Paediatric Multisystem Inflammatory Syndrome – Temporally Associated with SARS-CoV-2: infectious diseases perspective

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PIMS-TS AND SICKLE CELL DISEASE WEBINAR, 15TH JUNE 2020

COVID-19 in children – what we thought would happen

Low numbers of cases of COVID-19

Similar rates of infection

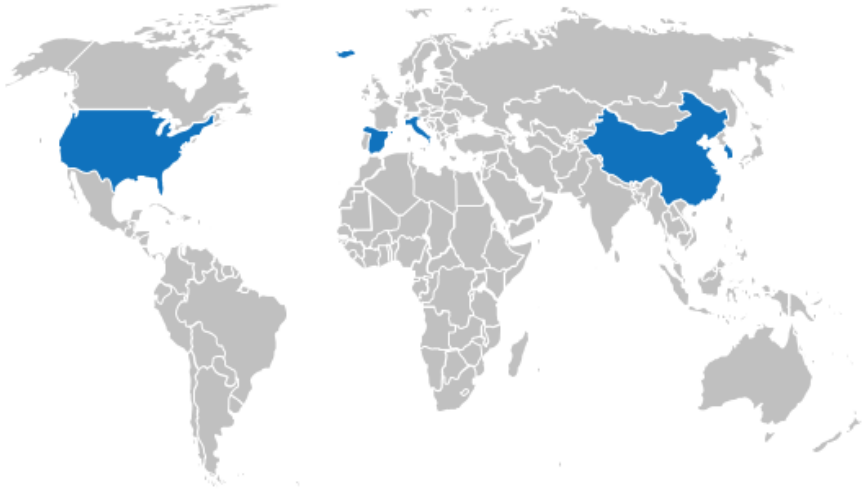
Asymptomatic or mild disease

Critical illness and death extremely rare

No risk factors

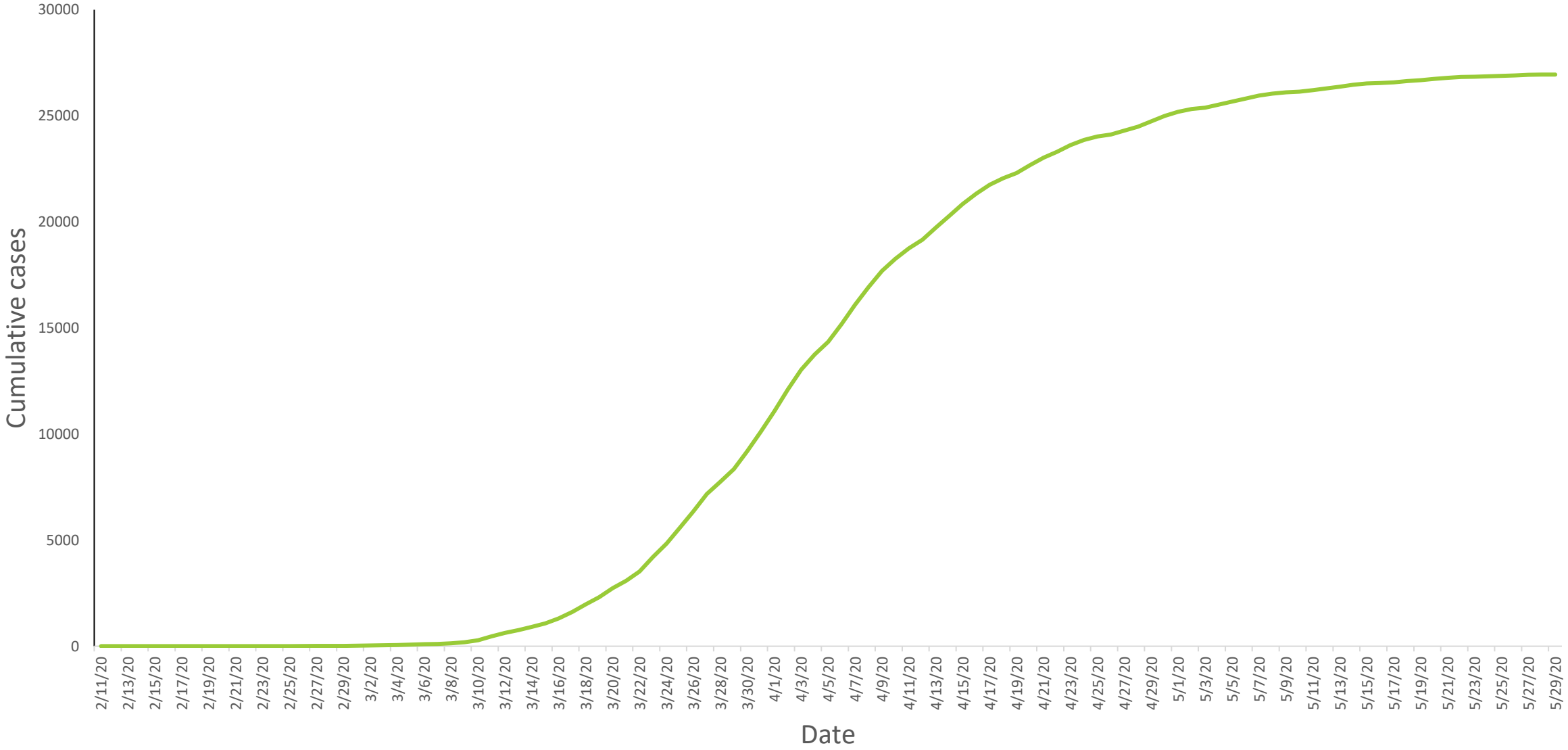
Blood parameters **not** like severe COVID-19 in adults

