Supplemental Tables

Supplemental Table S1. Median and interquartile range (IQR) of the highest (Max) and lowest (Min) lab values for patients diagnosed with multisystem inflammatory syndrome (MIS-C) and severe COVID-19 infection. Statistical significance determined with two-tailed Mann-Whitney Test with significance set at $p<0.05$. Correction for multiple comparisons not performed.

Supplemental Table S2. Criteria for complete (typical) and incomplete (atypical) Kawasaki disease.

Supplemental Table S3. Details of clinical presentation of the Multisystem Inflammatory Syndrome in Children (MIS-C) cohort.

Supplemental Table S1. Median and interquartile range (IQR) of the highest (Max) and lowest (Min) lab values for patients diagnosed with multisystem inflammatory syndrome (MIS-C) and severe COVID-19 infection. Statistical significance determined with two-tailed Mann-Whitney Test with significance set at $p<0.05$. Correction for multiple comparisons not performed.

	MIS-C			Severe COVID-19			
COAGULATION (Normal Range)	**Median**	**IQR**	**N**	**Median**	**IQR**	**N**	**P-value**
Max D-Dimer (0.27 - 0.60 μg/ml FEU)	13.3	4.0-37.9	5	2.6	0.7-22.1	9	0.2977
Max PT (11.6-13.8 secs)	16.6	14.7-21.5	6	16	13.4-33.9	9	0.9301
Max PTT (22-36 secs)	31.8	28.6-36.8	5	52.4	41.6-69.3	9	0.004*
Min Fibrinogen (172-471 mg/dL)	183	141-461	5	286	220.3-304	8	0.7242
CHEMISTRY							
Min Sodium (136-145 mmol/L)	130.5	129-132.8	6	136	131.5-139.5	9	0.0705
Max Potassium (3.8- 5.4 mmol/L)	4.4	4.0-5.0	6	2.8	2.1-9.6	9	0.3095
Max BUN (7-18 mg/dL)	26.5	11.3-68.3	6	27	14.5-52	9	0.8899
Max Creatinine (0.3-0.8 mg/dL)	0.9	0.45-2.2	6	0.7	0.25-2.4	9	0.6665
Max AST (10-30 U/L)	91.5	53.3-121.5	6	123	65.5-746	9	0.2721
Max ALT (5-30 U/L)	53	22-86.8	6	54	24.5-306	9	0.4559
Min Albumin (3.7-5.6 g/dL)	2.7	2.5-3.1	6	2.6	2.2-3.1	9	0.7536
HEMATOLOGY							
Max WBC (4.2-9.4 K/μL)	23.2	16.1-48.4	6	14.7	6.3-26.8	9	0.1369
Min WBC (4.2-9.4 K/μL)	9.6	7-11.6	6	3.6	3.1-5.1	9	0.0134*
Max ANC (1800-8000 cells/μL)	20660	12463-36115	6	9680	4880-21055	9	0.1447
Min ANC (1800- 8000 cells/μL)	7685	5535-9008	6	1950	770-3765	9	0.0048*
Max ALC (1200-5200 cells/μL)	2760	1180-5498	6	3610	1675-4225	9	>0.999
Min ALC (1200-5200 cells/μL)	310	215-847.5	6	510	175-1045	9	0.7990
Max Platelet (150-400 K/μL)	331	245-497	6	296	179-382	9	0.5868
Min Platelet (150-400 K/μL)	114.5	77.3-179.8	6	90	57.5-138.5	9	0.3277
Min Hemoglobin (12-16 g/dL)	7.9	6.9-9.4	6	8.3	6.5-11.2	9	>0.999
INFLAMMATORY/CARDIAC							
Max C-Reactive Protein (0-0.9 mg/dL)	26.3	18.9-33.6	6	30.9	6.5-39.5	9	0.9546
Max Ferritin (10.0-82.0 ng/ml)	804.2	680.6-2361	5	677	172.9-13417	8	0.7242
Max Erythrocyte Sedimentation rate (0-20 mm/hr)	40	24.5-93.5	5	20	13-33	3	0.1429
Max B-Natriuretic protein (≤100 pg/mL)	1719	647.1-10215	5	395	46.8-671.4	5	0.0556

