19, 2020. To de-confound the effect of the timing of diagnosis/healthcare visit on subsequent diagnosis of eating disorder, matching was stratified by the time of diagnosis into 2-month strata, and propensity score matching was applied separately in each stratum. SMD=Standardised mean difference.

	COVID-19	Visit	SMD
Number	37988	37988	-
Demographics			
Age; mean (SD); y	19.3 (7.2)	19.2 (7.3)	0.01
Sex; n (%)			
Female	21034 (55.4)	20930 (55.1)	0.006
Male	16858 (44.4)	16962 (44.7)	0.006
Other	96 (0.3)	96 (0.3)	0
Race; n (%)			
White	21707 (57.1)	21811 (57.4)	0.006
Black or African American	6500 (17.1)	6433 (16.9)	0.005
Asian	742 (2.0)	748 (2.0)	0.001
American Indian or Alaska Native	120 (0.3)	104 (0.3)	0.008
Native Hawaiian or Other Pacific Islander	135 (0.4)	136 (0.4)	4.00E-04
Unknown	8784 (23.1)	8756 (23.0)	0.002
Ethnicity; n (%)			
Hispanic or Latino	6469 (17.0)	6273 (16.5)	0.01
Not Hispanic of Latino	21780 (57.3)	21832 (57.5)	0.003
Unknown	9739 (25.6)	9883 (26.0)	0.009
Problems related to housing and economic circumstances; n (%) (Z59)	154 (0.4)	117 (0.3)	0.02
Comorbidities; n (%)			
Overweight and obesity (E66)	2572 (6.8)	2345 (6.2)	0.02
Hypertensive diseases (I10-I16)	1062 (2.8)	882 (2.3)	0.03
Type 1 diabetes mellitus (E10)	198 (0.5)	195 (0.5)	0.001
Type 2 diabetes mellitus (E11)	445 (1.2)	337 (0.9)	0.03
Bronchitis (J40)	720 (1.9)	630 (1.7)	0.02
Asthma (J45)	3137 (8.3)	3020 (8.0)	0.01
Nicotine dependence (F17.2)	1172 (3.1)	1079 (2.8)	0.01
Substance use disorder (F10-F19)	2026 (5.3)	1870 (4.9)	0.02
Psychotic disorder (F20-F29)	188 (0.5)	165 (0.4)	0.009
Mood disorder (F30-F39)	2784 (7.3)	2571 (6.8)	0.02
Anxiety disorder (F40-F48)	4254 (11.2)	4032 (10.6)	0.02
Heart disease (I30-I52)	1617 (4.3)	1440 (3.8)	0.02
Chronic kidney disease (N18)	195 (0.5)	147 (0.4)	0.02
Fatty liver disease (K76.0)	266 (0.7)	214 (0.6)	0.02
Neoplasm (C00-D49)	1625 (4.3)	1555 (4.1)	0.009
Haematological cancer (C81-C96)	116 (0.3)	83 (0.2)	0.02

18

Lupus (M32)	65 (0.2)	45 (0.1)	0.01
Psoriasis (L40)	128 (0.3)	108 (0.3)	0.009
Certain disorders involving the immune mechanism (D80-D89)	261 (0.7)	220 (0.6)	0.01
Medications; n (%)			
Previous use of antimicrobial agents	16507 (43.5)	16215 (42.7)	0.02

19

Supplementary Table 7: Baseline characteristics of the matched cohorts of patients who were diagnosed with COVID-19 or made a visit to a healthcare organisation for another reason between September 20, 2020, and November 19, 2020. To de-confound the effect of the timing of diagnosis/healthcare visit on subsequent diagnosis of eating disorder, matching was stratified by the time of diagnosis into 2-month strata, and propensity score matching was applied separately in each stratum. SMD=Standardised mean difference.

	COVID-19	Visit	SMD
Number	61265	61265	-
Demographics			
Age; mean (SD); y	18.6 (8.0)	18.5 (8.0)	0.01
Sex; n (%)			
Female	33514 (54.7)	33349 (54.4)	0.005
Male	27385 (44.7)	27534 (44.9)	0.005
Other	366 (0.6)	382 (0.6)	0.003
Race; n (%)			
White	38070 (62.1)	38074 (62.1)	1.00E-04
Black or African American	7468 (12.2)	7418 (12.1)	0.002
Asian	1189 (1.9)	1184 (1.9)	6.00E-04
American Indian or Alaska Native	262 (0.4)	223 (0.4)	0.01
Native Hawaiian or Other Pacific Islander	297 (0.5)	311 (0.5)	0.003
Unknown	13979 (22.8)	14055 (22.9)	0.003
Ethnicity; n (%)			
Hispanic or Latino	10690 (17.4)	10302 (16.8)	0.02
Not Hispanic of Latino	34991 (57.1)	34957 (57.1)	0.001
Unknown	15584 (25.4)	16006 (26.1)	0.02
Problems related to housing and economic circumstances; n (%) (Z59)	202 (0.3)	171 (0.3)	0.009
Comorbidities; n (%)			
Overweight and obesity (E66)	4215 (6.9)	3930 (6.4)	0.02
Hypertensive diseases (I10-I16)	1671 (2.7)	1428 (2.3)	0.03
Type 1 diabetes mellitus (E10)	410 (0.7)	382 (0.6)	0.006
Type 2 diabetes mellitus (E11)	702 (1.1)	580 (0.9)	0.02
Bronchitis (J40)	1277 (2.1)	1099 (1.8)	0.02
Asthma (J45)	5744 (9.4)	5551 (9.1)	0.01
Nicotine dependence (F17.2)	1896 (3.1)	1725 (2.8)	0.02
Substance use disorder (F10-F19)	3044 (5.0)	2764 (4.5)	0.02
Psychotic disorder (F20-F29)	278 (0.5)	240 (0.4)	0.01
Mood disorder (F30-F39)	5165 (8.4)	4807 (7.8)	0.02
Anxiety disorder (F40-F48)	7871 (12.8)	7430 (12.1)	0.02
Heart disease (I30-I52)	2696 (4.4)	2387 (3.9)	0.03
Chronic kidney disease (N18)	305 (0.5)	228 (0.4)	0.02
Fatty liver disease (K76.0)	381 (0.6)	286 (0.5)	0.02
Neoplasm (C00-D49)	3085 (5.0)	2862 (4.7)	0.02
Haematological cancer (C81-C96)	170 (0.3)	134 (0.2)	0.01

20

Lupus (M32)	100 (0.2)	86 (0.1)	0.006
Psoriasis (L40)	214 (0.3)	206 (0.3)	0.002
Certain disorders involving the immune mechanism (D80-D89)	453 (0.7)	393 (0.6)	0.01
Medications; n (%)			
Previous use of antimicrobial agents	27470 (44.8)	26950 (44.0)	0.02

21