

Severe Infections due to Group A Streptococcus: Learning from Extreme Clinical Phenotypes

Shiranee Sriskandan

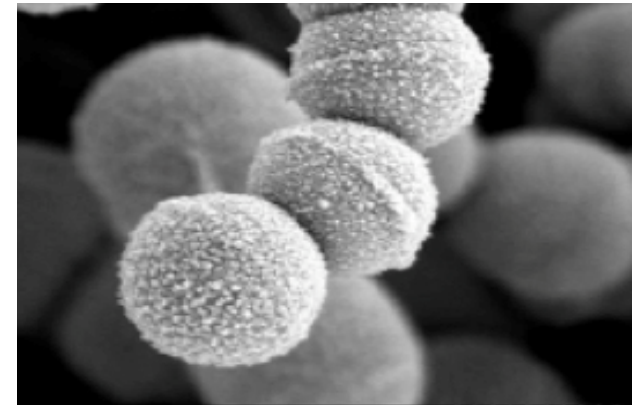
Imperial College
London



January 31st 2025 Paris | ICU Infections meeting

Talk today?

- Two cases of invasive GAS (iGAS) presenting in the ICU
- Both February 2015, both 51 years, both same serotype
- Necrotising soft tissue infection resistant to treatment?
- Necrotising pneumonia- why so severe?
- What can we learn from these rare cases?
- Link to the marked upsurge in iGAS in 2022-2023...

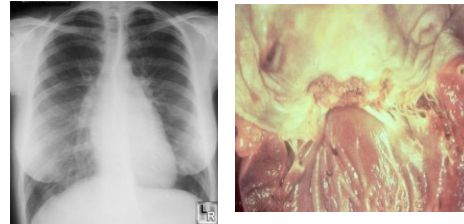


Some background!

Non-invasive infection



Immunological sequelae



Acute rheumatic fever &
Post-strep
glomerulonephritis

Invasive infections



SSTI

Pneumonia Bacteremia

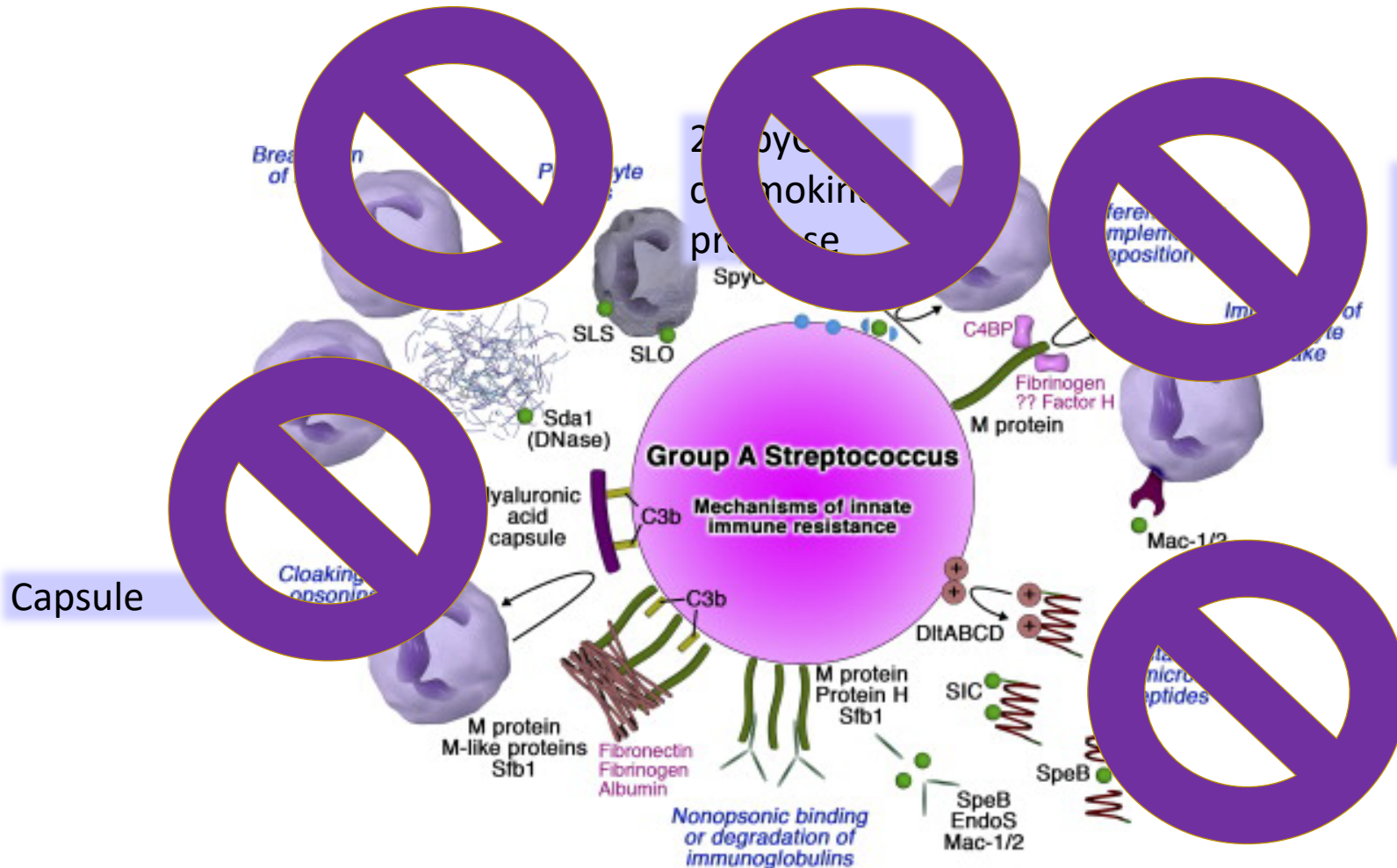
Necrotising
fasciitis

Peripartum
sepsis

Toxic shock
STSS

Rare; Overall mortality 12% (US data)

Virulence factors of *S. pyogenes* -repressed by CovRS



1. M protein- used for serotyping and genotyping (>200 types)

M1 oldest serotype, and most associated with invasive infections in developed nations (usually 20% of iGAS)

3. Secreted superantigens 'scarlet fever toxins'

A case of bilateral swollen legs after a long drive

51 year old man. Brought to hospital with 5d fever, severe pain in legs, no urine output, CRP >400

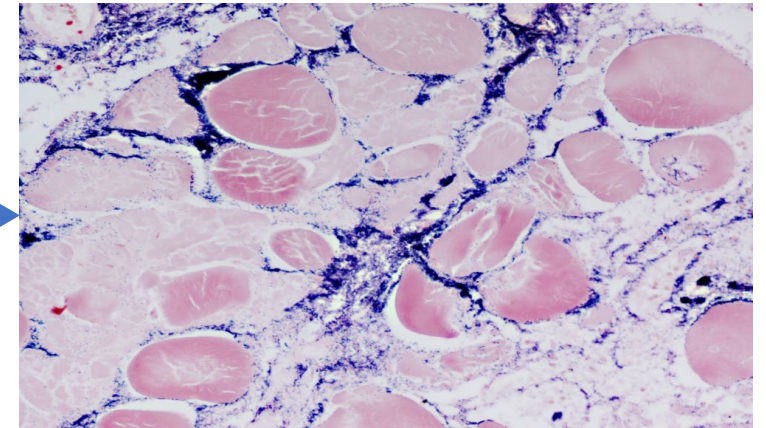


Day 1
ICU
2 filters (pH 6.9)
Antibiotics
IVIg



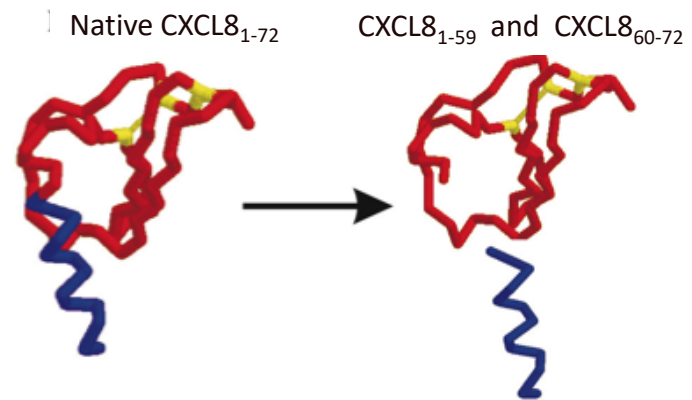
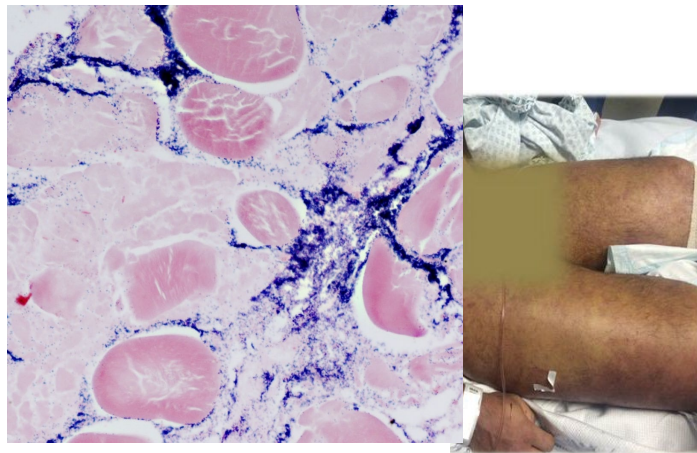
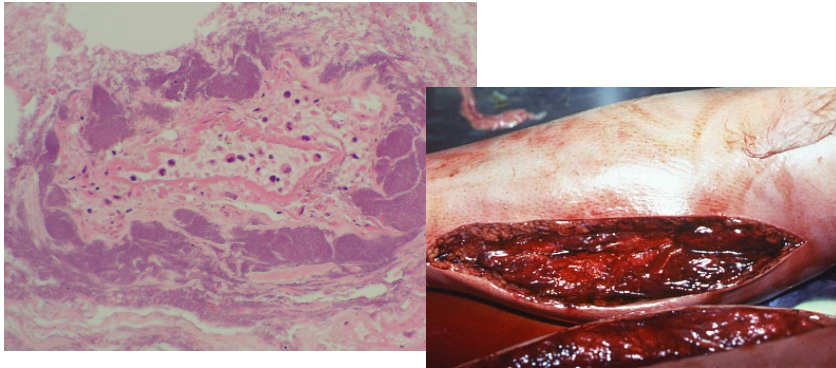
Day 2 debrided muscle- growing group A strep despite antibiotics

(WGS: GAS **covS mutant emm1**)



Day 5 bilateral below knee amputations;
No neutrophils seen in tissues despite multiple Gram positive cocci.
Viable strep growing on prolonged culture.

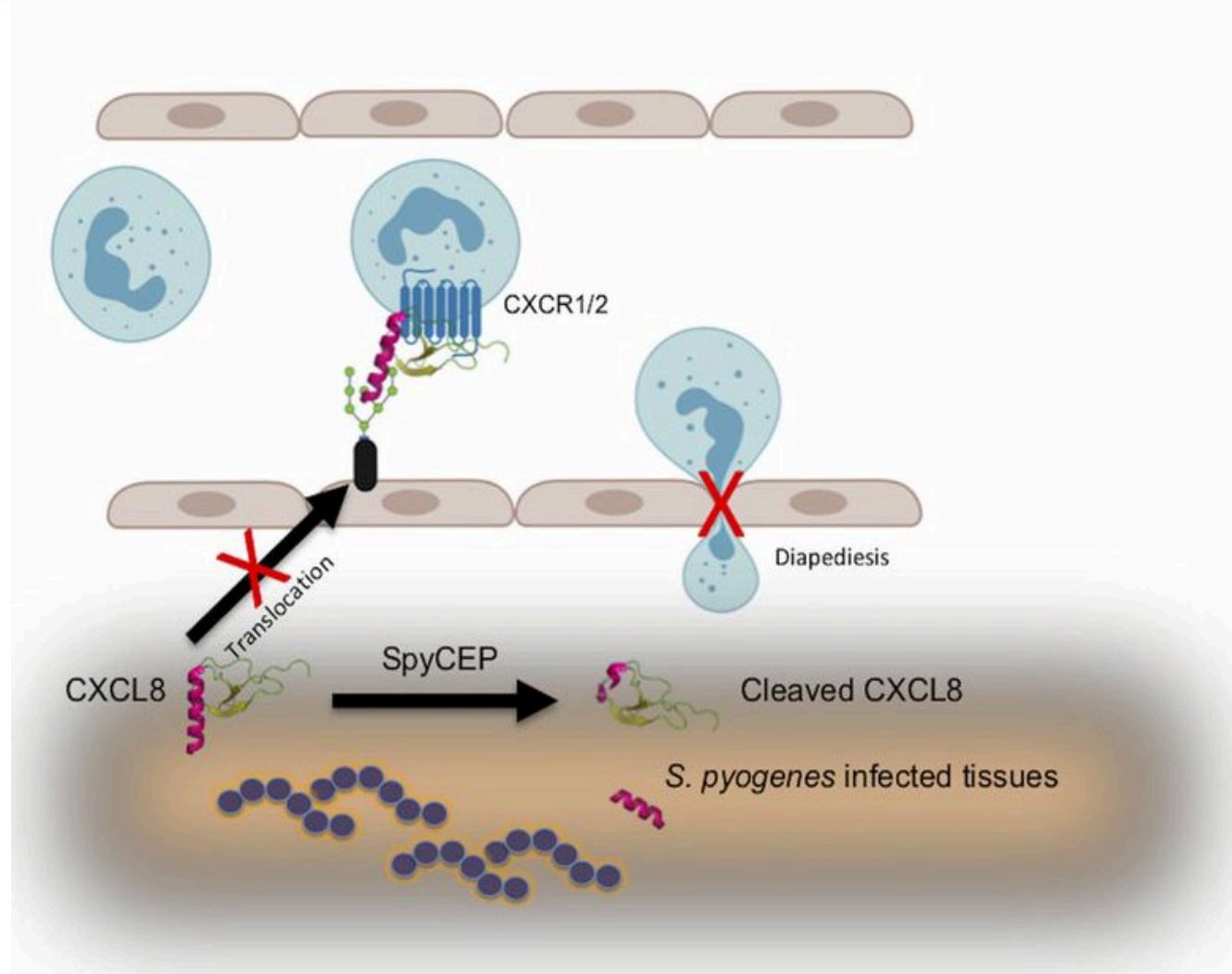
Day 6- Patient died
Did antibiotics fail to clear the bacteria?



