Annals of Internal Medicine RESEARCH AND REPORTING METHODS

COVID-19 Case Age Distribution: Correction for Differential Testing by Age

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Background: Despite expected initial universal susceptibility to a novel pandemic pathogen like SARS-CoV-2, the pandemic has been characterized by higher observed incidence in older persons and lower incidence in children and adolescents.

Objective: To determine whether differential testing by age group explains observed variation in incidence.

Design: Population-based cohort study.

Setting: Ontario, Canada.

Participants: Persons diagnosed with SARS-CoV-2 and those tested for SARS-CoV-2.

Measurements: Test volumes from the Ontario Laboratories Information System, number of laboratory-confirmed SARS-CoV-2 cases from the Integrated Public Health Information System, and population figures from Statistics Canada. Demographic and temporal patterns in incidence, testing rates, and test positivity were explored using negative binomial regression models and standardization. Sources of variation in standardized ratios were identified and test-adjusted standardized infection ratios (SIRs) were estimated by metaregression.

Results: Observed disease incidence and testing rates were highest in the oldest age group and markedly lower in those younger than 20 years; no differences in incidence were seen by sex. After adjustment for testing frequency, SIRs were lowest in children and in adults aged 70 years or older and markedly higher in adolescents and in males aged 20 to 49 years compared with the overall population. Test-adjusted SIRs were highly correlated with standardized positivity ratios (Pearson correlation coefficient, 0.87 [95% CI, 0.68 to 0.95]; $P < 0.001$) and provided a case identification fraction similar to that estimated with serologic testing (26.7% vs. 17.2%).

Limitations: The novel methodology requires external validation. Case and testing data were not linkable at the individual level.

Conclusion: Adjustment for testing frequency provides a different picture of SARS-CoV-2 infection risk by age, suggesting that younger males are an underrecognized group at high risk for SARS-CoV-2 infection.

Primary Funding Source: Canadian Institutes of Health Research.

Ann Intern Med. doi:10.7326/M20-7003 **Annals.org**
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 17 August 2021.

The COVID-19 pandemic has many unusual features that have created controversy around optimal control strategies. One such unexpected feature is the apparent low incidence of SARS-CoV-2 infection in children and adolescents (1, 2). Indeed, early in the pandemic, there was a question of whether children might lack susceptibility to SARS-CoV-2 infection, although an early report noted an asymptomatic child with pulmonary infection associated with a family cluster (3). A subsequent study in Shenzhen, China, showed that infection in children is not rare (4). Early studies conducted under strict public health interventions found less evidence of active infection and seropositivity in children than in older adults (5).

The failure to recognize pediatric infection early in the pandemic may have been due to the relative rarity of severe illness in younger people (2, 6), the large proportion of asymptomatic infections in children, or the nonspecificity of SARS-CoV-2 symptoms in children (7, 8), with resultant decreased testing rates. Although severe illness and even death due to COVID-19 have been reported in children younger than 10 years, this is uncommon (6, 9–11). In Ontario, Canada, early challenges with laboratory testing for SARS-CoV-2 led to limited testing in persons without severe symptoms; furthermore, the invasive nature of nasopharyngeal sampling for polymerase chain reaction (PCR) testing makes it an unappealing modality for use in children.

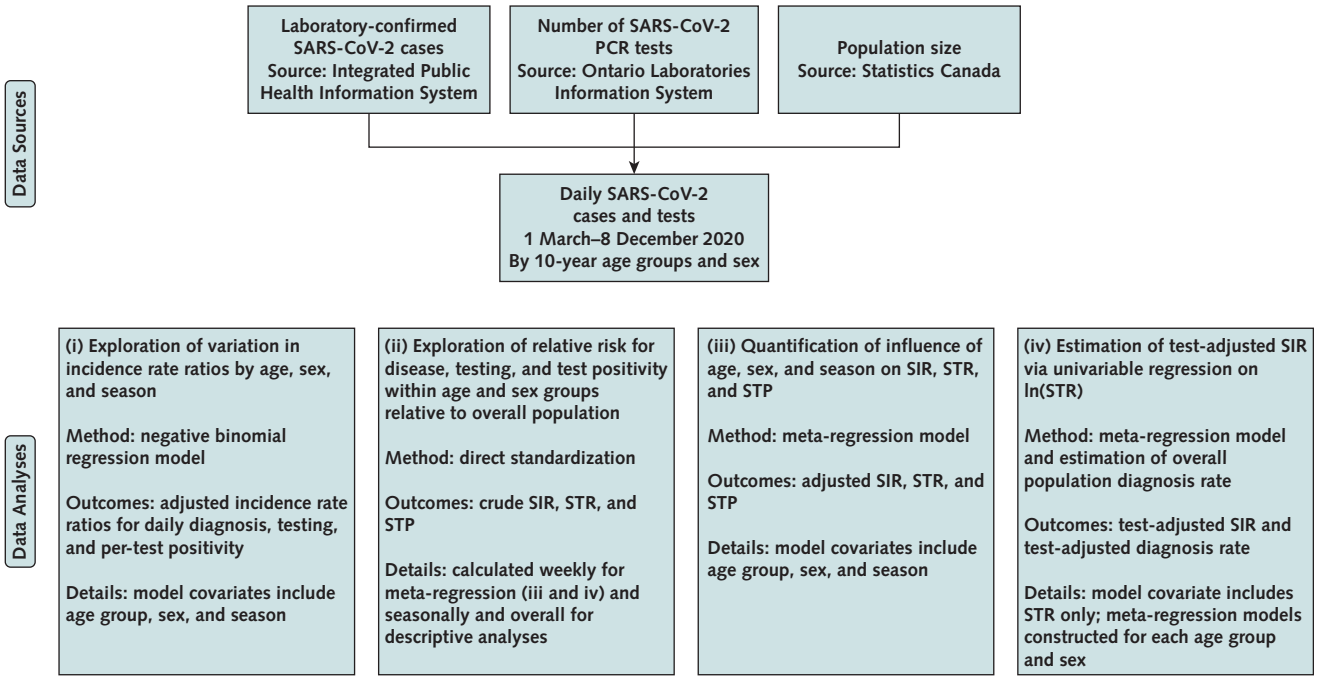
Universal susceptibility to a novel disease in the context of a pandemic is expected to result in attack rates that are proportional to contact rates in a given age group. Because children have the highest contact rates in society under normal circumstances, one might expect attack rates in this age group to be higher rather than lower than those seen in the overall population (12). We postulated that the apparent decreased incidence of SARS-CoV-2 infection in children might reflect differential patterns of testing in this age group rather than biological differences in susceptibility.

