

# PIMS-TS - MIS-C



HANNEKE VAN HAMERSVELT  
AIOS ANESTHESIOLOGIE

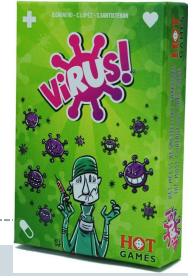
PICU

# Quiz tijd



- Waar staat de afkorting PIMS-TS voor?
- En MIS-C?
- Is er een verschil tussen deze 2?
- Wat is het meest voorkomende symptoom?
- Hoeveel procent heeft pericardvocht/pericarditis?

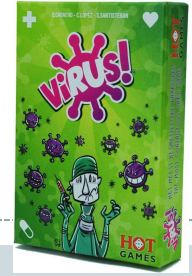
# Definitie PIMS-TS en MIS-C



**Table 1** Abbreviate case definitions from the UK Royal College of Paediatrics and Child Health (RCPCH) for PIMS-TS, the US Centre for Disease Control and Prevention (CDC) for MIS-C, and the World Health Organization (WHO) for multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19

Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-CoV-2 (PIMS-TS; RCPCH 2020)	Multisystem Inflammatory Syndrome in Children (MIS-C; CDC 2020)	Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 (WHO 2020)
A child presenting with persistent fever, inflammation and evidence of single or multi-organ dysfunction	An individual aged <21 years presenting with fever, inflammation, and severe illness requiring hospitalization, with multisystem (>2) organ involvement	Children and adolescents 0–19 years of age with fever > 3 days
This may include children meeting full or partial criteria for Kawasaki disease	No alternative plausible diagnoses	AND two of the following: - Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs - Hypotension or shock - Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities - Evidence of coagulopathy - Acute gastrointestinal problems
Exclusion of any other microbial cause	Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms	AND Elevated markers of inflammation
SARS-CoV-2 PCR testing may be positive or negative	Some individuals may fulfil full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C	AND No other obvious microbial cause of inflammation
	Consider MIS-C in any paediatric death with evidence of SARS-CoV-2 infection	AND Evidence of COVID-19, or likely contact with patients with COVID-19

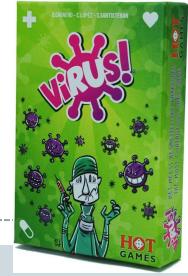
# Definitie



- 6 elementen:
  - 1) kinderen
  - 2) koorts
  - 3) verhoogde inflammatoire markers
  - 4) manifestatie/tekenen van orgaan dysfunctie
  - 5) afwezigheid van andere diagnose
  - 6) relatie met COVID-19
    - ✦ RCPCH: erkenning associatie, geen 'bewijs'
    - ✦ CDC/WHO: bewijs van infectie of exposure nodig



