test spending that was out of network increased from 5.2% during 2008-2010 to 11.5% during 2014-2016 (**Figure**), an adjusted annual growth of 0.98 (95% CI, 0.82-1.15) percentage points per year ($P < .001$). This was driven primarily by toxicology, for which the share of spending out of network increased 6.92 percentage points per year (95% CI, 6.03-7.80; $P < .001$), from 11.9% in 2008-2010 to 48.2% in 2014-2016 (**Table**).

The number of in-network laboratory tests increased 2.3% per year (from 1794 per 1000 enrollees per year in 2008-2010 to 2129 per 1000 enrollees per year in 2014-2016), whereas out-of-network laboratory tests increased by 18.9% per year (from 55 per 1000 enrollees per year in 2008-2010 to 139 per 1000 enrollees per year in 2014-2016). This was similarly driven primarily by toxicology, which increased from 37.9 per 1000 enrollees to 93.2 per 1000 enrollees in network and from 2.6 per 1000 enrollees to 45.6 per 1000 enrollees out of network. Out-of-network prices per test exceeded in-network prices (Table).

Discussion | This study found an increasing share of laboratory spending that was out of network, with both increased utilization and higher prices of out-of-network laboratory tests relative to in-network tests, especially for toxicology tests.

Toxicology tests are frequently ordered for patients with substance use disorders, with treatment programs potentially playing a larger role.[6] Laboratory services may be increasingly contracted to large suppliers, who may have sufficient market power to set high prices outside of insurer networks. Moreover, clinician discretion in test ordering and the lack of guidelines for many tests may render utilization more susceptible to financial incentives. These factors could help explain the increasing prices of toxicology tests and their out-of-network share.

Limitations of the study include the lack of generalizability of the employer-sponsored insurance context to individuals with other forms of coverage and the lack of further information on the laboratories. Moreover, claims may not capture the full cost of tests for patients who received balance bills (including surprise bills) in excess of the claim amounts.

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Accepted for Publication: January 19, 2021.

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Concept and design: Song, Wallace.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: All authors.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Song, Lillehaugen.
Obtained funding: Song.
Administrative, technical, or material support: Song.
Supervision: Song, Wallace.

Conflict of Interest Disclosures: Dr Song reported receipt of grants from the National Institutes of Health and the Laura and John Arnold Foundation and personal fees from the Research Triangle Institute for work on risk adjustment, from the International Foundation of Employee Benefit Plans for a lecture, and for providing consultation in legal cases. Mr Lillehaugen reported currently working as a full-time employee of IBM Watson Health; his contributions to this manuscript were completed while working at Harvard Medical School and prior to employment with IBM Watson Health. Dr Wallace reported that his spouse is employed by Aurrera Health Group LLC.

Funding/Support: This work was supported by the National Institutes of Health Director's Early Independence Award DP5-OD024564 (to Dr Song).

Role of the Funder/Sponsor: The National Institutes of Health had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Additional Contributions: We thank Andrew Hicks, MS, Harvard Medical School, for the derivation of diagnostic cost-group risk scores (without compensation).

1. Centers for Medicare & Medicaid Services; Centers for Disease Control and Prevention; Office for Civil Rights. CLIA program and HIPAA privacy rule; patients' access to test reports: final rule. *Fed Regist*. 2014;79(25):7289-7316.

2. Song Z, Johnson W, Kennedy K, Biniek JF, Wallace J. Out-of-network spending mostly declined in privately insured populations with a few notable exceptions from 2008 to 2016. *Health Aff (Millwood)*. 2020;39(6):1032-1041. doi:10.1377/hlthaff.2019.01776

3. American Society of Addiction Medicine. *Appropriate Use of Drug Testing in Clinical Addiction Medicine: Consensus Statement*. Published 2017. Accessed November 25, 2020. https://www.asam.org/Quality-Science/quality/drug-testing

4. Schulte F, Lucas E. Liquid gold: pain doctors soak up profits by screening urine for drugs. Kaiser Health News. Published November 6, 2017. Accessed November 22, 2020. https://khn.org/news/liquid-gold-pain-doctors-soak-up-profits-by-screening-urine-for-drugs/

5. IBM Watson Health. *IBM MarketScan Research Databases for Life Sciences Researchers*. Published April 2018. Accessed November 25, 2020. https://www.ibm.com/downloads/cas/0NKLE57Y

6. Song Z, Lillehaugen T, Busch SH, Benson NM, Wallace J. Out-of-network spending on behavioral health, 2008-2016. *J Gen Intern Med*. 2021;36(1):232-234. doi:10.1007/s11606-020-05665-w

Reasons for Admissions to US Children's Hospitals During the COVID-19 Pandemic

Measures to mitigate the COVID-19 pandemic affected children's access to health services and their physical and mental health. Reductions in hospitalizations for children occurred in 2020 compared with prior years.[1] Little is known about the reasons for the decline and whether it varied by patient characteristics.