Our objective was to evaluate whether differences in COVID-19 incidence between children and adults in Ontario are accounted for by differences in testing. To answer this question, we developed an approach that permits adjustment for differential relationships between testing and risk in different age and sex groups in the population. Our approach differs from the typical means

See also:

Web-Only
Supplement

Figure 1. Schematic diagram outlining the relationship among data sources (*top*) and the analytic approach (*bottom*).



PCR = polymerase chain reaction; SIR = standardized infection ratio; STP = standardized test positivity; STR = standardized testing ratio.

of correcting for differential testing (over time or by risk group) in infectious disease surveillance by using percentage positivity of testing rather than case incidence (as in the Canadian FluWatch system [13]). However, such an approach implicitly assumes that testing is applied independent of risk in tested persons; in the context of the pandemic, where testing may be focused on case contacts or persons associated with an outbreak, this assumption is likely incorrect. Our exploration of this question was facilitated by the existence of a single master record of all COVID-19 PCR tests completed in Ontario, a single master line list of all COVID-19 cases in this jurisdiction, and aggregated blood donor serologic data from Ontario collected by Canadian Blood Services. Furthermore, we were able to evaluate a period that included both restriction of in-person learning due to school closures (March to August 2020) and reopening of schools (September to December 2020), with associated changes in testing patterns.

METHODS

Ontario is Canada's most populous province, with a current population of 14.7 million (14). The province identified imported COVID-19 cases from China and Iran in January and February 2020 (15); local epidemic spread of SARS-CoV-2 has been evident since late February 2020 (16). Each of Ontario's 34 public health units is responsible for local case investigation and uploading of case information into Ontario's Integrated Public Health Information System (iPHIS), which is used for surveillance and case management of notifiable diseases in the province (17). Ontario's definition of a confirmed case of SARS-CoV-2 infection requires a positive result on a validated nucleic acid amplification test, including real-time PCR and nucleic acid sequencing (18). Data were available on age (10-year intervals) and sex of case patients and on date. We defined children as persons aged 0 to 9 years and adolescents as those aged 10 to 19 years.

Data sources for the analysis are described in Figure 1. Test volumes were obtained from the Ontario Laboratories Information System (OLIS), which includes testing and reporting dates for all PCR tests performed in the province (19). Although most SARS-CoV-2 testing is done in the province's public health laboratory system, OLIS also contains records of testing performed at hospital and private laboratories, which have been contributing to testing since April 2020 in an effort to increase the province's test capacity. As such, OLIS is believed to be a complete record of SARS-CoV-2 PCR testing in Ontario during the period under study. When a person had multiple tests on a given day, we included only the first test from that person on that day; however, subsequent testing on that person could be incorporated into test counts. Cases were defined on the basis of a first (positive) SARS-CoV-2 PCR test, but cases were identified in the case (iPHIS) data set and not in the OLIS data set, such that repeated positive test results for the same person (in OLIS) would not be represented as multiple cases.