SpyCEP
Serine protease
Attached to *S. pyogenes*
Cleaves IL-8

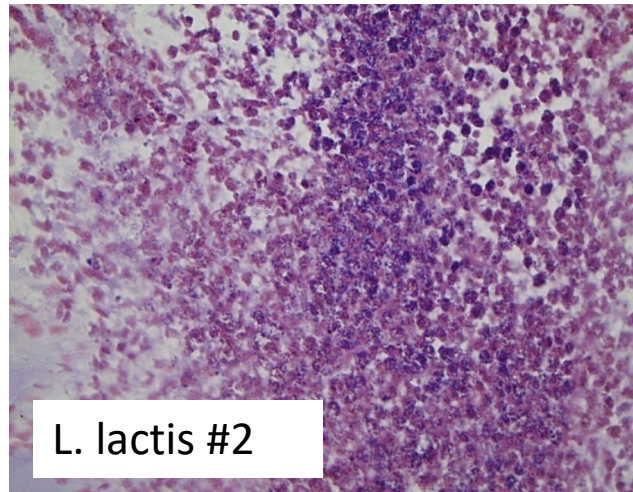
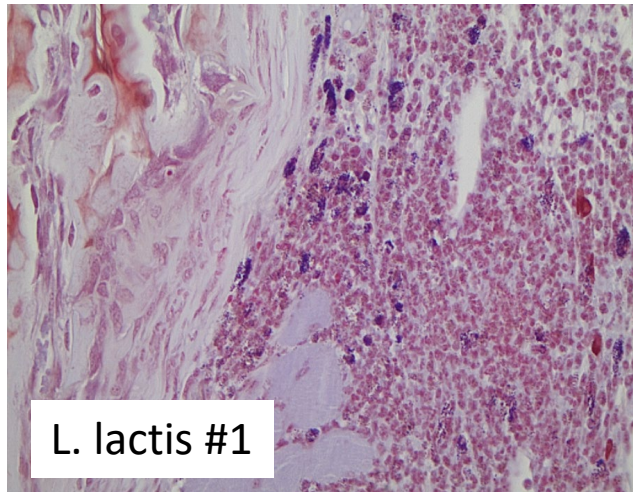
How does SpyCEP work?-

Cleavage and inactivation of CXC chemokines



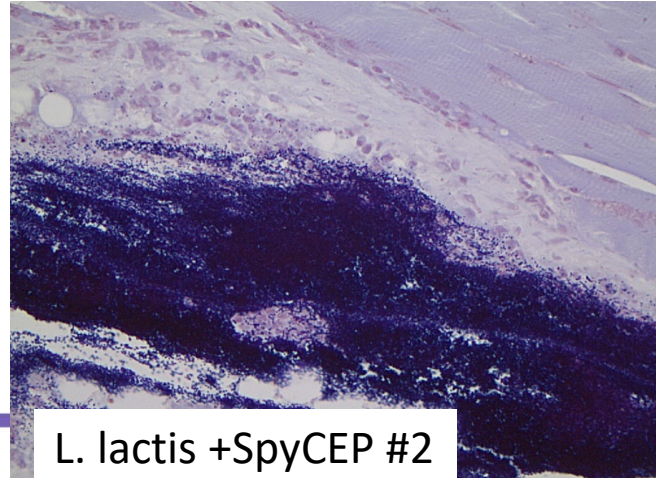
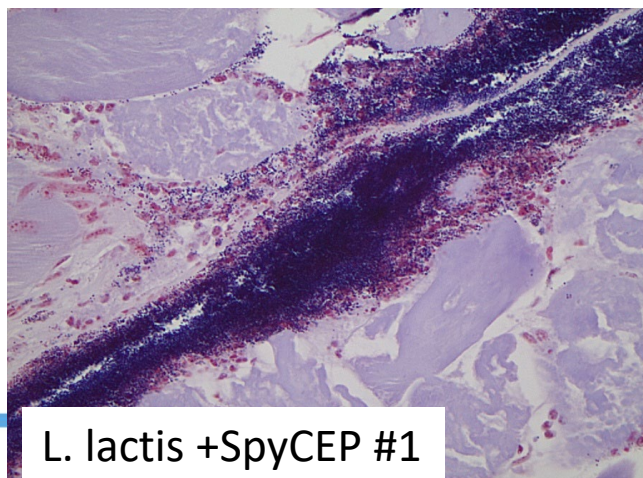
What is SpyCEP capable of doing?

L. lactis injected into soft tissue for 3h is rapidly cleared

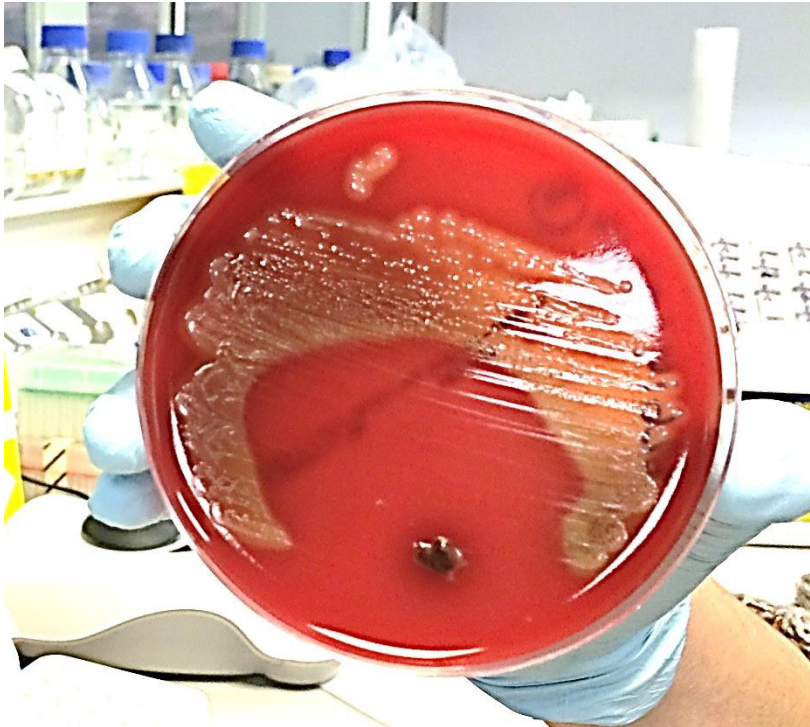


Gram stain

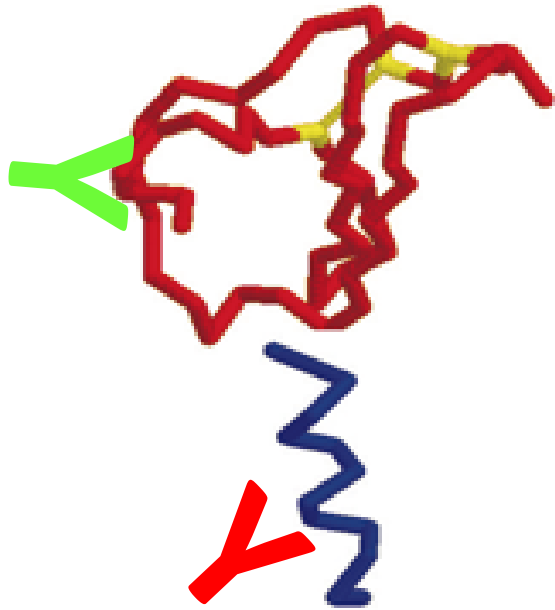
L. Lactis + SpyCEP is not



Group A strep can survive in deep tissue despite antibiotics



Is SpyCEP present after treatment starts?



Bioassay for SpyCEP activity

- Commercial antibodies to IL-8 all detect **full length IL-8** via the **C-terminal** alpha helix
- Raised **specific Ab** to detect cleaved IL-8 to detect cleavage events

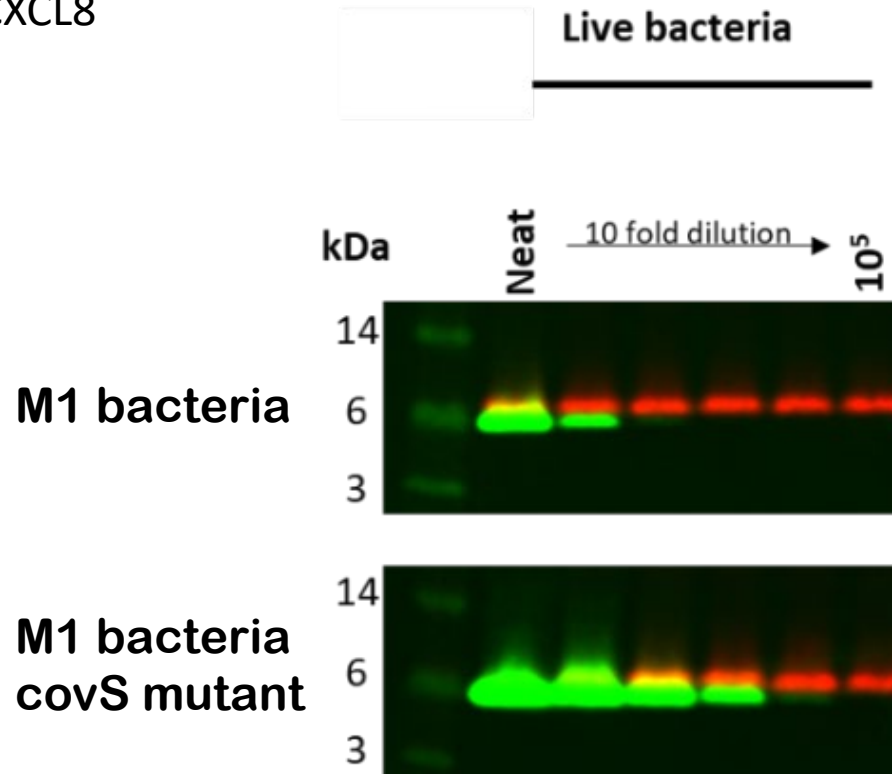
SpyCEP activity on surface of intact live & dead streptococci

Bioactivity assay

Incubate CXCL8 (IL8) with whole streptococci

Determine cleavage of CXCL8

Red intact CXCL8
Green cleaved CXCL8



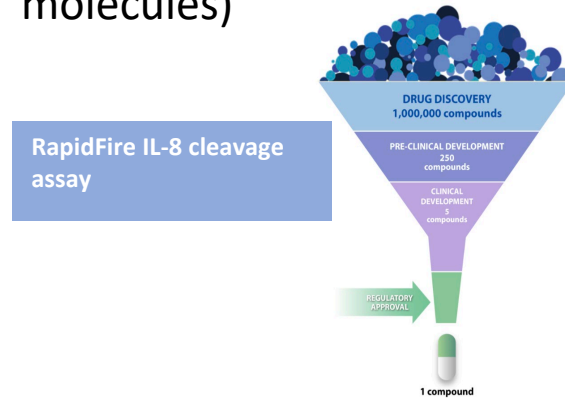
Even penicillin-killed bacteria express bioactive SpyCEP ?Zombie bacteria

SpyCEP bioactivity persists despite antibiotics



Strategies to combat SpyCEP?

