IMPACT OF COVID- 19 STATE OF EMERGENCY ON

FEVIALE REPRODUCTION



info@kstrategic.com

AVAILABLE OHIP DATA

Included **OHIP Codes** Specialist Specialist Working In Working in Community Hospital Referral **Primary Care** Physician

Not Included

ICD-10

If salaried may not be billed

Acute Care & Potentially Emergency Room

Miscarriages in emergency may not be captured. Nic U would be ICD-10

AVAILABLE OHIP DATA

Jan 2015 to December 2022



How to make a Freedom of Information request

Learn how to request records from public-sector institutions like Ontario government ministries, colleges, universities, school boards, hospitals, municipalities and police services.

FOI request submitted November 2021/April 2023 to Ministry of Health Ontario

How to make a Freedom of Information request

OHIP Codes

ncidence Rates For I	Registered Persons For Specified Diagnostic Codes	
M Request#IMSC-00	0018707	
Data Source(s): Claim	s History Database (BIDA environment)	
Run Date: 2022-12-1	3	
General Criteria		
O	ario registered physicians only, approved claims only, service date between 2015-01-01 and 2022-04- isted in Table 1.	
Community laborato	ry groups excluded, duplicate claims excluded.	
Notes		
Patient age was calcu	slated as of the last day of each calendar year.	
Counts are distinct pa	atient counts are the respective reporting level of granularity.	
Table 1		_
	Description Fe	emale 🛚
042	A.I.D.S.	
053	HERPES ZOSTER, SHINGLES	
070	VIRAL HEPATITIS	
075	INFECTIOUS MONONUCLEOSIS, GLANDULAR FEVER	
079	OTHER VIRAL DISEASES	
150	MALIGNANT NEOPLASMS - ESOPHAGUS	
157	MALIGNANT NEOPLASMS - PANCREAS	
174	MALIGNANT NEOPLASMS - FEMALE BREAST	
180	MALIGNANT NEOPLASMS - CERVIX	
182	MALIGNANT NEOPLASMS - BODY OF UTERUS	
183	MALIGNANT NEOPLASMS - OVARY, FALLOPIAN TUBE, BROAD LIGAMENT	
186	MALIGNANT NEOPLASMS - TESTIS	
201	MALIGNANT NEOPLASMS - HODGKIN'S DISEASE	
203	MULTIPLE MYELOMA, PLASMA CELL LEUKEMIA	

OHIP BILLING CODES

- OHIP billing codes are <u>diagnostic codes used by</u> the Ontario Health Insurance Program for claims submission by healthcare professionals (HCPs) in an outpatient setting
 - Does not include hospital data sources
 - Community laboratory groups excluded
- Code numbers and diagnostic assignments are similar to the ICD-9 system, although not necessarily the same
- All claims must be submitted through medical claims electronic data transfer; they include:
 - HCP claim for services rendered by physicians or private medical labs
 - WSIB claim for services rendered to patients with Ontario health insurance coverage who have work related injuries
 - RMB claim for services rendered by physicians to a patient insured under another Canadian provincial/territorial health coverage plan, excluding Quebec