Max Troponin (<0.3 ng/ml)	0.97	0.4-1.6	5	0.13	0.02-2.13	7	0.7866
Max Procalcitonin (0-0.1 ng/mL)	27.2	8.7-135	5	17.3	0.4-61.4	9	0.4585
Max Lactate (0.5-1.6 mmol/L)	2.6	1.8-4.0	5	2.8	2.1-9.6	8	0.6465
Max LDH (390-580 U/L)	1059	656-1928	5	2874	691.5-9702	5	0.4206

ANC, absolute neutrophil count; ALC, absolute lymphocyte count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; LDH, lactic dehydrogenase; WBC, white blood cell; PT, prothrombin time; PTT, partial thromboplastin time.

Supplemental Table S2. Criteria for complete (typical) and incomplete (atypical) Kawasaki disease.

Complete (typical) Kawasaki Disease criteria:	Incomplete (atypical) Kawasaki Disease criteria:
≥ 5 days of fever, PLUS at least 4/5: - Rash (polymorphous exanthem) - Bilateral, non-purulent limbic-sparing conjunctivitis - Mucocutaneous changes (cracked/red lips, strawberry tongue, erythema of oral or pharyngeal mucosa) - Extremity changes (erythema, edema, desquamation) - Prominent cervical node (unilateral, > 1.5 cm diameter)	≥ 5 days of fever, PLUS 2-3 criteria for complete KD, or infants < 6 months with fever for ≥ 7 days without other explanation, PLUS elevated inflammatory markers (CRP ≥ 3.0 mg/dL and/or ESR ≥ 40 mm/hr) AND 3 or more supplemental criteria: - Anemia for age - Thrombocytosis (platelets ≥ 450,000 after day 7 of fever) - Hypoalbuminemia (albumin ≤ 3.0 g/dL) - Elevated ALT (>50 U/L) - WBC Count ≥ 15,000/µL - Sterile pyuria (> 10 leukocytes/high-power field) OR Positive echocardiogram*

*Positive echocardiogram: Presence of one of the following: *Z* score of left anterior descending artery (LAD) or right coronary artery (RCA) ≥2.5; coronary artery aneurysm; or ≥3 other suggestive features including decreased left ventricular function, mitral regurgitation, pericardial effusion, lack of tapering, perivascular brightness or *Z* scores in LAD or RCA of 2-2.5.[1,2]

Supplemental Table S3. Details of clinical presentation of children in the Multisystem Inflammatory Syndrome in Children (MIS-C) cohort.

ID	Days of Fever	Evidence of SARS-CoV-2 (Cycle Threshold)	Classification	Major criteria	Minor criteria	Max CRP, ESR*	Coronary artery changes	Cardiac dysfunction	Treatment+: response
12	7	RT-PCR (39.72)	Complete (4 major)	Rash, conjunctivitis, cracked lips, extremity edema	Anemia	33, 82	No	No	Aspirin, IVIG, IVMP; fevers resolved
18	9	RT-PCR (40.21)	Complete (4 major)	Rash, conjunctivitis, cracked lips, extremity edema	Anemia, albumin	19, 105	No	LV dilation and dysfunction	Aspirin, IVIG, IVMP; resolution and then recurrence; anakinra given and resolved.
19	8	SARS-CoV-2 IgG positive	Incomplete (2 major, 5 minor)	Conjunctivitis, cracked lips	Anemia, albumin, ALT, platelets, WBC	1, 21	No	LV dilation and dysfunction	Aspirin, IVIG, IVMP: fevers resolved
22	7	RT-PCR (39.17)	N/A	None	Anemia, albumin, ALT, WBC	18, ND	LAD dilation (Z = 2.4)	LV dysfunction	Aspirin, IVIG, IVMP; fevers resolved
24	7	RT-PCR (35.17)	Incomplete (3 major, 4 minor)	Conjunctivitis, cracked lips, foot swelling	Anemia, albumin, ALT, WBC	35, 28	No	No	Aspirin, IVIG, IMVP; response after 2nd IVIG
26	5	RT-PCR (35.25)	N/A	None	Anemia, albumin, WBC, platelets	22,40	No	LV/RV dysfunction	Aspirin, IVIG, IVMP; fevers resolved