- Specific inhibitors (small molecules)



- Vaccination against SpyCEP- 3 candidate vaccines



- Protein synthesis inhibitors



- Antibody-based inhibitors



Management of NSTI needs to be a combined approach



THE LANCET
Infectious Diseases

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REVIEW · Volume 23, Issue 3, E81-E94, March 2023

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Necrotising soft-tissue infections

[Camille Hua, MD](#) ^{a,d,e,f} · [Tomas Urbina, MD](#) ^g · [Romain Bosc, MD](#) ^b · [Tom Parks, MD](#) ^h · [Prof Shiranee Seneviratne, MD](#) ⁱ
[Prof Nicolas de Prost, MD](#) ^{c,j,t} · [Prof Olivier Chosidow, MD](#) ^{a,d,f,k,t} [Show less](#)

[Affiliations & Notes](#) [Article Info](#)

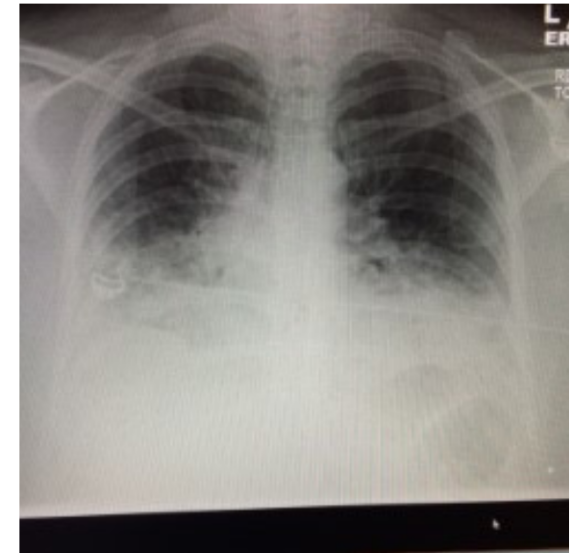
- Source control critical
- Prompt antibiotics essential
 - ICU and supportive care
- **Be aware of IPC risks if iGAS/notify**

A case of severe iGAS pneumonia

- 51 years female

Presenting complaint

- Flu like symptoms 3d. GP Rx paracetamol,
- 3d later Increased cough GP Rx trimethoprim for LRTI
- 1d later sister visited found her more unwell; called ambulance
- LAS – Patient on floor; T 39.1C; RR 40;
- Crackles and wheeze; cyanosed



Examination

- “Looks very sick’
- Slumped; not verbalising; squeezes hand to command
- **Widespread crackles; RR40** ; Sats unrecordable (peripherally shut down)
- **BP 50 systolic HR 140 regular**
- Abdo soft non tender

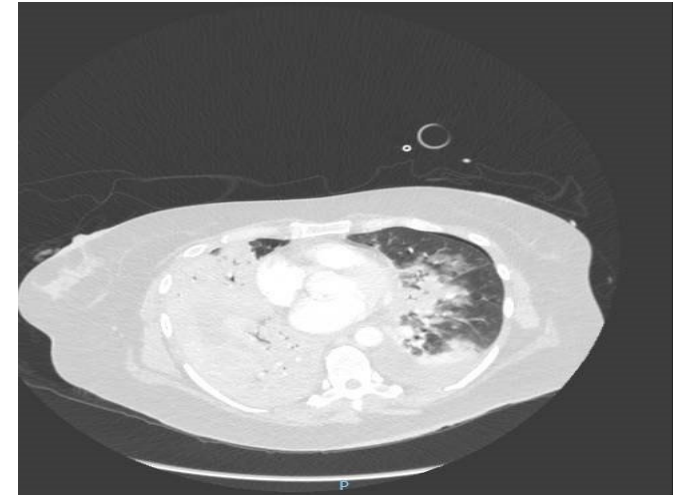
pO₂ 6.5
SaO₂ 70%

Actions

- Cannulated/femoral line; iv fluids; ABG/NIV
- Catheterised (clear urine) ; Bloods drawn incl cultures
- Antibiotics (NB Levofloxacin initially due to ‘penicillin allergy’)

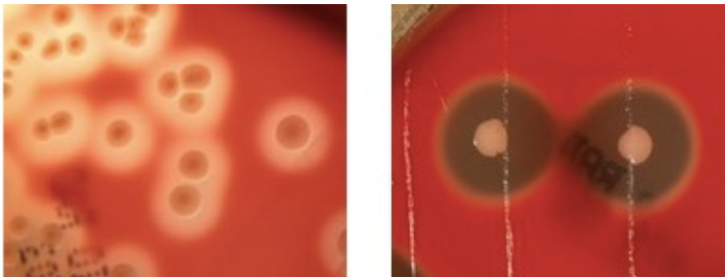
pH 7.09
pCO₂ 4.2
pO₂ 9.9
Lactate 10.1
Base excess -20
Bic 9.4

- **Hypoxaemia:** Intubated; ventilated FiO2 1.0 SaO2 89% pO2 8.4
 - L. intercostal drain (fluid sent to lab)
 - ECMO discussed- too unstable
 - **Persistent acidosis:** CVVHF; fluids; Sodium bicarbonate. Lactate >14
 - **Persistent hypotension** (MAP 60) noradrenaline/vasopressin/dobutamine & adrenaline/noradrenaline/vasopressin
 - **Coagulopathic-** FFP; platelets
 - **Septic:** sputum (brown; sticky); pleural fluid
- Hb 118
 - Wcc 2.8
 - Plt 175
 - Na 136
 - K 4.2
 - U 19
 - Cr 495
 - CRP 594



- Pleural fluid Gram stain: Gram positive cocci +++ Culture: *Streptococcus pyogenes* *emm1.0*
- Sputum Day 1: *Streptococcus pyogenes*
- Sputum Day 2: *Streptococcus pyogenes*

- **WGS- NO covRS mutation**



Patient did not survive beyond 2nd day

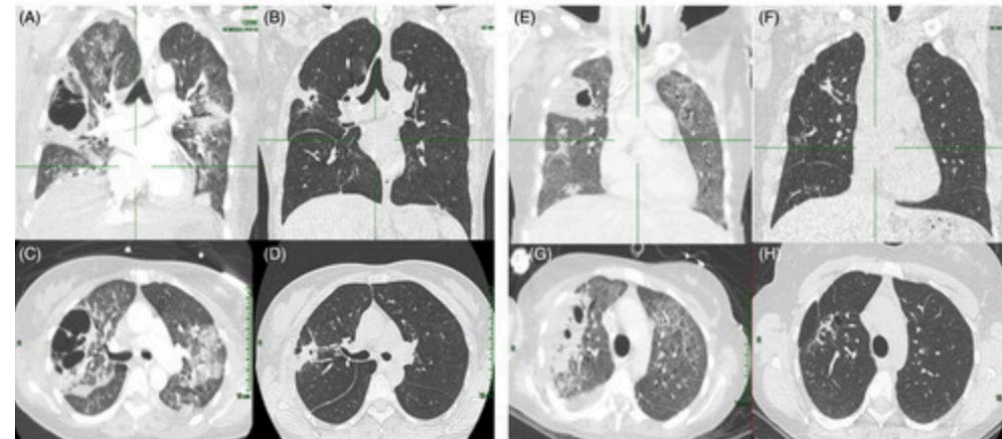
Group A Strep pneumonia is known to be lethal

Short and long-term outcomes of *Streptococcus pyogenes* pneumonia managed in the intensive care unit

Marie Lecronier , Alexandre Elabbadi, Armand Mekontso Dessap & Nicolas de Prost

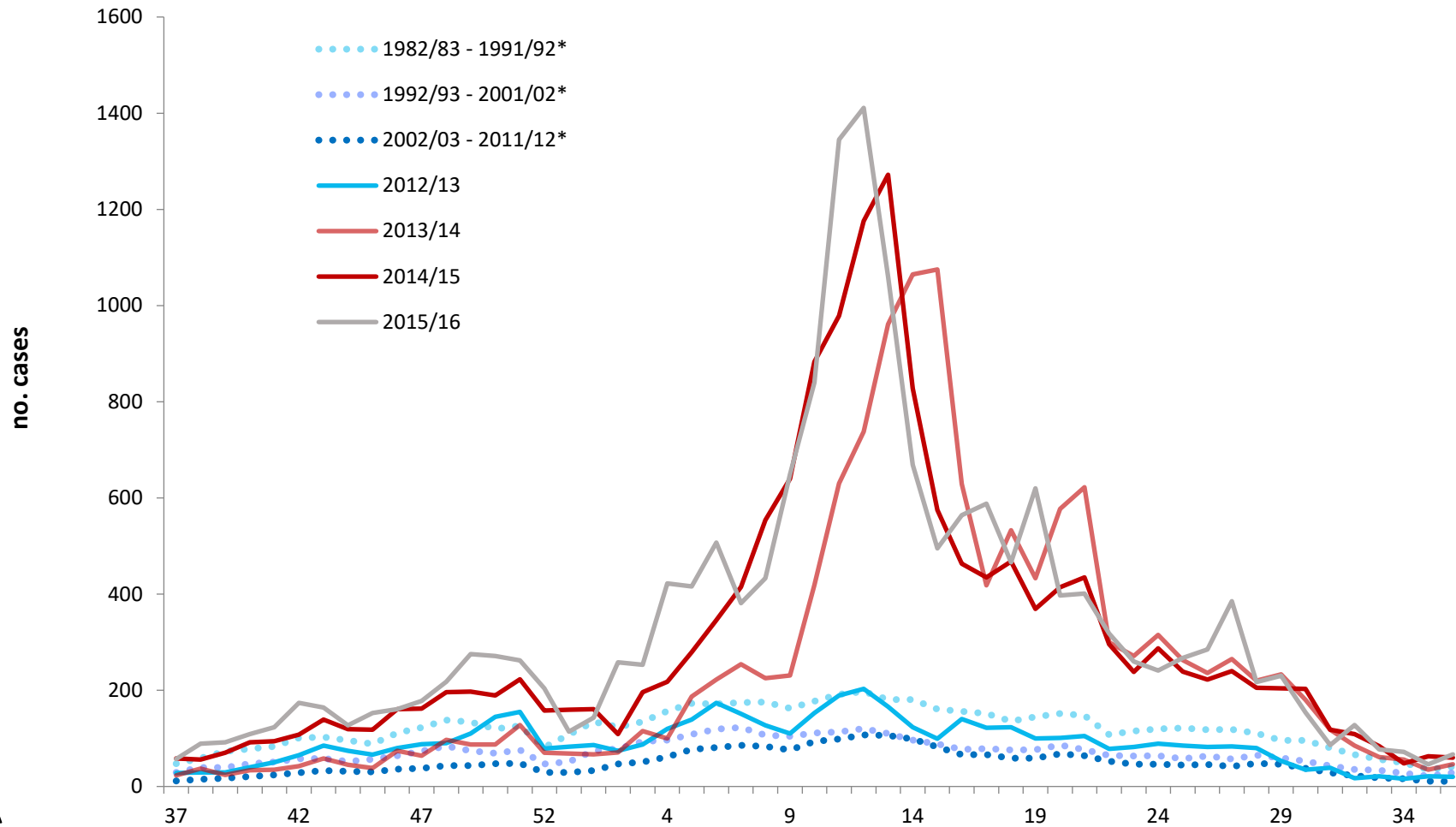
Six cases of iGAS pneumonia admitted to ICU
Creteil, France
Only 1/6 had comorbidity (HbSS)

50% required ECMO
50% died

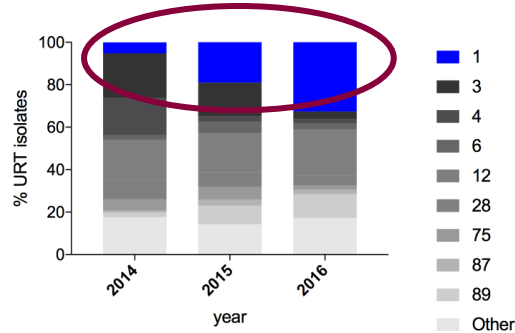


2 cases in one week is a lot.....?

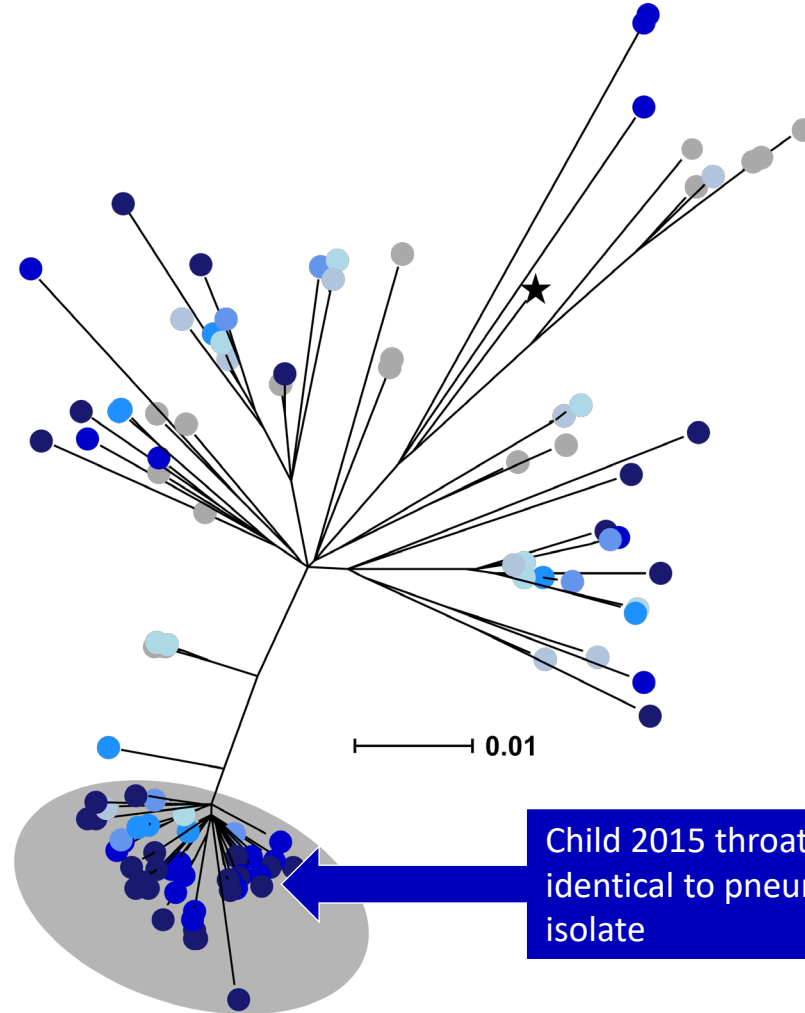
Weekly scarlet fever notifications by year and week/season, England



