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Sex differences Among Children, Adolescents, and Young Adults for Mental Health Service Use Within In-patient and Outpatient Settings, Before and During the COVID-19 Pandemic: A Population-based Study in Ontario, Canada.

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Sex differences Among Children, Adolescents, and Young Adults for Mental Health Service Use Within In-patient and Outpatient Settings, Before and During the COVID-19 Pandemic: A Population-based Study in Ontario, Canada.

ABSTRACT (282 words)

BACKGROUND: The COVID-19 pandemic and public health response to contain the spread of the virus had impacts on many aspects of young people's lives including disruptions to their daily routines, opportunities for social, academic, recreational engagement, and early employment. As a consequence, children, adolescents, and young adults may have experienced mental health challenges that required use of mental health services. This study compared rates of use for in- and out-patient mental health services during the pandemic to pre-pandemic rates.

METHODS: This population-based repeated cross-sectional study used linked health administrative databases in Ontario, Canada to model expected visit rates based on trends prior to the pandemic (March 2016-February 2020) and compared these to observed rates during the pandemic (March 2020 to November 2021). The absolute and relative differences in observed versus expected rates were examined by sex and age (6-24 years) diagnosis type, and healthcare provider.

RESULTS: N=6,039,275 children, adolescents and young adults were identified during the study period. The analysis showed that during the pandemic, observed out-patient visit rates were higher among young adult by 19.01% (CI: 15.56,22.37; 209 vs. 175 per 1000) and adolescent females 24.17% (CI: 18.93,29.15; 131 vs. 105 per 1000) for mood and anxiety disorders and remained higher than expected. Results also showed that female adolescents had higher than expected utilization of in-patient care (emergency departments and hospitals) for deliberate self-harm, eating disorders, and assault-related injuries.

CONCLUSION: Our study raises concerns over prolonged high rates of mental health use during the pandemic, particularly in female adolescents and young women, and highlights the need to better monitor and work to identify possible determinants related to COVID-19 containment policies and other factors at the individual, family, community, and society level.

Strengths and Limitations:

- (+) Large population-based study, representative of the Ontario population
- (+) Well-established mental health and quality indicators based on health administrative billing codes, many have been validated and used in routine reporting and peer-reviewed studies
- (+) Strong methodological design and analysis over time
- (-) Studies with outcomes based on healthcare utilization, may underestimate the true prevalence of those health outcomes, due to non-seeking of care, or the seeking of care in private clinics
- (-) Did not account for individuals characteristics beyond age and sex

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Conflict of Interest: none to report.

REB Approval: RIS 41386.

BACKGROUND:

The COVID-19 pandemic was declared by the World Health Organization on March 11th, 2020 (1). On March 15th, the Office of the Premier responded by declaring a provincial state of emergency in Ontario, Canada, which resulted in successive closure of all non-essential shops and services (2). For nearly two years, health officials and institutional decision makers attempted to mitigate population-level risk of infection by implementing non-pharmaceutical interventions (NPI), such as social distancing, masking, and the closing and reopening of various sectors, which included daycares, primary and secondary schools, and post-secondary institutions (2, 3). The use of various NPIs throughout the COVID-19 pandemic resulted in major disruptions to nearly all aspects of life and routines of children, adolescents, and young adults, due to mass closures of schools, recreation centers, organizational activities, and early employment opportunities. According to the CDC (2021) and other literature in the field, youth up to 24 years of age experienced many challenges during this time, some distinct to specific age groups, others shared across age bands, including major changes in their daily routine (e.g., having to physically distance from friends, family, places of worship and other social communities); breaks in the continuity of learning (e.g., switching from in-person to virtual learning, missing out on supplementary and early education opportunities, access limitations to personal workspace, technology, and connectivity at home) (4, 5); breaks in continuity of healthcare (e.g., missed well-child and immunization visits, limited access to mental, speech, occupational and other health services). Within some households, youth also suffered loss in security and safety (e.g., housing and food insecurity, increased exposures to domestic violence and online harms, threats of physical illness, and uncertainty for the future). For all youth but particularly late teens and young adults, they missed out on significant life events and rites of passage (e.g., missing celebrations, prom, graduations, dating, frosh-week and in-person college activities, early employment opportunities, and other milestone life events) (6).

Studies and reports have begun to surface, indicating both direct and indirect impacts of COVID-19, which may have implications on the development and mental health of youth. In worse circumstances, the effects of these events may result in adverse childhood experiences (ACEs) which may have lasting mental health impacts well into adulthood (6, 7). In England over a quarter of children and young people reported sleep disruptions, and high cases of isolation, feeling lonely and fearful of leaving home because of COVID-19 early in the pandemic (8). Another study found increases in depressive symptoms among youth (9). The socioeconomic impact on parents due to job losses, working from home, and social isolation also impacted children, particularly when there was job loss in the family and social isolation, showing elevated stress and cortisol levels among parents and their children (10). Adolescents and young adults were also directly impacted by layoffs, loss of early employment opportunities, and earnings to pay for expenses such as post-secondary education (11). In Ontario, Canada, there are indications that use of acute care services was higher for eating disorders during the pandemic (12, 13). Another study in Ontario found that there was a major increase in the use of mental health care services during the pandemic, particularly among adolescent females (14). A

systematic review and meta-analysis of 137 studies, found that while mental health symptoms may not have increased substantially after the pandemic, that women and females may have experienced mental health challenges disproportionate to the rest of the population (15). Therefore, there is growing evidence showing signs of mental health concerns among youth, particularly among females, and a growing and persistent use of mental health services both within in-patient and out-patient settings.

The following study aims to build on current evidence (13, 14, 16) by examining critical mental health care service indicators both within physician-based outpatient services and in-patient settings such as ED and hospitals. We are also building on prior studies by extending the age range to include young adults, as research on them in this regard have been less frequent. We are also building on current evidence by examining additional mental health outcomes such as deliberate self-harm (DSH) and assault-related injuries, with observational data for the first 20-months of the pandemic. Using routinely collected health administrative data from Ontario, Canada, we sought to examine whether the rates of mental health visits had changed during the pandemic (March 2020 to November 2021) versus (vs.) pre-COVID-19 patterns, and to identify possible variations by sex, provider type, and clinical diagnoses, among children, adolescents, and young adults.

METHODS

We designed a population-based, repeated cross-sectional study, using unique encrypted identifiers at the individual level, including all children (6-12 years of age), adolescents (13-17 years) and young adults (18-24 years), living in Ontario, Canada and eligible for provincial health insurance between March 2016 to November 2021. The Ontario Registered Persons Database provides sex, age, postal code, and dates of birth for all Ontario residents. Outpatient visits for physicians and psychiatrists were obtained from the provincial health insurance plan (OHIP) database, which contains billing records for all publicly funded mental health services provided. The Canadian Institute for Health Information's National Ambulatory Care Reporting System (NACRS), Discharge Abstract Database (DAD), and Ontario Mental Health Reporting System (OMHRS) were used to identify mental health-related emergency department (ED) visits and hospitalizations. All study data were accessed through Data Analytic Services (DAS) at ICES (formerly the Institute for Clinical Evaluative Sciences), an independent research institute with the legal status permitting it to collect and analyze health care and demographic data without individual patient consent for health system evaluation and improvement under the Ontario's health information privacy law.

A baseline measure of mental health rates of use was obtained from the pre-pandemic period (March 2016 to February 2020). Rates of use during the pandemic are based on utilization starting from March 2020 till the end of November 2021. Data were provided by DAS for analysis in a quarterly format, providing 23 cross-sectional measures over time. All persons between the ages of 6 to 24 years, and who were OHIP insured were considered for inclusion in the study. Persons with missing IKN (ICES Key Number - unique encrypted identifier), birth date,

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sex, OHIP eligibility, non-Ontario residential status, or who had died prior to index date were excluded. Three cohorts were generated based on age: 1) children 6-12 years of age, 2) adolescents 13-17 years of age, and 3) young adults 18-24 years of age. We used open cohorts and assessed at-risk time to allow for individuals to contribute time at risk for outcomes. Data for sex, age and service use were provided at the individual level.

Outcome measures:

Primary outcomes were outpatient visits for mental illness by primary care providers and psychiatrists derived from physician billing claims using the International Classification of Disease (ICD), 8th revision from OHIP, and inpatient emergency department (ED) visits and hospitalizations using ICD-9 and ICD-10 codes from OMHRS, DAD, and NACRS. Given the large proportion of virtual visits after the pandemic (14), especially in primary care, both in person and virtual were aggregated. Outcomes for each cohort are as follows: *Outpatient outcomes*: mood and anxiety disorders (OHIP DXCODES 296, 300, 311), alcohol and substance abuse disorders (OHIP DXCODES 303, 304), other non-psychotic mental health disorders (OHIP DXCODES 301, 302, 306, 309), and social problems (OHIP DXCODES: 897, 898, 899, 900, 901, 902, 904, 905, 906, 909). *Inpatient outcomes: (ED and Hospitalizations)*: substance-related and addictive disorders, anxiety disorders, assault-related injuries, deliberate self-harm (DSH), and eating disorders. For full list of diagnostic codes see supplementary section (Supplemental Table 1).