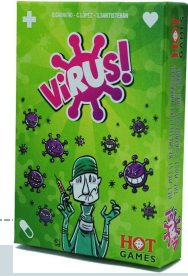
# Toxic shock syndroom



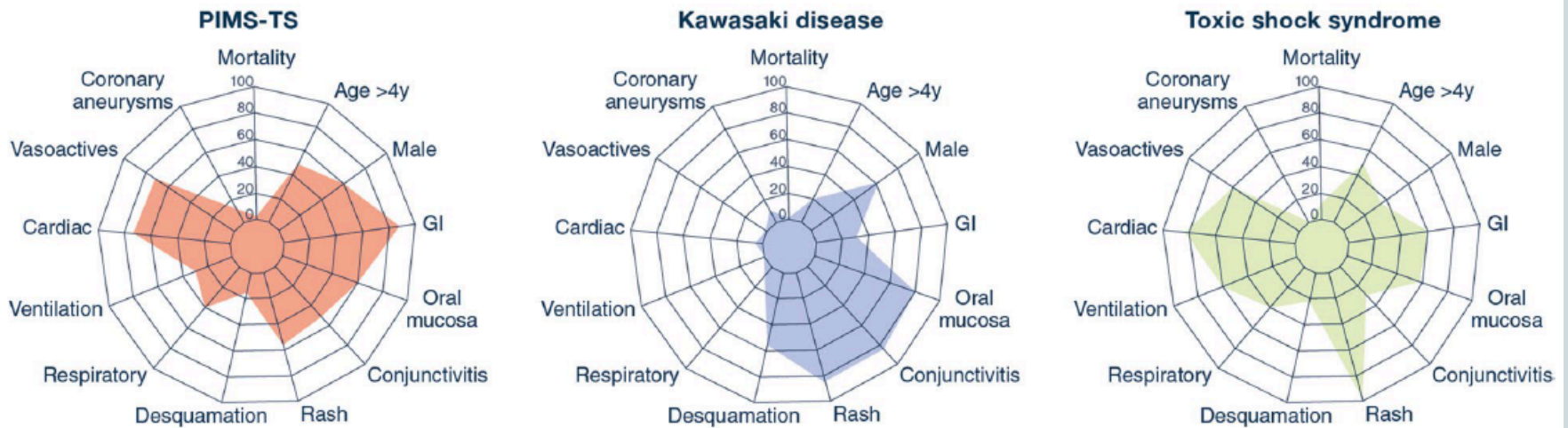
## **Toxisch shock syndroom**

Dit syndroom wordt gekenmerkt door hoge koorts, hypotensie, diffuus erythmateus exantheem met schilfering en vervelling (handpalmen en voetzolen) en verschijnselen van één of meer orgaansystemen: braken en diarree, conjunctivitis en pharyngitis, hoofdpijn en verwardheid, en stoornissen in nier- en leverfuncties. Dit syndroom kwam begin tachtiger jaren epidemisch voor, voornamelijk bij menstruerende vrouwen die nieuwe, sterk absorberende, tampons gebruikten. Daarnaast is het een syndroom dat wel eens bij kinderen voorkomt. Toxisch shock syndroom wordt veroorzaakt door *S. aureus*-stammen die een specifiek exotoxine (TSST-1) produceren, dat verantwoordelijk is voor de shockverschijnselen.

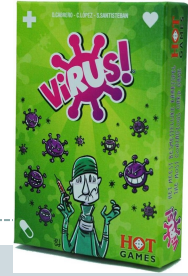
# Definitie



**B** Prevalence of clinical features across cohorts of PIMS-TS, Kawasaki disease and Toxic shock syndrome



# Systematic Review – Lancet sept 2020



Research Paper

## Multisystem inflammatory syndrome in children: A systematic review

Mubbasheer Ahmed<sup>a</sup>, Shailesh Advani<sup>b,c,1</sup>, Axel Moreira<sup>a</sup>, Sarah Zoretic<sup>d</sup>, John Martinez<sup>d</sup>, Kevin Chorath<sup>e</sup>, Sebastian Acosta<sup>a</sup>, Rija Naqvi<sup>a,b,c,d,e</sup>, Finn Burmeister-Morton<sup>d</sup>, Fiona Burmeister<sup>d</sup>, Aina Tarriela<sup>d</sup>, Matthew Petershock<sup>d</sup>, Mary Evans<sup>d</sup>, Ansel Hoang<sup>d</sup>, Karthik Rajasekaran<sup>e</sup>, Sunil Ahuja<sup>d</sup>, Alvaro Moreira<sup>d,\*</sup>