Sequencing of local non invasive north-west London Strep A *emm1* isolates



- - 2016
- - 2015
- - 2014
- - 2012
- - 2011
- - 2010
- - 2009
-



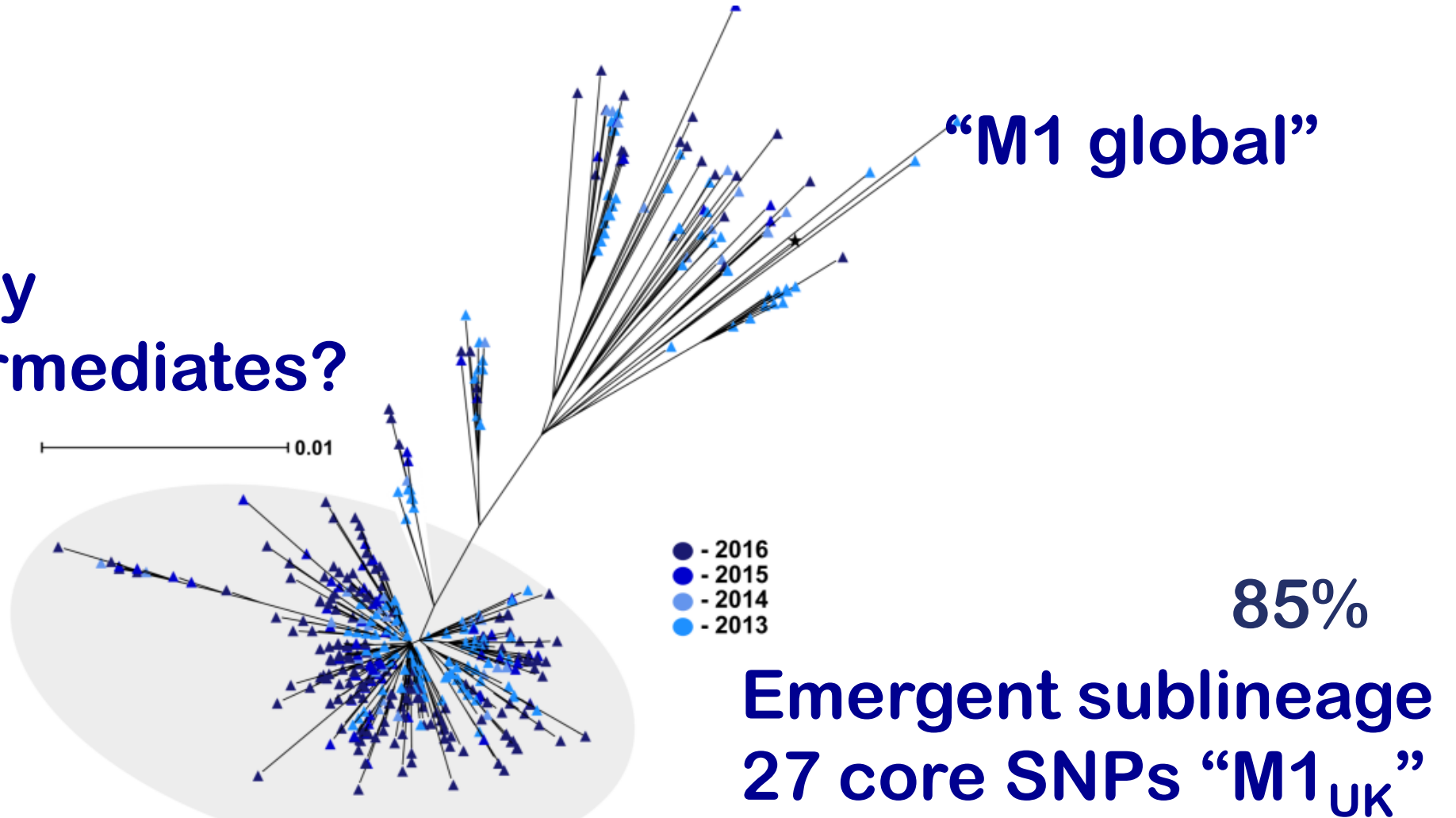
The strains that cause scarlet fever and sore throat are the same as the strains that cause invasive infections

Child 2015 throat isolate identical to pneumonia isolate

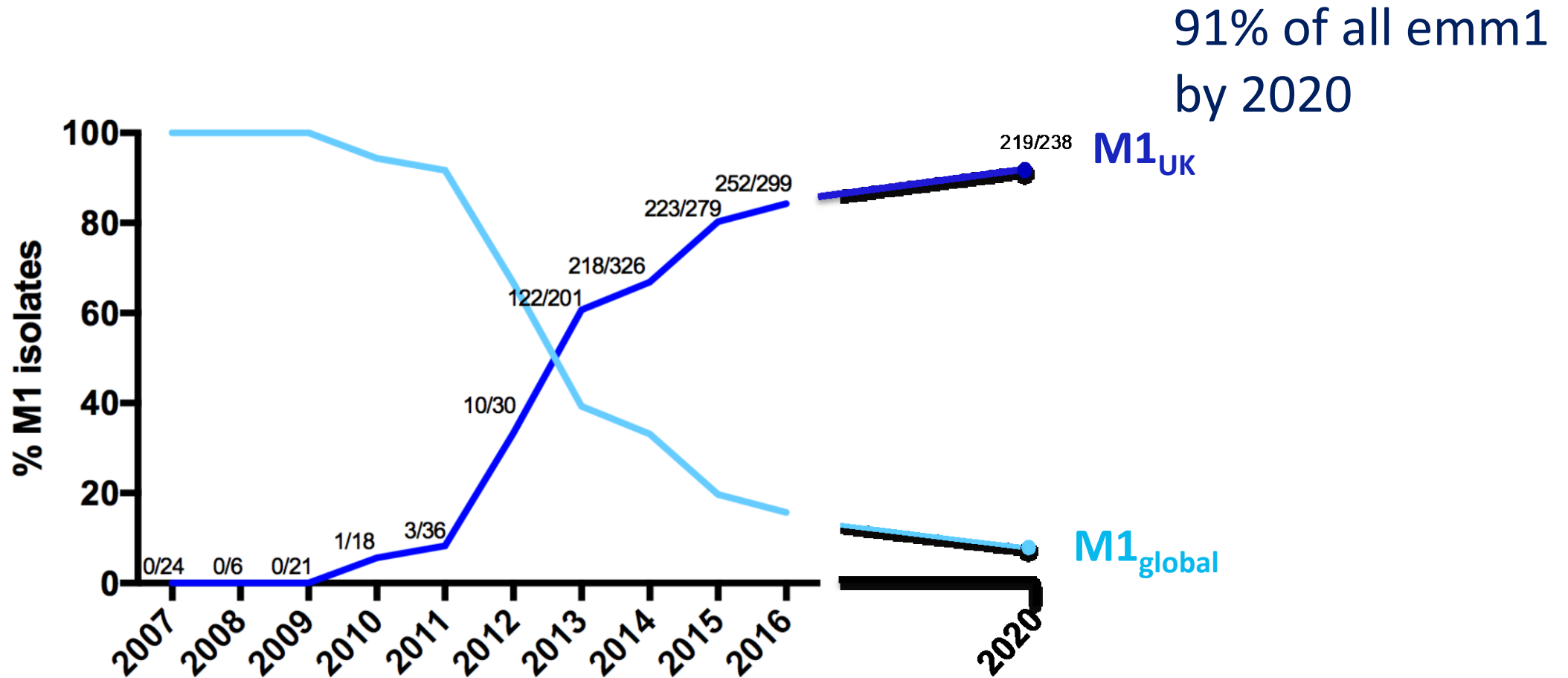
Sublineage of strains enriched by 2015-2016 isolates and SF cases

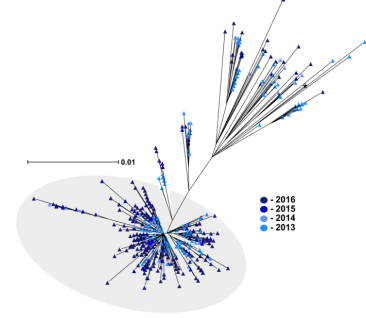
Sequencing of 552 invasive *emm1* strains from England and Wales 2013-2016

funny intermediates?



M1_{UK} lineage expansion in England





RNAseq comparing 4x M1UK and 4x other M1 (M1global)

| Gene | Description | Avg log ₂ fold-change | Average padj |
|---------------|-------------------------------------|----------------------------------|--------------|
| speA2 | enterotoxin | 2.361 | 3.731 E-09 |
| glpF.2 | glycerol uptake facilitator protein | -2.423 | 5.143E-09 |
| mipB | transaldolase | 1.043 | 0.0002 |
| gldA | glycerol dehydrogenase | 1.024 | 0.0006 |
| pflD | formate acetyltransferase | 0.963 | 0.0007 |
| NA | PTS system, cellobiose-specific IIC | 0.653 | 0.0061 |
| NA | PTS system, cellobiose-specific IIB | 0.749 | 0.0204 |

Phenotypic comparison of SpeA in *emm1* strains

A. Transcription of *spea*

10^6

B.

(mL)

125

Expression of SpeA

5x conc.

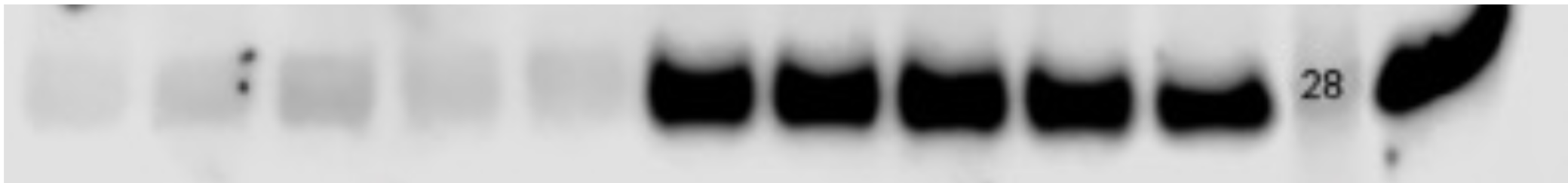
$M1_{global}$

5x conc.

$M1_{UK}$

Neat

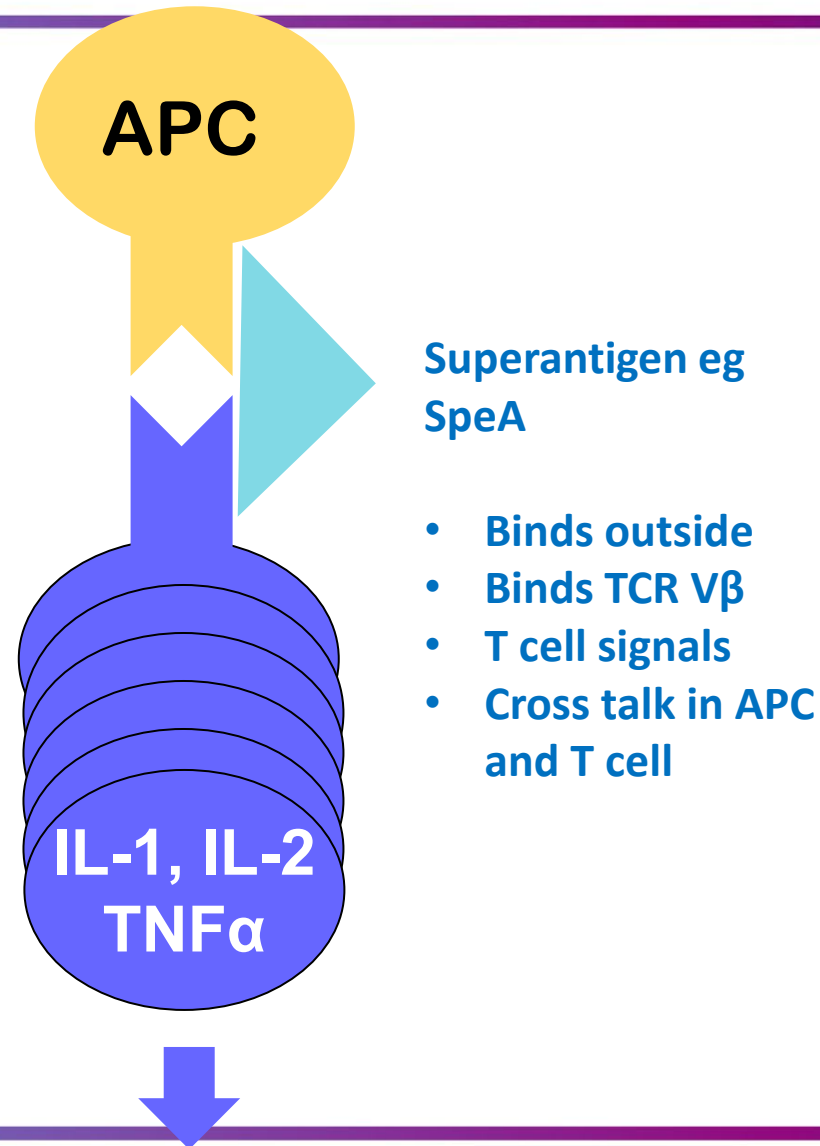
H305



Li, HK et al, Microbial Genomics, 2023

SpeA, a bacteriophage-encoded superantigen

- Scarlet Fever Toxin A



Toxic shock, scarlet fever (but also B cell Ab inhibition)