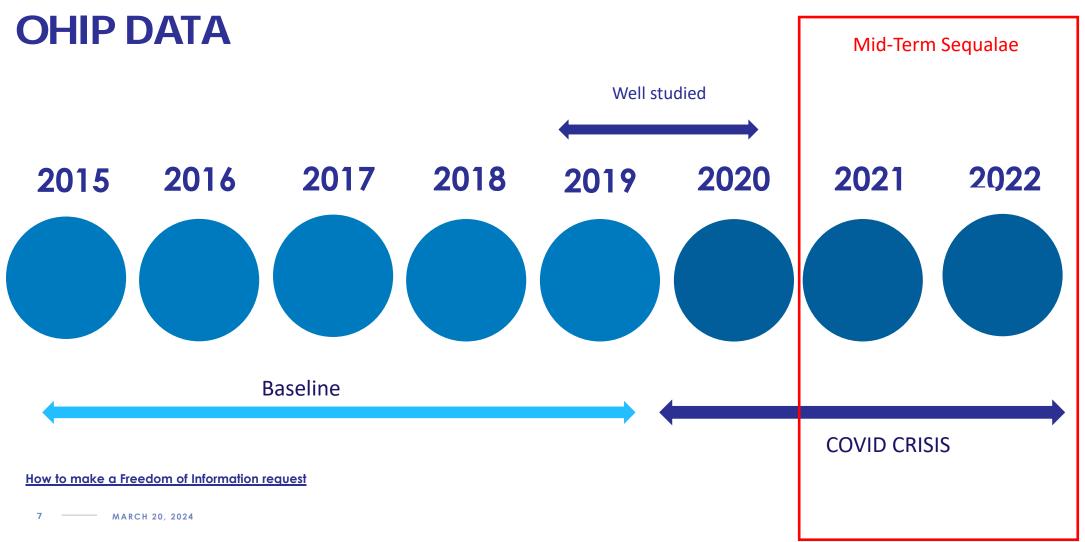
OHIP DATA REQUESTS AND QUERIES

- Two data requests were performed
 - Initial request at end of 2022 for female reproductive health and female cancer codes; OHIP database queried on Dec 13, 2022; includes billing code data from Jan 1 2015 to Apr 30 2022
 - Second request mid 2023 for the initial set of codes plus an extended set; OHIP database queried on Aug 25, 2023; includes billing code data for the full year of 2022; although requested, no historical (2015-2021) data was provided for the additional set of codes
- Includes unique patient claims only; duplicate claims excluded
- OHIP: "The reported counts of distinct patients was performed at the reported level of granularity"
 - o Granularity-defining variables: year, diagnosis, sex (M/F), age band (0-17, 18-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+ years)
 - This means that care should be taken when adding granular values although it is reasonable to assume that patient counts across different sexes and age bands in a given year are of distinct patients, the same patient may be diagnosed with different conditions

OHIP DATA REQUESTS AND QUERIES

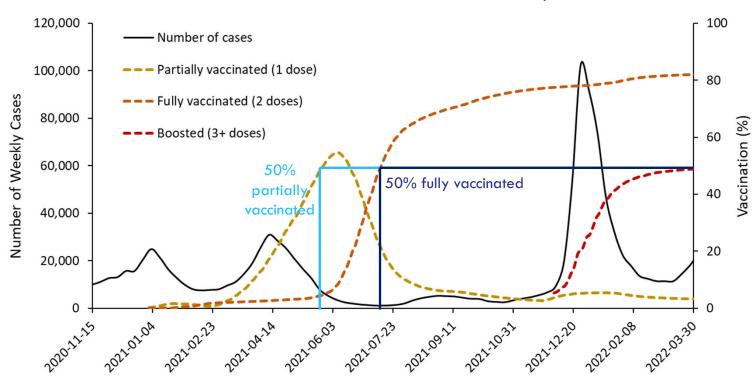
- OHIP: "Incidence was defined as the first time a patient received the diagnosis code. Therefore each patient
 was only counted once for a given diagnostic code within the entire reporting period (2015-01-01 to 2022-1231)"
 - OHIP: "In an attempt to align 2015 volumes with subsequent years the following logic was applied: In order to be counted the patient could not have had the diagnosis in the prior calendar year (2014)"
 - o This means that earlier years (and particularly 2015 and 2016) effectively have shorter "look-back" or reference periods which may contribute to overestimation of incidence
 - It is a common limitation of estimating incidence particularly from populational (registry) data^{1,2}
 - Its impact is reduced with longer study periods (ideally by using constant reference periods for each year); affects more chronic conditions than acute conditions¹
 - It has been shown that for most conditions the impact is small when look-back periods are extended to 3-5 years¹
 - Impact can be estimated using sensitivity analysis^{1,2}
 - Does not affect patient count numbers
- OHIP: [Patient counts] "Each patient was counted once per year, sex type code, diagnostic code and age band." [irrespective of data from previous years]

6 MARCH 20, 2024



VACCINE ROLLOUT IN ON

Number of COVID-19 cases and vaccine uptake



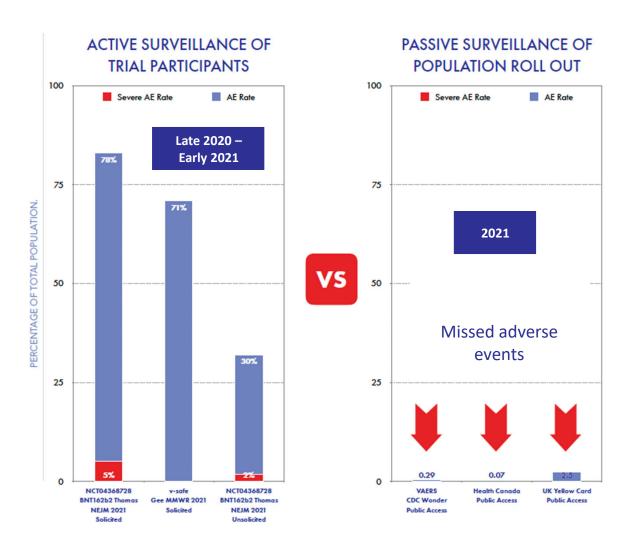
MARCH 20, 2024

ROLL OUR SURVEILLANCE YOU DON'T FIND WHAT YOU DON'T LOOK FOR

There is a dramatic difference between passive vs active monitoring of adverse events

- When participants were actively followed for adverse events (AEs) in the trials, high percentages of adverse events were reported.
- Once the vaccine was rolled out at the population level, **passive** surveillance was used with Health Canada, VAERS or the European Yellow Card system.

