Multisystem Inflammatory Syndrome in Children

(Philippine Experience)

IMELDA ASETRE-LUNA, M.D., FPPS, FPIDSP

Vaccinology 2022: 4th International Symposium for Asian Experts

Sofitel Philippine Plaza Manila

December 1, 2022

OUTLINE

- Introduction: History, Case Definition, Pathophysiology
- Local Epidemiology of Acute COVID-19
- Profile of MIS-C cases from 2 tertiary hospitals
- Risk Factor and Prevention of MIS-C

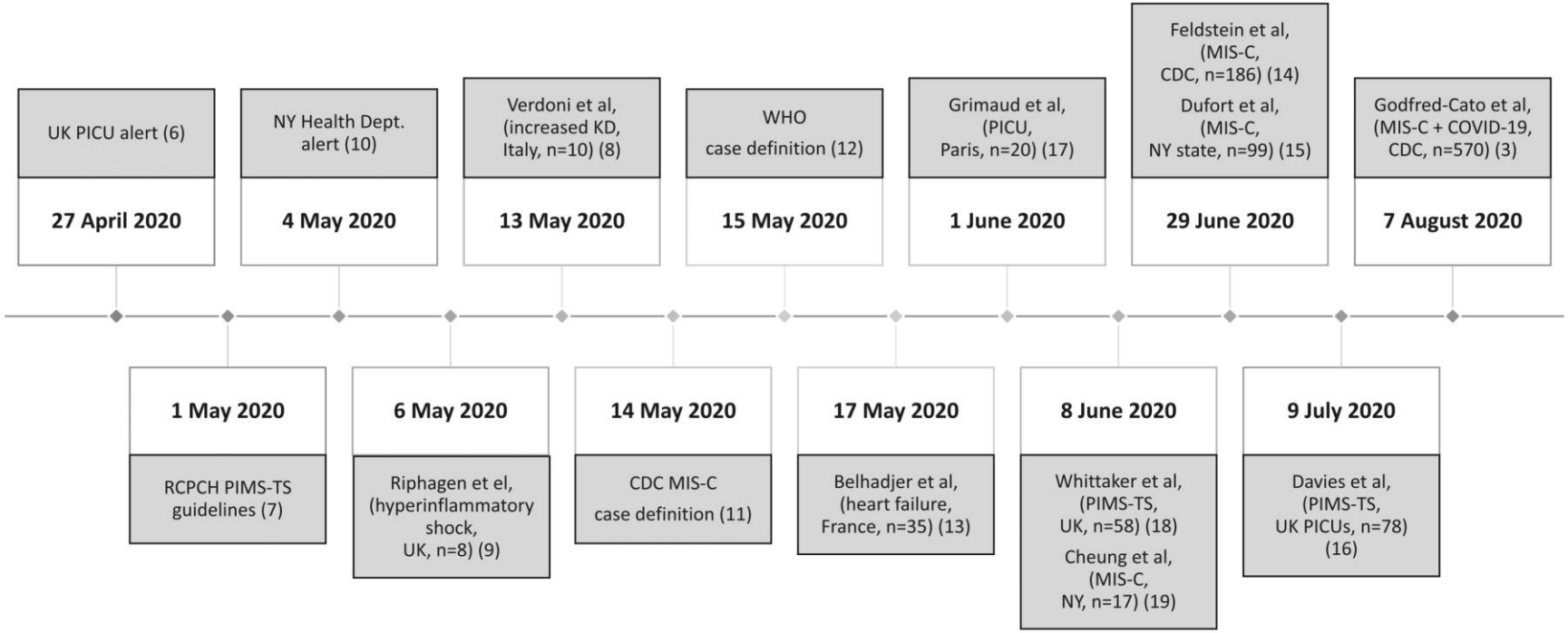


Fig. 1. Timeline of initial recognition and description of MIS-C.Abbreviations: UK, United Kingdom; PICU, pediatric intensive care unit; RCPCH, Royal College of Paediatricians and Child Health; PIMS-TS, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2; NY, New York; Dept., department; KD, Kawasaki Disease; CDC, Centers for Disease Control and Prevention; MIS-C, multisystem inflammatory syndrome in children; WHO, World Health Organization.

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

Existing Case Definitions of Multisystem Inflammatory Syndromes

	Pediatric: RCPCH	Pediatric: CDC	Pediatric: WHO	Adult: CDC
Age (years)	“child”	<21	0–19	≥21
Fever	persistent	≥ 1 day	≥ 3 days	no comment
Laboratory Evidence of Inflam-mation	Yes	Yes	Yes	Yes

RCPCH, Royal College of Paediatrics and Child Health; CDC, Centers for Disease Control and Prevention; WHO, World Health Organization

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

	Pediatric: RCPCH	Pediatric: CDC	Pediatric: WHO	Adult: CDC
Hospitaliza-tion	No	Yes	No	Yes
Number of Organ Systems Involved	≥1	≥2	≥2	≥1 extra-pulmonary

RCPCH, Royal College of Paediatrics and Child Health; CDC, Centers for Disease Control and Prevention; WHO, World Health Organization

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

	Pediatric: RCPCH	Pediatric: CDC	Pediatric: WHO	Adult: CDC
Organ Systems Named	shock, cardiac, respiratory, renal, gastrointesti-nal, neurologic	cardiac, renal, respiratory, hematologic, gastrointesti-nal, dermatologic, neurologic	mucocuta-neous, hypotension/ shock, cardiac, gastrointesti-nal	hypotension/ shock, cardiac, thrombosis/ thromboem-bolism, acute liver injury

RCPCH, Royal College of Paediatrics and Child Health; CDC, Centers for Disease Control and Prevention; WHO, World Health Organization

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

	Pediatric: RCPCH	Pediatric: CDC	Pediatric: WHO	Adult: CDC
Exclusion of Other Causes	Yes	Yes	Yes	Yes + exclu-sion of severe respiratory illness
(+) SARS-CoV-2 RT-PCR/antigen /serology	No	Yes	Yes	Yes (within 12 weeks)

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

	Pediatric: RCPCH	Pediatric: CDC	Pediatric: WHO	Adult: CDC
COVID-19 epidemio-logic link allowed in place of viral test	N/A	exposure within 4 weeks	“likely contact”	No

RCPCH, Royal College of Paediatrics and Child Health; CDC, Centers for Disease Control and Prevention; WHO, World Health Organization

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

Pathophysiology of MIS-C: unknown

Immune dysregulation (abnormal immune response to the virus)

The molecular mechanisms that lead to hyperinflammation in MIS-C are largely unknown and limited to phenotypic characterizations

It appears to be a consequence of massive release of inflammatory mediators with exaggerated activation of the immune system like cytokine storm

Nationwide Cases Data

Total Cases	Active Cases	Recovered	Died
4,035,487	18,250	3,952,617	64,620
+801 added on 11/29			

View Detailed Case Information

Confirmed cases are those that tested RT-PCR positive by a DOH-RITM certified lab.

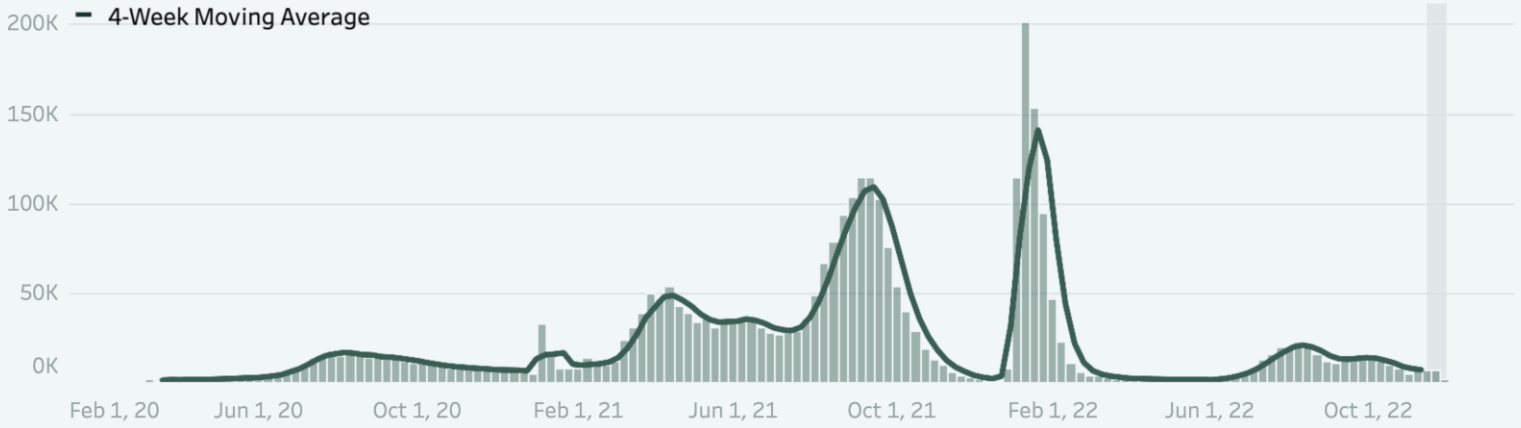
Weekly Cases by Date of Onset of Illness

For 64.4% or 2,600,711 of cases where date of onset of illness is unreported, date of specimen collection was used as proxy.