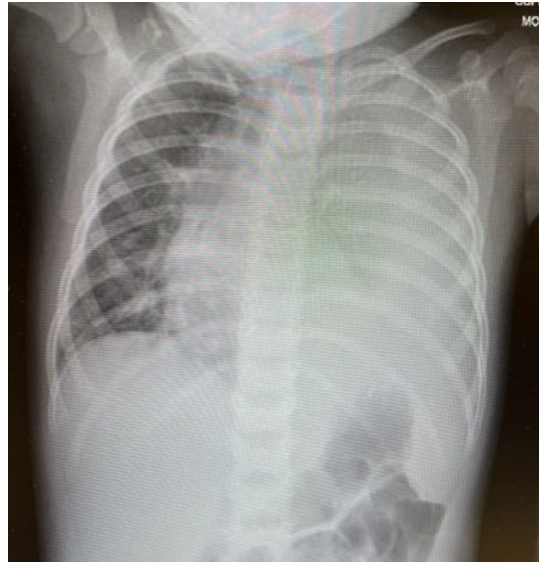
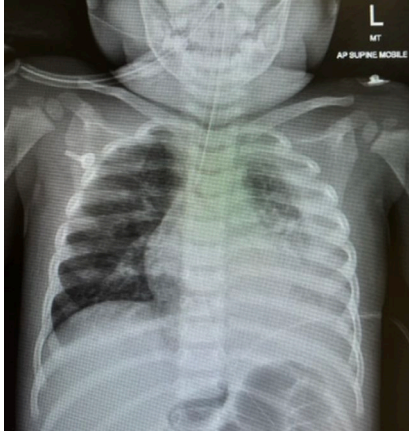
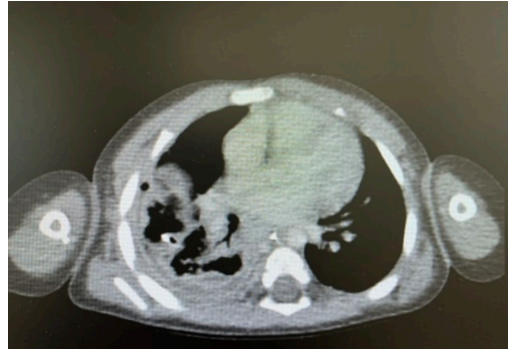
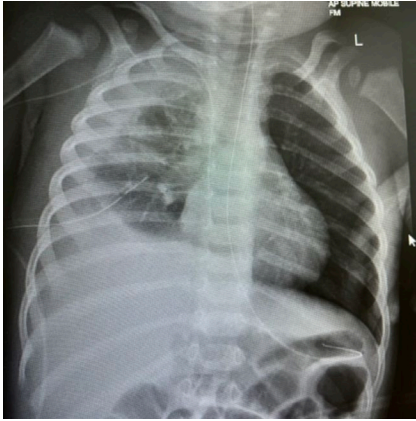
What happened next?

Scarlet fever notifications- iGAS followed similar pattern. Almost no Emm1 infections for 2 years

? A normal season




England lockdown



Similar reports from all centres and media reports of unexplained deaths over next 2 weeks led to..

- Nov 30th Incident team convened –UKHSA, NHS, etc
- Dec 2nd Urgent Central Alerting System (CAS alert) to GPs, Emergency Departments, paediatrics, microbiology/ID
- Briefing Note to micro/ID depts
- Press Release



Medicines & Healthcare products
Regulatory Agency

UKHSA - Urgent public health message to all GP practices, urgent care centres, emergency departments, paediatric and infectious disease/microbiology services regarding an increase in invasive Group A streptococcal infections in children, including lower respiratory tract infections with viral co-infection. UKHSA - Urgent public health message: Invasive Group A Strep

Current invasive Group A streptococcus (IGAS) infection notifications remain unusually high for this time of year, particularly in children. Marked increases in scarlet fever notifications are also being seen. Investigations are underway following reports of an increase in lower respiratory tract GAS infections in children over the past few weeks, which have caused severe illness. A high burden of co-circulating viral infections may be contributing to the increased severity and complications through co-infection. Clinicians should continue to be mindful of potential increases in invasive disease and maintain a high index of suspicion in relevant patients as early recognition and prompt initiation of specific and supportive therapy for patients with IGAS infection can be life-saving. Urgent notification to UKHSA Health Protection Teams of IGAS infection is essential to facilitate immediate public health actions including assessment of contacts.

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Health

What is strep A and what are the symptoms?

9 December 2022




NEWS

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Six children die with Strep A bacterial infection

There has been at least one death of a child in Wales but the data is not yet available for other nations.

3h | Health

- Strep A: Why it can be dangerous and what to know

News > Health

Strep A concerns create 'carnage' and 'eyewatering demand' for the NHS

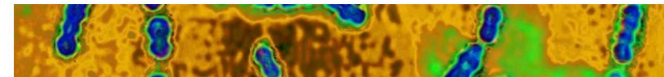
'We don't know where this wave is going to end up. So we have to take it seriously,' said Dr Shamez Ladhani

Rebecca Thomas Health Correspondent • Tuesday 06 December 2022 20:00



Strep A: GPs are struggling to cope and demand more help from Government

Ministers urged to boost resources for 'overspill' services such as out-of-hours and NHS 111 as scarlet fever cases reach 1,062 in a week



Strep A home-test kits sell out after spate of UK deaths sparks panic buying

Pharmacists also report difficulties finding supplies of antibiotics to treat the infection



Strep A tests are changing hands for £100 online, but are viewed as unreliable. Photograph: Alamy

News > Liverpool News > Alder Hey Children's Hospital

Alder Hey records 'highest ever' A&E attendance after Strep A fears

UK pharmacists report shortages of strep A antibiotics

Health secretary says government 'not aware' of issue but some independent outlets say stocks running low

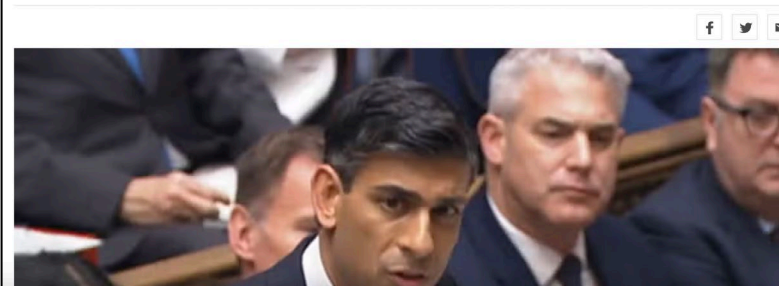
UK politics live - latest news updates



Demand for penicillin and amoxicillin has increased in recent days. Photograph: Murdo MacLeod/the Guardian

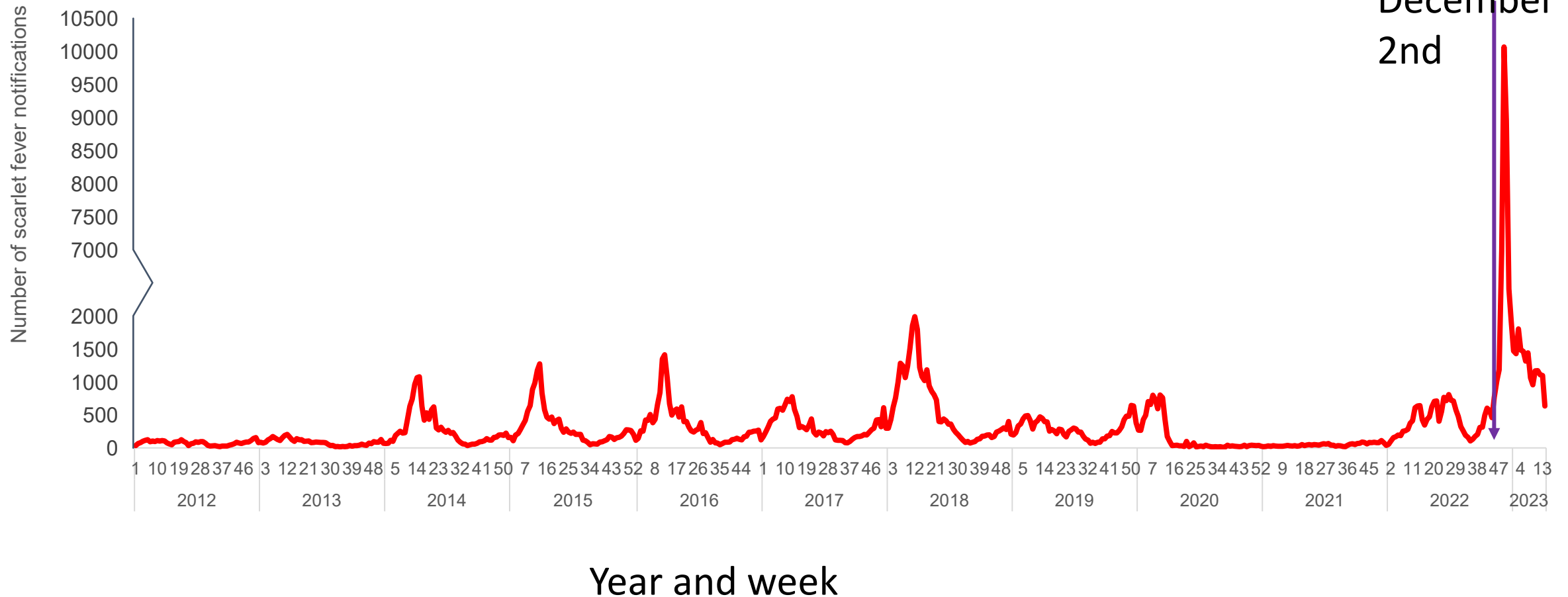
PM says 'there are no current shortages of drugs' to tackle Strep A cases

Sir Keir Starmer described Rishi Sunak as a 'blancmange Prime Minister' who 'sold out the aspirations of those who want to own their own home'.



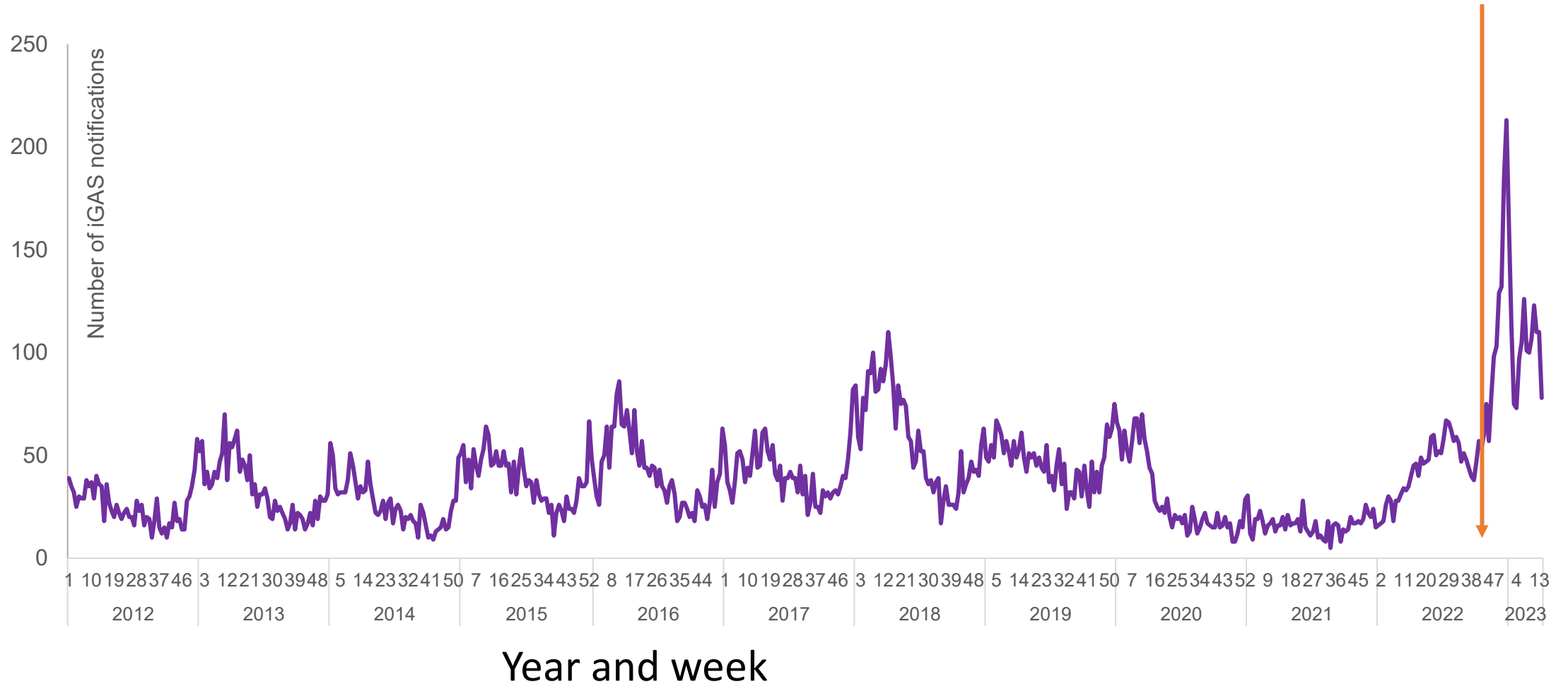
“There are no current shortages of drugs available to treat this and there are well-established procedures in place to ensure that that remains the case and the (UKHSA) are monitoring the situation at pace and what they have confirmed is that this is not a new strain of Strep A, so people should be reassured about that.:

