In a multicenter study of patients diagnosed with either multisystem inflammatory syndrome in children (MIS-C) or Kawasaki disease (KD), the authors explored the role of obesity as a comorbidity associated with the clinical course and outcome. The study was motivated by the well-established association of adiposity with inflammation. In their analysis of 338 patients with KD and 1429 patients with contemporaneous MIS-C, overweight and obesity were more common in the MIS-C cohort and were associated with a greater likelihood of shock, admission to the intensive care unit (ICU), administration of inotropic medications, and higher blood levels of inflammation markers. The authors found only a single association between obesity and ICU admission for the KD cohort. They concluded that obesity should be considered a risk factor for a more severe clinical course when evaluating children with MIS-C.

Certain features of the cohorts are worthy of closer inspection. When dealing with 2 diseases that share some clinical features and for which there is no standard diagnostic test, misclassification of patients is always a concern. To address this concern, the authors excluded 499 children with KD because of either recent evidence of SARS-CoV-2 infection or missing data for this variable. A reciprocal exclusion for the MIS-C cohort might have been exclusion of patients with coronary artery aneurysms, as this is a complication of KD but not MIS-C, but this was not implemented. A potential solution to the concern regarding misclassification of patients would have been to compare patients with MIS-C vs KD diagnosed before the pandemic.

The finding that obesity was associated with admission to the ICU for patients with KD is of interest but unexplained. Neither administration of inotropic agents nor diagnosis of KD shock syndrome was associated with obesity in patients with KD, so it is not clear what the indication was for admission to the ICU or why that might be associated with obesity. Variability among the 42 sites for criteria guiding admission to the ICU was not addressed in this study.

It is well established that during the pandemic, social determinants of health influenced exposure to SARS-CoV-2 and increased the risk of MIS-C among lower income families. Obesity is also related to these social factors. The first waves of MIS-C associated with the Wuhan and Alpha variant of SARS-CoV-2 were the most severe. The percentage of patients with MIS-C admitted to the ICU and requiring inotropic support decreased with the later Omicron variants. Therefore, it would have been helpful in analyzing these data to know the timing of the MIS-C cases relative to the emergence of the different variants. It is possible that obesity was a marker for lower socioeconomic status that resulted in increased SARS-CoV-2 exposures and, consequently, severe MIS-C outcomes early in the pandemic. The various strains circulated at well-defined times worldwide, and this knowledge, coupled with the timing of hospital admission for patients with MIS-C, could have helped identify whether the worst MIS-C outcomes occurred earlier in the pandemic.

Kawasaki disease and MIS-C are fundamentally different diseases with different long-term consequences. Kawasaki disease is a vasculitis that predominantly affects the coronary arteries and can result in long-term morbidity and mortality. In contrast, MIS-C is a systemic inflammatory condition associated with elevated levels of cardiac biomarkers and decreased ventricular function that normalizes within weeks of fever onset. Cardiac magnetic resonance imaging studies have shown a small percentage of patients with MIS-C (17.4%) with persistent late gadolinium enhancement at 6 months, but given that MIS-C is a new disease, long-term follow-up studies are not available.
yet available. The role of obesity as a contributor to a more severe clinical course in patients with MIS-C is difficult to disentangle from the complexities of social determinants of health and exposure to different variants. Given the global decrease in MIS-C case numbers, the data presented by Khoury and colleagues may be the final word on the possible role of obesity in influencing clinical disease severity in MIS-C.

ARTICLE INFORMATION
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Corresponding Author: Kirsten Dummer, MD, Division of Pediatric Cardiology, Department of Pediatrics, Rady Children's Hospital San Diego, 2020 Children’s Way, MC 5004, San Diego, CA 92123 (kdummer@rchsd.org).

Author Affiliations: Division of Pediatric Cardiology, Department of Pediatrics, University of California, San Diego, Rady Children's Hospital, San Diego, Rady Children’s Hospital, San Diego (Dummer); Department of Pediatrics, University of California, San Diego, Rady Children's Hospital, San Diego (Burns).

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