Early questions – **why is COVID-19 less common and less severe in children?**



Reviewed by: Zimmermann et al. PIDJ 2020, Castagnoli et al. JAMA Ped 2020, Ludvigsson Acta Ped 2020, Mehta et al. CID 2020, Henry et al. Clin Chem Lab Med 2020, Liguoro et al. Eur J Ped 2020, Lu et al. Arch Dis Paed, Mustafa et al. J Clin Viro 2020. Further reports: de Caeno Vivas et al. Arch Dis Child 2020, Tagarro et al Jama Ped 2020

London cumulative lab-confirmed SARS-CoV-2 cases



Data source: Public Health England

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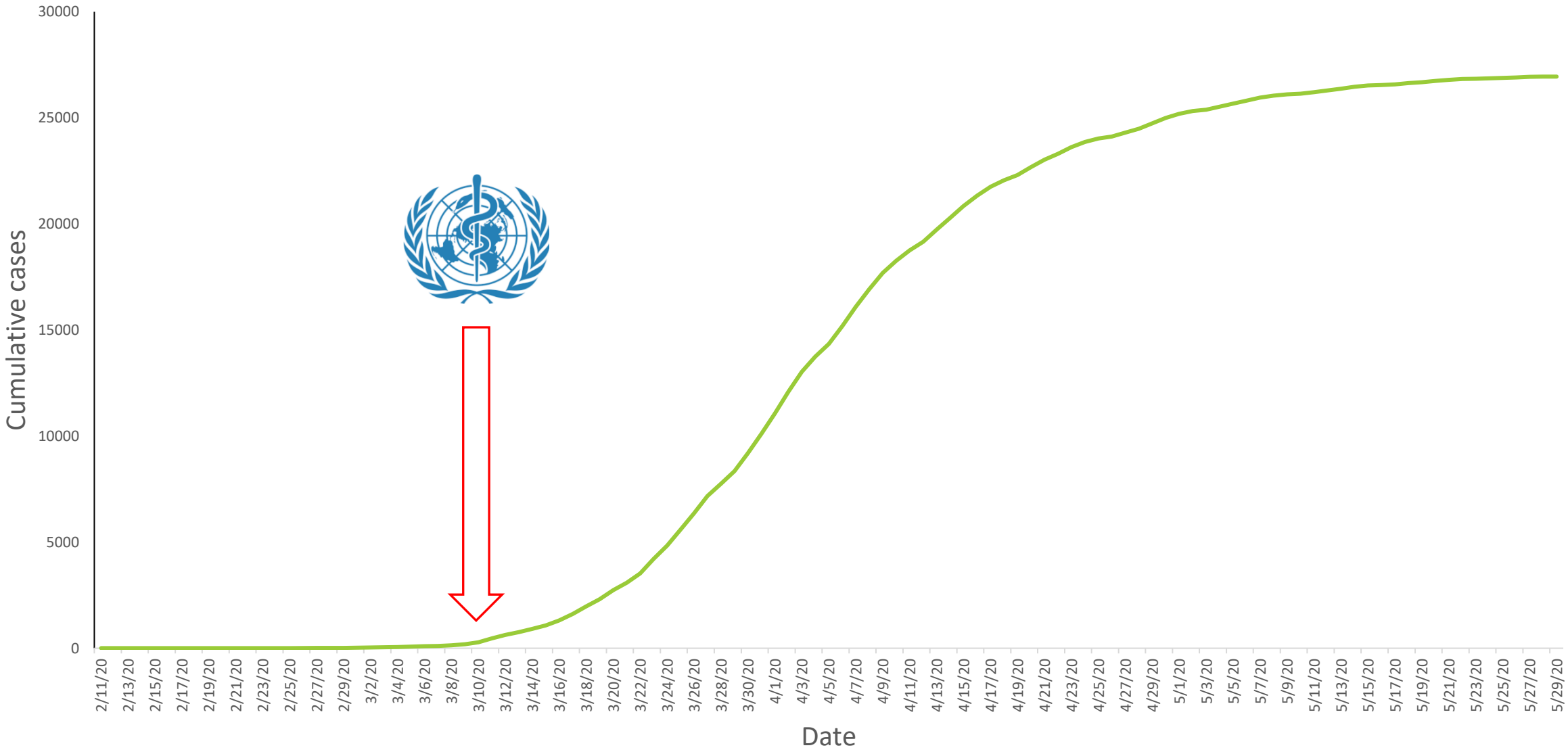