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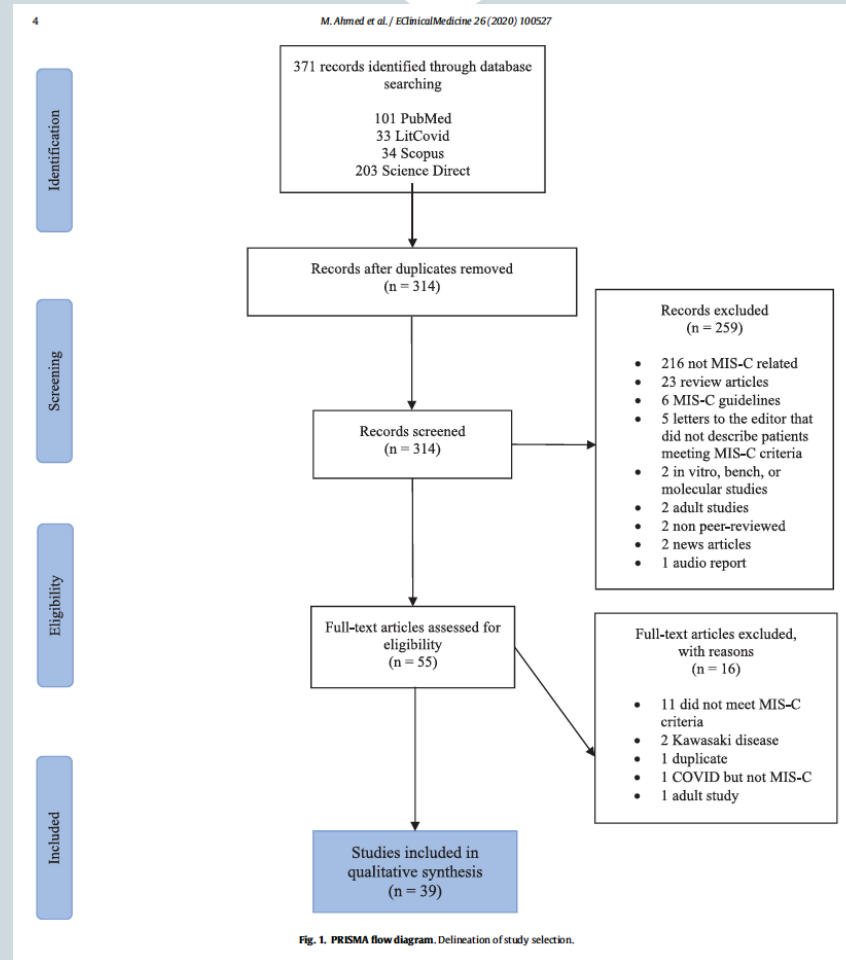
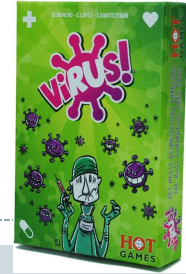
<sup>c</sup> Social Behavioral Research Branch, National Human Genome Research Institute, National Institutes of Health, USA

<sup>d</sup> Department of Pediatrics, University of Texas Health Science Center San Antonio, San Antonio, TX 78229-3900, USA

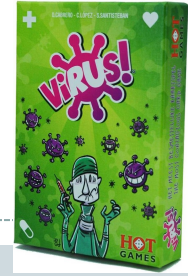
<sup>e</sup> Department of Otorhinolaryngology, The University of Pennsylvania, Philadelphia, PA, USA



# Studie selectie

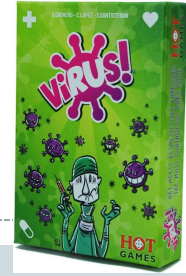


# Studie selectie



- Totale inclusie 39 artikelen, 662 kinderen
- 23 case series (59%)
- 2 grootste studies vanuit US
  - 43% data
  - n=285
- Gemiddelde leeftijd 9.3 jr ( $\pm 0.5$ ), 52.3% man
- Aantal overlijdens: 11 (1.7%)

# Patiënt karakteristieken



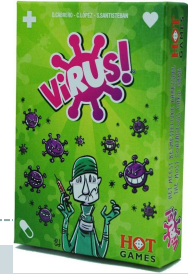
M. Ahmed et al. / EClinicalMedicine 26 (2020) 100527

**Table 2**  
Patient characteristics.

	# Patients with available data	N (%)
Male gender	662	346 (52.3)
Mean age (years)	528	9.3 ± 0.5
Race/Ethnicity	471	
African American/Afro-Caribbean/African		164 (34.8)
White/European/Caucasian		130 (27.6)
Hispanic/Latino		91 (19.3)
Asian/Indian/Middle Eastern		38 (8.1)
Other		48 (10.2)
Co-morbidities*	558	268 (48.0)
Overweight/Obese		136 (50.8)
Respiratory		71 (26.5)
Immunologic/Allergic		17 (6.3)
Cardiac		8 (2.9)
Hematologic		4 (1.5)
Endocrine/Gastrointestinal		5 (1.9)
Neurologic/Behavioral		3 (1.1)
Other		24 (9.0)
SARS-CoV-2 positive (RT-PCR/antibody)	628	532 (84.7)
Number of days symptomatic before presenting to hospital	294	4.8 ± 0.3
Hospital length of stay (days)	422	7.9 ± 0.6
Admission to intensive care unit	662	470 (71.0)