Testing data and case data are not linkable at the individual level, but daily case counts and test counts by 10-year age category and sex were linked by report date, a field common to both the OLIS and iPHIS data

Table 1. Negative Binomial Models of COVID-19 Disease Incidence, Testing Incidence, and Per-Test Positivity

Covariate	Reported Incidence per Population		Testing Rate per Population		Per-Test Positivity	
	Incidence Rate Ratio (95% CI)	*P* Value	Incidence Rate Ratio (95% CI)	*P* Value	Incidence Rate Ratio (95% CI)	*P* Value
Male sex	1.01 (0.96–1.07)	0.62	0.69 (0.66–0.72)	<0.001	1.45 (1.40–1.51)	<0.001
Age group						
0–9 y	0.36 (0.32–0.40)	<0.001	0.38 (0.34–0.41)	<0.001	1.02 (0.93–1.12)	0.55
10–19 y	0.67 (0.60–0.75)	<0.001	0.40 (0.36–0.44)	<0.001	1.59 (1.46–1.73)	<0.001
20–29 y	1.41 (1.27–1.57)	<0.001	0.85 (0.77–0.93)	0.001	1.61 (1.49–1.75)	<0.001
30–39 y	1.13 (1.01–1.25)	0.026	0.95 (0.87–1.04)	0.28	1.13 (1.04–1.22)	0.003
40–49 y	1.07 (0.96–1.18)	0.25	0.94 (0.86–1.03)	0.178	1.11 (1.03–1.21)	0.008
50–59 y	1 (reference)	–	1 (reference)	–	1 (reference)	–
60–69 y	0.78 (0.70–0.86)	<0.001	0.99 (0.90–1.08)	0.78	0.79 (0.73–0.86)	<0.001
70–79 y	0.67 (0.60–0.74)	<0.001	0.93 (0.85–1.02)	0.114	0.74 (0.68–0.81)	<0.001
≥80 y	1.69 (1.52–1.88)	<0.001	1.98 (1.81–2.17)	<0.001	0.88 (0.81–0.96)	0.003
Season						
Spring	1 (reference)	–	1 (reference)	–	1 (reference)	–
Summer	0.31 (0.30–0.34)	<0.001	2.19 (2.08–2.31)	<0.001	0.14 (0.13–0.15)	<0.001
Autumn	1.89 (1.78–2.01)	<0.001	3.67 (3.48–3.87)	<0.001	0.50 (0.48–0.53)	<0.001

sets. Our analysis was restricted to the period between 1 March 2020 and 8 December 2020, with the earlier date representing the start of the first month during which community transmission of SARS-CoV-2 was clearly occurring in Ontario (16, 20). Age- and sex-specific populations derived from Statistics Canada were used for estimation of cumulative incidence of disease and testing (21). Age data were complete for all records, but data on sex were missing for 754 case records (0.6%) and 309 test records (0.005%), which were excluded from the analysis. Cumulative incidence estimates were annualized by dividing populations by the period under study to convert them to "person-years at risk."

Negative Binomial Models

Our approach to data analysis is outlined in Figure 1. We began by evaluating trends in cases, diagnostic testing, and test positivity using count-based regression models, a common approach for the analysis of such data. Daily rates of testing, diagnosis, and per-test positivity were evaluated using negative binomial regression models, with populations (for testing and diagnosis rates) or test volumes (for per-test positivity) as offsets. In instances with no testing in an age and sex stratum on a given day (141 such instances occurred in March 2020, early in Ontario's epidemic), we added 0.5 to cells to avoid zeros in model offsets for per-test positivity models. Age categories were treated as (0,1) indicator variables, with age 50 to 59 years used as a reference. Because there were clear differences in case counts and testing over the course of the epidemic, we included indicator variables for seasons, defined as summer (June, July, and August) and autumn (September, October, November, and the first week of December) in models, with spring (March, April, and May) used as a reference.

Standardization

Given the marked changes in disease epidemiology and testing during our study period, we used direct standardization to isolate the risk for disease, the likelihood of testing, and test positivity within each age and sex group over time. Standardized infection ratios (SIRs), standardized testing ratios (STRs), and standardized test positivity (STP) by week, by season, and overall were estimated by calculating cumulative incidence of infection or testing or per-test positivity for the overall population and then by age and sex subgroups. Ratios were then calculated by dividing subgroup-specific estimates by estimates for the overall population. Daily counts were aggregated to the level of weeks, seasons, or the duration of the entire time series to avoid instability resulting from small denominators. Confidence intervals for ratios were calculated using estimates of the SE of ln(ratios), calculated as

$$\mathrm{SE}[\ln(\mathrm{SIR}_{ijk},\ \mathrm{STR}_{ijk},\ \text{or}\ \mathrm{STP}_{ijk})] = \sqrt{[(1/a_{ijk}) + (1/b_{ijk}) + (1/c_{ijk}) + (1/d_{ijk})]},$$