*ESR values all pre-IVIg

+ IVIG dose = 2g/kg, IVMP = 30 mg/kg/day x 3 days pulse or 2mg/kg/day daily anakinra = 2 – 4 mg/kg/day

CRP - C-reactive protein; ECHO - echocardiogram; ESR - erythrocyte sedimentation rate; IgG – dioriocimmunoglobulin G; IVIG - intravenous immunoglobulin; IVMP - intravenous methylprednisolone; LAD - left anterior descending; LV - left ventricle; RT-PCR – reverse transcriptase polymerase chain reaction; RV – right ventricle; SARS-CoV-2 – Severe Acute Respiratory Coronavirus 2; WBC, white blood cell;

Supplemental Figures

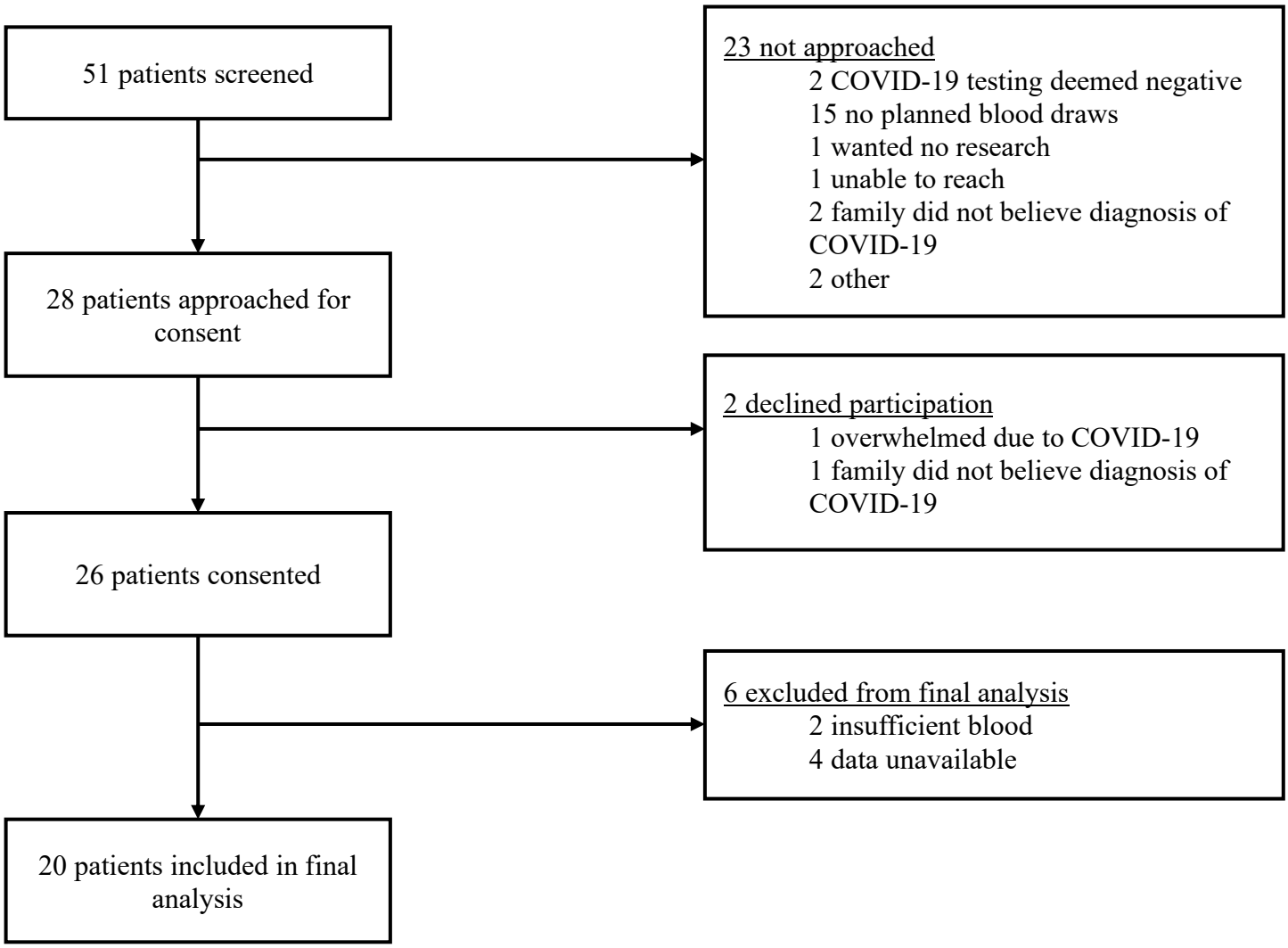
Supplemental Figure S1. Flow diagram of patient cohort selection.