Continuous data presented as Mean ± SD. Multiple co-morbidities in a subset of patients \*. RT-PCR=reverse transcriptase polymerase chain reaction; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

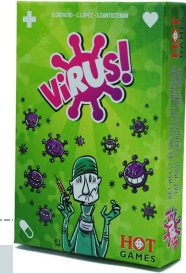
# Symptomen



**Table 3**  
Clinical signs and symptoms.

	# Patients with available data	N (%)
<b>CONSTITUTIONAL</b>		
Fever	662	662 (100.0)
Myalgia, fatigue	662	89 (13.4)
Lymphadenopathy	662	92 (13.9)
<b>GASTROINTESTINAL</b>		
Abdominal pain, diarrhea	662	488 (73.7)
Vomiting	662	452 (68.3)
Loss of appetite	662	73 (11.0)
<b>HEAD, EYES, EARS, NOSE, THROAT</b>		
Conjunctivitis	662	343 (51.8)
Cheilitis	662	216 (32.6)
Tongue swelling	662	31 (4.7)
Sore throat	662	59 (8.9)
<b>RESPIRATORY</b>		
Dyspnea, shortness of breath	662	121 (18.3)
Cough	662	86 (13.0)
Rhinorrhea, nasal congestion	662	47 (7.1)
<b>NEUROLOGIC</b>		
Headache, dizziness	662	129 (19.5)
Somnolence, altered mental status, lethargy, fussy	662	66 (10.0)
<b>DERMATOLOGIC</b>		
Rash	662	372 (56.2)
Edema to extremities	662	128 (19.3)

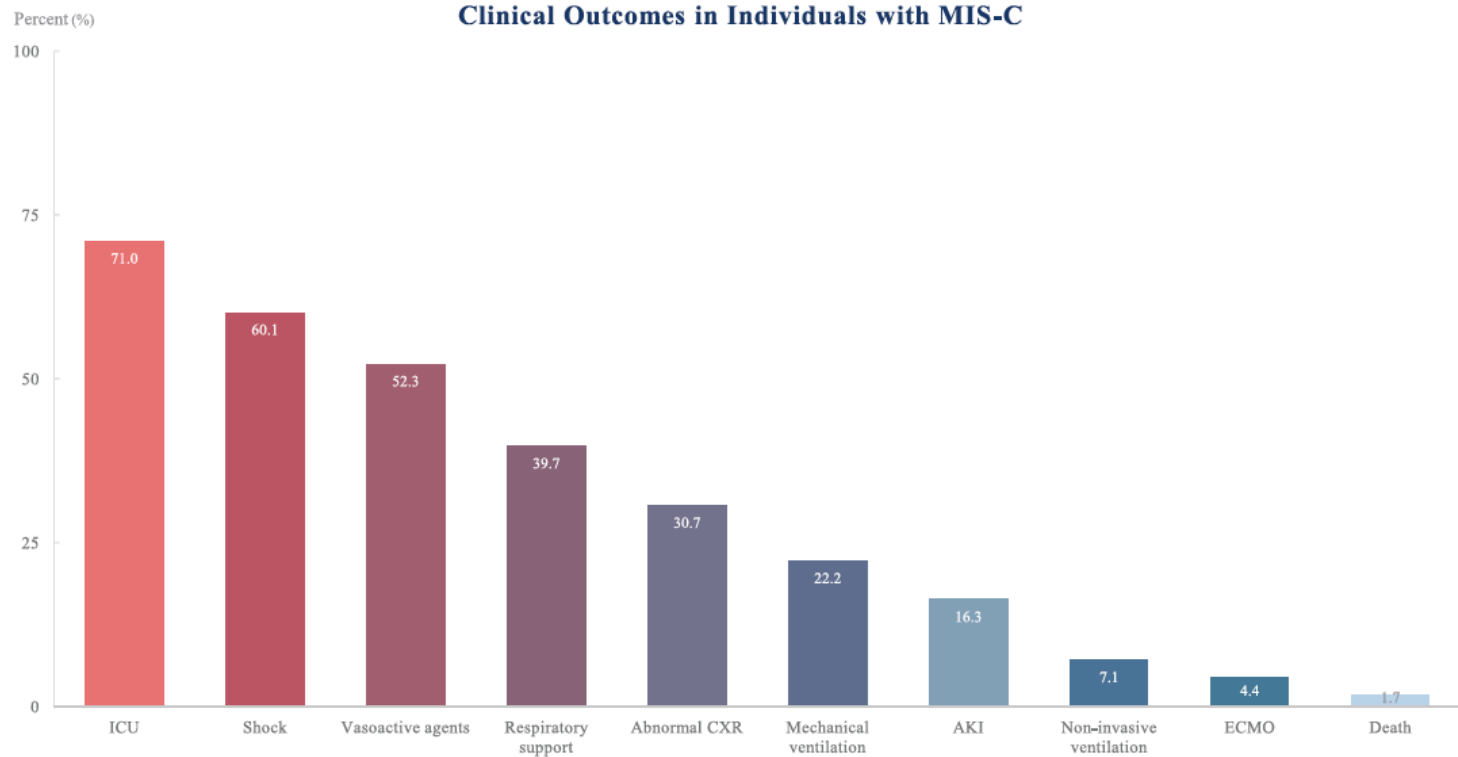
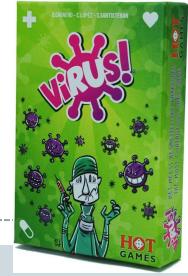
# Diagnostiek