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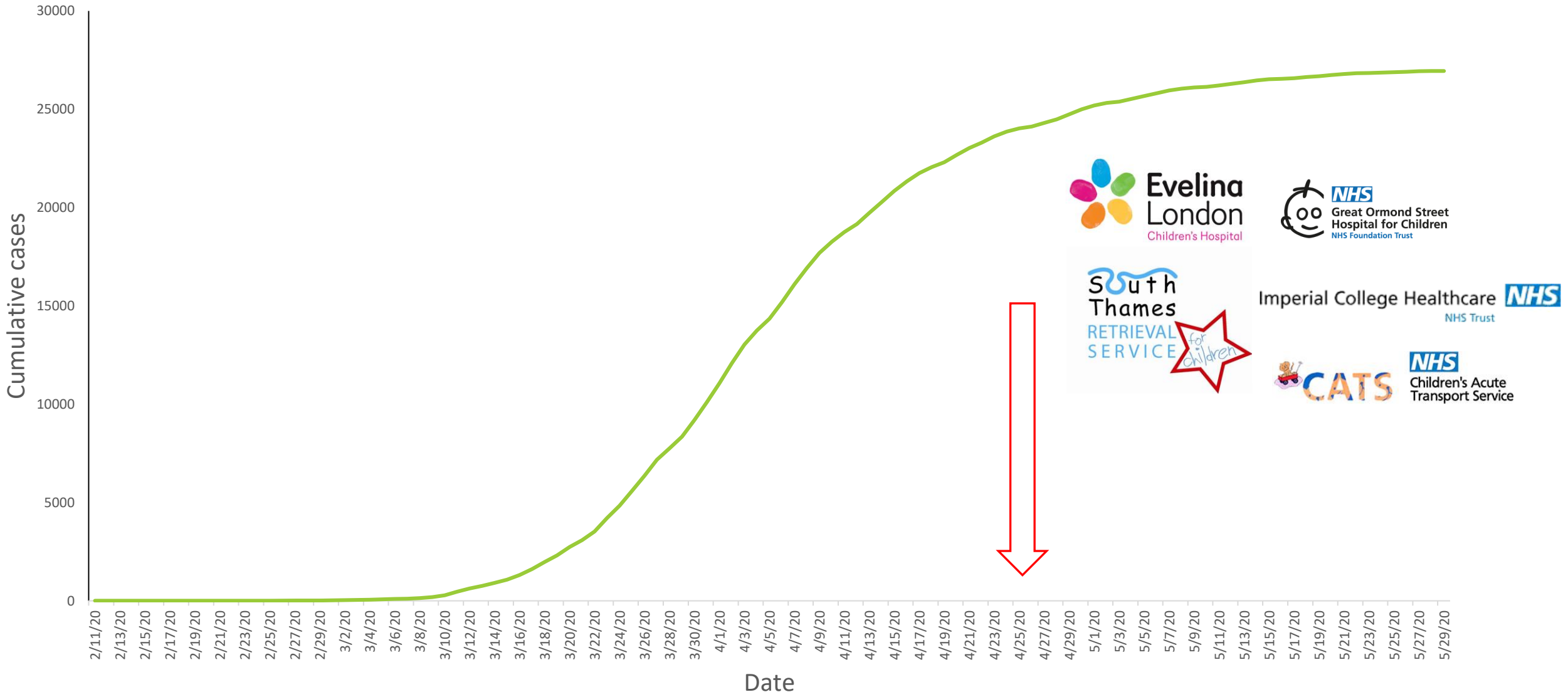