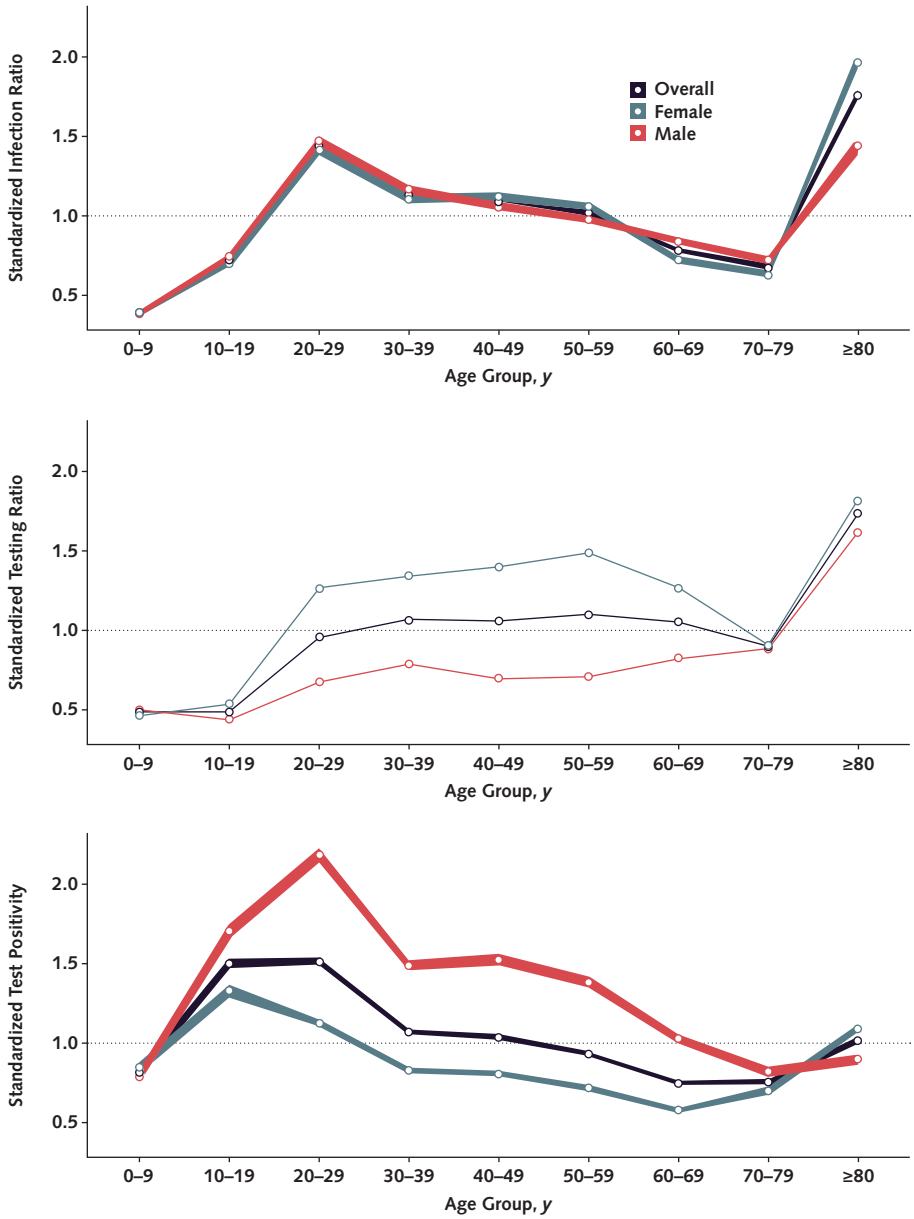
where a is the test or case count in the population subgroup; b is the population (or test count in the case of positivity) in the population subgroup; c is (overall test or case count − a); d is (overall population or test count − b); and i, j, and k represent age, sex, and period, respectively. Such a normal approximation is reasonable when cell sizes are large, as was the case after March 2020 (22). We evaluated the robustness of estimates by performing sensitivity analyses that excluded data for March 2020. By convention, the SIR would be multiplied by 100, but we did not use this multiplier, for methodological reasons described later.

We explored the effects of age, sex, and season on observed differences in SIR, STR, and STP using metaregression models. We used weekly standardized ratio estimates, which provided a straightforward means of evaluating effects in a manner that accounted for differential precision of standardized ratio estimates by using SE estimates as weights. These models followed the form

$$\ln(\mathrm{SIR}_{ijk},\ \mathrm{STR}_{ijk},\ \text{or}\ \mathrm{STP}_{ijk}) = \alpha + \beta_i X_i + \beta_j X_j + \beta_k X_k,$$

where α is the model intercept and each β represents a coefficient for the ith age, jth sex, and kth season (23).

Figure 2. Standardized infection and testing ratios and standardized test positivity during the SARS-CoV-2 pandemic in Ontario, Canada, 1 March to 8 December 2020.



Ratios were calculated by dividing disease incidence (standardized infection ratio [*top*]), test incidence (standardized testing ratio [*middle*]), or test positivity (standardized test positivity [*bottom*]) within a given age and sex group by incidence or test positivity in the overall population. Circles represent point estimates, and bands represent 95% CIs (confidence bands around standardized testing ratios are too narrow to be observed because of the large numbers of tests). A ratio of 1 indicates that within-group incidence or positivity is equivalent to that in the overall population. Ratios broken down by season are presented in section 2 of the Supplement (available at Annals.org).