**Table 4**  
Laboratory measures.

	# Patients	Mean ± SD	Ref. range
<b>HEMATOLOGY</b>			
White blood cell count ( $10^3/\mu\text{L}$ )	395	13.2 ± 0.8	4.0–12.0
Neutrophil (%)	276	80.7 ± 7.8	54–62
Lymphocyte (%)	306	9.8 ± 0.8	25–33
Hemoglobin (g/dL)	211	10.2 ± 0.8	11.5–14.5
Platelets ( $10^3/\mu\text{L}$ )	394	215 ± 11.4	150–450
<b>LIVER and RENAL FUNCTION</b>			
Albumin (g/dL)	337	2.8 ± 0.2	4.0–5.3
Creatinine (mg/dL)	158	0.9 ± 0.1	0.22–0.59
Alanine transaminase (U/L)	226	59.8 ± 4.1	5–45
Aspartate aminotransferase (U/L)	145	57.3 ± 5.3	15–50
<b>INFLAMMATORY MARKERS</b>			
C-reactive protein (mg/L)	439	160 ± 7.0	Male 0.6–7.9 Female 0.5–10.0
Ferritin (ng/mL)	303	977 ± 55.8	10–60
Procalcitonin (ng/mL)	312	30.5 ± 2.1	≤0.15
Lactate dehydrogenase (U/L)	300	478 ± 45.4	150–500
Interleukin-6 (pg/mL)	257	184 ± 15.6	≤1.8
Creatine kinase (U/L)	49	135 ± 46.0	5–130
<b>COAGULATION</b>			
D-dimer (mg/L)	349	3.5 ± 0.4	<0.4
Fibrinogen (mg/dL)	267	499 ± 58.3	220–440
Erythrocyte sedimentation rate (mm/h)	191	59.4 ± 9.1	0–20
<b>CARDIAC*</b>			
Troponin (ng/L)	281	494 ± 38.3	<10
Brain natriuretic peptide (pg/mL)	147	3604 ± 352	0–100
Prohormone of brain natriuretic peptide (ng/L)	164	5854 ± 743	0–450