Data courtesy of Rebecca Guy, UKHSA



Data courtesy of Rebecca Guy, UKHSA

Most iGAS was in adults



Communications to healthcare professionals and public

06.12.2022 Letters to all schools in England

09.12.2022 **Interim prescribing guidance to clinicians** (revoked 16-Feb-2023)

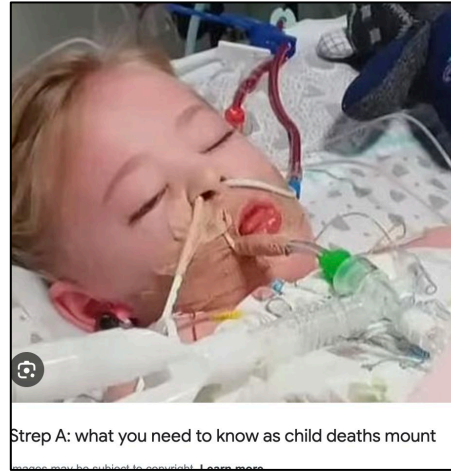
09.12.2022 Helpline for schools established

15.12.2022 **Updated household invasive Strep A (iGAS) guidelines** published

16.12.2022 Serious shortage protocols issued for oral penicillin V

Recognition that >50% had detected respiratory viral co-infection eg RSV

Daily reporting by media



Incident stood down May 18th

60 child deaths
Almost 500 adult deaths

Strep A has now killed 15 children as illness continues to spread

Comment

 Emma Brazell
Thursday 8 Dec 2022 3:12 pm

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Health

Strep A: At least 30 children have died in UK since mid-September

30 December 2022

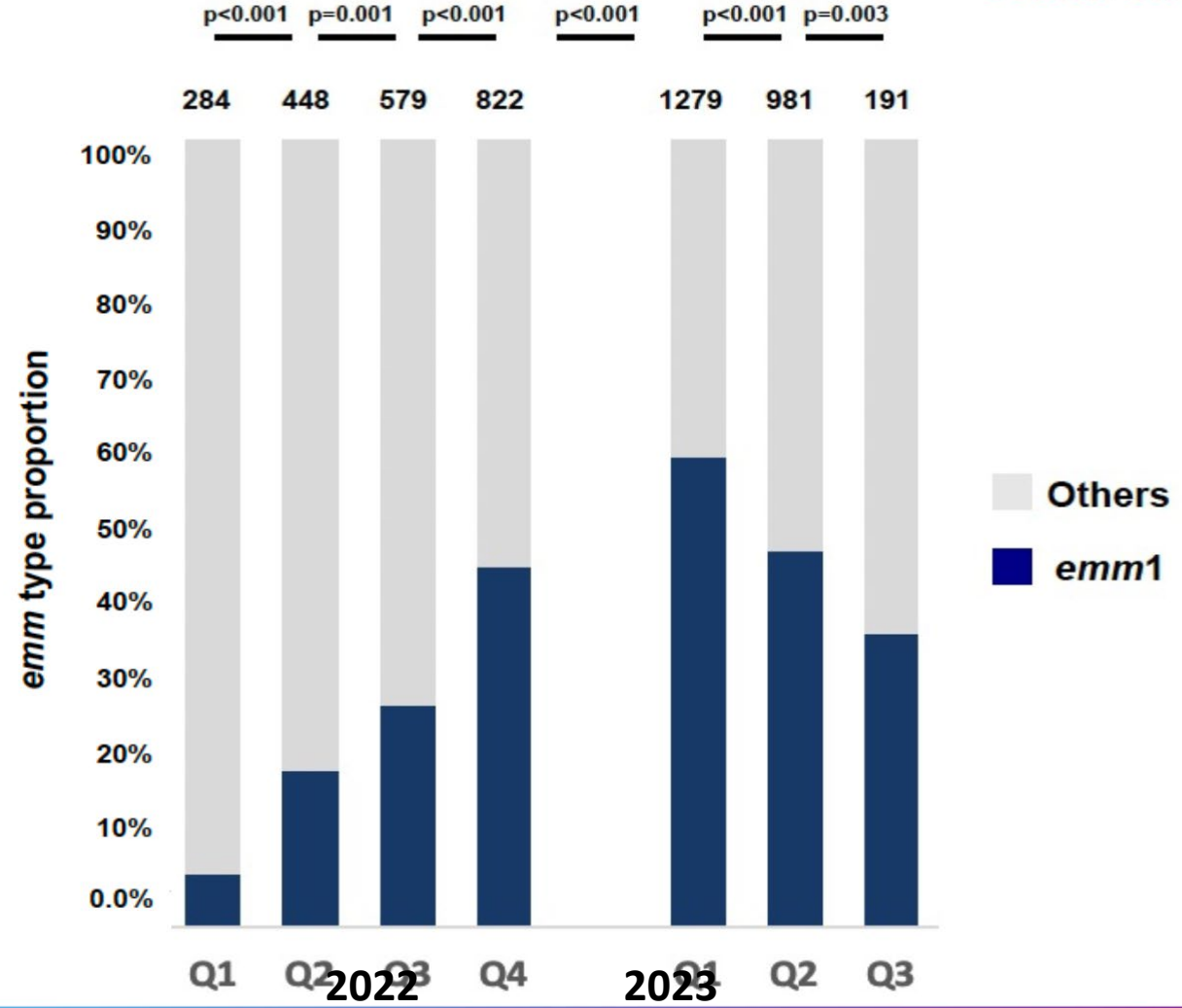



Health > News Health

KILLER BUG At least 48 children have died from Strep A in the UK as cases of deadly infection continue to rise

Most of the invasive cases were due to emm1 (M1_{UK})

Children <15y

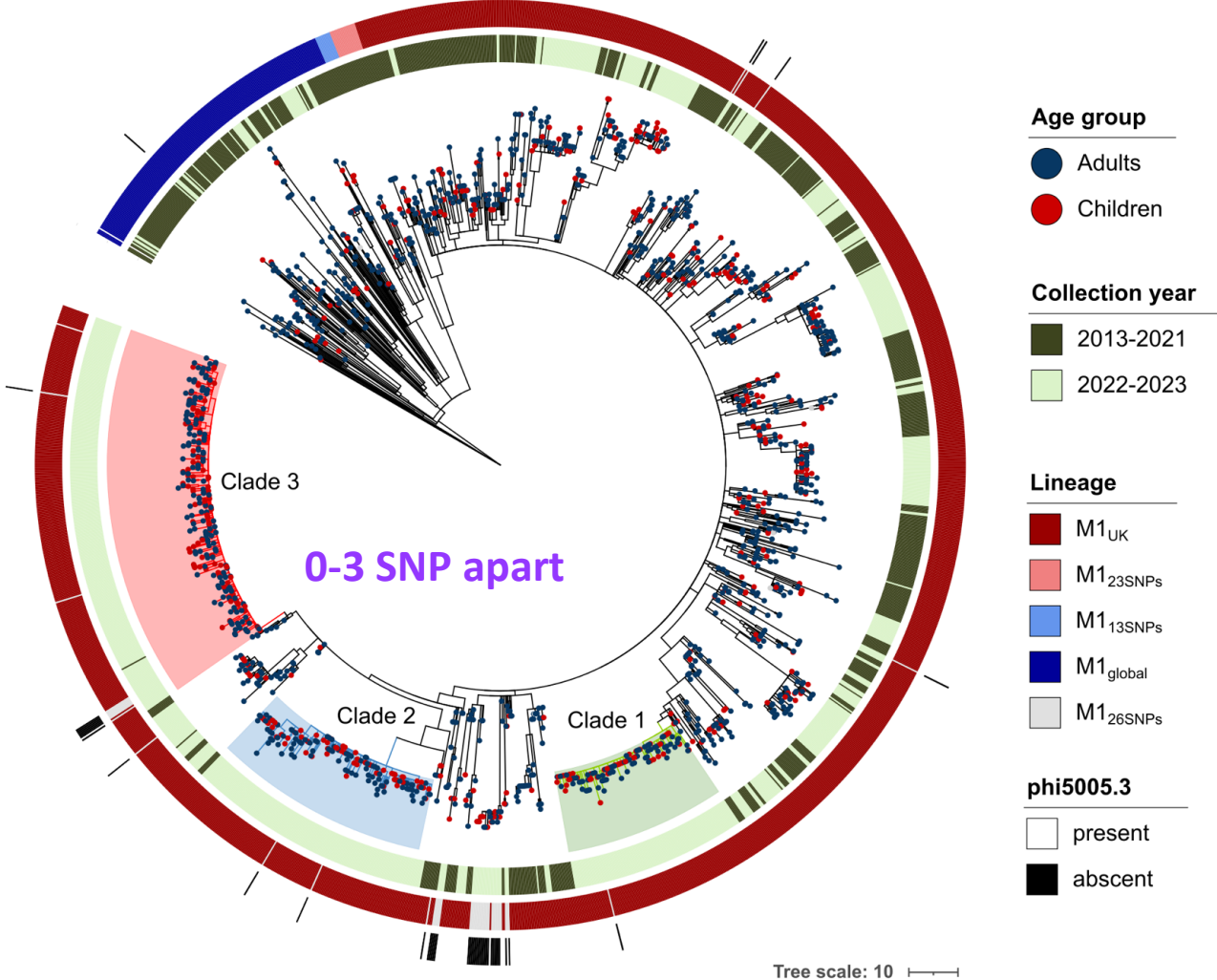


Lees et al, PIDJ 2024
 185 parapneumonic effusions due to iGAS
 (October 2022-February 2023) 85% emm1

Genomic analyses of invasive emm1 during upsurge



very little change and explosive expansion



Upsurge isolates 97% M1_{UK}

Early 2020

THE LANCET Infectious Diseases

CORRESPONDENCE | VOLUME 19, ISSUE 13, P1284-1285, DECEMBER 01, 2019

Identification of *Streptococcus pyogenes* M1_{UK} clone in Canada

Walter Demczuk · Irene Martin · Francesca Reyes Domingo · Diane MacDonald · Michael R Mulvey

Published: December, 2019 · DOI: [https://doi.org/10.1016/S1473-3099\(19\)30622-X](https://doi.org/10.1016/S1473-3099(19)30622-X)

CORRESPONDENCE | VOLUME 20, ISSUE 5, P539-540, MAY 01, 2020

Dominance of M1_{UK} clade among Dutch M1 *Streptococcus pyogenes*

Lidewij W Rümke · Brechje de Gier · Stefan M T Vestjens · Arie van der Ende · Nina M van Sorge · Bart J M Vlamincx · et al. Show all authors

Published: May, 2020 · DOI: [https://doi.org/10.1016/S1473-3099\(20\)30278-4](https://doi.org/10.1016/S1473-3099(20)30278-4)

CORRESPONDENCE | VOLUME 20, ISSUE 5, P538-539, MAY 01, 2020

M1_{UK} lineage in invasive group A streptococcus isolates from the USA

Yuan Li · Srinivas Acharya Nanduri · Chris A Van Beneden · Bernard W Beall

Published: May, 2020 · DOI: [https://doi.org/10.1016/S1473-3099\(20\)30279-6](https://doi.org/10.1016/S1473-3099(20)30279-6)

Europe 2023-2024

Rapid communication

Sustained increase of paediatric invasive *Streptococcus pyogenes* infections dominated by M1_{UK} and diverse *emm12* isolates, Portugal, September 2022 to May 2023

Home > Infection > Article

Population of invasive group A streptococci isolates from a German tertiary care center is dominated by the hypervirulent M1_{UK} genotype

Brief Report · Open access · Published: 08 December 2023

This Issue Views 4,075 Citations 2 Altmetric 23

Research Letter

April 7, 2023

Group A Streptococcal Meningitis With the M1_{UK} Variant in the Netherlands

Boas C. L. van der Putten, PhD¹, Bart J. M. Vlamincx, MD, PhD², Brechje de Gier, PhD³, et al.

Author Affiliations

Rapid communication

Increase in bloodstream infections caused by *emm1* group A *Streptococcus* correlates with emergence of toxigenic M1_{UK}, Belgium, May 2022 to August 2023

Juan Pablo Rodriguez-Ruiz^{1,2}, Qiang Lin^{1,2}, Christine Lammens^{1,2}, Pierre R Smeesters^{2,4}, Stefanie van Kleef⁵, Vaerla Mathanirajan^{1,2,5}, Surbhi Malhotra-Kumar^{1,2}

Rapid communication

Increase in invasive group A streptococcal infections and emergence of novel, rapidly expanding sub-lineage of the virulent *Streptococcus pyogenes* M1 clone, Denmark, 2023

Rapid communication

Increase in invasive *Streptococcus pyogenes* M1 infections with close evolutionary genetic relationship, Iceland and Scotland, 2022 to 2023

Stephen B Beres¹, Randall J Olsen^{1,2}, S Wesley Long^{1,2}, Ross Langley³, Thomas Williams⁴, Helga Erlendsdottir^{5,6}, Andrew Smith^{7,8}, Karl G Kristinnsson⁹, James M Musser^{1,2}

Outside Europe 2023-2024

Deadly new UK strep A variant leading to disease surge in Australia

Latest research finds the invasive variant produces significantly higher levels of a toxin than previous strain

- Follow our Australia news live blog for the latest updates
- Get our morning and afternoon news emails, free app or daily news podcast

A worldwide population of *Streptococcus pyogenes* strains circulating among school-aged children in Auckland, New Zealand: a genomic epidemiology analysis

Jake A. Lacey · Julie Bennett · Taylah B. James · Benjamin S. Hines · Tiffany Chen · Darren Lee · et al.