Statistical Analysis:

Negative binomial regression with time and season as predictor variables, were used to model utilization trends before the pandemic (March 2016 – February 2020) and visits rates per 1000. In the case of rare events in ED and hospitals, they were reported per 100,000. The log of the persons in each quarter was used as the offset. Residuals were modeled as an autoregressive AR(1) process to account for serial correlation and to account for seasonality. The fitted model was used to predict the expected rates of use from March 2020 to the end of November 2021. For the main analysis, we calculated actual observed rates of use during the pandemic as compared to expected rates. Absolute difference of use for each quarter from March 2020 to the end of November 2021 was calculated by subtracting expected rates from observed rates. We calculated the relative difference (95% confidence interval [CI]) between the observed and expected rates by subtracting the expected rate from the observed, divided by expected and multiplied by 100. We also stratified results from the primary analysis by individual diagnoses and sex. Data preparations, analyses, and visualizations were performed using SAS 9.4.

RESULTS

Over 6 million youth between the ages of 6 to 24 years from Ontario, Canada were included in this study. The child cohort had a mean age of 7.7 years of which 48.6% were female, the adolescent cohort a mean age of 13.9, 48.6% female, and the young adult cohort a mean age of 19.9 years with 48.8% female (Supplemental Table 2).

Overall Outpatient Mental Health Care Utilization:

Overall baseline expected rates of mental health service utilization were lowest in the children cohort, followed by adolescent and then young adult cohorts (Figure 1). In all three groups, the first quarter of the pandemic was associated with lower than expected rates. In the child cohort, the highest relative difference in rates for overall service utilization were among females in March to May 2021 by 22.57 % (CI: 18.14, 26.8; 33 vs. 27 per 1000). In the adolescent cohort, the highest difference in the rate of use was in June to August 2021 by 24.17% (CI: 18.93,29.15; 131 vs. 105 per 1000) among females. Female young adults had the highest difference in service use, during December 2020 to February 2021 quarter, up by 19.01% (CI: 15.56,22.37; 209 vs. 175 per 1000). For females in all three cohorts, overall rates of mental health care use remained above expected rates during the pandemic. In contrast, males showed lower overall utilization of mental health services relative to pre-pandemic levels, especially among children and adolescents. For more details (Supplemental Table 3).

Outpatient Mental Health Care Utilization by Individual Diagnoses:

Examining the change in individual diagnoses during the pandemic, revealed that the highest difference in mental health care use is attributable to mood and anxiety disorders, increasing with age across cohorts, particularly among females (Figure 2). The highest relative difference in utilization for mood and anxiety disorders was among female children 27.42% (CI: 22.93,31.72; 23 vs. 18/1000), although absolute rates remained low. Adolescent females and young adults showed much higher and persistent overall differences in service utilization for mood and anxiety disorders. The highest differences in adolescent females were observed in the March to May 2021 guarter 19.8% (CI: 14.23, 25.14; 118 vs. 112 per 1000) and June to August 2021 quarter 23.18% (CI: 17.4, 28.64; 117 vs. 95 per 1000). The highest differences in adult females were observed in the December 2020 to February 2021 guarter 19% (CI: 15.09, 22.93; 183 vs. 154 per 1000) and March to May 2021 quarter 18.2% (CI: 13.6, 22.6; 200 vs. 169 per 1000). Other non-psychotic disorders were also higher during the pandemic, predominantly among female adolescents, but with low overall rates. Among all three male cohorts, we saw significantly lower utilization of outpatient care for all disorders during the pandemic, especially among adolescents and young adults. However, higher rates of substance and alcohol abuse was observed among young male adults in March to May 2021 by 16% (CI: 11.4, 20.33; 15 vs. 13 per 1000) (Supplemental Figure 1). Other conditions did not show any substantial change between expected rates of use versus observed rates.

Inpatient Mental Health Care Utilization in ED and Hospitals:

The difference in mental health service utilization during the pandemic for ED and hospital services (Supplemental Figure 2) showed that there was a general decrease in seeking care for mental health services within those settings, although care was available after the pandemic. The overall decrease during the pandemic was evident among all three cohorts, with exception of certain ED and hospital services among female adolescents (Figure 3).

ED visits for DSH were up among adolescent females, with the highest difference in September to November 2021 by 42.8% (CI: 22.4, 59.7; 258 vs. 181/100,000). In the same timeframe, there was also a higher number of ED visits for DSH requiring hospitalization by 46.1% (CI: 26.5, 62.6; 110 vs. 80/100,000). Hospitalizations for DSH were also up among female adolescents, in September to November 2021 by 102.4% (CI: 76.4, 123; 354 vs. 175/100,000).

Assault-related ED visits that required hospitalization were up nearly five-fold for female adolescents 493.4% (CI: 238.5, 565.2; 2 vs. 0.4/100,000) in September to November 2021. Assault-related hospitalizations were up more than two-fold among female adolescents 272.7% (CI: 151.2, 372.6; 3 vs. 1/100,000) during the September to November 2021 quarter.

Eating disorders were also higher among female adolescents, with a two-fold difference in ED relative to expected rates 225.1% (CI: 178.6, 256.9; 59 vs. 18/100,000), observed in September to November 2021 and comparably in March to May 2021. ED visits for eating disorders requiring hospitalization were also up among adolescents, highest in September to November 2021 by 221.3% (CI: 162.4, 258.4; 27 vs. 8/100,000). The highest absolute difference in hospitalizations for eating disorder among adolescents was in March to May 2021 by 139.7% (CI: 112.4, 161; 64 vs. 26/100,000).

DISCUSSION

In this population-based repeated cross-sectional study, we observed substantially higher rates for clinical mental health outpatient visits for mood and anxiety disorders, relative to expected patterns prior to the pandemic, in adolescent and young female adults. Overall mental health visits to emergency departments and hospitalizations were down relative to expected rates, with exception of DSH, eating disorders, and assault-related injuries among female adolescents. This is further evidence, using mental health service use as an indicator, that there have been significant mental health challenges among young female adults and particularly female adolescents, during the pandemic.

Examining physician-based mental health service use by sex, revealed that a large proportion of the elevated use can be attributed to mood and anxiety disorders among female adolescents and adults. This finding was not unexpected and has been reported in Canada and elsewhere in North American and European countries (14, 17, 18). Female adolescents showed the highest relative increase indicative of various stressors and other factors, which may have been further exacerbated during the pandemic. Female adults had the highest absolute increase, which is not surprising given the same impacts on adolescents during the pandemic, in addition to preexisting economic stressors placed on young adults in terms of finances, education, employment prospects, housing and other added pressures early in adulthood. In contrast to lower overall mental health service use among males, we noted higher alcohol and substance abuse among male young adults. The literature is mixed with respect to increased alcohol and substance use in this population during the pandemic (19). This may be because these studies often utilize cross-sectional data, which depending on the demographics, timepoint, and

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sampling frame may yield different results. The increase in substance and alcohol abuse detected by this study was not substantial. The overall lower than expected rates of seeking mental health care among adolescent and young adult males is not surprising and is consistent with the literature, where this demographic is known for seeking less care, which may have worsened during the pandemic (20). Alternatively, it has been suggested that boys took part in more physical activity during the pandemic and enjoyed reduced stresses associated with lockdowns such as not going to school every day, which may have been protective (21). There may be a greater prevalence of mental health challenges among males, especially young adults, however, due to various factors available care is usually underutilized in this population (22-24).

Inpatient services revealed that ED visits and hospitalizations were down relatively across the board and for most conditions, except for DSH, eating disorders, and assault-related injuries among female adolescents. Similar findings have been reported elsewhere (13, 25, 26). To our knowledge, a similar study regarding DSH found no increase in ED and hospitalization among adolescents and young adults (16). This is likely a result of methodology as they combined their sample of adolescent and young adults. Our study did not find any increase in DSH among young female adults but did find an increase among female adolescents. There is also indication of greater case severity based on relatively flat ED visits but increased ED visits requiring hospitalization and overall hospitalization numbers for DSH, eating disorders, and assaultrelated injury. The increase in cases and severity has been reported in a prior study for eating disorders (13). While absolute numbers for these visits remain low, any increase within these segments of mental health warrants attention. Especially, for visits resulting from assault, neglect, and domestic abuse, among other risk factors for ACEs, which can lead to short-term and long-term psychological and physical health consequences (26-29). This is the first study to our knowledge to have examined service use for assault-related injuries at the population level during the pandemic within this segment of the population in Ontario. Studies elsewhere have noted increases in abusive physical and verbal interactions towards teens and children because of pandemic stressors on parents (25, 26, 30). Even though absolute rates remain low among the population for DSH, eating disorders, and assault-related injuries, we find it troubling that ED and hospitalizations have increased during the pandemic, for these critically serious outcomes.