Adjustment for Intensity of Testing

We postulated that observed low SIRs in children might be explained by lower testing rates. To estimate "test-adjusted" SIR, we created age- and sex-specific metaregression models for SIR by week, with SEs of log-ratios used as weights, as described earlier. Because there was uncertainty in both SIR and STR estimates, within-stratum SEs were approximated by taking the square root of the summed variance of both SIR and STR. Although this approach would overestimate SEs, we found the results to be identical to those obtained using only SEs of SIR as weights. In these models, ln(STR) is used as the independent variable, such that the models follow the form $\ln(SIR_{ij}) = \alpha_{ij} + \beta_{ij}\ln(STR_{ij})$. Here, *i* and *j* represent age and sex groupings. Because $\ln(STR_{ij})$ is zero when testing in a given age group is equivalent to the overall population test rate (that is, when STR = 1), SIR under these circumstances is simply e^{α},

which can be interpreted as the test-adjusted SIR that would be expected in a given age and sex group if it were tested at the same rate as the overall population. Test-adjusted SIRs were used to back-calculate test-adjusted incidence, which would be perceived if all age and sex groups were tested at the same rate as the most frequently tested age and sex group. If I_{ijTmax} is observed cumulative incidence in the maximally tested *i*th age group and *j*th sex, and I_o is incidence in the overall population, then I_o in a maximally tested population is I_{ijTmax}/SIR_{ij}. For any other *i*th age group and *j*th sex, test-adjusted incidence with maximal testing is then simply SIR_i multiplied by I_o. We validated this approach by comparing test-adjusted SIR derived in this way with STP (based on the overall fraction of positive test results) by age group and sex, with calculation of Pearson correlation coefficients and 95% CIs (based on the Fisher transformation, using the ci2 command in Stata), given that test positivity has been used to account for differential testing in surveillance systems.

Analysis and Data Sharing

All analyses were performed using Stata SE, version 15.0 (StataCorp). Stata code for all analyses and a glossary of nonstandard abbreviations are provided in the **Supplement** (available at Annals.org). Aggregate data sets needed for replication of the results are available at https://doi.org/10.6084/m9.figshare.14036528. The study received ethics approval from the Research Ethics Board at the University of Toronto. Patients and the public were not involved in the conduct of this research.

Role of the Funding Source

The Canadian Institutes of Health Research provided funding for this study but had no role in the design, conduct, or analysis of the study or the decision to submit the manuscript for publication.

RESULTS

Between 1 March and 8 December 2020, 132 075 cases of COVID-19 were diagnosed in Ontario. Results of 6 315 449 tests on unique person-days were reported during that interval. Daily testing rates increased 20-fold, from a mean of 12.5 tests per 100 000 persons in March to 239 per 100 000 persons in autumn. Changes in testing patterns were age-specific. The highest testing rates in older persons were seen during a long-term care "testing blitz" in mid-May, with up to 862 tests per 100 000 persons aged 80 years or older. A surge in testing in children younger than 10 years was seen with return to school; they were tested at a maximum rate of 543 per 100 000 children in early October. Two distinct waves were seen, with daily incidence increasing to 4.6 cases per 100 000 persons by mid-April before decreasing to an average of 1 case per 100 000 persons during the summer and then rebounding to a peak of 14 cases per 100 000 persons by 5 December 2020 (**Appendix Figure**, available at Annals.org).

In negative binomial models, incidence and testing rates were lowest in persons younger than 20 years and highest in those older than 80 years. Males were less likely to be tested but had higher per-test positivity than females. Testing rates increased significantly in the autumn of 2020 (**Table 1**). Both STRs and SIRs (**Figure 2**) were below 1 in children and above 1 in older persons. Standardized test positivity was lowest in those aged 60 years or older and above 1 in older children, adolescents, and young adults. In metaregression models, age and sex effects were similar to those seen in negative binomial models, but time trends were diminished, with a significantly higher STR seen only in autumn (**Table 2**; section 2 of the **Supplement**). Metaregression models for STP showed elevated positivity in males, adolescents, and young adults; decreased positivity in older adults; and a slight decrease in autumn.

Intercepts from univariable metaregression models (interpreted as SIR when testing in a given age and sex group is equivalent to that in the overall population) are presented in **Table 3**. Notably, the test-adjusted SIR was less than 1 in both children younger than 10 years and adults older than 60 years, signifying lower infection rates

Table 2. Metaregression Models of Effects of Sex, Age, and Month on Standardized Infection Ratios, Standardized Testing Ratios, and Standardized Test Positivity

Covariate	Standardized Infection Ratio (95% CI)	*P* Value	Standardized Testing Ratio (95% CI)	*P* Value	Standardized Test Positivity (95% CI)	*P* Value
Male sex	1.02 (0.95–1.09)	0.61	0.71 (0.67–0.75)	<0.001	1.48 (1.41–1.57)	<0.001
Age group						
0–9 y	0.30 (0.26–0.35)	<0.001	0.28 (0.25–0.32)	<0.001	1.01 (0.90–1.14)	0.84
10–19 y	0.58 (0.50–0.67)	<0.001	0.32 (0.29–0.37)	<0.001	1.67 (1.49–1.87)	<0.001
20–29 y	1.37 (1.19–1.58)	<0.001	0.82 (0.72–0.94)	0.003	1.64 (1.47–1.83)	<0.001
30–39 y	1.13 (0.97–1.30)	0.108	0.96 (0.84–1.09)	0.52	1.15 (1.03–1.28)	0.011
40–49 y	1.06 (0.91–1.22)	0.45	0.95 (0.84–1.09)	0.46	1.11 (1.00–1.24)	0.059
50–59 y	1 (reference)	–	1 (reference)	–	1 (reference)	–
60–69 y	0.78 (0.68–0.91)	0.001	1.02 (0.90–1.16)	0.74	0.78 (0.70–0.87)	<0.001
70–79 y	0.65 (0.56–0.76)	<0.001	0.92 (0.81–1.04)	0.186	0.71 (0.64–0.80)	<0.001
≥80 y	1.30 (1.12–1.51)	0.001	1.68 (1.48–1.91)	<0.001	0.75 (0.67–0.84)	<0.001
Season						
Spring	1 (reference)	–	1 (reference)	–	1 (reference)	–
Summer	1.04 (0.95–1.14)	0.40	1.03 (0.95–1.11)	0.40	0.99 (0.92–1.06)	0.80
Autumn	1.05 (0.97–1.15)	0.24	1.12 (1.04–1.21)	0.002	0.93 (0.87–0.99)	0.023