# Uitkomst

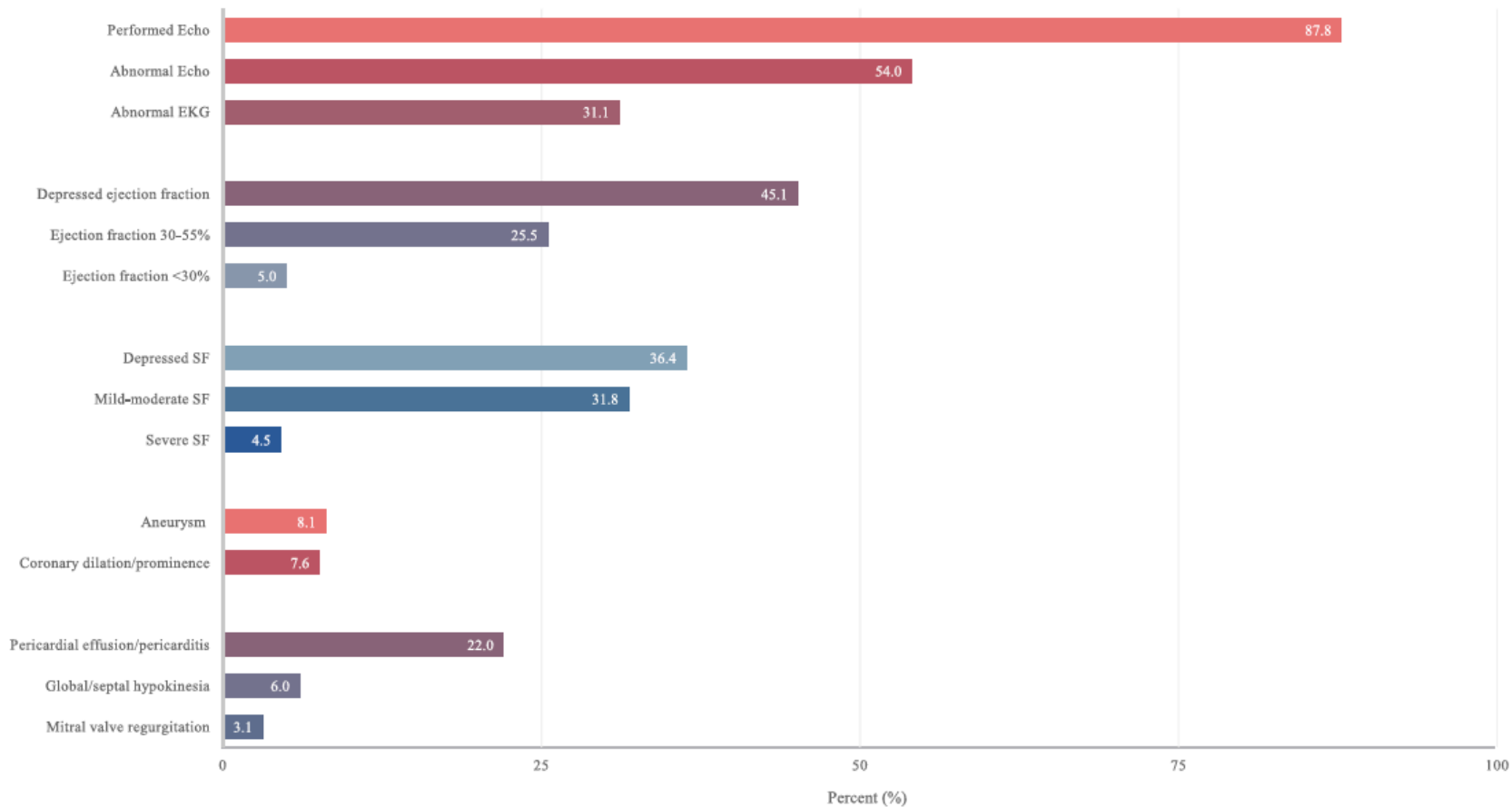


**Fig. 2. Overall clinical outcomes in individuals with MIS-C.** All 662 patients were considered in these findings. ICU-intensive care unit, CXR-chest x-ray, AKI-acute kidney injury, ECMO-extracorporeal membrane oxygenation.