Children's hospitals provide inpatient care for the most diverse, high-severity, and complex illnesses[2] and are located in large urban areas, which were particularly affected by COVID-19 outbreaks. Centralization of pediatric inpatient care into children's hospitals was urged to free beds in non-children's hospitals for adult COVID-19 patients. We compared hospitalizations in US children's hospitals before and during the pandemic.

Methods | We conducted a retrospective study of admissions for children aged 0 to 18 years in 42 US freestanding children's hospitals in the Pediatric Health Information System database. Admissions were categorized by spring (March 15 to May 31) and summer (June 1 to August 31). Using quantile

Table 1. Weekly Number of Admissions to Children's Hospitals Before and During the COVID-19 Pandemic by Patient Characteristics

Characteristics	Spring (March 15 to May 31)			Summer (June 1 to August 31)		
	No. of admissions per wk, median (IQR)		Adjusted change, % (95% CI)[a]	No. of admissions per wk, median (IQR)		Adjusted change, % (95% CI)[a]
	2017-2019	2020		2017-2019	2020	
All admissions	12 830 (12 468-13 095)	7033 (6187-8231)	−48.3 (−58.0 to −38.6)	11 697 (11 495-11 947)	9178 (8739-9358)	−23.5 (−27.8 to −19.2)
Age at admission, y						
<1	2990 (2796-3070)	1961 (1840-2081)	−37.1 (−44.9 to −29.3)	2723 (2616-2784)	2003 (1934-2129)	−27.8 (−32.8 to −22.8)
1-4	3355 (3203-3469)	1452 (1248-1744)	−64.3 (−73.9 to −54.8)	2840 (2757-2966)	1964 (1858-2008)	−35.0 (−41.2 to −28.8)
5-9	2344 (2268-2421)	1089 (979-1389)	−52.5 (−64.7 to −40.3)	2115 (2029-2192)	1552 (1516-1620)	−27.0 (−33.8 to −20.1)
10-14	2453 (2377-2532)	1435 (1186-1664)	−41.1 (−53 to −29.1)	2339 (2281-2375)	2004 (1836-2074)	−17.2 (−23.4 to −11.0)
15-18	1650 (1613-1714)	1096 (916-1238)	−36.1 (−48.6 to −23.5)	1674 (1627-1726)	1597 (1440-1649)	−9.6 (−17.5 to −1.8)
Sex						
Male	6903 (6703-7067)	3692 (3290-4319)	−49.9 (−59 to −40.7)	6284 (6212-6445)	4809 (4661-4932)	−26.5 (−31.5 to −21.4)
Female	5937 (5748-6054)	3339 (2900-3863)	−46.5 (−56.2 to −36.8)	5364 (5259-5491)	4336 (4075-4498)	−22.6 (−27.6 to −17.7)
Payer						
Public	6965 (6817-7133)	3673 (3260-4269)	−50.3 (−60.7 to −39.9)	6201 (6082-6383)	4741 (4533-4872)	−26.2 (−31.4 to −21.0)
Private	5006 (4897-5122)	2742 (2386-3287)	−46.3 (−57.1 to −35.5)	4681 (4515-4717)	3607 (3455-3670)	−24.6 (−28.4 to −20.8)
Race/ethnicity[b]						
Non-Hispanic White	6323 (6104-6463)	3539 (3086-4229)	−45.2 (−56.1 to −34.3)	5804 (5716-5940)	4677 (4427-4806)	−20.5 (−24.7 to −16.4)
Non-Hispanic Black	2517 (2365-2596)	1281 (1166-1496)	−53.9 (−63.4 to −44.4)	2193 (2117-2287)	1693 (1662-1725)	−26.9 (−32.1 to −21.6)
Hispanic	2496 (2442-2536)	1369 (1187-1540)	−48.7 (−58.6 to −38.8)	2257 (2169-2309)	1735 (1641-1755)	−27.7 (−33.1 to −22.2)