Explanations for these findings are complex and studies as to possible causes are ongoing.
Plausible theories have centered around closure of schools, reduced access to family and friends, and isolation due lockdown measures which have been associated with sleep disturbance, anxiety, depression among teens and post-secondary students (18, 31-35).
Students also experienced elevated stress, loneliness, and had fears of missing out on social life, their own health, friends and family's, and uncertainties about the future (36). Economic pressures on families have also shown to impact the mental health of youth within the household, especially when there was loss of employment and trouble keeping up with household bills (10, 32, 37). With increased cost of living and economic pressures, it is also important to acknowledge the link between food insecurity, depression, anxiety and eating

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disorders. Food insecurity has been associated with poor physical and mental outcomes, possibly due to feelings of helplessness, shame, and stress (38). Additionally, food insecurity has been associated with eating disorders (39-41). This is considering global challenges in supply chain disruptions, cost, access barriers, and growing demand for food banks post-pandemic (42-44). Additionally, disturbance in pre-pandemic routines and general reduction in physical activity during the pandemic may also be a contributing factor, given the wealth of evidence regarding physical and psychological benefits of exercise versus deleterious effects of a sedentary lifestyle (32, 45). Lastly, schools are not simply a place for learning, they are a place where students socialize, make connections with peers and staff, find a sense of purpose and a sense of self, and for many where they access critical services, such as tools for personal development, education, special learning and peer support, and for some, food programs or an escape from domestic troubles at home (4, 30, 46). Much of these benefits and critical services delivered at school were simply not available in a remote learning environment during the pandemic.

Limitations

Studies with outcomes based on healthcare utilization, may underestimate the true prevalence of those health outcomes, due to non-seeking of care, or the seeking of care outside the medical establishment such as private clinics. We did not control for history of mental illness among study participants, which may have impacted our results to some extent, as we know a history of mental illness is a risk factor for subsequent mental health needs. We were unable to account for factors beyond age and sex, such as race, ethnicity, sexual orientation, self-gender identification, and disability. Some of these factors could certainly be important in further studying mental health of youth during COVID-19, as indicated elsewhere (46, 47). Lastly, the results of this study while generalizable to the population of Ontario, Canada, may not be generalizable to other jurisdictions where COVID-19 cases, containment policies, boundaries and population characteristics are different.

CONCLUSIONS

Over a 20-month course of the COVID-19 pandemic, we observed substantially higher rates of use for mental health physician services relative to pre-pandemic levels, predominantly among female adolescents and young adults. Higher utilization was largely driven by services for mood, anxiety, and depressive disorders within outpatient settings. The only notable difference in mental health care needs among males was for alcohol and substance use in young adults, which should be monitored in the future. We noted higher cases and severity for eating disorders, deliberate self-harm, and assault-related injuries among adolescent females in EDs and hospitals. Our study raises concerns about growing mental health needs among female adolescents and young adults during the pandemic, especially in critical areas such as depression, anxiety, DSH, eating disorders, and assault-related injury and call for urgent action in policy and healthcare response. We also need to ensure that more research and

interventions are mobilized to identify and address underlying causes of worsening mental

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health among female adolescents and young adults.

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Authors Contributions:

MJS - formal analysis, visualization, validation, writing – original draft, review & editing.

VS – conceptualization, validation, writing – original draft, review & editing.

PL: data curation, project administration, writing – review & editing.

TN: data curation, project administration, writing – review & editing.

AM: validation, writing - review & editing.

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PI: validation, writing - review & editing.

WW: validation, writing - review & editing.

AG - conceptualization, funding acquisition, methodology, supervision, validation, writing – review & editing.

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Supplemental Table 1: Service and Diagnostic Codes:

Study Outcome Categories	OHIP Diagnostic CodesIndividual Diagnostic Codes and Theirfor OutcomesDescription				
Outpatient Mental Healt	th Fee Codes				
		296	Bipolar Disorder		
Mood and anxiety	206 200 211	300	Anxiety and related disorders		
disorders	296, 300, 311	311	Depressive or other non-psychotic disorders		
		301	Personality Disorder		
Non-psychotic and	201 202 206 200	302	Sexual deviations		
other disorders	301, 302, 300, 309	306	Psychosomatic illness		
		309	Adjustment reaction		
Alcohol/substance	202 204	303	Alcoholism		
abuse disorder	303, 304	304	Drug dependence		
		897	Economic problems		
		898	Marital difficulties		
		899	Parent-child problems		
		900	Problems with aged parents or in-laws		
Social problems	897, 898, 899, 900, 901, 902, 904, 905, 906, 909	901	Family disruption/divorce		
		902	Education problems		
		904	Social maladjustment		
		905	Occupational problems		
		906	Legal problems		
		000	Other problems of		
		909	social adjustment		
Inpatient Mental Health	Fee Codes (Definitions 20	16/2017 – 2018/2019 (DS	6M-5 Manual)		
Substance-related and addictive disorders	ICD-9-CM Code (OMHRS) (all 303 codes), 304.x (all ICD-10-CA (DAD/NACRS)	: 291.x (all 291 codes), 29 304 codes), 305.x. Provisi : F10-19, F55	2.x (all 292 codes), 303.x onal=16		
Anxiety disorders	ICD-9-CM Code (OMHRS) Provisional=5 ICD-10-CA (DAD/NACRS)	: 293.84, 300, 300.0x, 300 : F06.4, F40, F41, F93.0-2,	.2x, 309.21, 313.23. F94.0		
Assault related injuries (victims of violence)	ICD-10-CA (DAD/NACRS)	: X85 - X99, Y00 - Y09, Y87	.1		
Deliberate self-harm	ICD-9-CM Code (OMHRS): N/A – DAD/NACRS only ICD-10-CA (DAD/NACRS): X60-X84, Y10-Y19, Y28 when DX10CODE1 ne F06- F99				
Eating disorders	ICD-9-CM (OMHRS): 307.1, 307.5, 307.51 ICD-10-CA (DAD/NACRS): F50				

Inpatient Mental Health 10-CM diagnostic codes	Fee Codes (Definitions 2019/2020 and onwards (DSM-5 manual with ICD-
Substance-related and addictive disorders	ICD-10-CA (OMHRS): F10.x-F19.x, Z72.0. Provisional=16 ICD-10-CA (DAD/NACRS): F10-19, F55
Anxiety disorders	ICD-10-CA (OMHRS): F06.4, F40.0x, F40.1x. F40.2x, F41.0x/1x, F41.8x/9x, F93.0, F94.0. Provisional=5 ICD-10-CA (DAD/NACRS): F06.4, F40, F41, F93.0-2, F94.0
Assault related injuries (victims of violence)	ICD-10-CA (DAD/NACRS): X85 - X99, Y00 - Y09, Y87.1
Deliberate self-harm	ICD-10-CA (OMHRS): N/A – DAD/NACRS only ICD-10-CA (DAD/NACRS): X60-X84, Y10-Y19, Y28 when DX10CODE1 ne F06- F99
Eating disorders	ICD-10-CA (OMHRS): F50, F98.3, F98.21 ICD-10-CA (DAD/NACRS): F50

ICD-10-CA (DAD/NACRS): F50

Supplemental Table 2: Study Population Characteristics:

Characteristics	Children 6-12 Years of Age (Cohort 1)	Adolescents 13-17 Years of Age (Cohort 2)	Young Adults 18- 24 Years of Age (Cohort 3)
Age at Index - N (Mean) SD			
	2,043,977 (7.73) 2.11	1,708,754 (13.98) 1.41	2,286,544 (19.96) 2.20
Sex - n (%)			
Female	994,914 (48.68)	831,269 (48.65)	1,116,421 (48.83)
Male	986,870 (51.32)	877 <i>,</i> 485 (51.35)	1,170,123 (51.17)
Services			
Total mental health physician visits (N)	924,158	2,096,136	5,321,633
Physician visits for mood and anxiety - N (proportion of total)	524,166 (57%)	1,774,345 (85%)	4,275,435 (80%)
Physician visits for social problems - N (proportion of total)	350,525 (38%)	165,982 (8%)	80,980 (2%)
Physician visits for other non-psychotic disorders - N (proportion of total)	45,562 (5%)	119,028 (6%)	247,841 (5%)
Physician visits for alcohol and substance abuse - N (proportion of total)	1,312 (0%)	29,100 (1%)	701,780 (13%)
Total mental health emergency Room visits (N)	12,398	111,028	282,687
Total mental health inpatient admissions (N)	1,120	20,523	30,376