Table 3. Test-Adjusted Standardized Infection Ratios Derived From Metaregression Models

Age Group	Test-Adjusted Standardized Infection Ratio (95% CI)		
	All	Female	Male
0–9 y	0.59 (0.45–0.77)	0.59 (0.38–0.92)	0.59 (0.42–0.83)
10–19 y	1.47 (1.26–1.73)	1.52 (1.27–1.82)	1.61 (1.27–2.05)
20–29 y	1.46 (1.35–1.57)	1.01 (0.90–1.14)	2.50 (2.11–2.96)
30–39 y	1.16 (1.11–1.21)	1.00 (0.89–1.11)	1.40 (1.24–1.57)
40–49 y	1.09 (1.05–1.12)	1.01 (0.87–1.17)	1.33 (1.14–1.54)
50–59 y	1.02 (0.98–1.06)	0.93 (0.75–1.16)	1.10 (1.00–1.22)
60–69 y	0.80 (0.76–0.85)	0.74 (0.62–0.89)	0.93 (0.87–0.99)
70–79 y	0.67 (0.62–0.73)	0.61 (0.54–0.69)	0.73 (0.66–0.81)
≥80 y	0.53 (0.45–0.62)	0.53 (0.42–0.69)	0.53 (0.42–0.66)

than expected. By contrast, elevated infection rates were seen between ages 10 and 39 years and were particularly marked in young males, with men aged 20 to 29 years infected at a rate 2.5 times that of the overall population after adjustment for test frequency. Test-adjusted SIRs were highly correlated with standardized positivity ratios (Pearson correlation coefficient, 0.88 [95% CI, 0.71 to 0.96]; $P < 0.001$) (section 4 of the **Supplement**). We performed sensitivity analyses for all regression models with the time series restricted to the period from 1 April 2020 onward; no differences in results were seen when data from March 2020 were excluded.

The most tested age and sex group was women aged 80 years or older (STR, 1.81). The cumulative incidence of infection in this group was used to anchor estimates for the overall population (**Figure 3**). We estimated that the test-adjusted cumulative incidence in the province as of 8 December 2020 was 4367 cases per 100 000 persons, 4 times higher than the observed cumulative incidence of 1167 per 100 000 persons. Test-adjusted incidence was markedly higher than observed incidence in all age groups below 80 years (**Figure 3**). Whereas observed incidence in the population seemed to be highest in the oldest age groups and greater in women than in men, test-adjusted cumulative incidence was highest in younger persons and markedly higher in young men than women. Of note, although the SIR in children younger than 10 years was less than 1, their test-adjusted risk for infection was similar to that in adults aged 70 to 79 years and higher than that in adults older than 80 years. The estimated fraction of infections identified using this method (defined as observed cumulative incidence divided by test-adjusted cumulative incidence) was 26.7%, compared with an estimate of 17.2% derived by comparing case counts with serologic data during the first pandemic wave in Ontario (24).

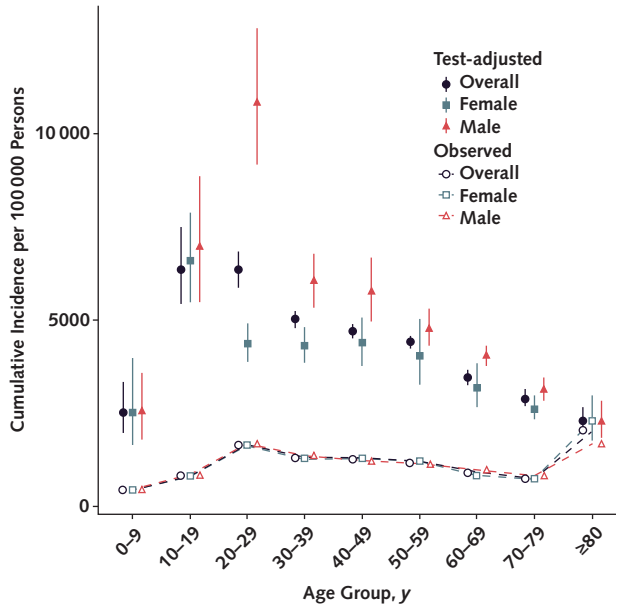
DISCUSSION

The observed epidemiology of reportable communicable diseases is often based exclusively on reports of test-positive cases without reference to how many people are tested. However, observed incidence depends on diagnostic testing, and differential testing volumes may dramatically alter how an epidemic is perceived. Most disease surveillance systems do not incorporate test denominators, with influenza surveillance being a notable exception (13). We were able to evaluate case counts and test counts for SARS-CoV-2 in a single large Canadian jurisdiction with a single testing authority. Standardized ratios had several attractive properties: They reproduced estimates of relative risk similar to those derived using more conventional count-based regression models; they remained stable over time, notwithstanding marked changes in disease risk and test frequency; and they allowed us to estimate relative risk without having to arbitrarily designate a particular age group, sex, or period as a reference.