When that happened, the **signal was** completely lost.



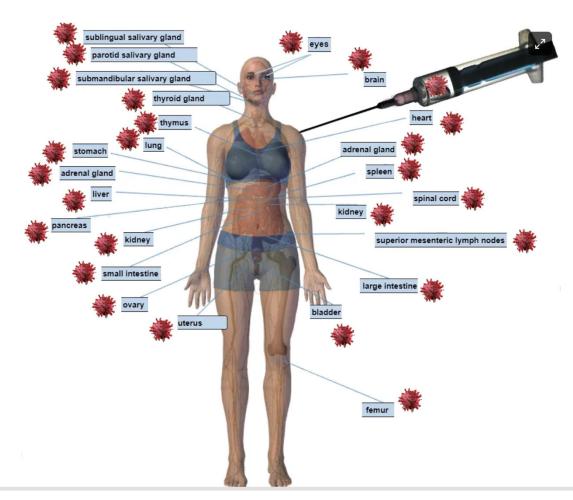
DISTRIBUTED SPIKE

Widespread distribution of synthetic mRNA coding **for** spike protein

Produces ORDERS OF MAGNITUDE longer than natures messenger RNA

has fragmented genetic instructions that come from a human factory environment

endless combination of extra protein producing burdens throughout the body



ENDOCRINE DISRUPTION?

NEWS | BIOLOGY Thousands report unusual menstruation patterns after covid-19... NEWS | BIOLOGY Thousands report unusual menstruation patterns after COVID-19 vaccination Survey aims to document breakthrough bleeding and heavier-than-usual periods postvaccine 15 JUL 2022 · 2:00 PM ET · BY JENNIFER COUZIN-FRANKEL



Unexpected vaginal bleeding and COVID-19 vaccination in nonmenstruating women



Unexpected vaginal bleeding and COVID-19 vaccination in nonmenstruating women

Table 1. SARS-CoV-2 mRNA Product (BNT162, PF-0 7302048): 2.6.5.5B. Adapted from Pharmacokinetics: *organ distribution*, report number: 185350, Pages 6-7

Sample	Mean total lipid concentration (μg lipid equivalent/g (or mL) (3 males and 3 females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Adrenal glands	0.271	1.48	2.72	2.89	6.80	13.80	18.20
Bone marrow (femur)	0.479	0.96	1.24	1.24	1.84	2.49	3.77
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068
Heart	0.282	1.03	1.40	0.99	0.79	0.45	0.55
Kidneys	0.391	1.16	2.050	0.924	0.590	0.426	0.425
Liver	0.737	4.63	11.00	16.50	26.50	19.20	24.30
Lung	0.492	1.21	1.83	1.50	1.15	1.04	1.09
Lymph node (mandibular)	0.064	0.189	0.290	0.408	0.534	0.554	0.727
Lymph node (mesenteric)	0.050	0.146	0.530	0.489	0.689	0.985	1.37
Ovaries (females)	0.104	1.34	1.64	2.34	3.09	5.24	12.30
Pancreas	0.081	0.21	0.414	0.380	0.294	0.358	0.599
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264
Skin	0.013	0.208	0.159	0.145	0.119	0.157	0.253
Small intestine	0.030	0.221	0.476	0.879	1.28	1.30	1.47
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112
Spleen	0.334	2.47	7.730	10.300	22.100	20.100	23.400
Testes (males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.000
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.446

WOMEN INORDINATELY HARMED

5.3.6 CUMULATIVE ANALYSIS OF POST-AUTHORIZATION ADVERSE EVENT REPORTS OF PF-07302048 (BNT162B2) RECEIVED THROUGH 28-FEB-2021

Report Prepared by:

Worldwide Safety

Pfizer

The information contained in this document is proprietary and confidential. Any disclosure, reproduction, distribution, or other dissemination of this information outside of Pfizer, its Affiliates, its Licensees, or Regulatory Agencies is strictly prohibited. Except as may be otherwise agreed to in writing, by accepting or reviewing these materials, you agree to hold such information in confidence and not to disclose it to others (except where required by applicable law), nor to use it for unauthorized purposes.