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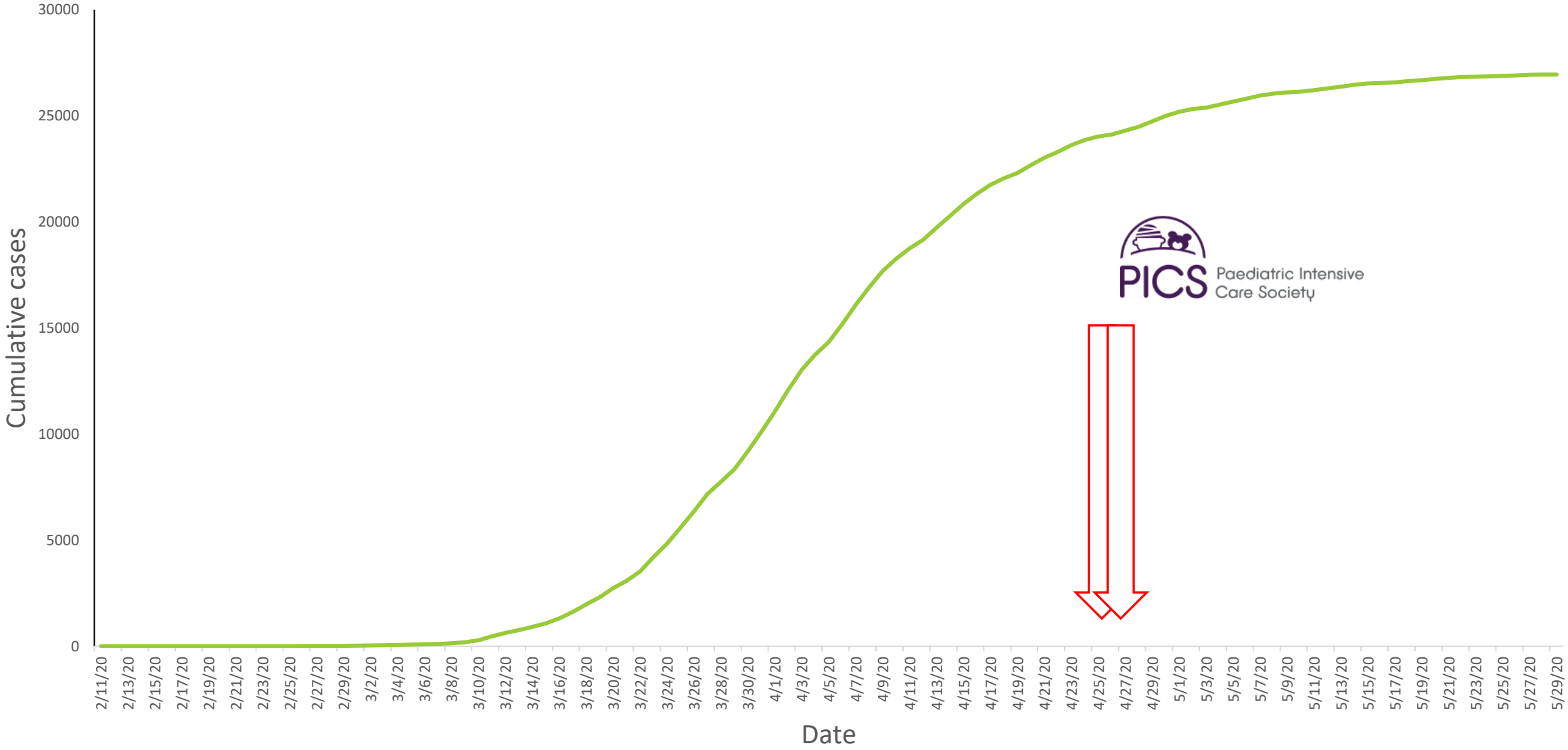

https://picsociety.uk/wp-content/uploads/2020/04/PICS-statement-re-novel-KD-C19-presentation-v2-27042020.pdf

Data source: Public Health England

Questions asked of the team

Is this real?

Is it an increase in the numbers of cases of a condition we know?

Is it linked to SARS-CoV-2?

Is it an outbreak of another infectious pathogen?

How can we raise awareness?

Where should the patients be looked after?

What investigations should be done?

Can we provide any guidance on specific treatment?

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https://www.rcpch.ac.uk/resources/guidance-paediatric-multisystem-inflammatory-syndrome-temporally-associated-covid-19

Data source: Public Health England

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Paediatric Inflammatory Multisystem Syndrome Temporally Associated with SARS-CoV2 (PIMS-TS)

Purpose of the case definition

To be broad enough to not miss cases

To include cases of other conditions that may have increased in frequency

To inform baseline surveillance

To raise awareness and promote early referral and entry in to research studies

Not to be dependent on a diagnosis of SARS-CoV-2 infection

Not to be the final case definition of a new syndrome (if one is identified)

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Case definition:

1. A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features (see listed in Appendix 1). This may include children fulfilling full or partial criteria for Kawasaki disease.

2. Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice).

3. SARS-CoV-2 PCR testing may be positive or negative

https://www.rcpch.ac.uk/resources/guidance-paediatric-multisystem-inflammatory-syndrome-temporally-associated-covid-19

Clinical and lab features

Fever

Rash

Conjunctivitis

Abdominal pain

Diarrhoea

Vomiting

Headache

Shock

Myocardial dysfunction

ECG abnormaliti

Cor

Low lymphocytes

neutrophils

gh C reactive protein

albumin

High ferritin

High fibrinogen

High D-dimers

High troponin

High NT-BNP

SARS-CoV-2 PCR often negative
SARS-CoV-2 IgG positive in most

https://www.rcpch.ac.uk/resources/guidance-paediatric-multisystem-inflammatory-syndrome-temporally-associated-covid-19