Supplemental Figure S2. Cytokine levels for all patients included in cohort. Each cytokine is plotted on a distinct axis to allow for fine visualization of cytokine levels across the whole panel in the entire cohort.

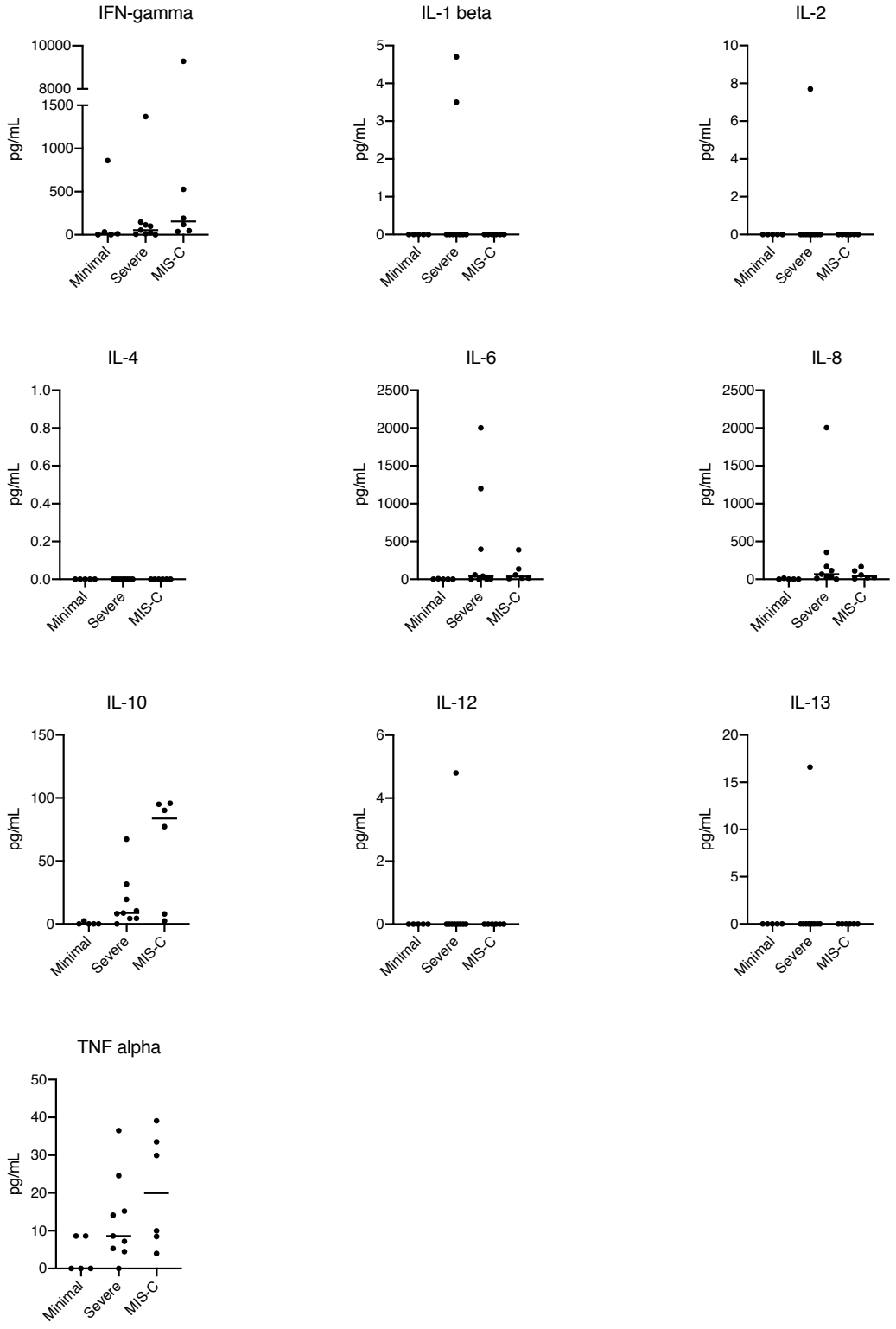
Supplemental Figure S3. Cytokine trajectories for MIS-C versus severe presentations of SARS-CoV-2 infections. Longitudinal graphs of plasma cytokine concentrations for all patients in the cohort where available. Patient IDs are listed above each plot. Day zero represents the day of first cytokine testing. Arrows denote time of each immunomodulatory therapy given.