(•) Weekly ( ) Daily

(•) Cases ( ) Recoveries ( ) Deaths

We urge caution when interpreting data during the highlighted period below, which may be incomplete because of delays in reporting.



Note: There are still 889062 cases with unreported date of onset of illness and date of specimen collection.

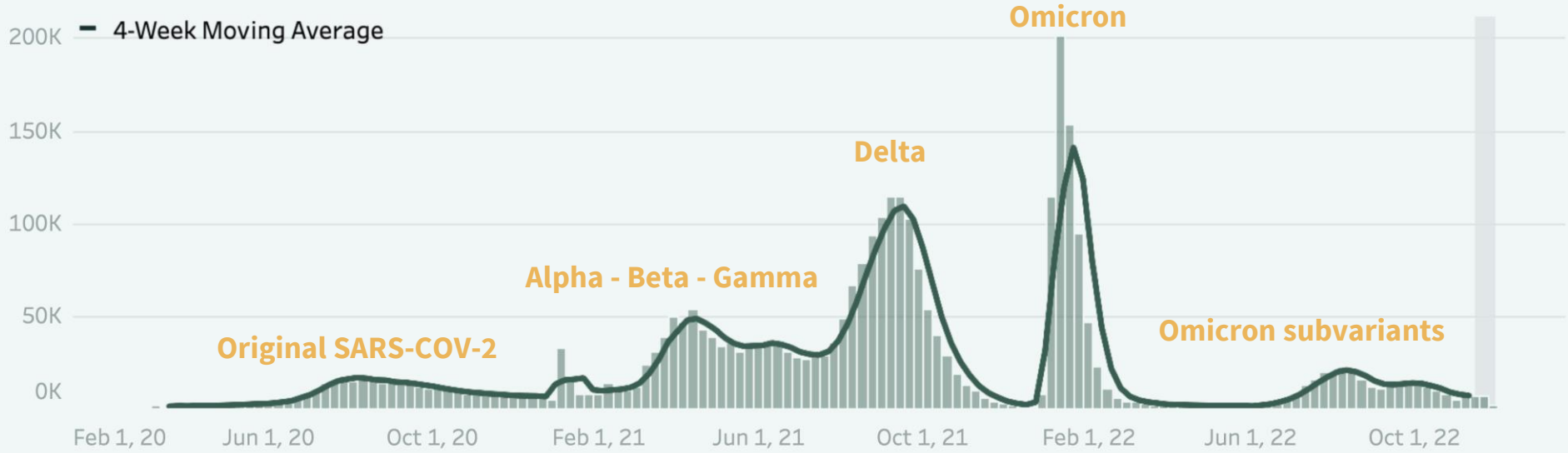
Weekly Cases by Date of Onset of Illness

For 64.4% or 2,600,711 of cases where date of onset of illness is unreported, date of specimen collection was used as proxy.

(•) Weekly
( ) Daily

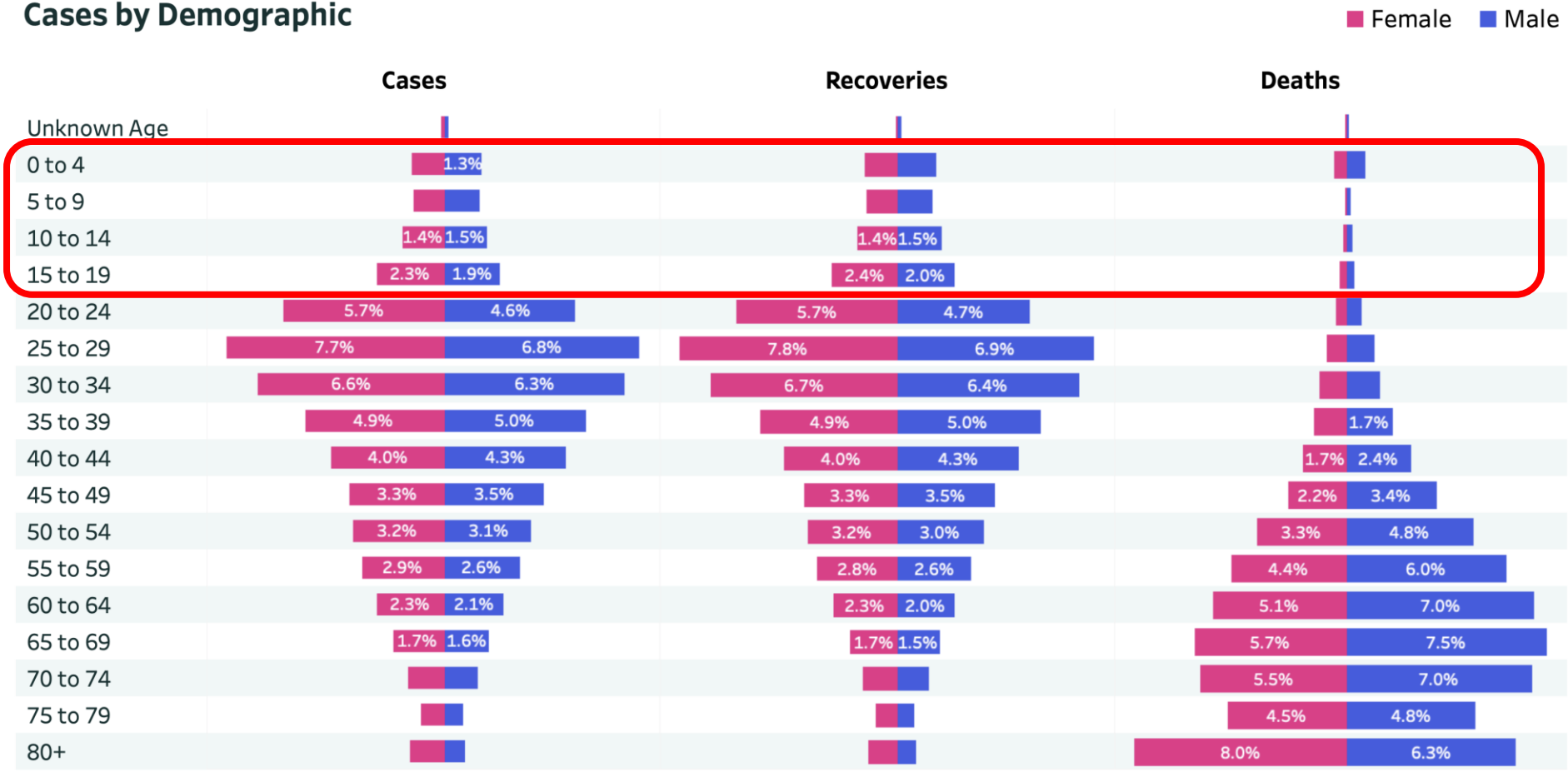
(•) Cases
( ) Recoveries
( ) Deaths

We urge caution when interpreting data during the highlighted period below, which may be incomplete because of delays in reporting.



Note: There are still 889062 cases with unreported date of onset of illness and date of specimen collection.

Cases by Demographic



National COVID-19 Vaccination Dashboard

Coverage date: March 1, 2021 to November 27, 2022. Data is refreshed daily at 12:00 PM.

Figures are pending addition of 3,564,941 total 2nd booster doses administered as of November 27, 2022.