Approved On: 30-Apr-2021 09:26 (GMT)

Table 1. General Overview: Selected Characteristics of All Cases Received During the Reporting Interval

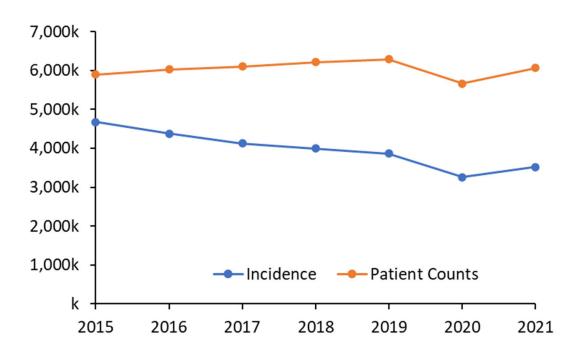
	Characteristics	Relevant cases (N=42086)
Gender:	Female	29914 71% in women
	Male	9182
	No Data	2990
Age range (years):	≤ 17	175 ^a 12% in prime childbear
0.01 -107 years	18-30	4953 age
Mean = 50.9 years	31-50	13886
n = 34952	51-64	7884
	65-74	3098
	≥ 75	5214
	Unknown	6876
Case outcome:	Recovered/Recovering	19582
	Recovered with sequelae	520 28% don't fully recove
	Not recovered at the time of report	11361
	Fatal	1223 3% prove fatal
	Unknown	9400

a. in 46 cases reported age was <16-year-old and in 34 cases <12-year-old.

CLAIMS DATA

- Claims data is extensively used for epidemiological and health care studies
- Strengths timely, widely available and inexpensive. Data generally aligns with medical records
 - Only one diagnostic code is claimed per visit
 - Trend based on assumption that billing practices remained constant over time
- Limitations some variability in coding dependent on transcriber, susceptible to changes over time due to shifts in coding and/or shifts between outpatient and in-hospital visits
 - Does not include claims from acute care settings or private clinics
 - Not as specific as ICD codes, with many catch-all categories
 - New diagnostic codes introduced during the study period may dilute claims to the original code
- ** Does hot include data on stage or progression of malignancies
 - Important to look at changes over time in order to detect trends.

OHIP SUMMARY DATA INCIDENCE AND PATIENT COUNTS ACROSS ALL CODES



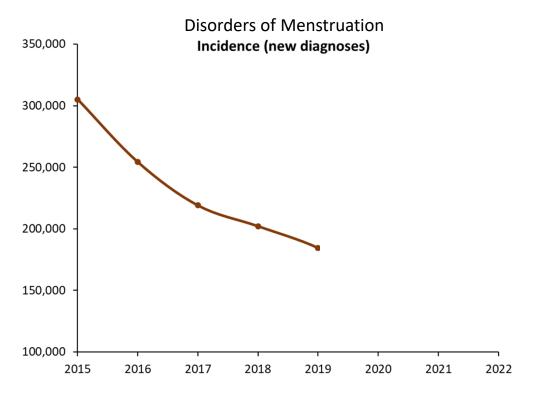
Unique patients with any of the requested billing codes in a given year (total patient counts) increases slightly from 2015-2019 (roughly 2% per year)

"New" unique patients with any of the requested billing codes (total incident patients) decreases slightly from 2015-2019 (roughly 4% per year)

Both have a stable pattern up to 2019

MENSTRUAL DISORDERS

OHIP: 626 - DISORDERS OF MENSTRUATION



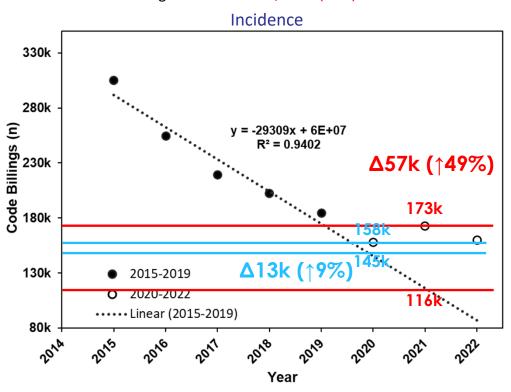
Factors that may explain a downward trend

- Changes in "true" rates of the condition as new technologies or treatments are administered
- Changes in screening practices or programs.
 For example the implementation of a healthcare program
- A move from community practice to salaried practices that are not captured by OHIP billing
- Overestimation in earlier years due to shorter look-back period

MENSTRUAL DISORDERS

OHIP: 626 - DISORDERS OF MENSTRUATION

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data



Percentual differences (Δ) for the years of 2020 (blue) and maximum of 2021/2022 (red) relative to expected values from a simple linear fit to 2015-2019 data (dotted line). May be affected by incidence overestimation in earlier years due to shorter lookback period.

Absolute and percentual differences (Δ) for the years of 2020 to 2022 relative to 2019 values. Does not account for historical trends; minimally affected by variable lookback period.