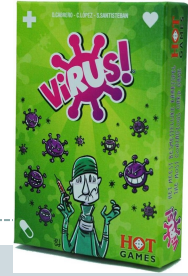
# Cardiovasculaire schade



Cardiovascular Outcomes in Individuals with MIS-C



# Medicatie

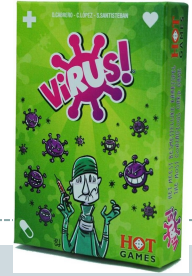


**Table 5**  
Medications.

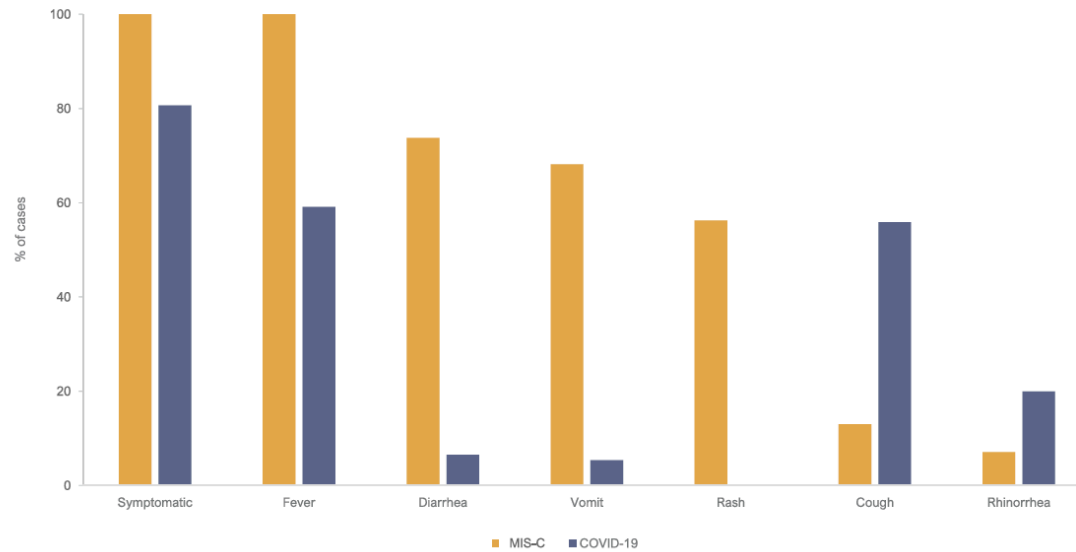
Total <i>n</i> = 662	N (%)
Intravenous immunoglobulin	506 (76.4)
Vasoactive support	347 (52.3)
Corticosteroids	347 (52.3)
Antibiotics	108 (16.3)
Anticoagulants	172 (25.9)
Aspirin	111 (16.8)
Interleukin-1ra inhibitor	56 (8.5)
Interleukin-6 inhibitor	40 (6.0)
Remdesivir	6 (0.9)
Hydroxychloroquine	5 (0.8)