Total Doses Administered

165,750,058

10,123 doses administered on Nov 27

First Dose

71,045,629 (**+2,385** doses administered on Nov 27)

Complete Dose

73,750,395 (**+3,181** doses administered on Nov 27)

Booster Dose

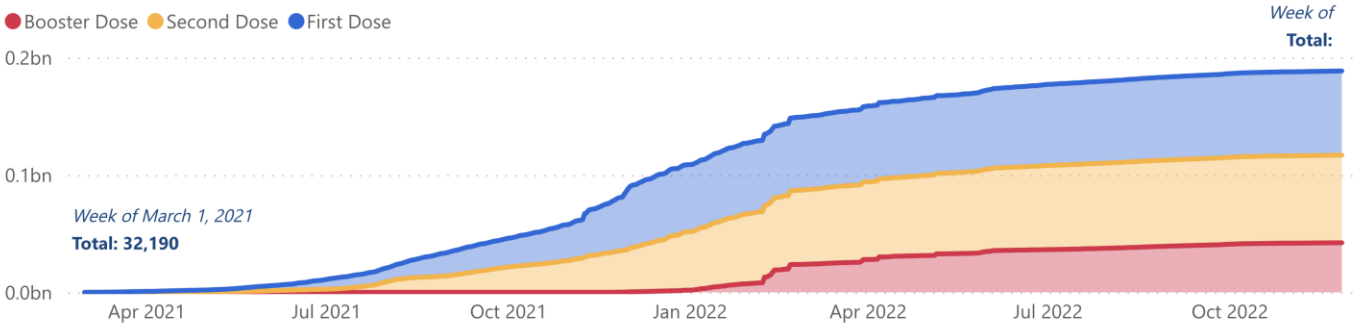
20,954,034 (**+4,557** doses administered on Nov 27)

24,121

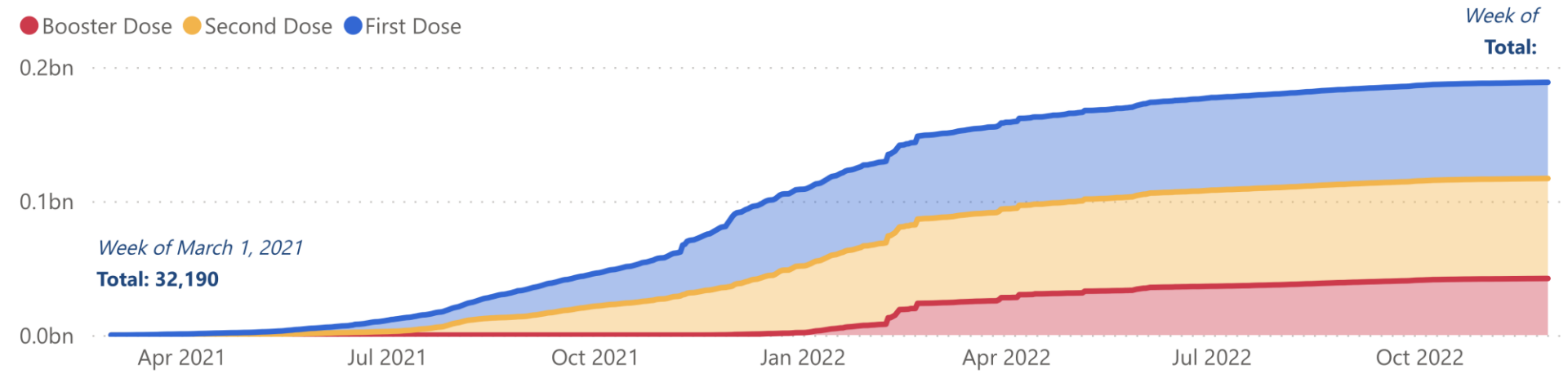
Average daily doses in the last 7 days

Tara na! Makipag-ugnayan na sa inyong LGU at magpa-booster na!

TOTAL DOSES ADMINISTERED



TOTAL DOSES ADMINISTERED



Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

14 October 2021

DEPARTMENT CIRCULAR
No. 2021 - 0464

TO: **ALL UNDERSECRETARIES AND ASSISTANT SECRETARIES; DIRECTORS OF BUREAUS, SERVICES AND CENTERS FOR HEALTH DEVELOPMENT; MINISTER OF HEALTH – BANGSAMORO AUTONOMOUS REGION IN MUSLIM MINDANAO); EXECUTIVE DIRECTORS OF SPECIALTY HOSPITALS AND NATIONAL NUTRITION COUNCIL; CHIEFS OF MEDICAL CENTERS, HOSPITALS, SANITARIA AND INSTITUTES; AND OTHERS CONCERNED**

SUBJECT : **Interim Operational Guidelines on the COVID-19 Vaccination of the Pediatric Population Ages 12-17 Years Old with Comorbidities**

Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

January 24, 2022

DEPARTMENT MEMORANDUM
No. 2022 - 0041

FOR: **ALL UNDERSECRETARIES AND ASSISTANT SECRETARIES; DIRECTORS OF BUREAUS, SERVICES AND CENTERS FOR HEALTH DEVELOPMENT; MINISTER OF HEALTH – BANGSAMORO AUTONOMOUS REGION IN MUSLIM MINDANAO); EXECUTIVE DIRECTORS OF SPECIALTY HOSPITALS AND NATIONAL NUTRITION COUNCIL; CHIEFS OF MEDICAL CENTERS, HOSPITALS, SANITARIA AND INSTITUTES; AND OTHERS CONCERNED**

SUBJECT : **Interim Guidelines on the Management and Administration of Tozinameran COVID-19 mRNA vaccine (nucleoside-modified) [Cominarty] Pfizer COVID-19 Vaccine to Pediatric Population Ages 5-11 Years Old**


ST LUKE'S MEDICAL CENTER
St. Luke's
Medical Center
Global City

St. Luke's Medical Center
Quezon City · Global City

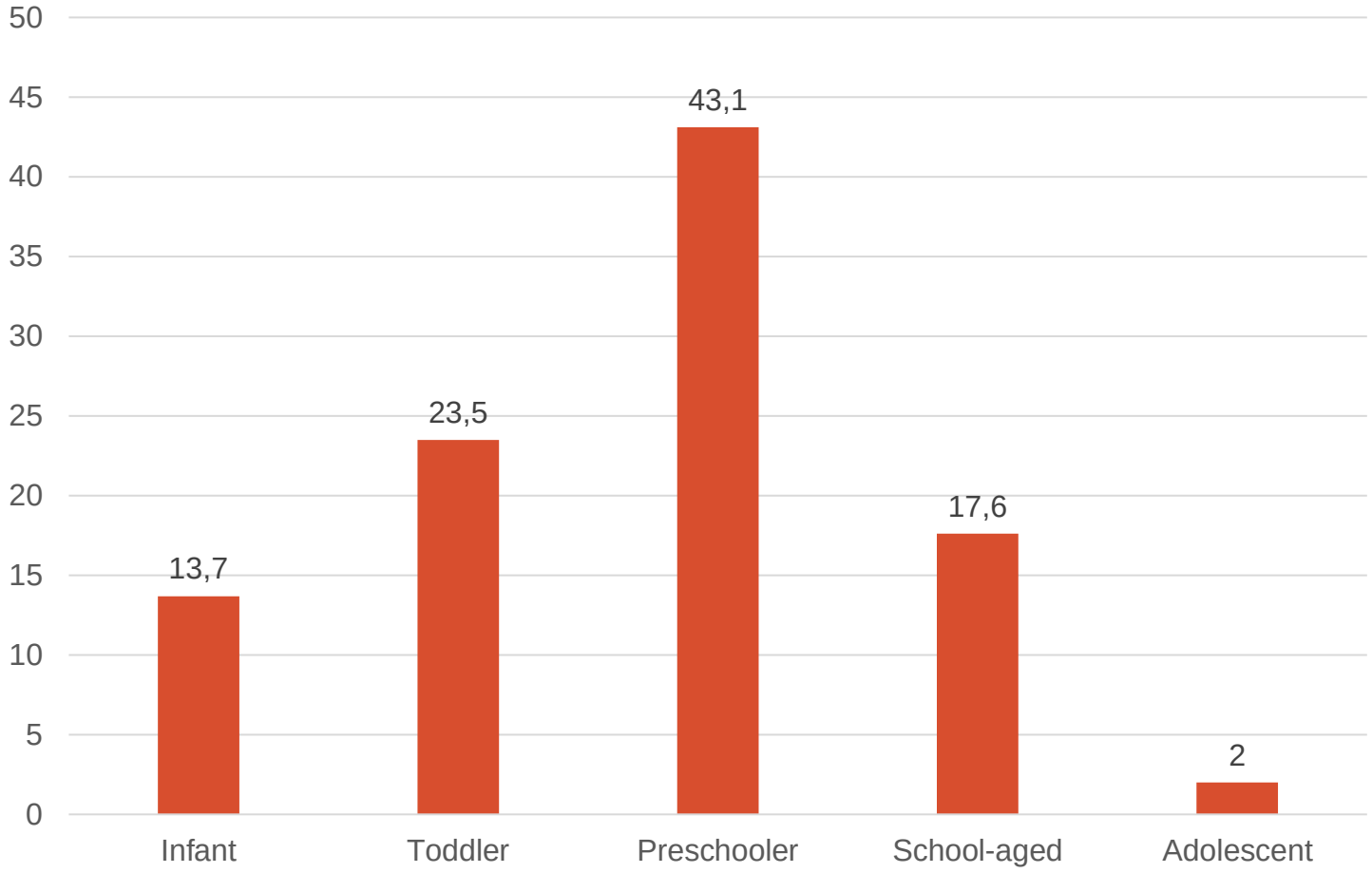
January 2021 to September 2022 COVID-19 related Admissions in Children (N:269)

- Acute COVID-19 cases 218
- MIS-C cases 51 (18%)

Age (Mean = 3.32, Median = 2)	**n**
Infant (1 month to Less than 1 year)	7
Toddler (1 to Less than 2 years)	12
Preschooler (2 to Less than 6 years)	22
School-aged Child (6 to Less than 12 years)	9
Adolescent (12 to 18 years old)	1