RCPCH guidance continued…

Early medical management

Monitoring

Treatment

Recruitment into observational studies and trials

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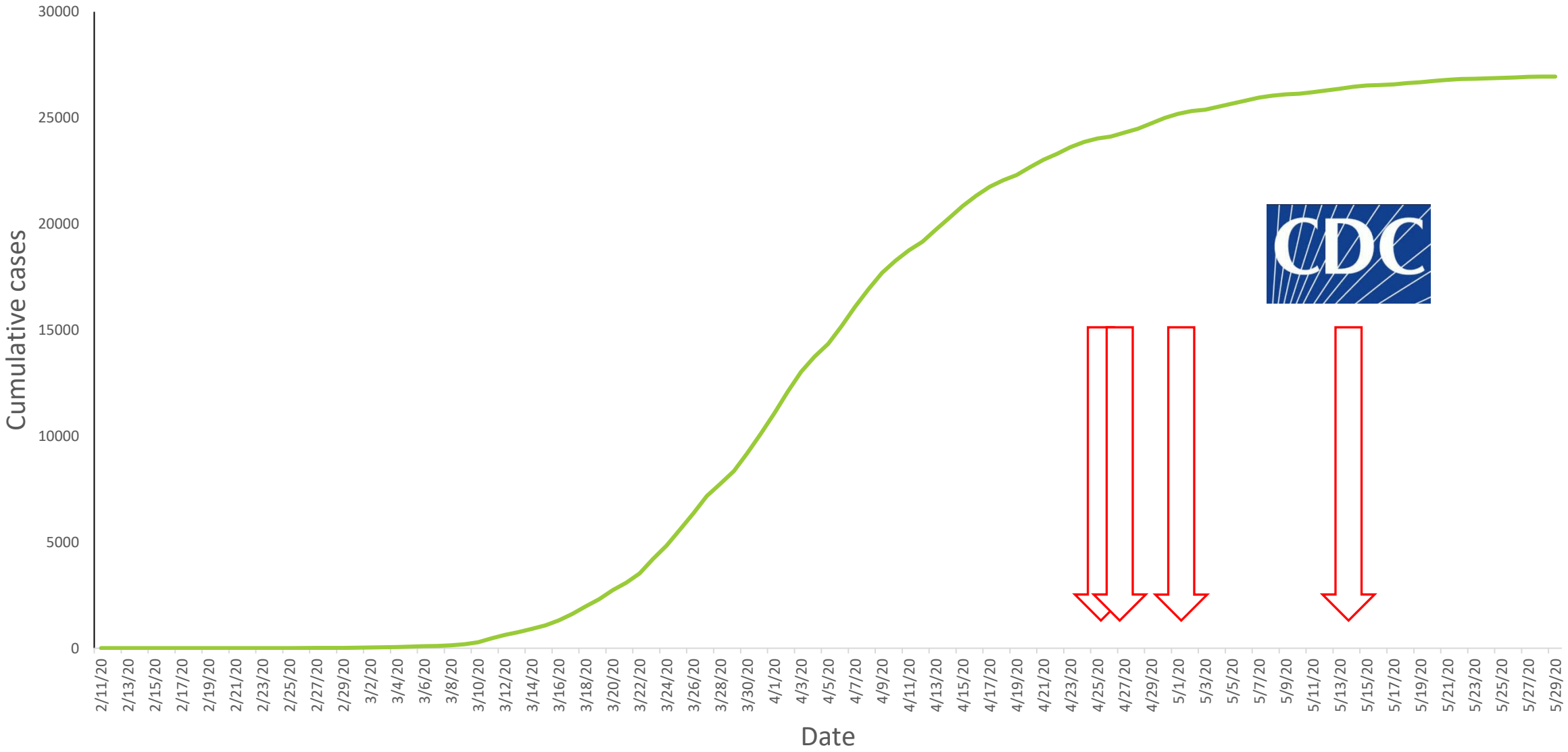

https://emergency.cdc.gov/han/2020/han00432.asp

Data source: Public Health England

Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], 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 COVID-19 exposure within the 4 weeks prior to the onset of symptoms