Time (Quarterly)	n 6 – 12 vears o	fage					
	Mar-May	lun-Aug	Sep-Nov	Dec-Feb	Mar-May	lun-Aug	Sep-N
	2020	2020	2020	2020	2021	2021	2021
			Male				-
Observed Rate/1000	25.29	25.30	34.39	30.68	33.80	25.84	32.40
Expected Rate/1000	33.36	26.49	32.61	30.62	34	27	33.24
Difference between	-8.07	-1.19	1.78	0.06	-0.2	-1.16	-0.84
observed and expected							
% Relative Difference	-24.1%	-4.5%	5.4%	0.1%	-0.5%	-4.3%	-2.5%
(95% CI)	(-27.96.	(-8.46, -0.69)	(1.57, 9.19)	(-3.97.	(-5.35.	(-9.24.	(-7.44.
(-20.55)	(/ /	(- <i>))</i>	4.16)	3.98)	0.39)	2.19)
	· · · ·		Female	, ,	, ,	<u> </u>	, ,
Observed Rate/1000	20.25	22.24	30.12	28.41	33.11	25.47	30.75
Expected Rate/1000	25.93	20.84	25.1	23.34	27.01	21.71	26.15
Difforanca batwaan	5.96	1 /	5.02	5.07	6.1	2.76	1.6
observed and expected	-5.80	1.4	5.02	5.07	0.1	3.70	4.0
% Relative Difference	-21.89%	6.71%	20%	21.73%	22.57%	17.31%	17.59%
(95% CI)	(-25.38,	(3.06,	(16.4,	(17.88,	(18.14,	(12.76,	(13.02,
	-18.53)	10.23)	23.47)	25.44)	26.8)	21.67)	21.96)
Cohort 2 – Adolescents 1	3 – 17 years of	age					
Time (Quarterly)	Mar-May	Jun-Aug	Sep-Nov	Dec-Feb	Mar-May	Jun-Aug	Sep-No
	2020	2020	2020	2020	2021	2021	2021
			Male				
Observed Rate/1000	51.91	49.36	60.79	59.25	64.09	53.44	63.88
Expected Rate/1000	67.53	54.01	65.13	62.06	70.04	56.02	67.54
Difference between	-15.62	-4.65	-4.34	-2.81	-5.95	-2.58	-3.66
observed and expected							
% Relative Difference	-23.12%	-8.59%	-6.65%	-4.53%	-8.5%	-4.6%	-5.41%
(95% CI)	(-25.33,	(-10.91,	(-8.92,	(-6.95,	(-11.29,	(-7.47,	(-8.30,
	-20.96)	-6.33)	-4.42)	-2.16)	-5.78)	-1.8)	-2.61)
			Female				
Observed Rate/1000	101.99	104.29	132.61	138.46	159.01	131.22	151.06
Expected Rate/1000	126.71	101.8	121.66	116.99	131.53	105.67	126.28
Difference between	-24.72	2.49	10.95	21.47	27.48	25.55	24.78
observed and expected							
% Relative Difference	-19.51%	2.44%	9%	18.35%	20.89%	24.17%	19.61%
(95% CI)	(-23.51,	(-1.75,	(4.86,	(13.94,	(15.8,	(18.93,	(14.35,
. ,	-15.65)	6.46)	12.97)	22.57)	25.72)	29.15)	24.61)
Cohort 3 – Young Adults	18 – 24 years o	fage					
Time (Quarterly)	Mar-May	Jun-Aug	Sep-Nov	Dec-Feb	Mar-May	Jun-Aug	Sep-No
	2020	2020	2020	2020	2021	2021	2021
			Male				
Observed Rate/1000	95.23	102.76	109.28	105.72	113.28	102	104.97
Expected Rate/1000	110	101.8	103.84	101.42	109.94	101.75	103.78
Difference hetureen	-14.77	0.96	5.44	4.3	3.34	0.25	1.19
Difference between							
observed and expected		0.94%	5.23%	4.23%	3.03%	0.24%	1.14%
observed and expected % Relative Difference	-13.42%	0.57/0			10 110	1 2 40	
observed and expected % Relative Difference (95% CI)	-13.42% (-15.5.	(-1.17.3.00)	(3.08.7.35)	(1.94.6.47)	(0.41.5.59	(-2.40.	(-1.5/.
observed and expected % Relative Difference (95% CI)	-13.42% (-15.5, -11.38)	(-1.17,3.00)	(3.08,7.35)	(1.94,6.47)	(0.41,5.59)	(-2.40, 2.82)	(-1.5 <i>7,</i> 3.79)
observed and expected % Relative Difference (95% Cl)	-13.42% (-15.5, -11.38)	(-1.17,3.00)	(3.08,7.35) Female	(1.94,6.47)	(0.41,5.59)	(-2.40, 2.82)	(-1.57, 3.79)
observed and expected % Relative Difference (95% Cl) Observed Rate/1000	-13.42% (-15.5, -11.38)	(-1.17,3.00)	(3.08,7.35) Female	(1.94,6.47)	(0.41,5.59)	(-2.40, 2.82)	(-1.57, 3.79)
observed and expected % Relative Difference (95% Cl) Observed Rate/1000	-13.42% (-15.5, -11.38) 165.8	(-1.17,3.00) 181.46	(3.08,7.35) Female 203.7	(1.94,6.47)	(0.41,5.59)	(-2.40, 2.82) 201.62	(-1.57, 3.79) 208.99
observed and expected % Relative Difference (95% CI) Observed Rate/1000 Expected Rate/1000	-13.42% (-15.5, -11.38) 165.8 185.78	(-1.17,3.00) 181.46 172.94	(3.08,7.35) Female 203.7 182.46 21.24	(1.94,6.47) 208.91 175.53 22.28	(0.41,5.59) 228.05 192.06	(-2.40, 2.82) 201.62 178.79	(-1.57, 3.79) 208.99 188.63
Observed and expected % Relative Difference (95% CI) Observed Rate/1000 Expected Rate/1000 Difference between	-13.42% (-15.5, -11.38) 165.8 185.78 -19.98	(-1.17,3.00) 181.46 172.94 8.52	(3.08,7.35) Female 203.7 182.46 21.24	(1.94,6.47) 208.91 175.53 33.38	(0.41,5.59) 228.05 192.06 35.99	(-2.40, 2.82) 201.62 178.79 22.83	(-1.57, 3.79) 208.99 188.63 20.36
Observed and expected % Relative Difference (95% CI) Observed Rate/1000 Expected Rate/1000 Difference between observed and expected % Relative Difference	-13.42% (-15.5, -11.38) 165.8 185.78 -19.98	(-1.17,3.00) 181.46 172.94 8.52	(3.08,7.35) Female 203.7 182.46 21.24 11.62%	(1.94,6.47) 208.91 175.53 33.38	(0.41,5.59) 228.05 192.06 35.99	(-2.40, 2.82) 201.62 178.79 22.83	(-1.57, 3.79) 208.99 188.63 20.36
Observed and expected % Relative Difference (95% CI) Observed Rate/1000 Expected Rate/1000 Difference between observed and expected % Relative Difference	-13.42% (-15.5, -11.38) 165.8 185.78 -19.98 -10.75% (13.2	(-1.17,3.00) 181.46 172.94 8.52 4.92% (1.72)	(3.08,7.35) Female 203.7 182.46 21.24 11.63% (8.42)	(1.94,6.47) 208.91 175.53 33.38 19.01% (15.56	(0.41,5.59) 228.05 192.06 35.99 18.73% (14.75	(-2.40, 2.82) 201.62 178.79 22.83 12.76%	(-1.57, 3.79) 208.99 188.63 20.36 10.79%

Supplemental Table 3: Total Expected Versus Observed Outpatient Mental Health Visits by Age and Sex:

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Supplemental Figure 1: Expected versus observed mental health visits by age and diagnosis (males):

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Supplemental Figure 2 – Expected versus observed mental health ED visits and hospitalization over time both male and female combined:



A. Total Mental Health Emergency Department Visits



B. Total Mental Health Hospitalizations

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Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data	3
Participants	6	(<i>a</i>) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3-4
		(b) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	3-4
Bias	9	Describe any efforts to address notential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	4
		(b) Describe any methods used to examine subgroups and interactions	4
		(c) Explain how missing data were addressed	n/a
		(d) If applicable, explain how loss to follow-up was addressed	n/a
		(e) Describe any sensitivity analyses	n/a
Results			

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of cohort studies

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed	n/a
		eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Supplemental file
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	Report numbers of outcome events or summary measures over time	4
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	4-6
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-6
Discussion			
Key results	18	Summarise key results with reference to study objectives	6-7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	7-8
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	1
i ununig			

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Sex differences Among Children, Adolescents, and Young Adults for Mental Health Service Use Within In-patient and Outpatient Settings, Before and During the COVID-19 Pandemic: A Population-based Study in Ontario, Canada.