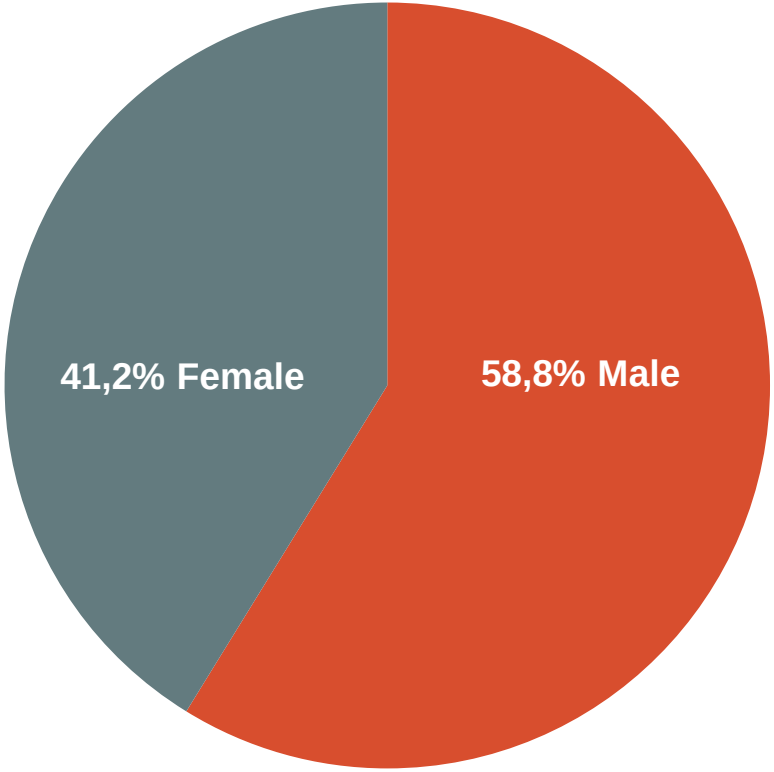
Gender	**n**
Male	30
Female	21

# **Age Distribution** by percentage
n = 51



Gender

n = 51



St. Luke's Medical Center
Quezon City · Global City

- Total number of **MIS-C** cases Jan 2021-September 2022: **51**

- Total Number of **Kawasaki Disease** cases 2021-September 2022: **38**

	MIS-C Patients	Kawasaki Disease Patients
Year 2021 (January to December)	13	12
Year 2022 (January to September)	38	26
Considering only January to September		
Year 2021	8	9
Year 2022	38	26
Change in cases	**375%**	**189%**

St. Luke's Medical Center
Quezon City · Global City

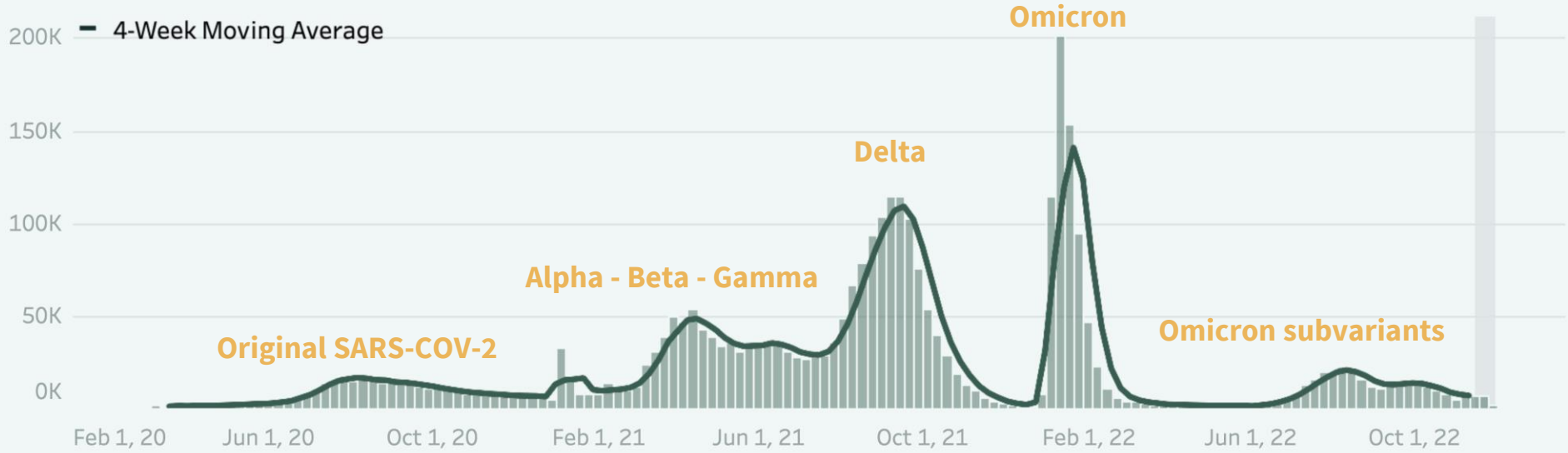
Weekly Cases by Date of Onset of Illness

For 64.4% or 2,600,711 of cases where date of onset of illness is unreported, date of specimen collection was used as proxy.

(•) Weekly
( ) Daily

(•) Cases
( ) Recoveries
( ) Deaths

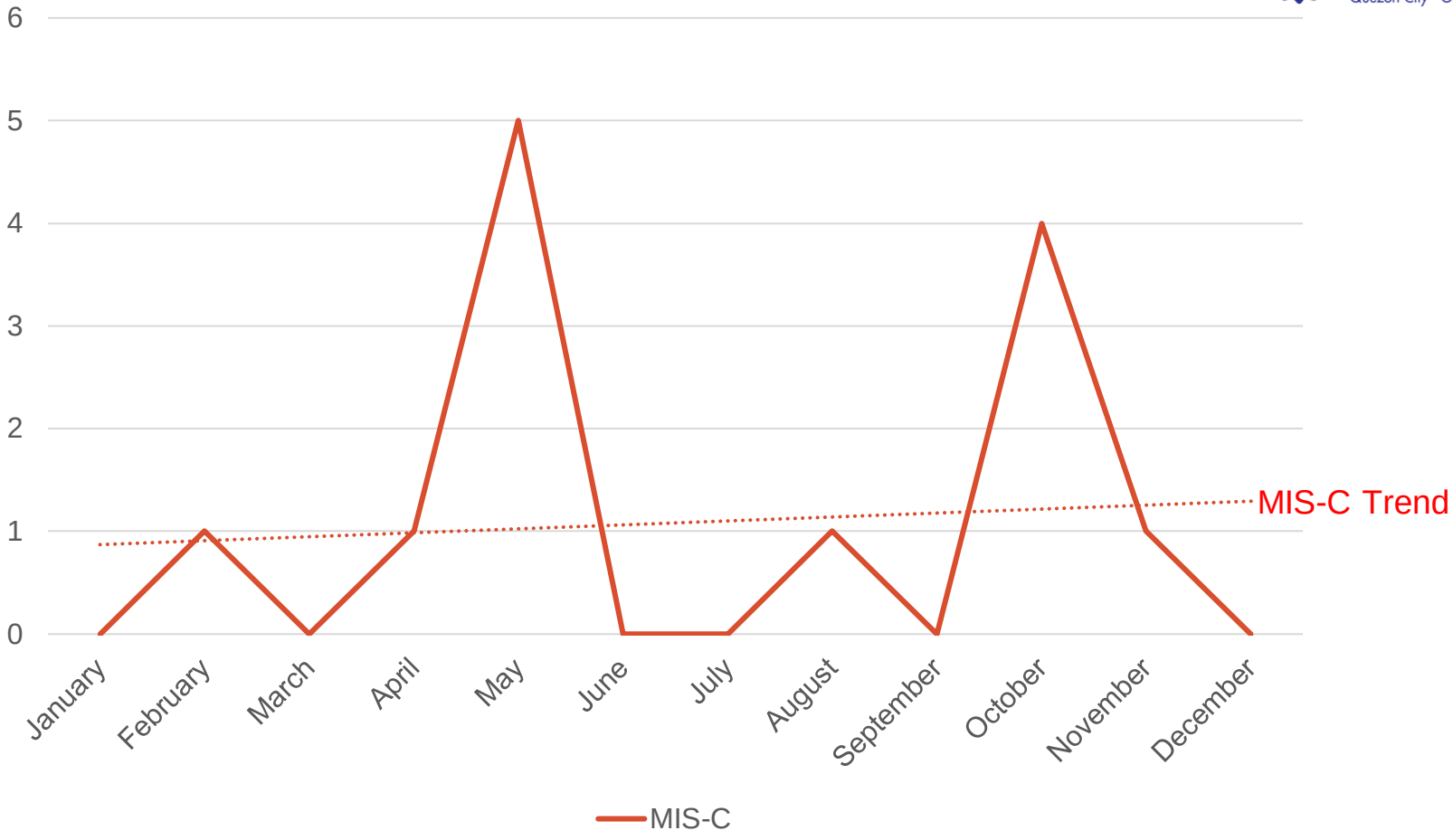
We urge caution when interpreting data during the highlighted period below, which may be incomplete because of delays in reporting.