Supplemental Figure S4. White blood cell trajectories for MIS-C versus severe presentations of SARS-CoV-2 infections. A) Longitudinal graphs of absolute neutrophil and lymphocyte counts for MIS-C and severe phenotypes. Day zero represents the day of first white blood cell count testing. B) Summary of trajectories from data from panel (A). Slopes of linear regression models are used to approximate trajectory of changes for each patient in each group for ANCs (left) and ALCs (right).

Supplemental Figure S1. Flow diagram of patient cohort selection.



Supplemental Figure S2. Cytokine levels for patients in minimal COVID-19, severe COVID-19 and MIS-C cohorts. Each cytokine is plotted on a distinct axis to allow for fine visualization of cytokine levels across the whole panel in the entire cohort.



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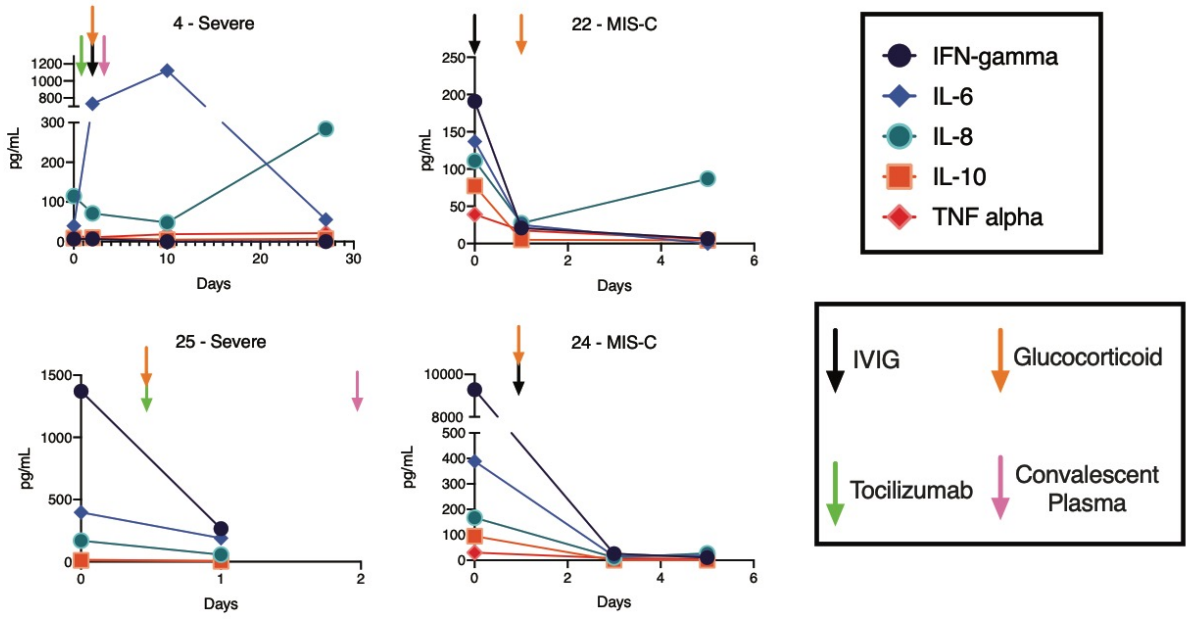