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Primary Subject Heading :	Epidemiology
Secondary Subject Heading:	Public health
Keywords:	MENTAL HEALTH, COVID-19, Primary Health Care, Depression & mood disorders < PSYCHIATRY, Eating disorders < PSYCHIATRY, PUBLIC HEALTH





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Sex differences Among Children, Adolescents, and Young Adults for Mental Health Service Use Within In-patient and Outpatient Settings, Before and During the COVID-19 Pandemic: A Population-based Study in Ontario, Canada.

ABSTRACT (297/300words)

OBJECTIVES: The pandemic and public health response to contain the virus had impacts on many aspects of young people's lives including disruptions to daily routines, opportunities for social, academic, recreational engagement, and early employment. Consequently, children, adolescents, and young adults may have experienced mental health challenges that required use of mental health services. This study compared rates of use for in- and out-patient mental health services during the pandemic to pre-pandemic rates.

DESIGN: Population-based repeated cross-sectional study.

SETTING: Publicly delivered mental health care in primary and secondary settings within the province of Ontario, Canada.

PARTICIPANTS: All children 6-12 years of age (n=2,043,977), adolescents 13-17 years (n=1,708,754), and young adults 18-24 years (n=2,286,544), living in Ontario and eligible for provincial health insurance between March 2016 and November 2021.

PRIMARY OUTCOME MEASURES: *Outpatient mental health visits* to family physicians and psychiatrists for: mood and anxiety disorders, alcohol and substance abuse disorders, other non-psychotic mental health disorders, and social problems. *Inpatient mental health visits* to emergency departments and hospitalizations for: substance-related and addictive disorders, anxiety disorders, assault-related injuries, deliberate self-harm, and eating disorders. All outcomes were analyzed by cohort and sex.

RESULTS: During the pandemic, observed out-patient visit rates were higher among young adult by 19.01% (CI: 15.56,22.37; 209 vs. 175 per 1000) and adolescent females 24.17% (CI: 18.93,29.15; 131 vs. 105 per 1000) for mood and anxiety disorders and remained higher than expected. Female adolescents had higher than expected utilization of in-patient care for deliberate self-harm, eating disorders, and assault-related injuries.

CONCLUSIONS: Study results raise concerns over prolonged high rates of mental health use during the pandemic, particularly in female adolescents and young women, and highlights the need to better monitor and identify mental health outcomes associated with COVID-19 containment measures and to develop policies to address these concerns.

Strengths and Limitations:

- (+) Strong observational study design using large, diverse, and population based cohorts
- (+) Outcomes are well-established mental health utilization indicators used in routine reporting and peerreviewed publications and are based on physician claims and data routinely provided by hospitals and emergency departments under Ontario's public health insurance that provides comprehensive care to all residents
- (-) Care received outside Ontario's public health insurance program for physician services, hospital and emergency departments are not included in the analysis
- (-) Observational study design cannot provide evidence of causality between specific public health measures and mental health outcomes
- (-) Analysis was stratified by age and sex but did not control for other potential individual-level confounders that might have changed over the study period

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Conflict of Interest: none to report.

REB Approval: This research was approved by the research ethics board at the University of Toronto (RIS protocol number 41386).

BACKGROUND:

The COVID-19 pandemic was declared by the World Health Organization on March 11th, 2020 (1). On March 15th, the Office of the Premier responded by declaring a provincial state of emergency in Ontario, Canada, which resulted in successive closure of all non-essential shops and services (2). For nearly two years, health officials and institutional decision makers attempted to mitigate population-level risk of infection by implementing non-pharmaceutical interventions (NPI), such as social distancing, masking, and the closing and reopening of various sectors, which included daycares, primary and secondary schools, and post-secondary institutions (2, 3). The use of various NPIs throughout the COVID-19 pandemic resulted in major disruptions to nearly all aspects of life and routines of children, adolescents, and young adults, due to mass closures of schools, recreation centers, organizational activities, and early employment opportunities. According to the Center for Diseases Control and Prevention⁽⁴⁾ and other literature in the field, youth up to 24 years of age experienced many challenges during this time, some distinct to specific age groups, others shared across age bands, including major changes in their daily *routine* (e.g., having to physically distance from friends, family, places of worship and other social communities); breaks in the continuity of learning (e.g., switching from in-person to virtual learning, missing out on supplementary and early education opportunities, access limitations to personal workspace, technology, and connectivity at home) (5, 6); breaks in continuity of healthcare (e.g., missed well-child and immunization visits, limited access to mental, speech, occupational and other health services). Within some households, youth also suffered loss in security and safety (e.g., housing and food insecurity, increased exposures to domestic violence and online harms, threats of physical illness, and uncertainty for the future). For all youth but particularly late teens and young adults, they missed out on significant life events and rites of passage (e.g., missing celebrations, prom, graduations, dating, frosh-week and in-person college activities, early employment opportunities, and other milestone life events) (4).

It has been hypothesized that these COVID-19-related challenges could result in long lasting mental health distress and symptoms, and in increased utilization of mental health services. Studies and reports have begun to surface in support of this hypothesis (4, 7). In England over a quarter of children and young people reported sleep disruptions, and high cases of isolation, feeling lonely and fearful of leaving home because of COVID-19 early in the pandemic (8). Another study found increases in depressive symptoms among youth in the United Kingdom (9). A study from the United States showed that the socioeconomic impact on parents due to job losses, working from home, and social isolation also impacted children, particularly when there was job loss in the family and social isolation, with elevated stress and cortisol levels among parents and their children (10). A study from 73 primary care clinics in the United States showed increases in visits for children for mood and eating disorders at the beginning of the pandemic (11). In Ontario, Canada, there are indications that use of acute care services for eating disorders were higher during the pandemic (12, 13). Another study in Ontario found that there was an increase in the use of mental health care services during the pandemic, particularly among adolescent females (14). A systematic review of studies of college students also found that mental health problems during the COVID-19 pandemic occurred more often in females than males (15). A systematic review of studies of emergency department use by children and adolescents, showed increased visits for suicide-related issues in girls but not boys and increased visit rates for self-harm in adolescents (16).

Our study builds on that literature by examining critical mental health care service indicators for both office-based physician services and in-patient settings such as emergency departments (EDs) and hospitals. We are also building on prior studies by extending the age range to include young adults, who were underrepresented in prior research. We are also building on current evidence by examining additional mental health outcomes such as deliberate self-harm (DSH) and assault-related injuries, with observational data for the first 20-months of the pandemic. Using routinely collected health administrative data from Ontario, Canada, we sought to examine whether the rates of mental health visits had changed during the pandemic (March 2020 to November 2021) versus (vs.) pre-COVID-19 patterns. Given the existing evidence on differences in the rates of use of specific mental health services related to the age and gender of children (14-16), we examined use by specific diagnostic categories and stratified the sample by age (children (6-12 years of age), adolescents (13-17 years) and young adults (18-24 years)) and sex.

METHODS

We designed a population-based, repeated cross-sectional study, using unique encrypted identifiers at the individual level, including all children (6-12 years of age), adolescents (13-17 years) and young adults (18-24 years), living in Ontario, Canada and eligible for provincial health insurance between March 2016 to November 2021. The physician billing codes have been completed in the same manner before and after COVID-19. The diagnosis code is provided independently by the physician after the assessment is completed. The Ontario Registered Persons Database provides sex, age, postal code, and dates of birth for all Ontario residents. Office visits for physicians and psychiatrists were obtained from the Ontario Health Insurance Plan (OHIP) database, which contains billing records for all publicly funded physician services provided. The Canadian Institute for Health Information's National Ambulatory Care Reporting System (NACRS), Discharge Abstract Database (DAD), and Ontario Mental Health Reporting System (OMHRS) were used to identify mental health-related emergency department (ED) visits

and hospitalizations. All study data were accessed through Data Analytic Services (DAS) at ICES (formerly the Institute for Clinical Evaluative Sciences), an independent research institute with the legal status permitting it to collect and analyze health care and demographic data without individual patient consent for health system evaluation and improvement under the Ontario's health information privacy law.

A baseline measure of mental health rates of use was obtained from the pre-pandemic period (March 2016 to February 2020). Rates of use during the pandemic are based on utilization starting from March 2020 till the end of November 2021. Data were provided by DAS for analysis in a quarterly format, providing 23 cross-sectional measures over time. All persons between the ages of 6 to 24 years, and who were OHIP insured were considered for inclusion in the study. Persons with missing IKN (ICES Key Number - unique encrypted identifier), birth date, sex, OHIP eligibility, non-Ontario residential status, or who had died prior to index date were excluded. Three cohorts were generated based on age: 1) children 6-12 years of age, 2) adolescents 13-17 years of age, and 3) young adults 18-24 years of age. We used open cohorts and assessed at-risk time to allow for individuals to contribute time at risk for outcomes. Data for sex, age and service use were provided at the individual level.