Asian	359 (337-379)	190 (173-216)	−52.4 (−64.7 to −40)	337 (316-351)	240 (224-253)	−35.9 (−43.7 to −28.1)
Other	1125 (1076-1202)	653 (583-707)	−47.1 (−57.5 to −36.8)	1089 (1040-1125)	817 (750-856)	−31.2 (−37.7 to −24.8)
Hospital region						
Midwest	3360 (3269-3440)	1657 (1480-1990)	−54 (−64.1 to −43.8)	3025 (2888-3116)	2279 (2181-2343)	−22.0 (−28.6 to −15.3)
Northeast	1754 (1687-1806)	851 (751-1100)	−51.9 (−65.6 to −38.1)	1582 (1517-1613)	1289 (1189-1337)	−19.8 (−25.8 to −13.8)
South	5137 (4978-5320)	2899 (2542-3388)	−50.1 (−60.2 to −39.9)	4785 (4597-4910)	3703 (3506-3768)	−28.5 (−33.4 to −23.5)
West	2546 (2419-2605)	1642 (1443-1749)	−35.5 (−45.3 to −25.7)	2322 (2242-2405)	1897 (1851-1944)	−25.2 (−29.3 to −21.1)
Severity of illness[c]						
1 (Lowest)	3310 (3097-3427)	1393 (1261-1555)	−56.4 (−65.1 to −47.7)	2661 (2574-2789)	1740 (1695-1808)	−36.1 (−43.3 to −28.9)
2	3249 (3153-3326)	1662 (1417-1969)	−46.6 (−57.3 to −35.8)	2915 (2831-2993)	2278 (2175-2309)	−22.4 (−27.2 to −17.6)
3	3137 (3008-3316)	1930 (1674-2209)	−49.4 (−60.2 to −38.7)	2910 (2848-3000)	2479 (2406-2511)	−19.1 (−23.7 to −14.5)
4 (Highest)	3090 (2999-3169)	2043 (1850-2457)	−37.6 (−49.4 to −25.8)	3197 (3056-3253)	2683 (2503-2818)	−17.1 (−22.9 to −11.4)
Chronic conditions, No.						
0	7666 (7348-7842)	3934 (3398-4508)	−49.1 (−57.8 to −40.5)	3233 (3131-3312)	2386 (2349-2423)	−28.9 (−33.8 to −23.9)
1	3027 (2965-3122)	1776 (1597-2172)	−49 (−58.8 to −39.2)	3450 (3387-3572)	2658 (2497-2706)	−24.7 (−30.3 to −19.2)
2-3	1831 (1771-1873)	1140 (1049-1299)	−43.4 (−55.8 to −30.9)	3430 (3403-3514)	2879 (2672-2945)	−19.1 (−25.1 to −13.2)
≥4	305 (287-328)	196 (175-219)	−46.5 (−56.5 to −36.5)	1552 (1495-1591)	1274 (1167-1324)	−22.4 (−28.5 to −16.2)
Hospital transfer[d]						
No	11 231 (10 856-11 461)	5940 (5187-7087)	−49.1 (−59.3 to −38.9)	6284 (6212-6445)	4809 (4661-4932)	−23.6 (−28.0 to −19.3)
Yes	1647 (1480-1736)	1075 (993-1136)	−48.1 (−56.9 to −39.3)	5364 (5259-5491)	4336 (4075-4498)	−32.3 (−39.3 to −25.3)

Abbreviation: IQR, interquartile range.

[a] Percent changes in median volume of admissions per week, estimated from quantile regression with a fixed effect for year; *P* < .01 for all percent changes except for age group 15 to 18 years in summer 2020 (*P* = .47); *P* values were adjusted for multiple comparisons using the Sidak correction.

[b] Assessed to determine whether trends in admissions varied by race and ethnicity before vs during the COVID-19 pandemic. Race and ethnicity were self-reported by patients and families using classification options defined by hospitals.

[c] Severity of illness determined from Hospitalization Resource Intensity Score for Kids (HRISK) quartiles.