Table with absolute and percentual differences relative to 2019

Year	Δ2019 (n)	Δ2019 (%)
2020	-26,967	-15
2021	-11,781	-6
2022	-24,881	-13
Sum of Δs 2020-2022	-63,629	-34

16 MARCH 20, 2024

MENSTRUAL DISORDERS

OHIP: 626 - DISORDERS OF MENSTRUATION

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

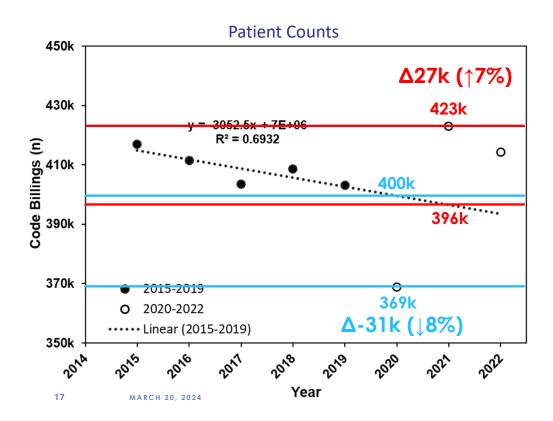


Table with absolute and percentual differences relative to 2019

Year	Δ2019 (n)	Δ2019 (%)
2020	-34,334	-9
2021	+19,905	+5
2022	+11,198	+3
Sum of Δs (2020-2022)	-3,231	-1

Not all menstrual changes were severe enough to go to physician

MENSTRUAL DISORDERS

OHIP: 627 — MENOPAUSE, POST- MENOPAUSAL BLEEDING

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

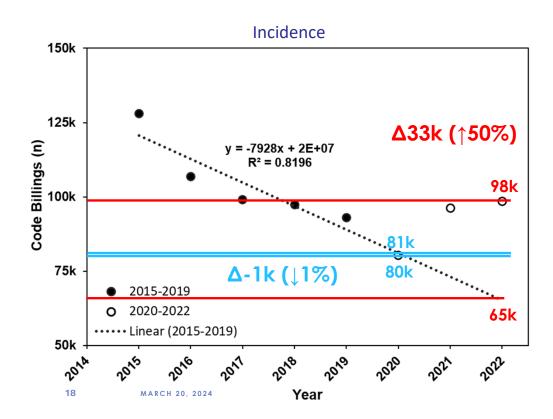


Table with absolute and percentual differences relative to 2019

Year	Δ2019 (n)	Δ2019 (%)
2020	-12,725	-14
2021	+3,267	+4
2022	+5,421	+6
Sum of Δs (2020-2022)	-4,037	-4

Not all menstrual changes were severe enough to go to physician

MENSTRUAL DISORDERS

OHIP: 627 — MENOPAUSE, POST- MENOPAUSAL BLEEDING

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

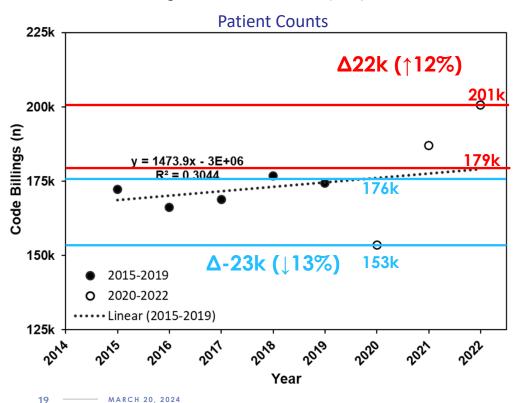


Table with absolute and percentual differences relative to 2019

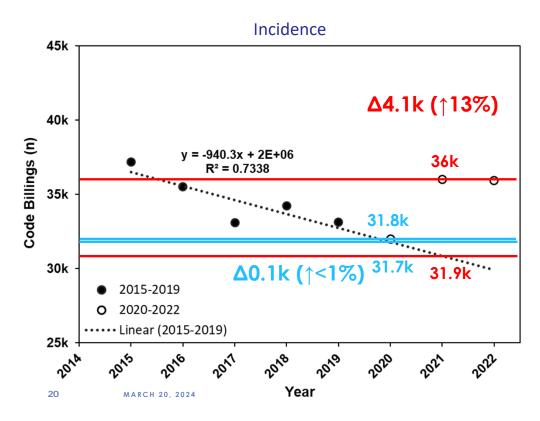
Year	Δ2019 (n)	Δ2019 (%)
2020	-20,888	-12
2021	+12,680	+7
2022	+26,373	+15
Sum of Δs (2020-2022)	+18,165	+10