Outcome measures:

Primary outcomes were outpatient visits for mental illness by primary care providers and psychiatrists derived from OHIP physician billing claims, and inpatient emergency department (ED) visits and hospitalizations using ICD-9 and ICD-10 codes from OMHRS, DAD, and NACRS. Given the large proportion of virtual visits after the pandemic (14), especially in primary care, both in person and virtual were aggregated. Outcomes for each cohort are as follows: *Outpatient outcomes*: mood and anxiety disorders (OHIP DXCODES 296, 300, 311), alcohol and substance abuse disorders (OHIP DXCODES 303, 304), other non-psychotic mental health disorders (OHIP DXCODES 301, 302, 306, 309), and social problems (OHIP DXCODES: 897, 898, 899, 900, 901, 902, 904, 905, 906, 909). *Inpatient outcomes: (ED and Hospitalizations)*: substance-related and addictive disorders, anxiety disorders, assault-related injuries, deliberate self-harm (DSH), and eating disorders. For full list of diagnostic codes see supplementary section (Supplemental Table 1).

Statistical Analysis:

Negative binomial regression with time and season as predictor variables, were used to model utilization trends before the pandemic (March 2016 – February 2020) and visits rates per 1000. In the case of rare events in ED and hospitals, they were reported per 100,000. The log of the persons in each quarter was used as the offset. Residuals were modeled as an autoregressive AR(1) process to account for serial correlation and to account for seasonality. The fitted model was used to predict the expected rates of use from March 2020 to the end of November 2021. For the main analysis, we calculated actual observed rates of use during the pandemic as compared to expected rates. Absolute difference of use for each quarter from March 2020 to

the end of November 2021 was calculated by subtracting expected rates from observed rates. We calculated the relative difference (95% confidence interval [CI]) between the observed and expected rates by subtracting the expected rate from the observed, divided by expected and multiplied by 100. We also stratified results from the primary analysis by individual diagnoses and sex. Data preparations, analyses, and visualizations were performed using SAS 9.4.

Patient and Public Involvement:

None.

RESULTS

Over 6 million youth between the ages of 6 to 24 years from Ontario, Canada were included in this study. The child cohort had a mean age of 7.7 (Standard Deviation [SD] 2.1) years of which 48.6% were female, the adolescent cohort a mean age of 13.9(1.4), 48.6% female, and the young adult cohort a mean age of 19.9(2.2) years with 48.8% female (Supplemental Table 2).

Overall Outpatient Mental Health Care Utilization:

Overall baseline expected rates of mental health service utilization were lowest in the children cohort, followed by adolescent and then young adult cohorts (Figure 1). In all three groups, the first quarter of the pandemic was associated with lower than expected rates. In the child cohort, the highest relative difference in rates for overall service utilization were among females in March to May 2021 by 22.57 % (CI: 18.14, 26.8; 33 vs. 27 per 1000). In the adolescent cohort, the highest difference in the rate of use was in June to August 2021 by 24.17% (CI: 18.93,29.15; 131 vs. 105 per 1000) among females. Young female adults had the highest difference in service use, during December 2020 to February 2021 quarter, up by 19.01% (CI: 15.56,22.37; 209 vs. 175 per 1000). For females in all three cohorts, overall rates of mental health care use remained above expected rates during the pandemic. In contrast, males showed lower overall utilization of mental health services relative to pre-pandemic levels, especially among children and adolescents. For more details (Supplemental Table 3).

Outpatient Mental Health Care Utilization by Individual Diagnoses:

Examining the change in individual diagnoses during the pandemic, revealed that the highest difference in mental health care use is attributable to mood and anxiety disorders, increasing with age across cohorts, particularly among females (Figure 2). The highest relative difference in utilization for mood and anxiety disorders was among female children 27.42% (CI: 22.93,31.72; 23 vs. 18/1000), although absolute rates remained low. Adolescent females and young adults showed much higher and persistent overall differences in service utilization for mood and anxiety disorders. The highest differences in adolescent females were observed in the March to May 2021 quarter 19.8% (CI: 14.23, 25.14; 118 vs. 112 per 1000) and June to August 2021 quarter 23.18% (CI: 17.4, 28.64; 117 vs. 95 per 1000). The highest differences in adult females were observed in the December 2020 to February 2021 quarter 19% (CI: 15.09, 22.93; 183 vs. 154 per 1000) and March to May 2021 quarter 18.2% (CI: 13.6, 22.6; 200 vs. 169

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per 1000). Other non-psychotic disorders were also higher during the pandemic, predominantly among female adolescents, but with low overall rates. Among all three male cohorts, we saw significantly lower utilization of outpatient care for all disorders during the pandemic, especially among adolescents and young adults. However, higher rates of substance and alcohol abuse was observed among young male adults in March to May 2021 by 16% (CI: 11.4, 20.33; 15 vs. 13 per 1000) (Supplemental Figure 1). Other conditions did not show any substantial change between expected rates of use versus observed rates.

Inpatient Mental Health Care Utilization in ED and Hospitals:

The difference in mental health service utilization during the pandemic for ED and hospital services (Supplemental Figure 2) showed that there was a general decrease in seeking care for mental health services within those settings, although care was available after the pandemic. The overall decrease during the pandemic was evident among all three cohorts, with exception of certain ED and hospital services among female adolescents (Figure 3).

ED visits for DSH were up among adolescent females, with the highest difference in September to November 2021 by 42.8% (CI: 22.4, 59.7; 258 vs. 181/100,000). In the same timeframe, there was also a higher number of ED visits for DSH requiring hospitalization by 46.1% (CI: 26.5, 62.6; 110 vs. 80/100,000). Hospitalizations for DSH were also up among female adolescents, in September to November 2021 by 102.4% (CI: 76.4, 123; 354 vs. 175/100,000).

Assault-related ED visits that required hospitalization were up nearly five-fold for female adolescents 493.4% (CI: 238.5, 565.2; 2 vs. 0.4/100,000) in September to November 2021. Assault-related hospitalizations were up more than two-fold among female adolescents 272.7% (CI: 151.2, 372.6; 3 vs. 1/100,000) during the September to November 2021 quarter.

Eating disorders were also higher among female adolescents, with a two-fold difference in ED relative to expected rates 225.1% (CI: 178.6, 256.9; 59 vs. 18/100,000), observed in September to November 2021 and comparably in March to May 2021. ED visits for eating disorders requiring hospitalization were also up among female adolescents, highest in September to November 2021 by 221.3% (CI: 162.4, 258.4; 27 vs. 8/100,000). The highest absolute difference in hospitalizations for eating disorder among female adolescents was in March to May 2021 by 139.7% (CI: 112.4, 161; 64 vs. 26/100,000).

DISCUSSION

In this population-based repeated cross-sectional study, we observed substantially higher rates for clinical mental health outpatient visits for mood and anxiety disorders, relative to expected patterns prior to the pandemic, in adolescent and young female adults. Overall mental health visits to emergency departments and hospitalizations were down relative to expected rates, with exception of DSH, eating disorders, and assault-related injuries among female adolescents. This is further evidence, using mental health service use as an indicator, that there have been significant mental health challenges among young female adults and particularly female adolescents, during the pandemic.

Examining physician-based mental health service use by sex, revealed that a large proportion of the elevated use can be attributed to mood and anxiety disorders among female adolescents and young adults. This finding was not unexpected and has been reported in Canada and elsewhere in North American and European countries (14, 17, 18). Female adolescents showed the highest relative increase, likely due to various stressors reported during the pandemic among female teenagers, such as disruptions to daily routines, school, and inability to see their peers in person (19). Female adults had the highest absolute increase, which is not surprising given the same impacts on adolescents during the pandemic, in addition to pre-existing economic stressors placed on young adults in terms of finances, education, employment prospects, housing and other added pressures early in adulthood (20).

In contrast to lower overall mental health service use among males, we noted higher alcohol and substance abuse among male young adults. The literature is mixed with respect to increased alcohol and substance use in this population during the pandemic (21). This may be because these studies often utilize cross-sectional data, which depending on the demographics, time point, and sampling frame may yield different results. It should be noted that the increase in substance and alcohol abuse detected in this study was not substantial. The overall lower than expected rates of seeking mental health care among adolescent and young adult males is not surprising and is consistent with the literature, where this demographic is known for seeking less care, which may have worsened during the pandemic (22). Alternatively, it has been suggested that boys took part in more physical activity during the pandemic and enjoyed reduced stresses associated with lockdowns such as less daily structure and not going to school, which may have been protective (19). There may be a greater prevalence of mental health challenges among males, especially young adults, however, due to various factors, available care is usually underutilized in this population (23-25).