Show all authors

Original Article

Detection of toxigenic M1_{UK} lineage group A *Streptococcus* clones in Taiwan

Chuan Chiang-Ni^{a,b,c,d,*}, Chih-Yun Hsu^a, Yu-Hsuan Yeh^e, Chia-Yu Chi^{f,g}, Shuying Wang^{g,h}, Pei-Jane Tsai^{h,i}, Cheng-Hsun Chiu^{b,c}

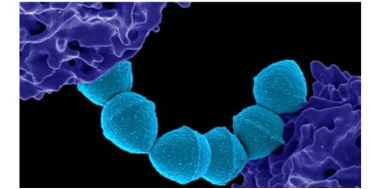
PAHO Epidemiological alert: Invasive disease caused by group A streptococci 28 November 2023

In December of 2022, the World Health Organization (WHO) released an alert on the increase in cases of invasive group A streptococcal (iGAS) infection in Europe, especially in children under 10 years of age. During the same period, the Pan-American Health Organization (PAHO) issued an information note following cases of invasive GAS disease reported by Uruguay. In November of 2023, Argentina reported a significant increase in the notification of cases and deaths from this agent, and recent reports highlighted the presence of M1_{UK} clones and a sub-lineage of M1 with the SpaC toxin in that country, which has been associated with this increase. In view of this situation, PAHO/WHO recommends that Member States conduct clinical and genomic surveillance, as well as ensure early diagnosis and timely treatment of cases of invasive group A streptococcal disease.

M1_{UK} successful globally



Tokyo issues warning as rare but deadly STSS bacterial infections rise



North Korea cancels World Cup qualifier against Japan

Last-minute decision on Tuesday's match leaves football bodies searching for alternative venue



North Korea's fans cheer before the World Cup 2026 qualifier football match in Tokyo on 21 March between Japan and North Korea. Photograph: Yuchi Yamazaki/APPI/Getty Images
North Korea has abruptly cancelled its 2026 World Cup qualifying match with Japan next week, leaving organisers frantically searching for an alternative venue.

RESEARCH

Open Access

Invasive group A streptococcal infections requiring admission to ICU: a nationwide, multicenter, retrospective study (ISTRE study)



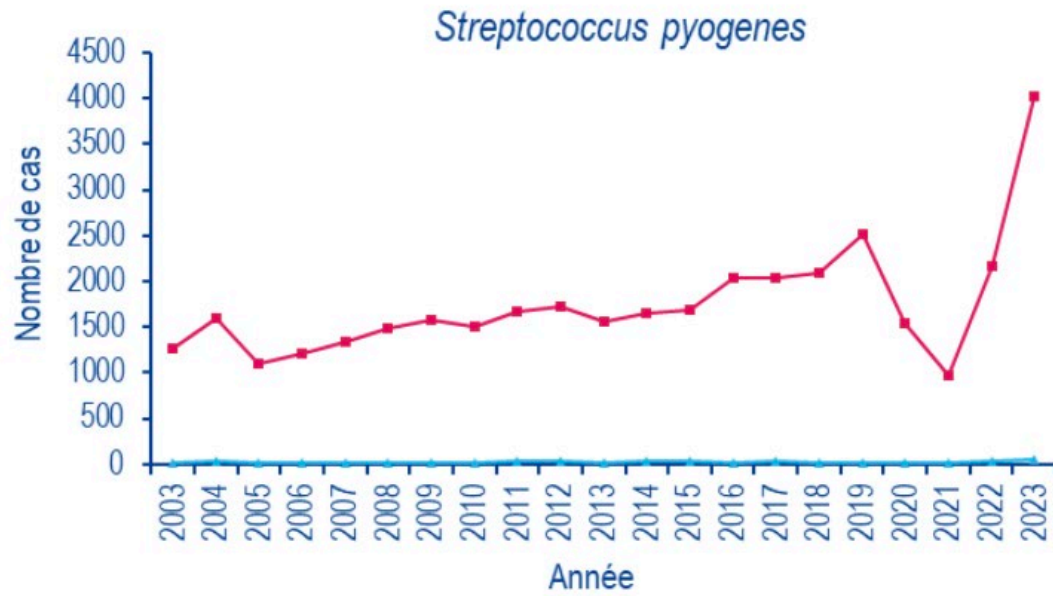
Arthur Orieux^{1*}, Renaud Prevel^{1,2}, Margot Dumery¹, Jean-Baptiste Lascarrou³, Noémie Zucman⁴, Florian Reizine⁵, Pierre Fillatre⁶, Charles Detollenaere⁷, Cédric Darreau⁸, Nadiejda Antier⁹, Mélanie Saint-Léger¹⁰, Guillaume Schnell¹¹, Béatrice La Combe¹², Charlotte Guesdon¹³, Franklin Bruna¹⁴, Antoine Guillon¹⁵, Caroline Varillon¹⁶, Olivier Lesieur¹⁷, Hubert Grand¹⁸, Benjamin Bertrand¹⁹, Shidasp Siami²⁰, Pierre Oudeville²¹, Céline Besnard²², Romain Persichini²³, Pierrick Bauduin²⁴, Martial Thyrault²⁵, Mathieu Evrard²⁶, David Schnell²⁷, Johann Auchabie²⁸, Adrien Auvet²⁹, Jean-Philippe Rigaud³⁰, Pascal Beuret³¹, Maxime Leclerc³², Asaël Berger³³, Omar Ben Hadj Salem³⁴, Julien Lorber³⁵, Annabelle Stoclin³⁶, Olivier Guisset¹, Léa Bientz³⁷, Pierre Khan³⁸, Vivien Guillotin¹, Jean-Claude Lacherade³⁹ and Alexandre Boyer^{1,2} on behalf of ISTRE Group

Retrospective study 37 ICU's Compared adult iGAS

- Oct-March 2018 & 2019 (pre COVID-19)
- Oct-March 2022/23 (post COVID-19)

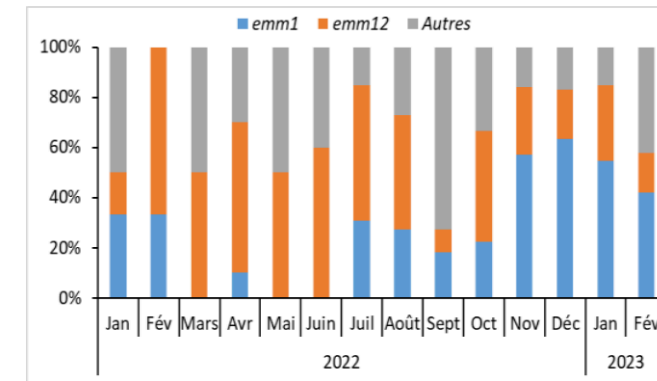
“...case rate during the period before and after COVID-19 pandemic was **205/100,000** and **949/100,000 ICU admissions**, respectively ($p < 0.001$), with more frequent STSS after the COVID-19 pandemic (61% vs. 45%, $p = 0.015$)”

What about France?



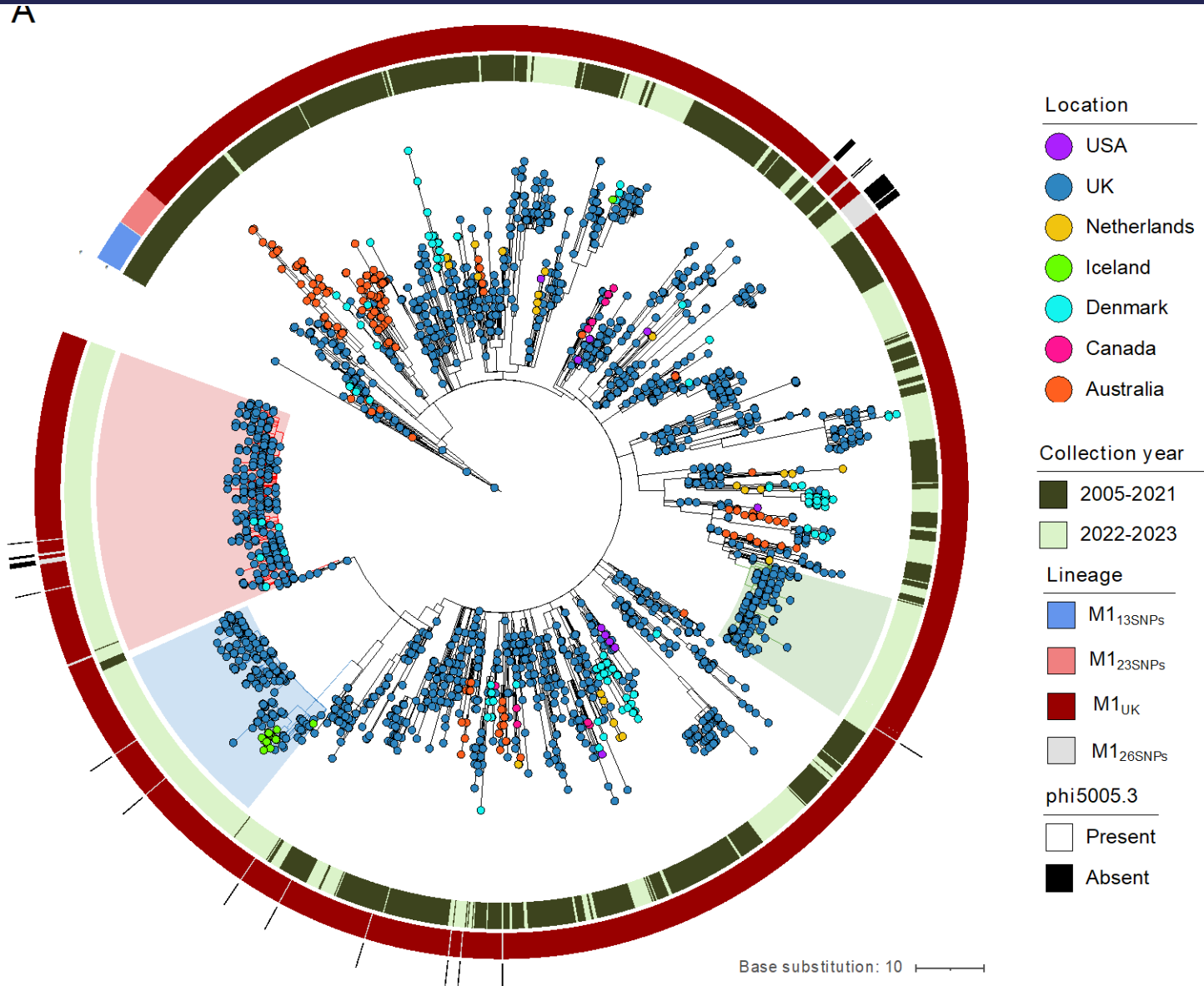
Sante publique France: “La situation épidémiologique actuelle des IISGA n’est pas liée à l’émergence d’une souche bactérienne nouvelle mais principalement à deux génotypes (emm12 et emm1) déjà connus.”

Figure 7B. Fréquence des principaux génotypes emm des souches de SGA responsables d’infections invasives chez l’enfant (<18 ans), France, janvier 2022- février 2023.



Sante publique France: “Le séquençage du génome complet de 39 souches pédiatriques dont la moitié de génotype emm1 isolées en 2022 a permis de mettre en évidence l’appartenance de ces dernières au variant M1UK décrit initialement au Royaume-Uni “

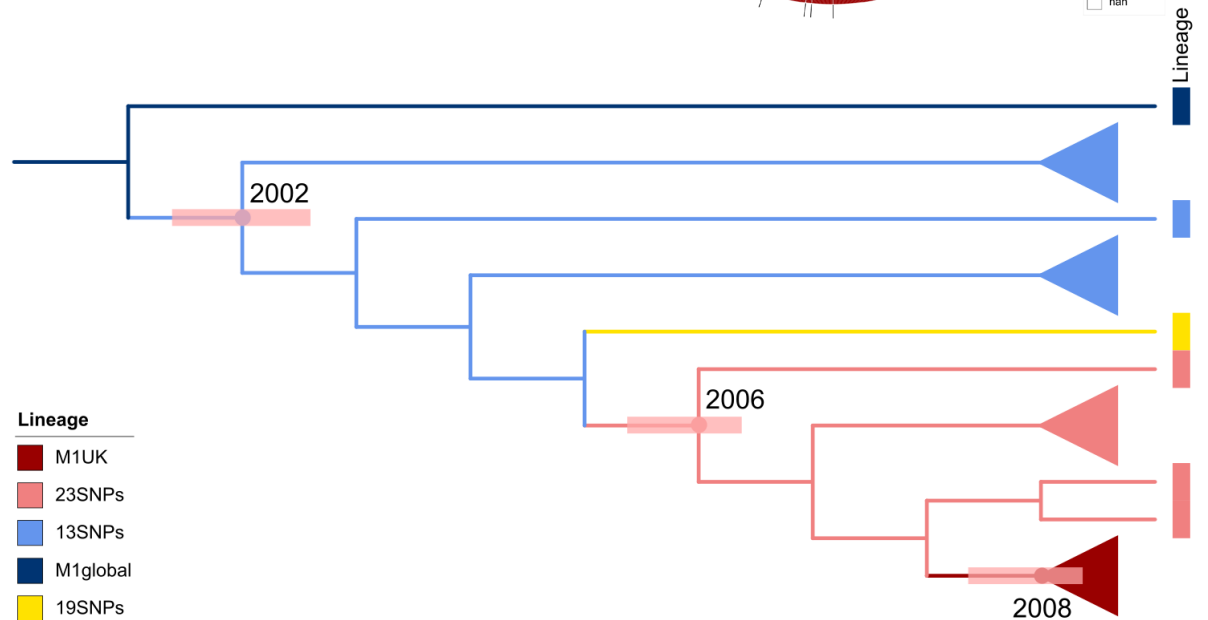
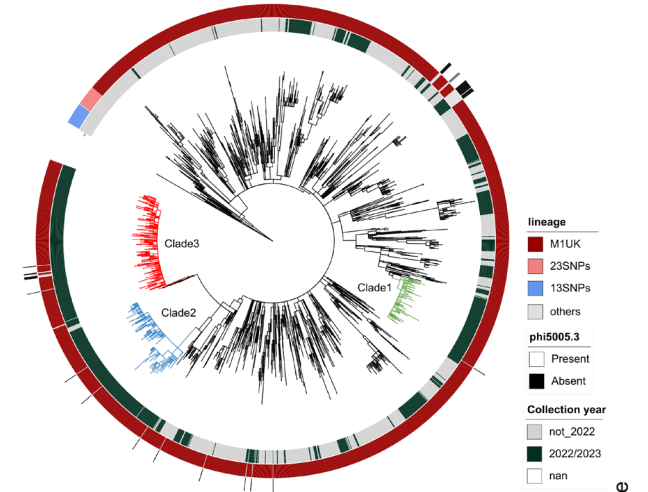
Global phylogeny of recent M1_{UK} isolates