Note: There are still 889062 cases with unreported date of onset of illness and date of specimen collection.

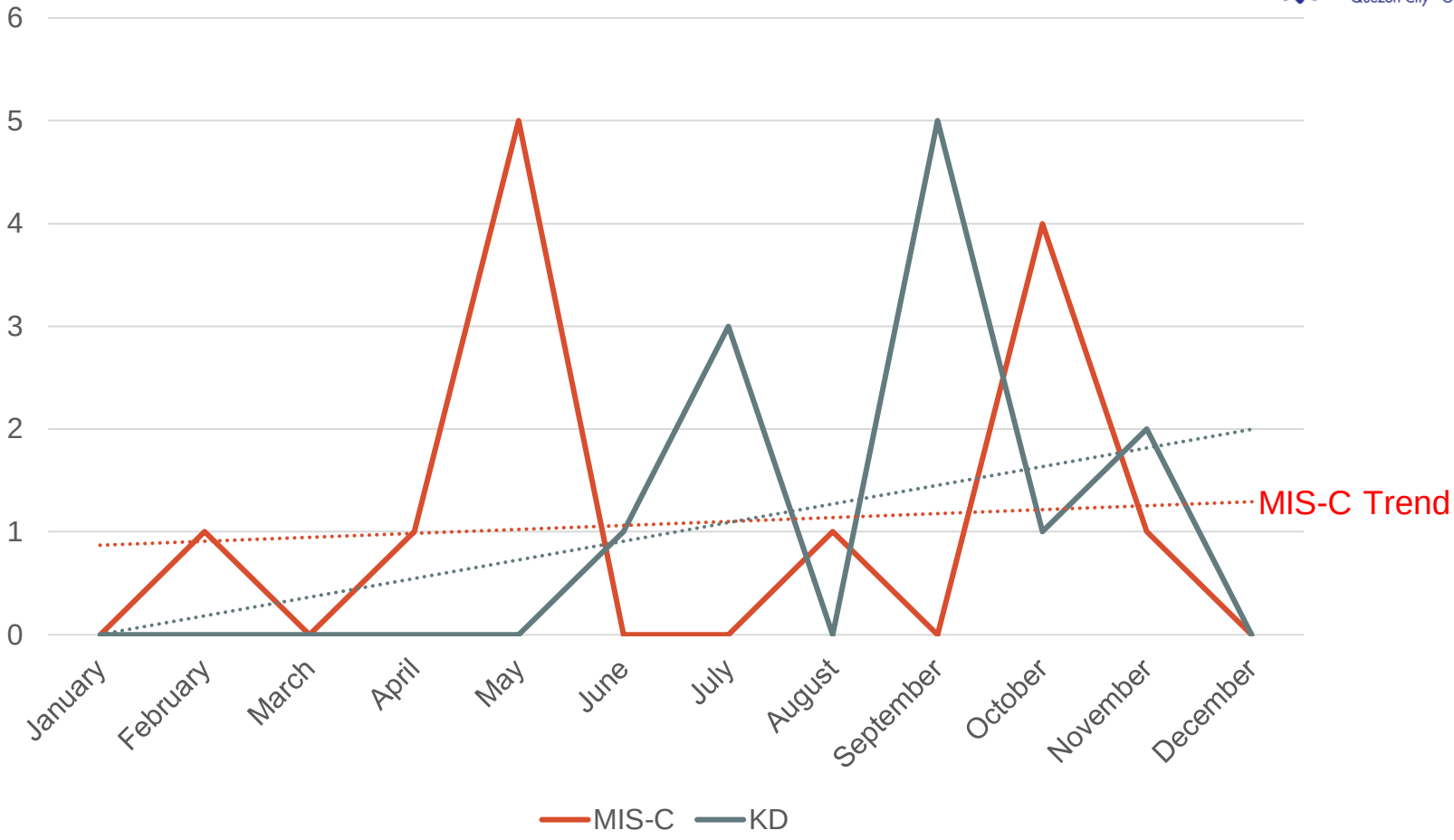
Number of Cases per Month in 2021

St. Luke's Medical Center
Quezon City · Global City



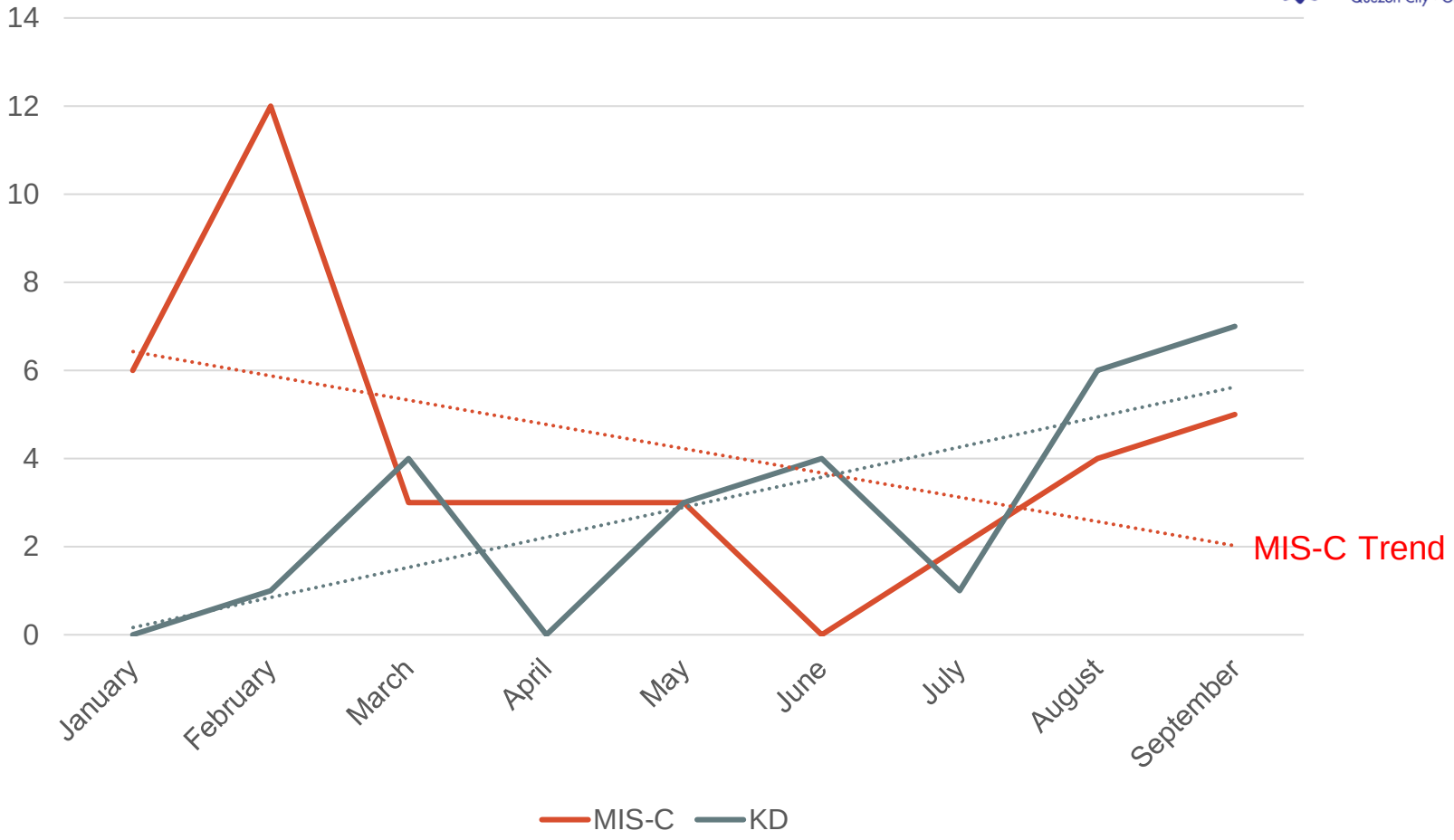
Number of Cases per Month in 2021

St. Luke's Medical Center
Quezon City · Global City



Number of Cases per Month in 2022

Number of Cases per Month in 2022



Symptoms		n	%
Fever		48	94.1
Mucocutaneous	Rash	17	33.3
	Red Lips	1	2.0
	Red eyes	9	17.6
	Oral sores	1	2.0

Symptoms		n	%
Gastrointestinal	Diarrhea	20	39.2
	Vomiting	8	15.7
	Abdominal pain	5	9.8
	Poor appetite	3	5.9