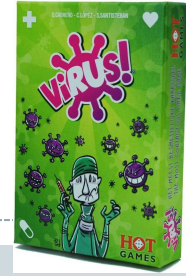
# MIS-C vs COVID-19



Signs and Symptoms in MIS-C vs. COVID-19

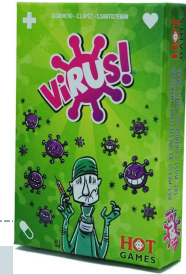


# MIS-C vs COVID-19



**TABLE 6**  
Differences between children with MIS-C and COVID-19.

	MIS-C	COVID-19
<b>GENERAL INFORMATION</b>		
Total number of patients	662	7780
Dates included	January 1, 2020 - July 25, 2020	December 1, 2019 - May 14, 2020
Number of studies	39	131
Data source	Multi-national	Multi-national
<b>DEMOGRAPHICS</b>		
Age	9.3 ± 0.5	8.9 ± 0.5
mean ± SD	[n = 528]	[n = 4517]
Male gender%	52.3	55.6
	[n = 662]	[n = 4640]
Comorbidity%	48.0	35.6
	[n = 558]	[n = 655]
<b>LABORATORY MARKERS</b>		
<b>Complete blood count</b>		
mean ± SD		
Leukocytes ( $10^3/\mu\text{L}$ )	13.2 ± 0.8	7.1 ± 0.3
	[n = 395]	[n = 811]
Neutrophil (%)	80.7 ± 7.8	44.4 ± 2.7
	[n = 276]	[n = 512]
Lymphocyte (%)	9.8 ± 0.8	39.9 ± 2.0
	[n = 306]	[n = 672]
Hemoglobin (g/dL)	10.2 ± 0.8	12.9 ± 0.9
	[n = 211]	[n = 211]
Platelets ( $10^3/\mu\text{L}$ )	215 ± 11.4	273 ± 8.5
	[n = 394]	[n = 115]
<b>Liver and renal function</b>		
mean ± SD		
Alanine transaminase (U/L)	59.8 ± 4.1	19.5 ± 1.0
	[n = 226]	[n = 656]
Aspartate aminotransferase (U/L)	57.3 ± 5.3	29.4 ± 2.2
	[n = 145]	[n = 469]
Creatinine (mg/dL)	0.9 ± 0.1	0.3 ± 0.0
	[n = 158]	[n = 449]



<b>Inflammatory markers</b>		
mean $\pm$ SD		
C-reactive protein (mg/L)	160 $\pm$ 7.0 [n = 439]	9.4 $\pm$ 0.5 [n = 643]
Ferritin (ng/mL)	977 $\pm$ 55.8 [n = 303]	51.6 $\pm$ 13.2 [n = 22]
Procalcitonin (ng/mL)	30.5 $\pm$ 2.1 [n = 312]	0.25 $\pm$ 0.0 [n = 259]
Lactate dehydrogenase (U/L)	478 $\pm$ 45.4 [n = 300]	277 $\pm$ 25.9 [n = 404]
Creatine kinase (U/L)	135 $\pm$ 46.0 [n = 49]	197 $\pm$ 23.1 [n = 193]
Interleukin-6 (pg/mL)	184 $\pm$ 15.6 [n = 257]	26.1 $\pm$ 3.7 [n = 92]
<b>Coagulation</b>		
mean $\pm$ SD		
D-dimer (mg/L)	3.5 $\pm$ 0.4 [n = 349]	0.7 $\pm$ 0.1 [n = 285]
Fibrinogen (mg/dL)	499 $\pm$ 58.3 [n = 267]	224 $\pm$ 1.3 [n = 179]
Erythrocyte sedimentation rate (mm/h)	59.4 $\pm$ 9.1 [n = 191]	14.1 $\pm$ 3.4 [n = 134]
<b>OUTCOME</b>		
Length of hospitalization		
mean $\pm$ SD	7.9 $\pm$ 0.6 [n = 423]	11.6 $\pm$ 0.3 [n = 652]
Intensive care unit admission	470 (71.0) [n = 662]	116 (3.3) [n = 3564]
In (%)	[n = 662]	[n = 3564]
Shock	398 (60.1) [n = 662]	19 (0.24) [n = 7780]
In (%)	[n = 662]	[n = 7780]
Mechanical ventilation	147 (22.2) [n = 662]	42 (0.54) [n = 7780]
In (%)	[n = 662]	[n = 7780]
Aneurysm	47 (7.1) [n = 662]	—
In (%)	[n = 662]	—
Death	11 (1.7) [n = 662]	7 (0.09) [n = 7780]
In (%)	[n = 662]	[n = 7780]
<b>TREATMENT</b>		
IVIG	506 (76.4) [n = 662]	19 (3.1) [n = 614]
In (%)	[n = 662]	[n = 614]
Corticosteroid	347 (52.3) [n = 662]	25 (4.1) [n = 614]
In (%)	[n = 662]	[n = 614]

# Discussie



- Inclusie van case reports en case reviews
- Risk of bias binnen de verschillende studies
- Data omgezet naar mean en SD

# Vragen?