Not all menstrual changes were severe enough to go to physician

FEMALE INFERTILITY

OHIP: 628 — INFERTILITY, SEX=FEMALE

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

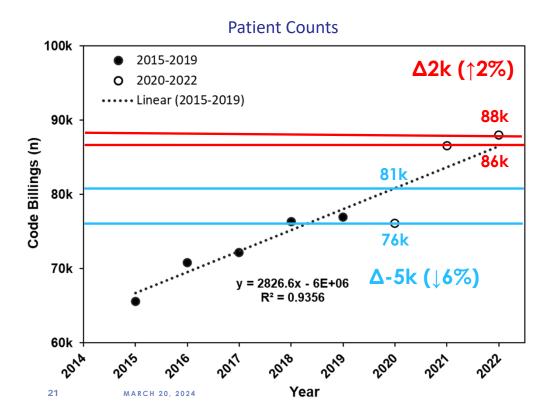


Year	Δ2019 (n)	Δ2019 (%)
2020	-1,123	-3
2021	+2,903	+9
2022	+2,802	+8
Sum of Δs (2020-2022)	+4,582	+14

FEMALE INFERTILITY

OHIP: 628 — INFERTILITY, SEX=FEMALE

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

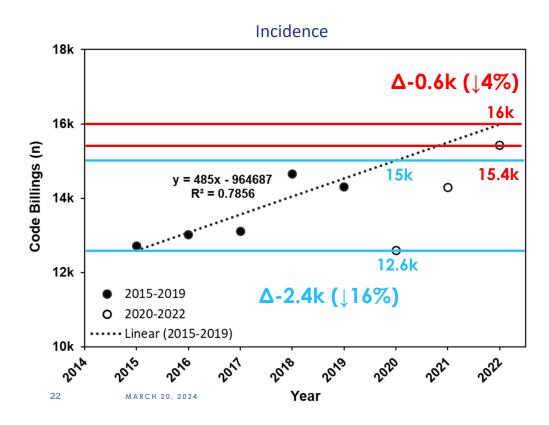


Year	Δ2019 (n)	Δ2019 (%)
2020	-815	-1
2021	+9,681	+13
2022	+11,117	+14
Sum of Δs (2020-2022)	+19,983	+26

MALE INFERTILITY

OHIP: 628 — INFERTILITY, SEX= MALE

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

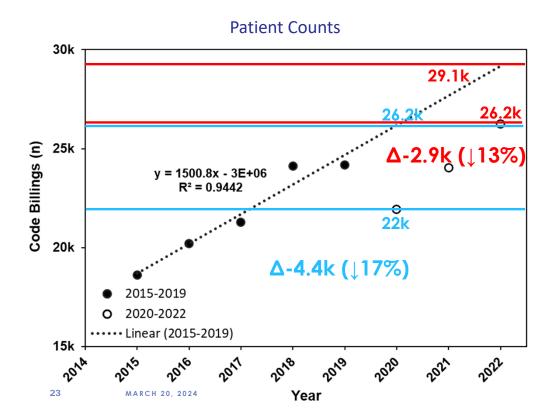


Year	Δ2019 (n)	Δ2019 (%)
2020	-1,713	-12
2021	-24	0
2022	+1,121	+8
Sum of Δs (2020-2022)	-616	-4

MALE INFERTILITY

OHIP: 628 — INFERTILITY, SEX= MALE

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

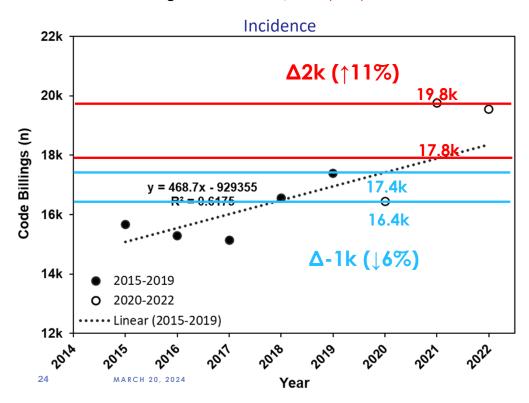


Year	Δ2019 (n)	Δ2019 (%)
2020	-2,232	-9
2021	-118	-1
2022	+2,072	+9
Sum of Δs (2020-2022)	-278	-1

MALE INFERTILITY

OHIP: 606 — MALE INFERTILITY, OLIGOSPERMIA, AZOOSPERMIA

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

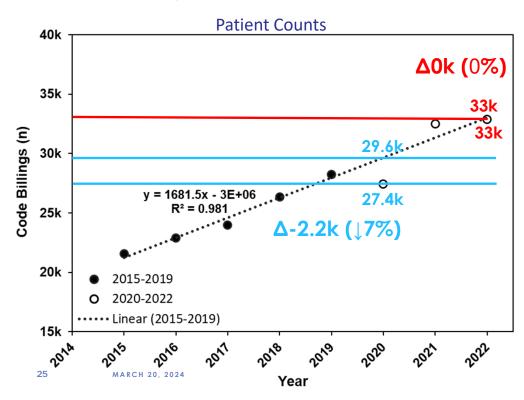


Year	Δ2019 (n)	Δ2019 (%)
2020	-940	-5
2021	+2,364	+14
2022	+2,161	+12
Sum of Δs (2020-2022)	3,585	+21