[d] Indicates that a patient was transferred from another acute care hospital for admission to the children's hospital in the study cohort.

regression, the median weekly volumes of admissions during spring and summer were compared between 2017-2019 and 2020 for all-cause admissions and the most common condition-specific reasons for admission.[3] We also assessed patients' demographic and clinical characteristics. Analyses were performed with SAS version 9.4 (SAS Institute Inc). To account for multiple comparisons, Sidak correction was applied to all *P* values. The threshold for statistical

Table 2. Weekly Number of Admissions for the 20 Most Common Conditions at Children's Hospitals Before and During the COVID-19 Pandemic

Condition-specific admissions	Spring (March 15 to May 31) No. of admissions per wk, median (IQR) 2017-2019	2020	Adjusted change, % (95% CI)[a]	P value	Summer (June 1 to August 31) No. of admissions per wk, median (IQR) 2017-2019	2020	Adjusted change, % (95% CI)[a]	P value
Respiratory conditions								
Viral infection	122 (110-133)	47 (39-60)	−70.8 (−90.3 to −51.3)	<.001	120 (104-131)	62 (55-64)	−61.1 (−75.0 to −47.2)	<.001
Respiratory failure	296 (253-464)	87 (85-136)	−167.7 (−205.9 to −129.6)	<.001	188 (148-225)	94 (87-97)	−93.6 (−125.2 to −62)	<.001
Pneumonia	352 (304-405)	71 (53-126)	−82.8 (−112.1 to 53.5)	<.001	192 (158-220)	42 (40-47)	−84.1 (−108.6 to 59.7)	<.001
Bronchiolitis	456 (373-553)	26 (15-121)	−121.8 (−159.8 to 83.9)	<.001	174 (145-218)	24 (13-27)	−98.6 (−143.5 to −53.6)	.001
Asthma	577 (528-630)	59 (51-73)	−79.4 (−91.6 to −67.1)	<.001	261 (219-341)	80 (55-98)	−68.1 (−105.2 to −31.1)	.01
Chronic conditions								
Diabetic ketoacidosis	125 (114-135)	132 (105-139)	3.2 (−19.9 to 26.3)	>.99	138 (125-146)	150 (142-162)	−0.7 (−13.5 to 12.0)	>.99
Suicide/intentional injury	139 (122-159)	116 (112-122)	−14.4 (−36.1 to 7.3)	.98	93 (87-102)	109 (93-128)	11.8 (−10.8 to 34.5)	.99
Major depressive disorder	238 (215-253)	128 (113-140)	−52.5 (−64.1 to −41)	<.001	156 (140-175)	143 (132-167)	−20.6 (−45.6 to 4.5)	.89
Epilepsy	586 (561-606)	300 (239-373)	−48 (−64.9 to −31.1)	<.001	596 (573-612)	500 (471-525)	−14.8 (−22.3 to −7.3)	.004
Sickle cell crisis	97 (86-113)	52 (43-58)	−50 (−72.3 to −27.7)	.001	84 (74-92)	66 (54-77)	−36.3 (−57.1 to −15.5)	.02
Nonrespiratory infections								
Appendicitis	340 (322-350)	296 (271-333)	−12.5 (−26.1 to 1.1)	.77	342 (322-352)	351 (321-367)	−1.8 (−10.5 to 7)	>.99
Septicemia	136 (102-157)	107 (99-114)	−65.4 (−87.7 to −43.1)	<.001	118 (101-134)	116 (98-129)	−32.3 (−54.2 to −10.5)	.09
Urinary tract infection	145 (136-156)	106 (89-112)	−26 (−42.4 to −9.5)	.05	152 (137-162)	138 (129-145)	−14.5 (−28.7 to −0.2)	.62
Cellulitis	221 (211-239)	120 (111-142)	−45.4 (−58.1 to −32.6)	<.001	250 (237-265)	175 (155-184)	−25.9 (−34.8 to −16.9)	<.001
Gastroenteritis	459 (413-507)	154 (138-179)	−81.8 (−101.7 to −61.8)	<.001	361 (329-391)	222 (210-228)	−55 (−64.6 to −45.4)	<.001
Other conditions								
Neoplasms and chemotherapy	297 (285-313)	263 (249-277)	−6.7 (−14 to 0.5)	.75	288 (280-298)	259 (246-269)	−13.2 (−19.5 to −6.9)	.002
Extremity fracture	313 (268-340)	231 (198-251)	−26.2 (−43.8 to −8.6)	.08	300 (281-312)	249 (236-275)	−19.4 (−30.2 to −8.5)	.02
Constipation	122 (109-132)	43 (29-63)	−67.9 (−95 to −40.8)	<.001	101 (92-117)	84 (68-91)	−21.4 (−41.9 to −0.9)	.57
Headache	96 (83-103)	27 (24-30)	−59.9 (−77.4 to −42.4)	<.001	62 (56-74)	43 (34-47)	−44.4 (−71.3 to −17.4)	.03
Hypertrophy of tonsils and adenoids	211 (194-230)	43 (20-103)	−69.8 (−98.6 to −41.1)	<.001	225 (206-243)	157 (137-167)	−38.7 (−53.1 to −24.2)	<.001