Accounting for testing rates in estimation of SIRs resulted in a different view of the epidemic than that seen with usual surveillance. Our method builds on earlier approaches to estimation of infection fatality ratio (25), requires few assumptions, and is easy to implement. Adjustment for test volume had marked effects on estimated infection risk at the extremes of age. Test-adjusted SIR was substantially higher than unadjusted SIR in children and adolescents and decreased in the oldest age groups. Although test-adjusted SIR in the youngest age group remained below 1, it increased 1.5-fold after adjustment. In older children and adolescents (10- to 19-year age group), the test-adjusted SIR was 2 times higher than the unadjusted SIR. By contrast, the oldest persons in the population (those aged ≥80 years) had a crude cumulative incidence of infection that was 80% higher than that seen in the overall population, but after adjustment for testing, their risk was estimated to be 50%*lower* than in the overall population. These results, which we were able to partially cross-validate with STP and which are also consistent with seroepidemiologic evidence, suggest that the elevated rates of reported COVID-19 in older adults are most likely attributable to increased testing due to increased disease severity (26).

Decreased infection risk at the extremes of age is consistent with serologic data from other centers (27). In older adults, this attenuation may reflect greater adherence to social distancing, mask wearing, and other protective behaviors (28). By contrast, adults aged 20 to 29 years and males were at higher risk for infection after adjustment for decreased testing frequency, which is also consistent with reported risk behaviors (28, 29). Although younger children have seemed less likely to be infected in both PCR-based population screening studies and serologic surveys (5, 30, 31), we caution against ascribing this apparent decrease in risk to biological or

Figure 3. Observed and test-adjusted estimates of cumulative incidence of SARS-CoV-2 infection, Ontario, Canada.



The lower lines represent annualized observed cumulative incidence of SARS-CoV-2 infection in Ontario, Canada, by age and sex, to 8 December 2020 (*dashed curves*). Estimates were test-adjusted using standardized infection ratios as described in the text, under the assumption that maximal testing was performed in women aged ≥80 years. The upper shapes and bands represent test-adjusted incidence by age group and sex; shapes represent point estimates, and bands indicate 95% CIs.

immunologic mechanisms. Younger children may have been more adherent to social distancing than adolescents with more autonomy, have been deprived of typical school-based contact networks, may have atypical presentations of SARS-CoV-2 infection (such as gastrointestinal illness) with resultant undertesting or underrecognition (7), or may have had COVID-19 misidentified as a non–COVID-19 respiratory infection (8). It has been suggested that only about 1% of children with SARS-CoV-2 infection are identified through clinical testing (32), and seroprevalence studies have found little difference in reported symptom history between seropositive and seronegative children (33), in contrast to adults (34). As such, surveillance data that do not include testing of asymptomatic children may result in misleading estimates of prevalence. With the emergence of novel SARS-CoV-2 variants of concern, epidemiology of infection in children in schools may have shifted further (35, 36). The Alpha (B.1.1.7) and Delta (B.1.617.2) lineages emerged after December 2020 in Ontario (37), and their effects would not have been captured by our data set.

Our study was made possible by the transparency of health agencies in a single large Canadian jurisdiction, which allowed linkage of testing and case data, including data on test volumes for both cases and noncases. This enabled us to evaluate the degree to which testing is a driver of the perceived severity of an epidemic. Our study is subject to limitations, most notably our inability to directly link people's case data with the test data set. Our ability to validate our test adjustment method is also limited by lack of concurrent serologic data, although we did find that our test-adjusted SIR estimates were highly correlated with estimates based on per-test positivity (STP), which has previously been used to capture variability in testing rates in infectious disease surveillance.

Finally, our results reflect epidemiology at the midpoint of the second COVID-19 pandemic wave in a high-income North American jurisdiction. We show that test adjustment provides a markedly different view of SARS-CoV-2, one that is consistent with both test positivity data and patterns seen in serosurveys and that differs markedly from a traditional case-based surveillance approach. Our approach highlights the likely importance of younger persons, particularly younger males, as silent drivers of virulent infection in older adults. Although the work presented here awaits validation in other settings, it provides a simple, inexpensive approach to more nuanced estimation of true infection risk by age, especially in jurisdictions that currently lack seroprevalence data.

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Grant Support: This research was supported by a grant to Dr. Fisman from the Canadian Institutes of Health Research (2019 COVID-19 rapid research funding OV4-170360).

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M20-7003.