[i]Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
[ii]Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Additional comments

- 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

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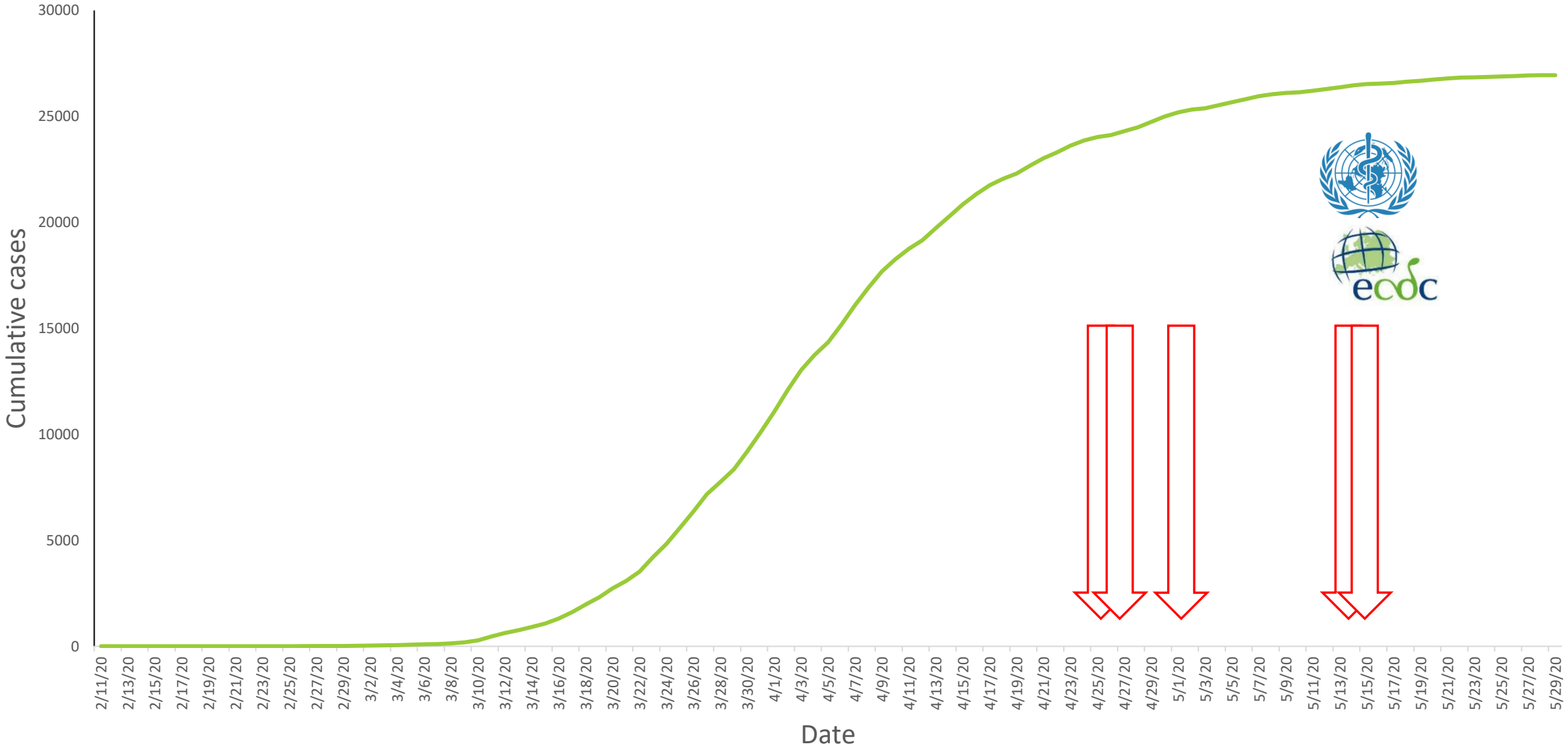


https://www.who.int/publications-detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19
https://www.ecdc.europa.eu/sites/default/files/documents/covid-19-risk-assessment-paediatric-inflammatory-multisystem-syndrome-15-May-2020.pdf