Abbreviation: IQR, interquartile range.

[a] Percent changes in median volume of admissions per week, estimated from quantile regression with a fixed effect for year; *P* values were adjusted for multiple comparisons using the Sidak correction.

significance was a 2-sided $P < .05$. The study was approved by the Boston Children's Hospital Institutional Review Board with a waiver of consent.

Results | There were 1 699 911 admissions included in the study; 54% were male. Weekly all-cause hospitalizations decreased in the spring from a median of 12 830 (interquartile range [IQR], 12 468-13 095) in 2017-2019 to 7033 (IQR, 6187-8231) in 2020 (48.3% [95% CI, 38.6%-58.0%] decrease) and in the summer from a median of 11 697 (IQR, 11 495-11 947) in 2017-2019 to 9178 (IQR, 8739-9358) in 2020 (23.5% [95% CI, 19.2%-27.8%] decrease) ($P < .001$ for both). The least percentage change per week was in summer 2020 among adolescents aged 15 to 18 years (−9.6% [95% CI, −17.5% to −1.8%]; $P = .47$) and the greatest change was in spring 2020 among those with the lowest illness severity (−56.4% [95% CI, −65.1% to −47.7%]; $P < .001$) (**Table 1**). Decreases in hospitalizations occurred in all demographic and clinical subgroups.

The largest decrease in weekly condition-specific hospitalizations occurred in spring 2020 with respiratory failure (from a median of 296 [IQR, 253-464] in 2017-2019 to 87 [IQR, 85-134] in 2020; 167.7% [95% CI, 129.6%-205.9%] decrease; $P < .001$) (**Table 2**). Decreases also occurred in spring 2020 with nonrespiratory conditions, including cellulitis (from a median of 221 [IQR, 211-239] in 2017-2019 to 120 [IQR, 111-142] in 2020; 45.4% [95% CI, 32.6%-58.1%] decrease; $P < .001$) and epilepsy (from a median of 585 [IQR, 561-606] in 2017-2019 to 300 [IQR, 239-373] in 2020; 48.0% [95% CI, 31.1%-64.9%] decrease; $P < .001$). Although not significant, the least percentage change per week was in summer 2020 for diabetic ketoacidosis (from a median of 138 [IQR, 125-146] in 2017-2019 to 150 [IQR, 142-162]; change, −0.7% [95% CI, 12.0% to −13.7%]; $P > .99$). Suicide/intentional injury was the only hospitalization with a (nonsignificant) percentage increase in summer 2020 (from a median of 93 [IQR, 87-102] to 109 [IQR, 93-128]; change, 11.8% [95% CI, −10.8% to 34.5%]; $P > .99$).

Discussion | In spring and summer 2020, during the COVID-19 pandemic, all-cause admissions and many condition-specific admissions for acute and chronic health problems decreased in US children's hospitals. These decreases exceeded those reported with prior initiatives to prevent hospitalizations.[4] In addition to social distancing, potential reasons include more watchful waiting for children with symptoms and increased thresholds for emergency department and hospital care, especially for lower-severity illnesses.

Diabetic ketoacidosis and suicide hospitalizations did not significantly change. Increased diabetic ketoacidosis during the COVID-19 pandemic has been reported in Germany.[5] Increased depression, anxiety, and suicidal ideation and planning in children have occurred during the COVID-19 pandemic.[6]

Limitations include the absence of data from non-children's hospitals. Transfers of pediatric patients from non-children's hospitals to children's hospitals did not increase, suggesting that changes in the location of where children received care did not influence the results. Data on the resurgence of COVID-19 in the fall and winter of 2020 were not available.