Reproducible Research Statement: *Study protocol:* See Figure 1. *Statistical code:* Provided in section 7 of the Supplement (available at Annals.org). *Data set:* Aggregate data sets are available at https://doi.org/10.6084/m9.figshare.14036528.

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Previous Posting: This manuscript was posted as a preprint on medRxiv on 18 September 2020. doi:10.1101/2020.09.15.20193862

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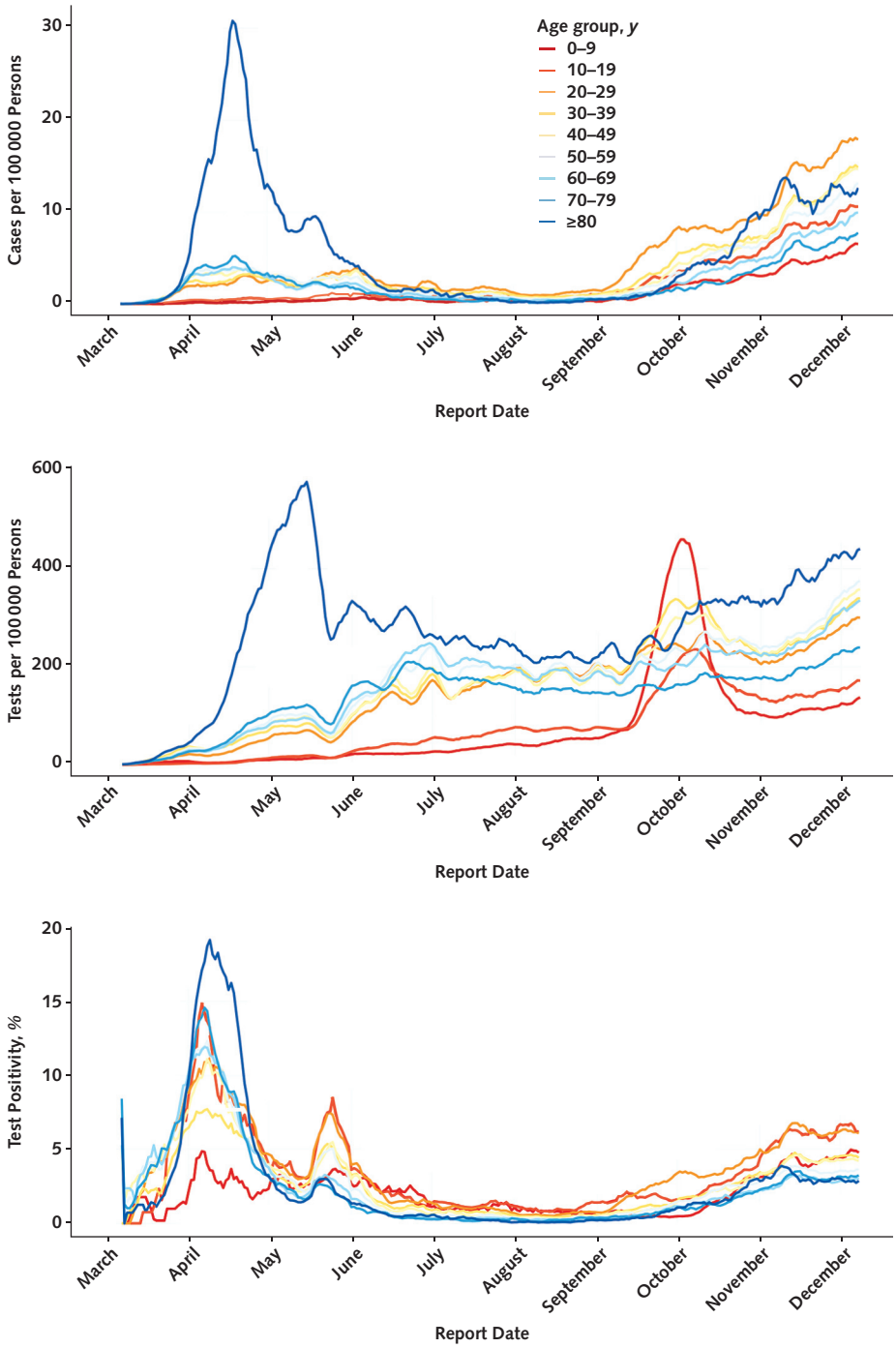
Appendix Figure. Epidemiology of the SARS-CoV-2 pandemic in Ontario, Canada, 1 March to 8 December 2020.



The panels show 7-day moving averages for annualized case incidence (*top*), annualized testing rates (*middle*), and per-test positivity (*bottom*), by age, for the population of Ontario during the SARS-CoV-2 pandemic. Each color represents a unique 10-year age category. Annualized rates can be converted to weekly rates by dividing by 52 or to daily rates by dividing by 365. Because of smoothing, rates estimated from this plot do not correspond exactly to estimates presented in the text. Two distinct pandemic waves can be seen in the top and bottom panels, a springtime testing surge in older persons due to a "nursing home testing blitz" can be seen in dark blue in the middle panel, and a surge in testing due to a return to school in children aged <10 years can be seen in red in the middle panel.