MALE INFERTILITY

OHIP: 606 — MALE INFERTILITY, OLIGOSPERMIA, AZOOSPERMIA

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

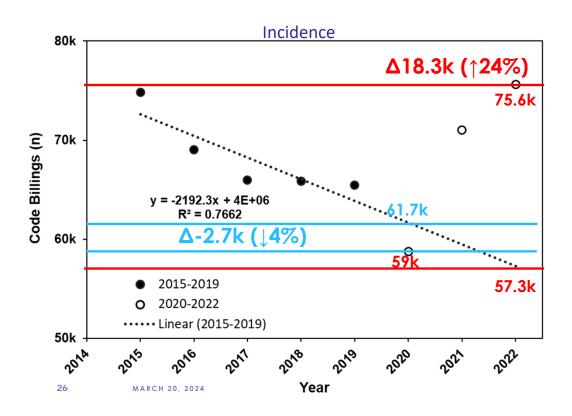


Year	Δ2019 (n)	Δ2019 (%)
2020	-795	-3
2021	4,287	+15
2022	4,631	+16
Sum of Δs (2020-2022)	8,123	+29

DISORDERS FEMALE GENITALS

OHIP: 629 - OTHER DISORDERS OF FEMALE GENITAL ORGANS

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

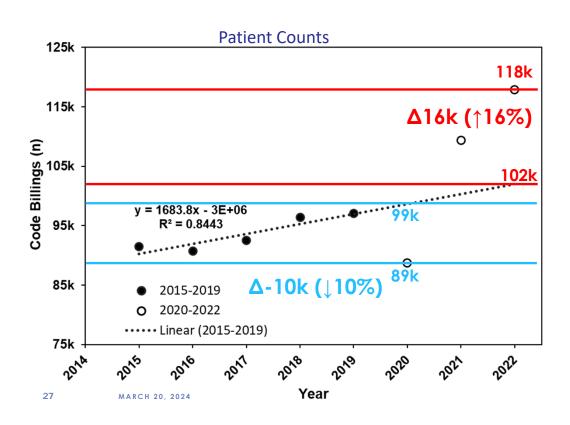


Year	Δ2019 (n)	Δ2019 (%)
2020	-6,711	-10
2021	+5,581	+9
2022	+10,135	+15
Sum of Δs (2020-2022)	+9,005	+14

DISORDERS FEMALE GENITALS

OHIP: 629 - OTHER DISORDERS OF FEMALE GENITAL ORGANS

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data



Year	Δ2019 (n)	Δ2019 (%)
2020	-8,305	-9
2021	+12,319	+13
2022	+20,836	+21
Sum of Δs (2020-2022)	+24,850	+26

FETAL LOSS

OHIP: 632+634 — MISSED, INCOMPLETE, OR COMPLETE ABORTION

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

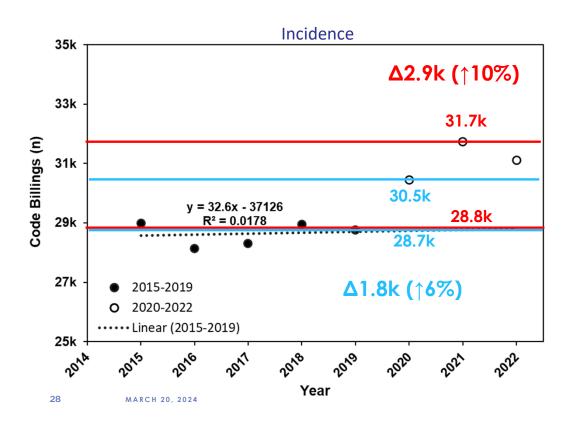


Table with absolute and percentual differences relative to 2019

Year	Δ2019 (n)	Δ2019 (%)
2020	+1,699	+6
2021	+2,986	+10
2022	+2,359	+8
Sum of Δs (2020-2022)	+7,044	+24