There was no major change in mental health service use among young children. However, we do not believe that this is an indication of there being an absence of mental health needs in this cohort but perhaps challenges in communication between children and their parents at this stage of development (26, 27). Based on the literature, we know that young children also experienced challenges due to changes in their routines, distancing from extended family and caretakers, missed opportunities for social and cognitive development, routine medical and wellness visits, in addition to potential exposures to stress as a result of economic pressures on parents in some households (4, 10, 28, 29). In one study, parents reported negative impacts associated with closure of early childhood education and care facilities, and schools (30). Some parents reported negative impacts of these closures on their children's social and emotional well-being, resulting in anxiety, boredom, under-stimulation, and tantrums (30). Another study also found deterioration of children's mental health during the pandemic, attributed largely to social isolation (31). It is possible that the early psychological impacts of the pandemic and

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related lock-down measures on children were not detectable based on this study design and data but will become more apparent downstream.

Inpatient services revealed that ED visits and hospitalizations were down relatively across the board and for most conditions, except for DSH, eating disorders, and assault-related injuries among female adolescents. Similar findings have been reported elsewhere (13, 32, 33). To our knowledge, a similar study regarding DSH found no increase in ED and hospitalization among adolescents and young adults (34). This is likely a result of methodology as they combined their sample of adolescent and young adults. Our study did not find any increase in DSH among young female adults but did find an increase among female adolescents. There is also indication of greater case severity based on relatively flat ED visits but increased ED visits requiring hospitalization and overall hospitalization numbers for DSH, eating disorders, and assaultrelated injury. The increase in cases and severity has been reported in a prior study for eating disorders (13). While absolute numbers for these visits remain low, any increase within these segments of mental health warrants attention. Especially, for visits resulting from assault, neglect, and domestic abuse, among other risk factors for ACEs, which can lead to short-term and long-term psychological and physical health consequences (33, 35-37). This is the first study to our knowledge to have examined service use for assault-related injuries at the population level during the pandemic within this segment of the population in Ontario. Studies elsewhere have noted increases in abusive physical and verbal interactions towards teens and children because of pandemic stressors on parents (32, 33, 38). Even though absolute rates remain low among the population for DSH, eating disorders, and assault-related injuries, we find it troubling that ED and hospitalizations have increased during the pandemic, for these critically serious outcomes.

Explanations for these findings are complex and studies as to possible causes are ongoing. Plausible theories have centered around closure of schools, reduced access to family and friends, and isolation due lockdown measures which have been associated with sleep disturbance, anxiety, depression among teens and post-secondary students (18, 29, 39-42). Students also experienced elevated stress, loneliness, and had fears of missing out on social life, their own health, friends and family's, and uncertainties about the future (43). Economic pressures on families have also shown to impact the mental health of youth within the household, especially when there was loss of employment and trouble keeping up with household bills (10, 28, 29). With increased cost of living and economic pressures, it is also important to acknowledge the link between food insecurity, depression, anxiety and eating disorders. Food insecurity has been associated with poor physical and mental outcomes, possibly due to feelings of helplessness, shame, and stress (44). Additionally, food insecurity has been associated with eating disorders (45-47). This is considering global challenges in supply chain disruptions, cost, access barriers, and growing demand for food banks post-pandemic (48-50). Additionally, disturbance in pre-pandemic routines and general reduction in physical activity during the pandemic may also be a contributing factor, given the wealth of evidence regarding physical and psychological benefits of exercise versus deleterious effects of a

sedentary lifestyle (29, 51). Lastly, schools are not simply a place for learning, they are a place where students socialize, make connections with peers and staff, find a sense of purpose and a sense of self, and for many where they access critical services, such as tools for personal development, education, special learning and peer support, and for some, food programs or an escape from domestic troubles at home (5, 38, 52). Much of these benefits and critical services delivered at school were simply not available in a remote learning environment during the pandemic.

Limitations

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Studies with outcomes based on healthcare utilization, may underestimate the true prevalence of those health outcomes, due to non-seeking of care, or the seeking of care outside the medical establishment such as private clinics. The diagnostic codes from OHIP billing submitted by physicians have been validated by chart audit and have found to be very sensitive and specific (53). These codes have been used for public reporting and for peer reviewed research publications (13, 14, 54). We stratified the analysis by age and sex to highlight important distinctions in mental health service utilization. However, we did not control for a range of other risk factors such as previous history of mental health diagnoses or social and racial factors known to be related to mental health service utilization at the individual level. Changes in prevalence of these factors over the course of this five-year study could confound our results. Our quasi-experimental study design cannot provide evidence of causality based on NPIs, other post-pandemic stressors, and increases in mental health service use. We acknowledge that the rapid shift to virtual care may have resulted in greater accessibility to some of the mental health services described in this study and as a result drive higher service utilization postpandemic. However, studies looking at the shift to virtual care from in-person services in Ontario have shown that in cases of mental health, the overall use in services decreased among the general population during the first 9-months of the pandemic (55). Therefore, it is quite possible that the increase detected among children, adolescents, and young adults in this study were unique to this sub-population. Lastly, the results of this study while generalizable to the population of Ontario, Canada, may not be generalizable to other jurisdictions where COVID-19 cases, containment policies, boundaries and population characteristics are different.

CONCLUSIONS

Over a 20-month course of the COVID-19 pandemic, we observed substantially higher rates of use for mental health physician services relative to pre-pandemic levels, predominantly among female adolescents and young adults. Higher utilization was largely driven by services for mood, anxiety, and depressive disorders within outpatient settings. The only notable difference in mental health care needs among males was for alcohol and substance use in young adults, which should be monitored in the future. We noted higher cases and severity for eating disorders, deliberate self-harm, and assault-related injuries among adolescent females in EDs and hospitals. Our study raises concerns about growing mental health needs among female adolescents and young adults during the pandemic, especially in critical areas such as

depression, anxiety, DSH, eating disorders, and assault-related injury and call for urgent action in policy and healthcare response. We also need to ensure that more research and interventions are mobilized to identify and address underlying causes of worsening mental health among female adolescents and young adults.

Figure 1: Total Expected and Observed Outpatient Mental Health Visits by Age and Sex Figure 2: Expected Versus Observed Mental Health Visits by Age and Diagnosis (Females) Figure 3: Total Hospitalizations (Females)

Contributorship Statement

MJS - formal analysis, visualization, validation, writing – original draft, review & editing. VS – conceptualization, validation, writing – original draft, review & editing. PL: data curation, project administration, writing – review & editing. TN: data curation, project administration, writing – review & editing. AM: validation, writing - review & editing. BS: validation, writing - review & editing. PI: validation, writing - review & editing. WW: validation, writing - review & editing. AG - conceptualization, funding acquisition, methodology, supervision, validation, writing – review & editing.

Competing Interests:

None declared.

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Data sharing statement:

The datasets from this study are held securely in coded form at ICES. While data sharing agreements prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS. The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Ethics approval statement:

This research was approved by the research ethics board at the University of Toronto (RIS protocol number 41386).

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Supplemental Table 1: Service and Diagnostic Codes:

Study Outcome Categories	OHIP Diagnostic Codes for Outcomes	OHIP Diagnostic Codes Individual Diagnostic Codes and Their for Outcomes Description			
Outpatient Mental Heal	th Fee Codes				
		296	Bipolar Disorder		
Mood and anxiety	206 200 211	300	Anxiety and related disorders		
disorders	296, 300, 311	311	Depressive or other non-psychotic disorders		
		301	Personality Disorder		
Non-psychotic and	201 202 206 200	302	Sexual deviations		
other disorders	301, 302, 306, 309	306	Psychosomatic illness		
		309	Adjustment reaction		
Alcohol/substance	202 204	303	Alcoholism		
abuse disorder	303, 304	304	Drug dependence		
		897	Economic problems		
		898	Marital difficulties		
		899	Parent-child problems		
		900	Problems with aged parents or in-laws		
Social problems	897, 898, 899, 900, 901, 902, 904, 905, 906, 909	901	Family disruption/divorce		
		902	Education problems		
		904	Social maladjustment		
		905	Occupational problems		
		906	Legal problems		
		000	Other problems of		
		909	social adjustment		
Inpatient Mental Health	Fee Codes (Definitions 20	16/2017 – 2018/2019 (DS	M-5 Manual)		
Substance-related and addictive disorders	ICD-9-CM Code (OMHRS) (all 303 codes), 304.x (all ICD-10-CA (DAD/NACRS)): 291.x (all 291 codes), 293 304 codes), 305.x. Provisi : F10-19, F55	2.x (all 292 codes), 303.x onal=16		
Anxiety disorders	ICD-9-CM Code (OMHRS) Provisional=5 ICD-10-CA (DAD/NACRS)): 293.84, 300, 300.0x, 300 : F06.4, F40, F41, F93.0-2,	.2x, 309.21, 313.23. F94.0		
Assault related injuries (victims of violence)	ICD-10-CA (DAD/NACRS)	: X85 - X99, Y00 - Y09, Y87.	1		
Deliberate self-harm	ICD-9-CM Code (OMHRS): N/A – DAD/NACRS only ICD-10-CA (DAD/NACRS): X60-X84, Y10-Y19, Y28 when DX10CODE1 ne F06- F99				
Eating disorders	ICD-9-CM (OMHRS): 307.1, 307.5, 307.51 ICD-10-CA (DAD/NACRS): F50				