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Accepted for Publication: March 8, 2021.

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Author Contributions: Drs Gill and Hall had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: All authors.
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Drafting of the manuscript: All authors.
Critical revision for important intellectual content: Gill, Mahant, Berry.
Statistical analysis: Hall.
Obtained funding: Berry.
Administrative, technical, or material support: Gill, Mahant, Berry.
Supervision: Berry.

Conflict of Interest Disclosures: Dr Gill reported receipt of grants from the Canadian Institute of Health Research (CIHR) and the Hospital for Sick Children, conference reimbursement from the EBMLive Steering Committee, and advisory board membership and meeting reimbursement from the CIHR Institute of Human Development, Child and Youth Health. Dr Mahant reported receiving grants from the CIHR. No other disclosures were reported.

Funding/Support: Drs Berry and Hall were supported by the Health Resources and Services Administration (HRSA) of the US Department of Health and Human Services (DHHS) under contract UA6MC31101, Children and Youth With Special Health Care Needs Research Network.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Disclaimer: This information or content and conclusions are those of the author and should not be construed as the official position or policy of nor should any endorsements be inferred by the HRSA, DHHS, or US government.

1. Wilder JL, Parsons CR, Growdon AS, Toomey SL, Mansbach JM. Pediatric hospitalizations during the COVID-19 pandemic. *Pediatrics*. 2020;146(6):e2020005983. doi:10.1542/peds.2020-005983

2. Berry JG, Hall M, Cohen E, et al. Hospitals' diversity of diagnosis groups and associated costs of care. *Pediatrics*. 2021;147(3):e2020018101. doi:10.1542/peds.2020-018101

3. Gill PJ, Anwar MR, Thavam T, Hall M, Rodean J, Mahant S. Pediatric clinical classification system for use in inpatient settings. *JAMA Pediatr*. Published online March 1, 2021. doi:10.1001/jamapediatrics.2020.6007

4. Coller RJ, Nelson BB, Sklansky DJ, et al. Preventing hospitalizations in children with medical complexity: a systematic review. *Pediatrics*. 2014;134(6):e1628-e1647. doi:10.1542/peds.2014-1956

5. Kamrath C, Mönkemöller K, Biester T, et al. Ketoacidosis in children and adolescents with newly diagnosed type 1 diabetes during the COVID-19 pandemic in Germany. *JAMA*. 2020;324(8):801-804. doi:10.1001/jama.2020.13445

6. Xie X, Xue Q, Zhou Y, et al. Mental health status among children in home confinement during the coronavirus disease 2019 outbreak in Hubei Province, China. *JAMA Pediatr*. 2020;174(9):898-900. doi:10.1001/jamapediatrics.2020.1619

COMMENT & RESPONSE

Depression and Incident Cardiovascular Disease

To the Editor In their recent pooled analysis[1] from 563 255 participants in 22 prospective cohorts, Dr Harshfield and colleagues demonstrated that depressive symptoms reported at baseline were associated with cardiovascular disease (CVD) incidence. It appears that there are several limitations to this study. First, the definition of fatal and nonfatal coronary heart disease was not well defined.

Second, it is important to highlight that takotsubo syndrome (TTS) may mimic acute coronary syndrome and fatal coronary artery disease, presenting with similar clinical symptoms, electrocardiographic changes, and elevated cardiac biomarkers. In addition, emotional and physical events may trigger both of these cardiac conditions.[2] It is therefore possible that some of the cases reported in this study were related to TTS. Of note, it has been reported that approximately 2% to 5% of patients with suspected acute coronary syndrome on the basis of coronary artery disease may have TTS.[3] In addition, TTS may be underestimated. Notably, several complications of TTS, such as stroke and long-term mortality, are estimated to be similar or increased compared with acute coronary syndrome from coronary artery disease.[4,5]

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Conflict of Interest Disclosures: None reported.

1. Harshfield EL, Pennells L, Schwartz JE, et al; Emerging Risk Factors Collaboration. Association between depressive symptoms and incident cardiovascular diseases. *JAMA*. 2020;324(23):2396-2405. doi:10.1001/jama.2020.23068

2. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. *N Engl J Med*. 2015;373(10):929-938. doi:10.1056/NEJMoa1406761