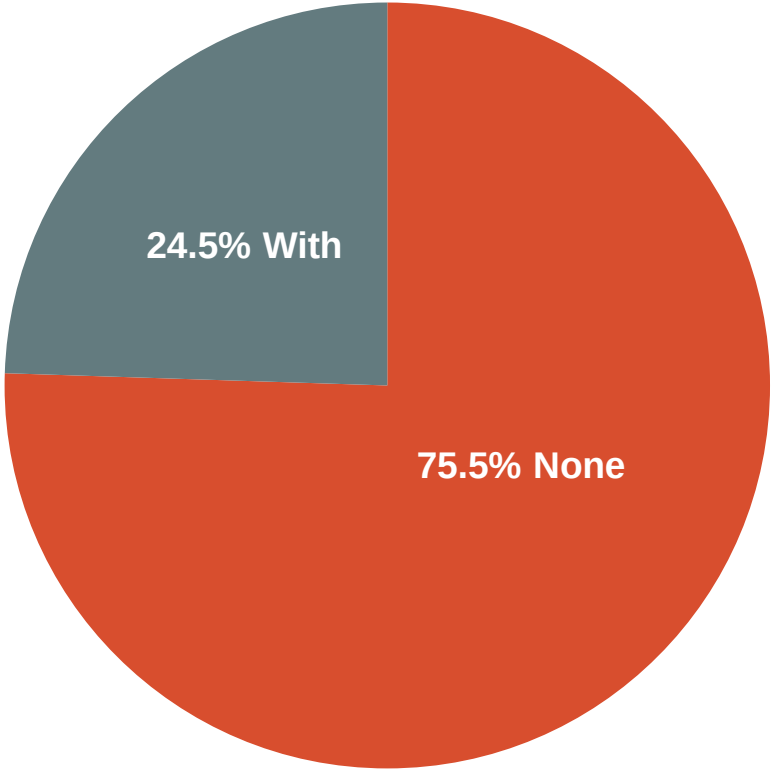
Symptoms		n	%
Respiratory	Cough/colds	16	31.4
	Dyspnea	3	5.9
	Chest pain	2	3.9
Neurologic	Headache	4	7.8
	Seizure	3	5.9
	Irritability	1	2.0

Symptoms		n	%
Cervical Lymph-adenopathy		1	2.0
Genitourinary	Dysuria	2	3.9
Edema of hands and Feet		1	2.0
Pallor		1	2.0

St. Luke's Medical Center
Quezon City · Global City

Underlying Illness

n = 49



Underlying illness	n	%
Cockayne Syndrome*	2	4.1
Congenital Microcephaly*		
Atopic Dermatitis	1	2.0
Malnutrition	1	2.0
UTI	2	4.1
Benign Febrile Convulsion	1	2.0
Typhoid Fever	1	2.0
G6PD	1	2.0
Obese	1	2.0
Intussusception	1	2.0
Chronic Liver disease s/p Liver transplant	1	2.0

*Mortality

Exposure to COVID-19 in the 6 weeks prior to MIS-C	n	%
With exposure to COVID	26	52.0
No exposure to COVID/denies exposure	24	48.0
No data	1	-

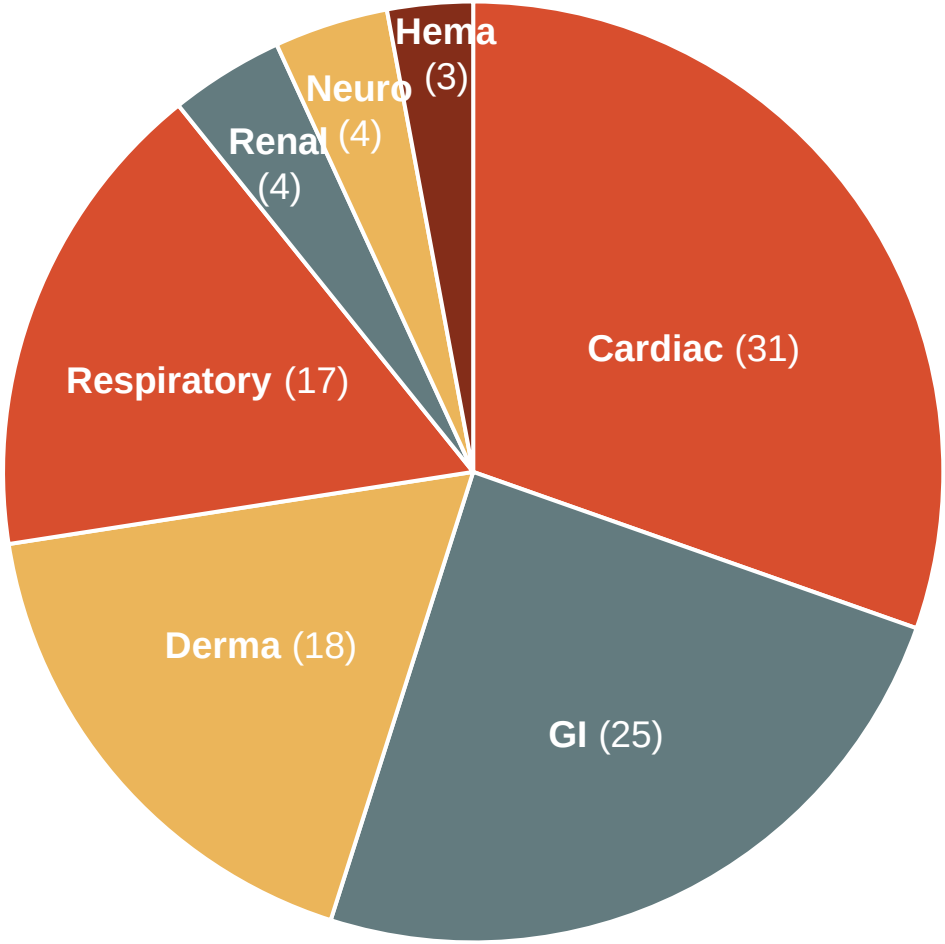
Past infection of COVID-19 in the 6 weeks prior to MIS-C	n	%
With past infection (+)	23	45.1
Without past infection (-)	28	54.9

COVID IgM	COVID IgG	n	%
Negative (-)	**Positive (+)**	**46**	**92.0**
Positive (+)	Negative (-)	1	2.0
Negative (-)	Negative (-)	3	6.0
Not done	Not done	1	-

RT-PCR	n	%
Positive (+)	17	37.8
Negative (-)	28	62.2
Not done	6	-

Cardiac: 2D Echo Findings	n	%
Normal echo	15	29.4
Abormal echo		
Pericardial effusion	**22**	**43.1**
Coronary artery dilation	**14**	**27.5**
Mitral regurgitation	9	17.6
Tricuspid regurgitation	5	9.8
Poor contractility	4	7.8
Ectasia	2	3.9
Pulmonic regurgitation	1	2.0
Atrial regurgitation	1	2.0
Left ventricular enlargement	1	2.0
Left ventricular hypertrophy	1	2.0
Left atrial enlargement	1	2.0

Organ Involvement

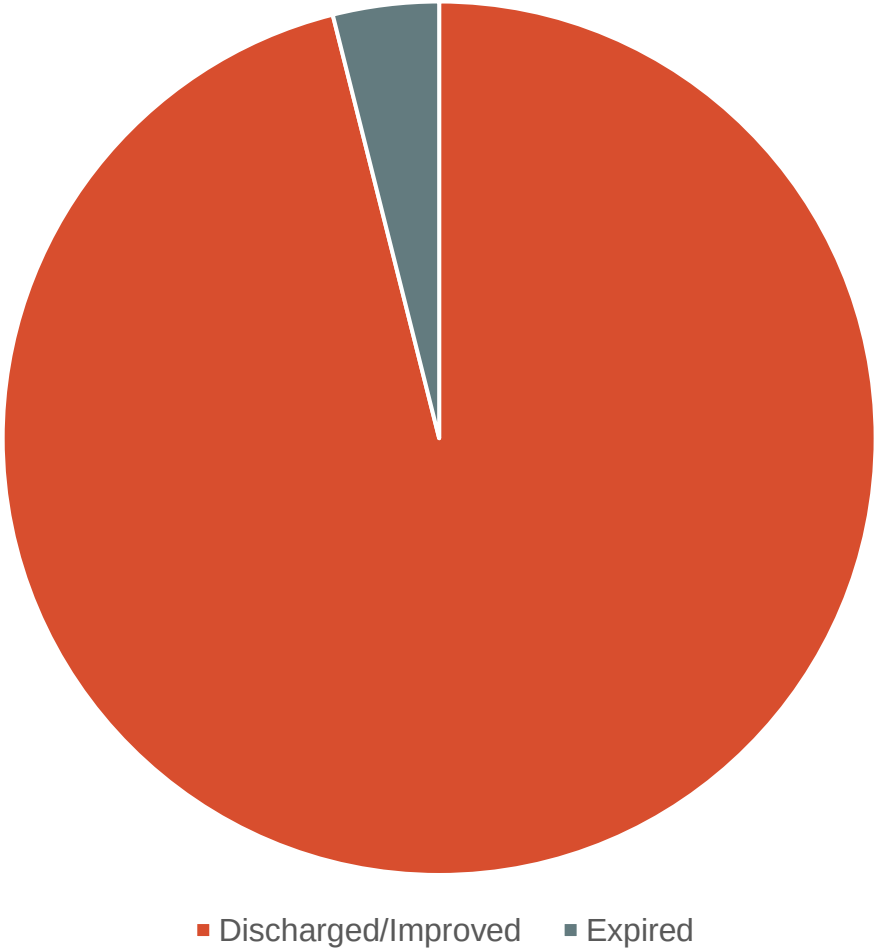


Elevated Results	n	N	%
Interleukin-6	32	33	97.0
ESR	27	28	96.4
CRP	41	43	95.3
D-Dimer	27	31	87.1
Procalcitonin	23	30	76.7
Ferritin	13	20	65.0
LDH	10	16	62.5
Pro-BNP	37	43	86.0
CPK-MB	3	6	50.0
Troponin-i	10	24	41.7
Sodium	1	1	100.0
SGPT	14	26	53.8
Creatinine	2	14	14.3