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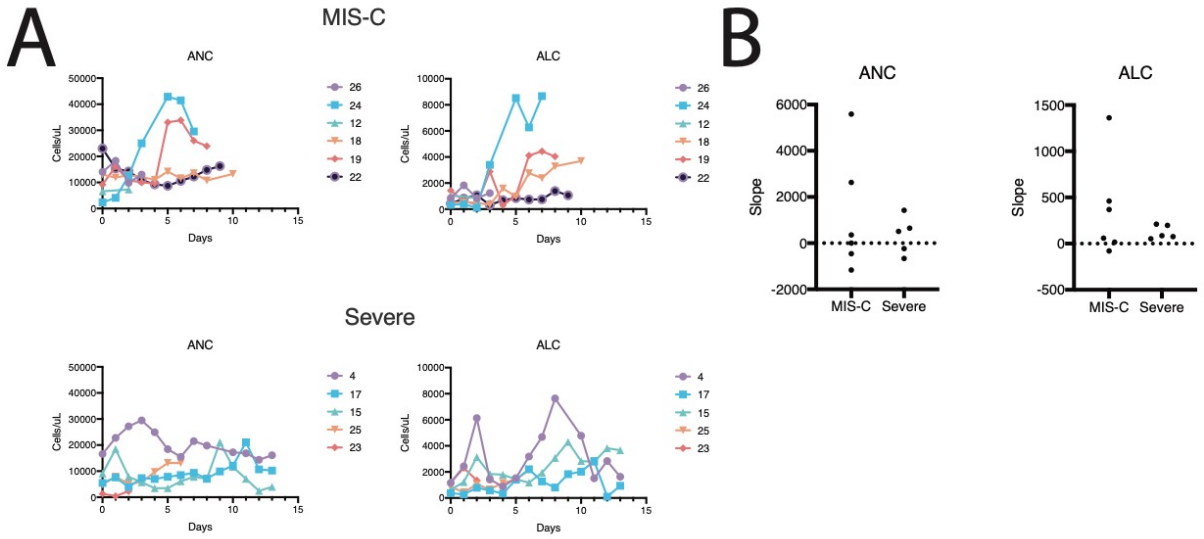

References

1. McCrindle, B. W. *et al.* Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. *Circulation* **135**, (2017).
2. Newburger, J. W. *et al.* Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Statement for Health Professionals From the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation* **110**, 2747–2771 (2004).

STROBE Checklist

Title and Abstract

1) Title and abstract – Design indicated in title (deferred due to space reasons), abstract is a balanced summary

Introduction

2) Background and rationale provided on page 5
3) Objective and hypothesis provided on page 6

Methods

4) Study Design present on pages 14
5) Setting provided on page 14
6) Participants for our cross-sectional study provided on page 14
7) Variables collected, and diagnostic and classification criteria used provided on pages 14
8) Measurement methodologies are provided on pages 15-16
9) Attempts to control bias are presented on page 14,15
10) Study size – As a prospective observational study, there was no a prior prescribed study size. The ultimate arrival at the size of the study cohort is presented on page 10 and supplemental Figure 1
11) Quantitate variable analysis is provided on page 6
12) Statistical methodology is provided on page 16,17 including analytic plan for interactions between variables. Confounding, missing data and sensitivity analysis do not apply to this study.

Results

13) Participants, reasons for non-participation, and a flow diagram are provided on page 10 and supplemental Figure 1
14) Descriptive data of participants in discussed on page 10-11, and in Tables 1 and 2.
15) Numbers of outcomes events for each measurement are provided in their respective sections of discussion.
16) Unadjusted means for each relevant variable are provided in text with 95% CIs. There is no categorizations of continuous variables, nor are there estimates of risk in this study. Additionally, data are presented as scatter plots to allow the reader to see the exact distribution of data in each analysis.
17) There is no subgroup analysis presented.

Discussion

18) Key results are presented on page 10-11, referring back to study objectives.
19) Study limitations are discussed on page 12-13
20) Interpretation of results are provided on pages 11-12, multiple measurements are address.
21) Statement regarding generalizability is provided on page 13.

Other Information

22) Source of funding is provided on page 3.