Would be good to consider relative to live births

FETAL LOSS

OHIP: 634+635 — MISSED, INCOMPLETE, OR COMPLETE ABORTION

Max vs Min billings 2020 and 2021/2022 (max) to linear fit to 2015-2019 data

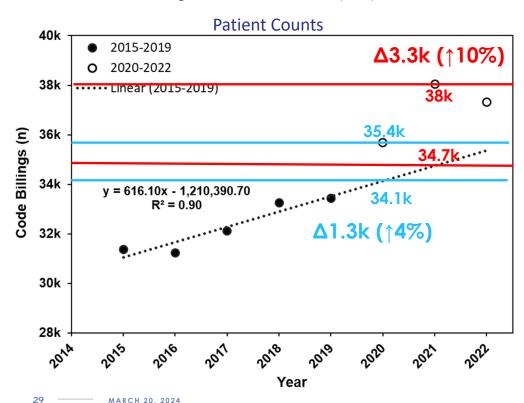
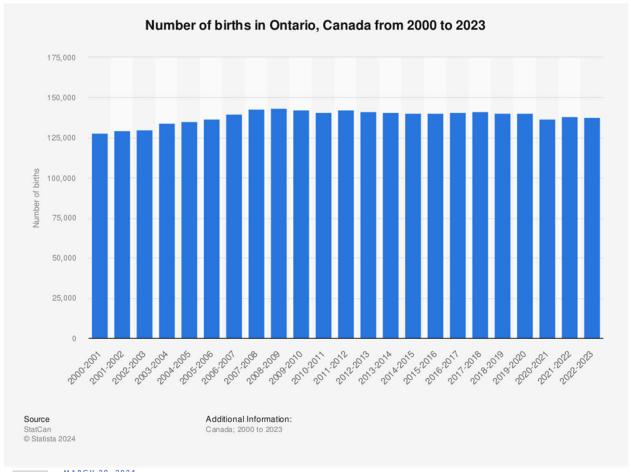


Table with absolute and percentual differences relative to 2019

Year	Δ2019 (n)	Δ2019 (%)
2020	+2,256	+7
2021	+4,619	+14
2022	+3,878	+12
Sum of Δs (2020-2022)	+10,753	+32

May be beneficial to consider relative to live births

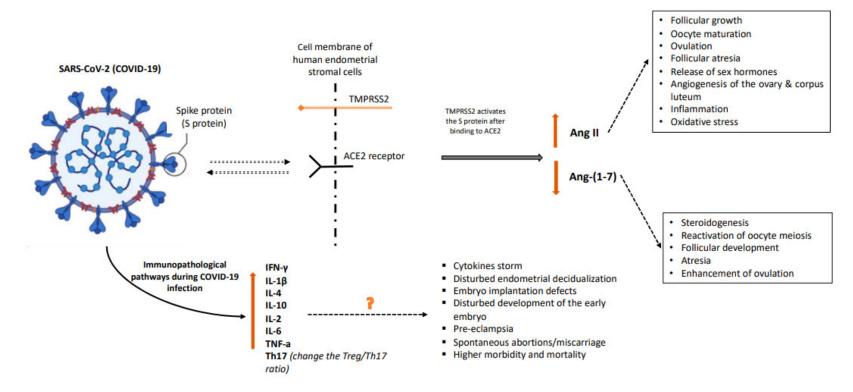
LIVE BIRTHS IN ONTARIO



Rates of live births remained fairly constant from 2015 to 2022 with exception of a slight drop in live births from 2020 -2021.

30

COVID- 19 AND REPRODUCTIVE HEALTH INFECTION- AND SPIKE- INDUCED MEACHANISMS



1 — MARCH 20, 2024 1. Chrysanthopoulos Diseases 2023

COVID- 19 AND FETAL LOSS

- Although there were several reports that that early pregnancy loss is associated with COVID-19 infection, this finding was not confirmed in meta-analysis and meta-reviews^{1,2}
- Similar to our findings other studies have identified increased fetal loss (missed and complete/incomplete abortions) in 2020-2022. A retrospective study from Turkey found that the frequency of first-trimester miscarriage was increased in 2020 (11.8%) relative to 2019 (9.2%)³
 - After applying mixed-effects Poisson regression model with random intercepts for matching months was used to adjust for seasonality the authors found that the number of miscarriages per 100 new pregnancies was significantly higher in 2020 compared with 2019 (IRR, 1.25 (95% CI, 1.16–1.35); P < 0.0001)
 - \circ However, the rate of positive SARS-CoV-2 test results did not have a significant effect on the miscarriage rate (P = 0.810)
 - This indicates that there may be other factors associated with the COVID crisis that may have had an impact on fetal loss

1. Van Baar Hum Reprod Update 2023

2. Chrysanthopoulos Diseases 2023

2. Sacinti Unitrasound Obs Gyn 2021

CALLS FOR ACTION

- Call for more research. Need to investigate this further in well-controlled prospective trials
- Pause on vaccination in pregnant, lactating and women and men of reproductive age until safety issues fully investigated