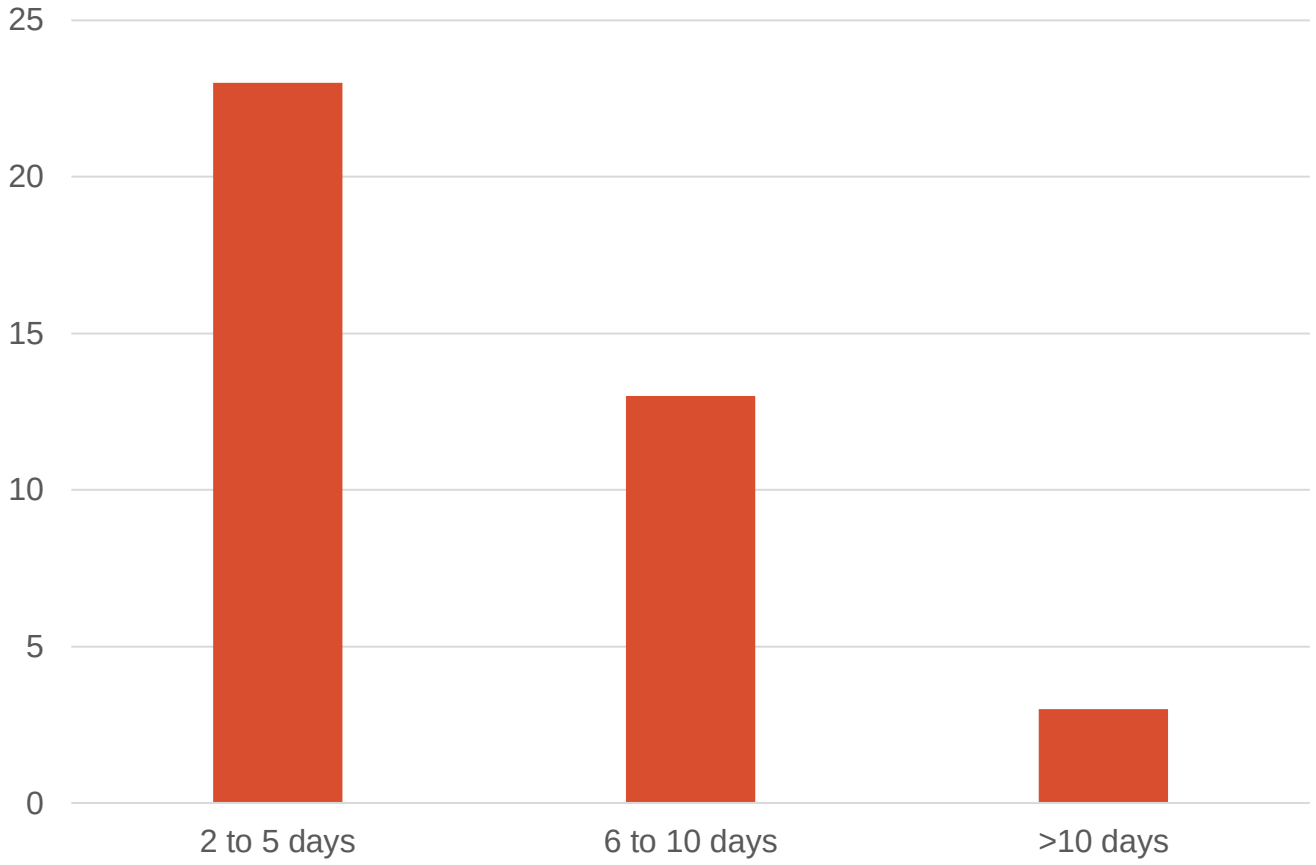
St. Luke's Medical Center
Quezon City · Global City

Treatment	n	%
With major treatment		
IVIG+Steroids	17	33.3
IVIG+ Aspirin+ Steroids	16	31.4
IVIG+Aspirin	10	19.6
IVIG only	4	7.8
Steroids +Aspirin	2	3.9
None	2	3.9
Other treatments		
Antibiotics	18	35.3
Enoxaparin	5	9.8
Inotropes	4	7.8
Hemoperfusion	1	2.0
Remdesivir	1	2.0

Outcome



Length of Hospital Stay



The Average Hospital Stay is 6 Days

St. Luke's Medical Center
Quezon City · Global City

Other Data

- Patients with significant PICU stay: 7 (13.7%)
- None of those who had MIS-C were vaccinated with COVID-19 vaccine

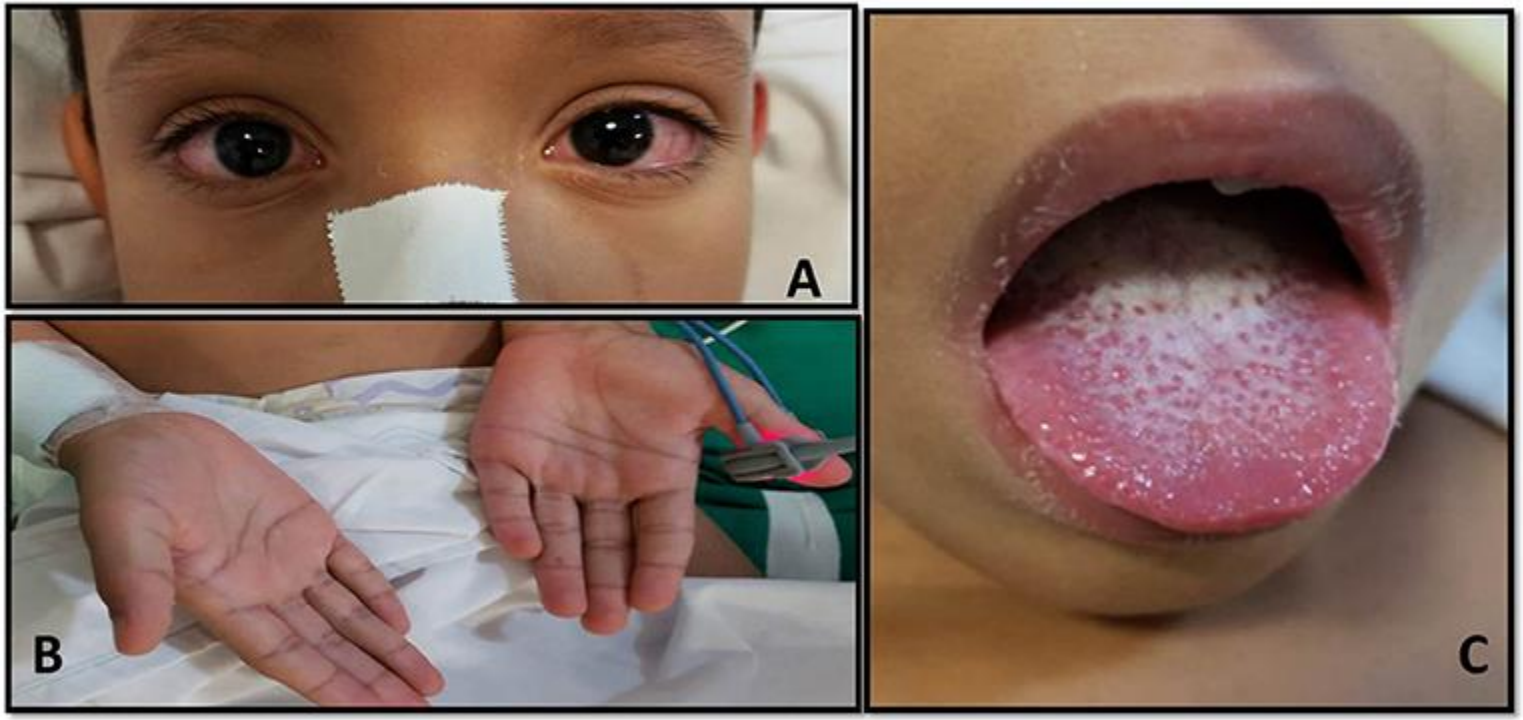
Challenges in Diagnosis and Management of MIS-C

1. Positive serologies for SARS Co-V-2 are no longer as informative for a diagnosis of MIS-C given widespread native infections as well as increasing vaccination.
    - The baseline rate of seropositivity for SARS-CoV-2 has increased significantly. There will be an increasing number of febrile children who may incidentally have positive serologies

CHALLENGES IN DIAGNOSIS AND MANAGEMENT OF MIS-C...