Data source: Public Health England

Preliminary case definition[a]

Children and adolescents 0–19 years of age with fever ≥ 3 days

AND two of the following:

a) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).

b) Hypotension or shock.

c) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),

d) Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).

e) Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

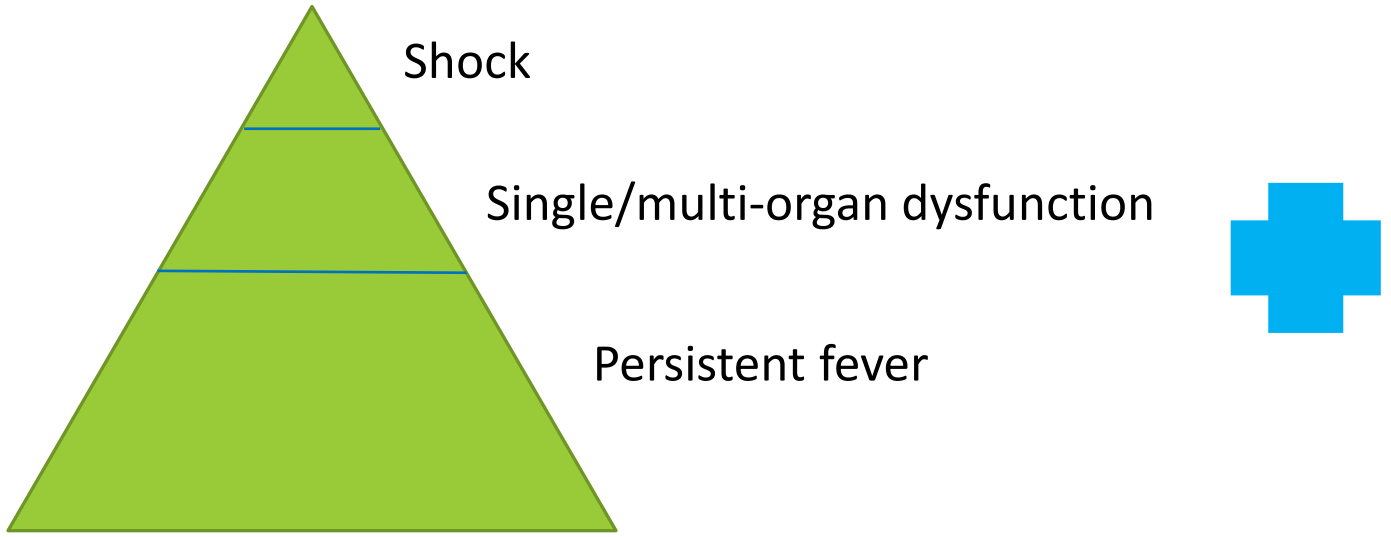
AND

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

[a] Consider this syndrome in children with features of typical or atypical Kawasaki disease or toxic shock syndrome.

https://www.who.int/publications-detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19

What should be the definition PIMS-TS v2?



A set of characteristic and unique clinical and laboratory features

Next steps…

Link to SARS-CoV-2

Direct viral effect vs. host response

Risk factors

Age range – young adults?

Pathophysiology and biomarkers

Treatment – supportive care vs. antivirals vs. immunomodulation - Delphi

Long term outcomes – MDT clinics?

Implications for vaccine development and convalescent plasma

Summary

Acknowledgements