Inpatient Mental Health 10-CM diagnostic codes	Fee Codes (Definitions 2019/2020 and onwards (DSM-5 manual with ICD-
Substance-related and addictive disorders	ICD-10-CA (OMHRS): F10.x-F19.x, Z72.0. Provisional=16 ICD-10-CA (DAD/NACRS): F10-19, F55
Anxiety disorders	ICD-10-CA (OMHRS): F06.4, F40.0x, F40.1x. F40.2x, F41.0x/1x, F41.8x/9x, F93.0, F94.0. Provisional=5 ICD-10-CA (DAD/NACRS): F06.4, F40, F41, F93.0-2, F94.0
Assault related injuries (victims of violence)	ICD-10-CA (DAD/NACRS): X85 - X99, Y00 - Y09, Y87.1
Deliberate self-harm	ICD-10-CA (OMHRS): N/A – DAD/NACRS only ICD-10-CA (DAD/NACRS): X60-X84, Y10-Y19, Y28 when DX10CODE1 ne F06- F99
Eating disorders	ICD-10-CA (OMHRS): F50, F98.3, F98.21 ICD-10-CA (DAD/NACRS): F50

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 Laces: x60-x84, V10-Y19, V28 when DX10CC

 LCD-10-CA (OMHRS): F50, F98.3, F98.21

 LD-10-CA (DAD/NACRS): F50

Supplemental Table 2: Study Population Characteristics:

Characteristics	Children 6-12 Years of Age (Cohort 1)	Adolescents 13-17 Years of Age (Cohort 2)	Young Adults 18- 24 Years of Age (Cohort 3)
Age at Index - N (Mean) SD			
	2,043,977 (7.73) 2.11	1,708,754 (13.98) 1.41	2,286,544 (19.96) 2.20
Sex - n (%)			
Female	994,914 (48.68)	831,269 (48.65)	1,116,421 (48.83)
Male	986,870 (51.32)	877,485 (51.35)	1,170,123 (51.17)
Services			
Total mental health physician visits (N)	924,158	2,096,136	5,321,633
Physician visits for mood and anxiety - N (proportion of total)	524,166 (57%)	1,774,345 (85%)	4,275,435 (80%)
Physician visits for social problems - N (proportion of total)	350,525 (38%)	165,982 (8%)	80,980 (2%)
Physician visits for other non-psychotic disorders - N (proportion of total)	45,562 (5%)	119,028 (6%)	247,841 (5%)
Physician visits for alcohol and substance abuse - N (proportion of total)	1,312 (0%)	29,100 (1%)	701,780 (13%)
Total mental health emergency Room visits (N)	12,398	111,028	282,687
Total mental health inpatient admissions (N)	1,120	20,523	30,376



Supplemental Table 3: Total Expected Versus Observed Outpatient Mental Health Visits by Age and Sex:

Cohort 1 – Young childre	n 6 – 12 years o	fage					
Time (Quarterly)	Mar-May	Jun-Aug	Sep-Nov	Dec-Feb	Mar-May	Jun-Aug	Sep-Nov
	2020	2020	2020	2020	2021	2021	2021
			Male		•		
Observed Rate/1000	25.29	25.30	34.39	30.68	33.80	25.84	32.40
Expected Rate/1000	33.36	26.49	32.61	30.62	34	27	33.24
Difference between	-8.07	-1.19	1.78	0.06	-0.2	-1.16	-0.84
observed and expected							
% Relative Difference	-24.1%	-4.5%	5.4%	0.1%	-0.5%	-4.3%	-2.5%
(95% CI)	(-27.96,	(-8.46, -0.69)	(1.57, 9.19)	(-3.97,	(-5.35,	(-9.24,	(-7.44,
	-20.55)		l	4.16)	3.98)	0.39)	2.19)
	20.05	22.24	Female	20.44	22.44	05.47	20.75
Observed Rate/1000	20.25	22.24	30.12	28.41	33.11	25.47	30.75
Expected Rate/1000	25.93	20.84	25.1	23.34	27.01	21.71	26.15
Difference between	-5.86	1.4	5.02	5.07	6.1	3.76	4.6
observed and expected							
% Relative Difference	-21.89%	6.71%	20%	21.73%	22.57%	17.31%	17.59%
(95% CI)	(-25.38,	(3.06,	(16.4,	(17.88,	(18.14,	(12.76,	(13.02,
Cohort 2 Adolosoonto 1	-18.53)	10.23)	23.47)	25.44)	26.8)	21.67)	21.96)
Time (Quarterly)	3 – 17 years of a	age	Son Nov	Doc Fob	Mar May		Son Nov
Time (Quarterly)	2020	Jun-Aug 2020	2020	2020	2021	Jun-Aug 2021	2021
	2020	2020	Male	2020	2021	2021	2021
Observed Rate/1000	51 91	49 36	60.79	59.25	64.09	53.44	63.88
Expected Rate/1000	67 53	54 01	65.13	62.06	70.04	56.02	67 54
Difference between	-15.62	-4.65	-4.34	-2.81	-5.95	-2.58	-3.66
observed and expected	10.02			2.01	5.55	2.50	5.00
% Relative Difference	-23.12%	-8.59%	-6.65%	-4.53%	-8.5%	-4.6%	-5.41%
(95% CI)	(-25.33,	(-10.91,	(-8.92,) (-6.95,	(-11.29,	(-7.47,	(-8.30,
· · ·	-20.96)	-6.33)	-4.42)	-2.16)	-5.78)	-1.8)	-2.61)
			Female	· · · ·			
Observed Rate/1000	101.99	104.29	132.61 🔪	138.46	159.01	131.22	151.06
Expected Rate/1000	126.71	101.8	121.66	116.99	131.53	105.67	126.28
Difference between	-24.72	2.49	10.95	21.47	27.48	25.55	24.78
observed and expected							
% Relative Difference	-19.51%	2.44%	9%	18.35%	20.89%	24.17%	19.61%
(95% CI)	(-23.51,	(-1.75,	(4.86,	(13.94,	(15.8,	(18.93,	(14.35,
	-15.65)	6.46)	12.97)	22.57)	25.72)	29.15)	24.61)
Cohort 3 – Young Adults	18 – 24 years of	age					
Time (Quarterly)	Mar-May	Jun-Aug	Sep-Nov	Dec-Feb	Mar-May	Jun-Aug	Sep-Nov
	2020	2020	2020	2020	2021	2021	2021
01 15 1/1000	05.00	400.70	Male	405 70	442.20	100	404.07
Observed Rate/1000	95.23	102.76	109.28	105.72	113.28	102	104.97
Expected Rate/1000	110	101.8	103.84	101.42	109.94	101.75	103.78
Difference between	-14.//	0.96	5.44	4.3	3.34	0.25	1.19
% Relative Difference	12 / 20/	0.04%	E 220/	4 220/	2 0 2 9/	0.24%	1 1 / 0/
	-15.42%	0.94%	5.25% (2.09.7.25)	4.25%	5.05%	0.24%	1.14%
	-11 38)	(-1.17,3.00)	(3.06,7.33)	(1.54,0.47))	(-2.40, 2.82)	3 79)
	11.50)	1	Female	1		2.021	5.75
Observed Rate/1000	165.8	181.46	203.7	208.91	228.05	201.62	208,99
Expected Rate/1000	185.79	172 0/	182.46	175 52	192.06	178 70	188 62
Difference between	-19 98	8 52	21 24	22.22	35.00	27.82	20 26
observed and expected	13.50	0.52	21.27	55.50	33.35	22.05	20.30
% Relative Difference	-10.75%	4.92%	11.63%	19.01%	18.73%	12.76%	10.79%
(95% CI)	(-13.9,	(1.73,	(8.40,	(15.56,	(14.76,	(8.75,	(6.69,
, ,	-7.70)	8.02)	14.77)	22.34)	22.55)	16.62)	14.73)

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Supplemental Figure 1: Expected versus observed mental health visits by age and diagnosis (males):

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Supplemental Figure 2 – Expected versus observed mental health ED visits and hospitalization over time both male and female combined:



A. Total Mental Health Emergency Department Visits



B. Total Mental Health Hospitalizations

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		STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of <i>cohort studies</i>	
Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2-3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3-4
		(b) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	4
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	4
		(b) Describe any methods used to examine subgroups and interactions	4
		(c) Explain how missing data were addressed	n/a
		(d) If applicable, explain how loss to follow-up was addressed	n/a
		(e) Describe any sensitivity analyses	n/a
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed	n/a
		eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Supplemental file
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	n/a
		(c) Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	Report numbers of outcome events or summary measures over time	4
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	4-6
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	n/a
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5-6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5-6
Discussion			
Key results	18	Summarise key results with reference to study objectives	6-7
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	7-8
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.