2. There is no readily available test to differentiate IgG resulting from COVID vaccine or IgG from a past infection

MIS-C and Kawasaki Disease (KD)



https://www.frontiersin.org/files/Articles/650697/fped-09-650697-HTML/image_m/fped-09-650697-g001.jpg

	MIS-C	KD
Age (mean)	8.5 years	3 years
Fever	+++	+++
Rash	++	+++
Conjunctivitis	++	++
Oromucosal change	++	++
Extremity Change	+/-	+

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

	MIS-C	KD
Cervical LAD	+/-	+
Coronary dilation	+	++
Cardiac dysfunction	++	–
GI symptoms	+++	+
Shock/hypotension	++	+/–
Death	2%	0.17%

Vogel TP, Top KA, Karatzios C, Hilmers DC, Tapia LI, Moceri P, Giovannini-Chami L, Wood N, Chandler RE, Klein NP, Schlaudecker EP, Poli MC, Muscal E, Munoz FM. Multisystem inflammatory syndrome in children and adults (MIS-C/A): Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2021 May 21;39(22):3037-3049. doi: 10.1016/j.vaccine.2021.01.054. Epub 2021 Feb 25. PMID: 33640145; PMCID: PMC7904456.

CHALLENGES IN DIAGNOSIS AND MANAGEMENT OF MIS-C…

3. With the overlapping clinical manifestations and the lack of a specific diagnostic test for either MIS-C or KD, distinguishing the two conditions in an individual patient can be challenging

- Though inflammatory markers are higher in MIS-C, there is no cut off to say specifically how high that of MIS-C rather than KD
- difficult to distinguish patients with incidental KD who have seroconverted from prior SARS Co-V2 infections from patients with MIS-C who meet KD criteria

US CDC Case Definition for MIS-C

An individual aged <21 years presenting with fever*, laboratory evidence of inflammation**, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **AND**

No alternative plausible diagnoses; **AND**

Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms

Addendum: ***Some individuals may fulfill full or partial criteria for Kawasaki Disease but should be reported if they meet the case definition for MIS-C***

Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

CHALLENGES IN DIAGNOSIS AND MANAGEMENT OF MIS-C…

3. With relaxed measures, persons with COVID-19 symptoms are not tested anymore unless hospitalized

4. Shortage of serologic test for COVID-19 recently

5. Shortage of IVIG

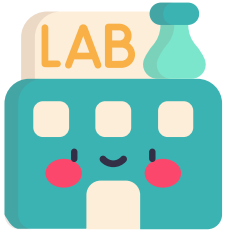
Known Risk Factor for MIS-C

- **Acute COVID-19 infection** → MIS-C
- PREVENT ACUTE COVID-19 → **PREVENT MIS-C**

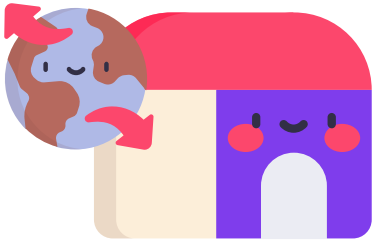
How to stop the spread of

COVID-19

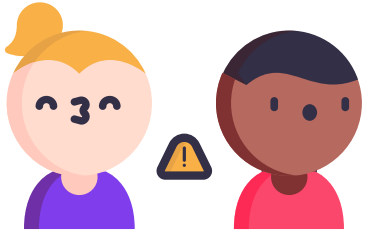
Get vaccinated and **boosted** if you're eligible



Get **tested** if you have symptoms of illness



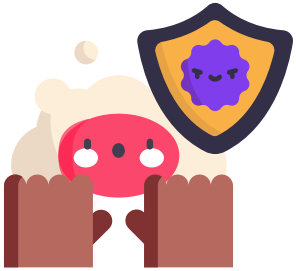
Choose **outdoor** gatherings instead of indoor ones



Practice **physical distancing** – the farther the better

Wear a **mask** indoors/ in public transportation

Wash your hands frequently



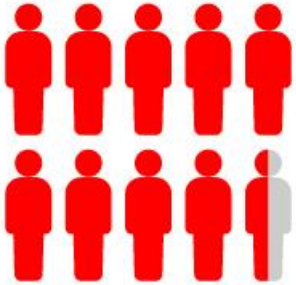
Disinfect high-touch surfaces

https://www.nebraskamed.com/COVID/omicron-variant-what-it-is-and-how-to-stop-the-spread / Icons by Slidesgo

COVID-19 vaccination protects against multisystem inflammatory syndrome in children (MIS-C) among 12–18 year-olds hospitalized during July–December 2021

Vaccination reduced likelihood of MIS-C by:

ADOLESCENTS HOSPITALIZED WITH MIS-C



No vaccinated MIS-C patients required life support

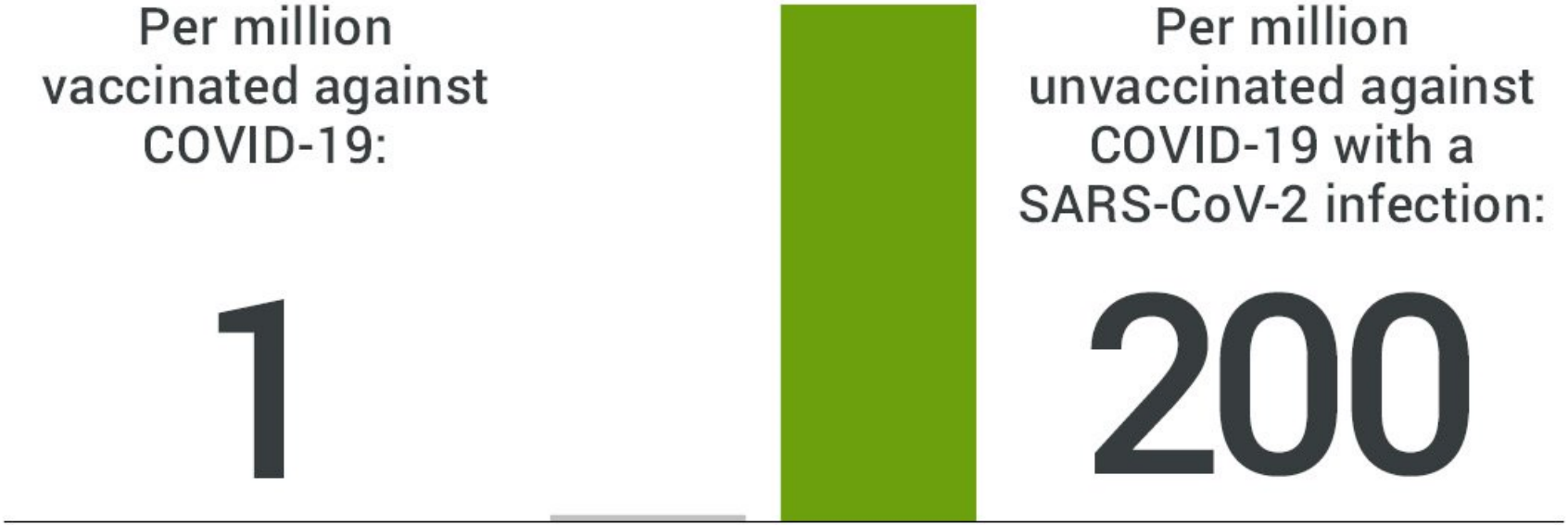
COVID-19 VACCINATION IS THE BEST PROTECTION AGAINST MIS-C

* Case-control study, 238 patients in 24 pediatric hospitals—20 U.S. states
† 2 doses of Pfizer-BioNTech vaccine received ≥28 days before hospital admission

bit.ly/MMWR7102

MMWR

Estimated U.S. rate of multisystem inflammatory syndrome in children:



Healio

https://www.healio.com/news/primary-care/20220223/misc-risk-after-covid19-vaccination-falls-to-one-in-a-million-study-finds

THANK YOU.

Do you have any questions?

emylunapedid@gmail.com

CREDITS: This presentation template was created by **Slidesgo**, including icons by **Flaticon**, and infographics & images by **Freepik**