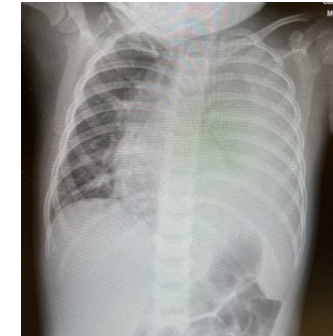
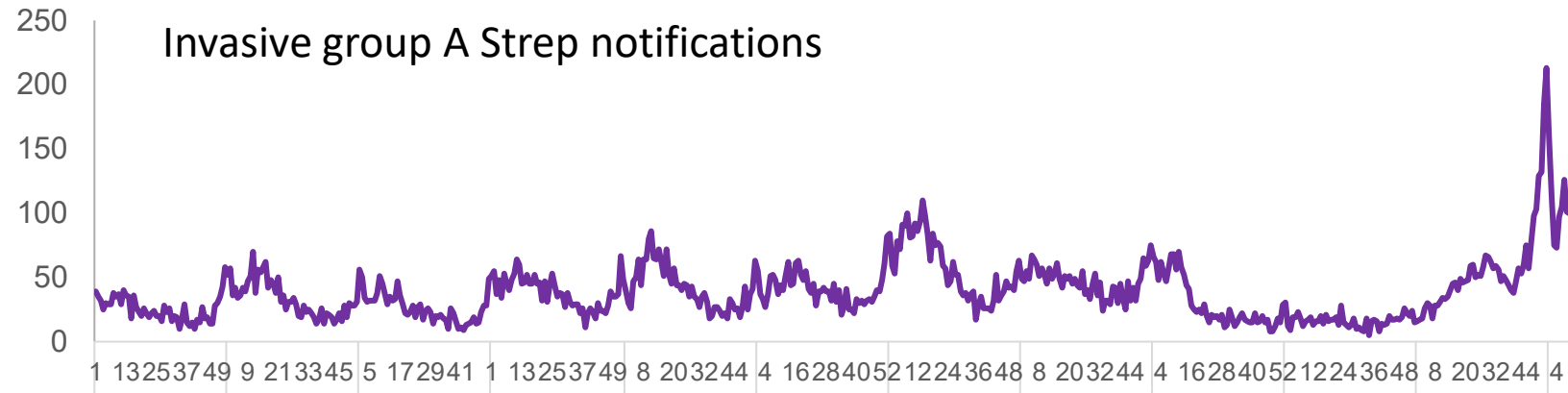
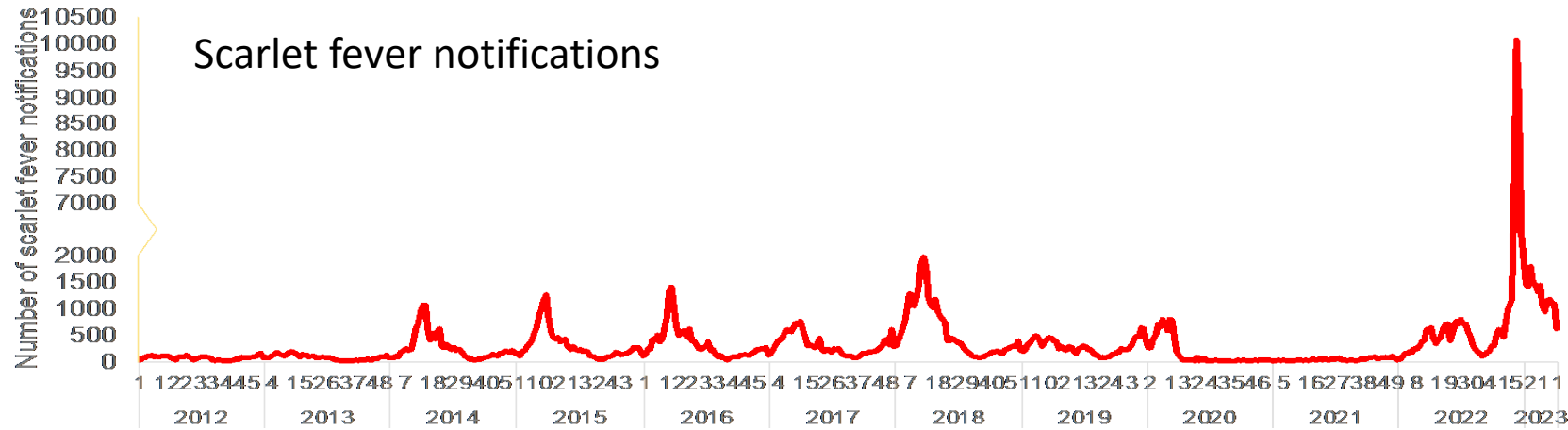
Suggests intermediates and M1_{UK} emerged in the UK followed by global dispersion.

When did M1_{UK} emerge?

- Dated phylogenetic tree of 2364 available M1_{UK}/intermediate genomes.
- 13SNP 2002 (95% CI 2000, 2004)
- 23SNP 2006 (95% CI 2004, 2007)
- M1_{UK} 2008 (95% CI 2006, 2009) ★
- 1.5 nucleotide substitutions/genome/year (average evolutionary rate)
- Evolutionary path:
- M1_{global} → M1_{13SNPs} → M1_{23SNPs} → M1_{UK}



Key questions- (1) is M1_{UK} more dangerous or is it just numbers ?



Health > News Health
KILLER BUG At least 48 children have died from Strep A in the UK as cases of deadly infection continue to rise

Data linkage study CFR iGAS M1_{UK} vs M1_{global}



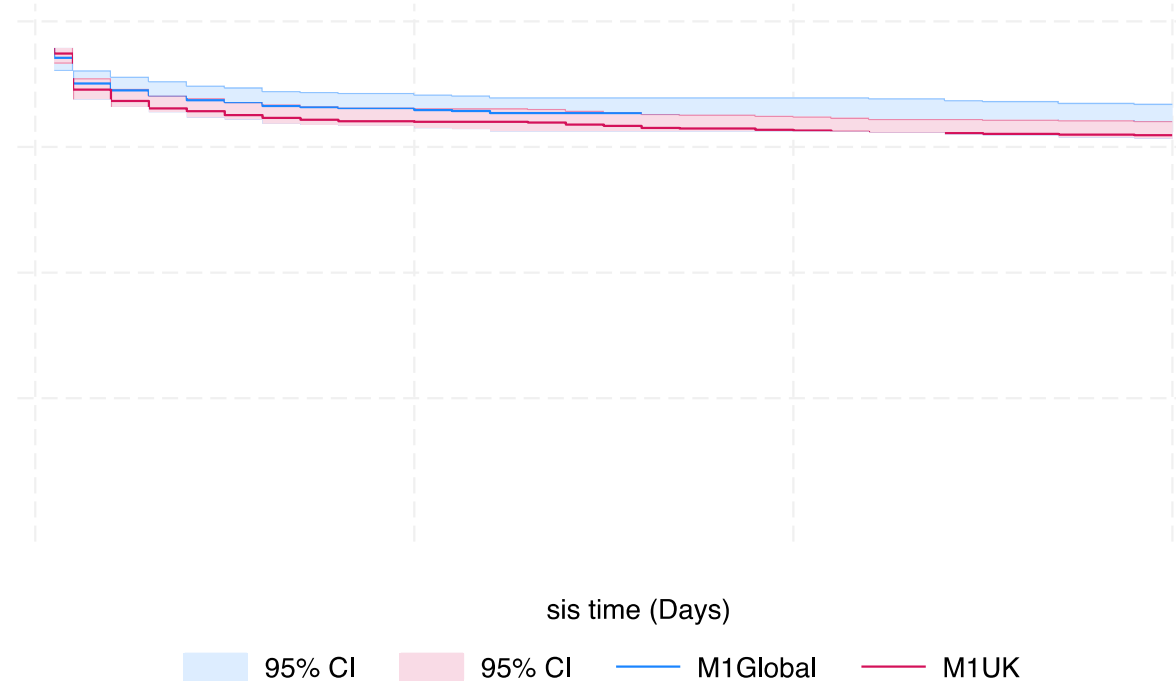
Used all available cases with genotyping available (~1500) from 2010-2020

CFR

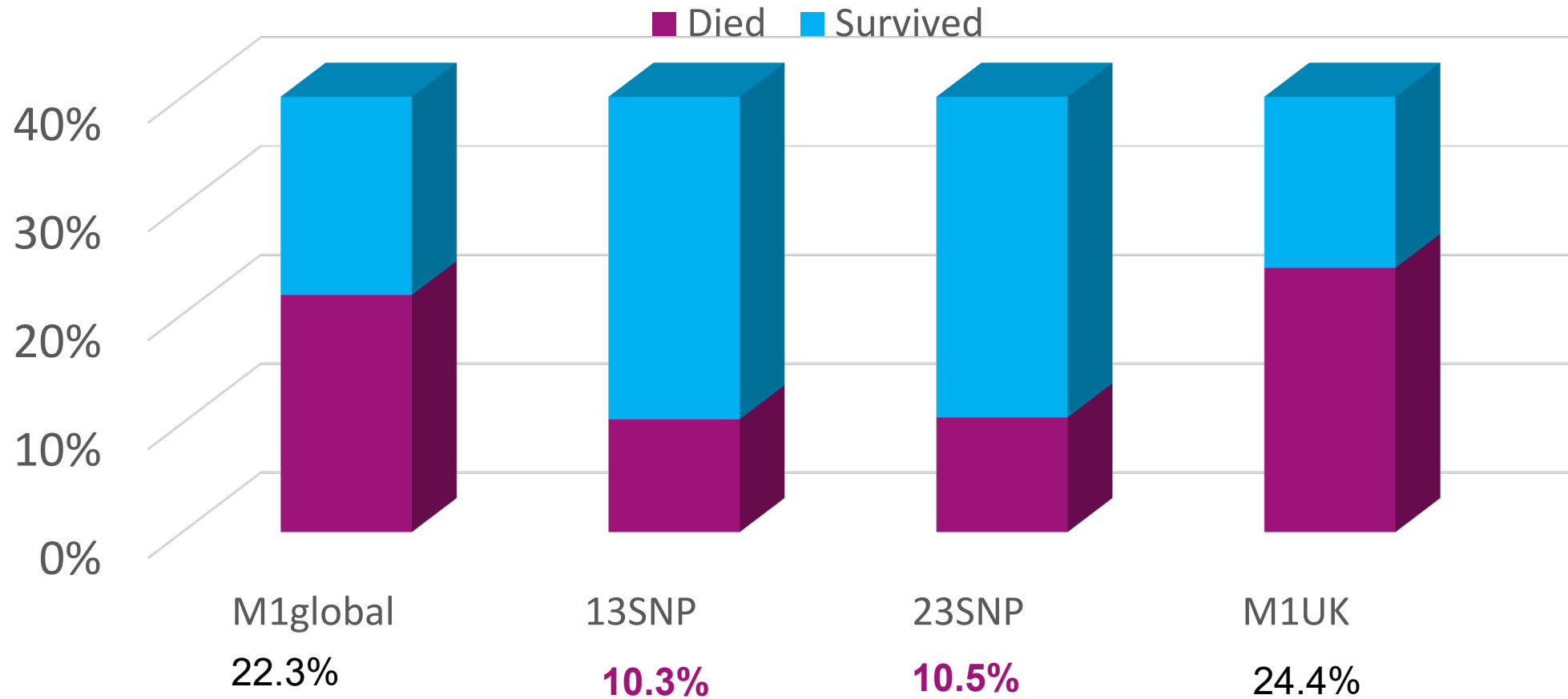
22.3% (95% CI: 18.1, 25.4%) M1_{global}

24.4% (95% CI: 21.2, 27.3%) M1_{UK}

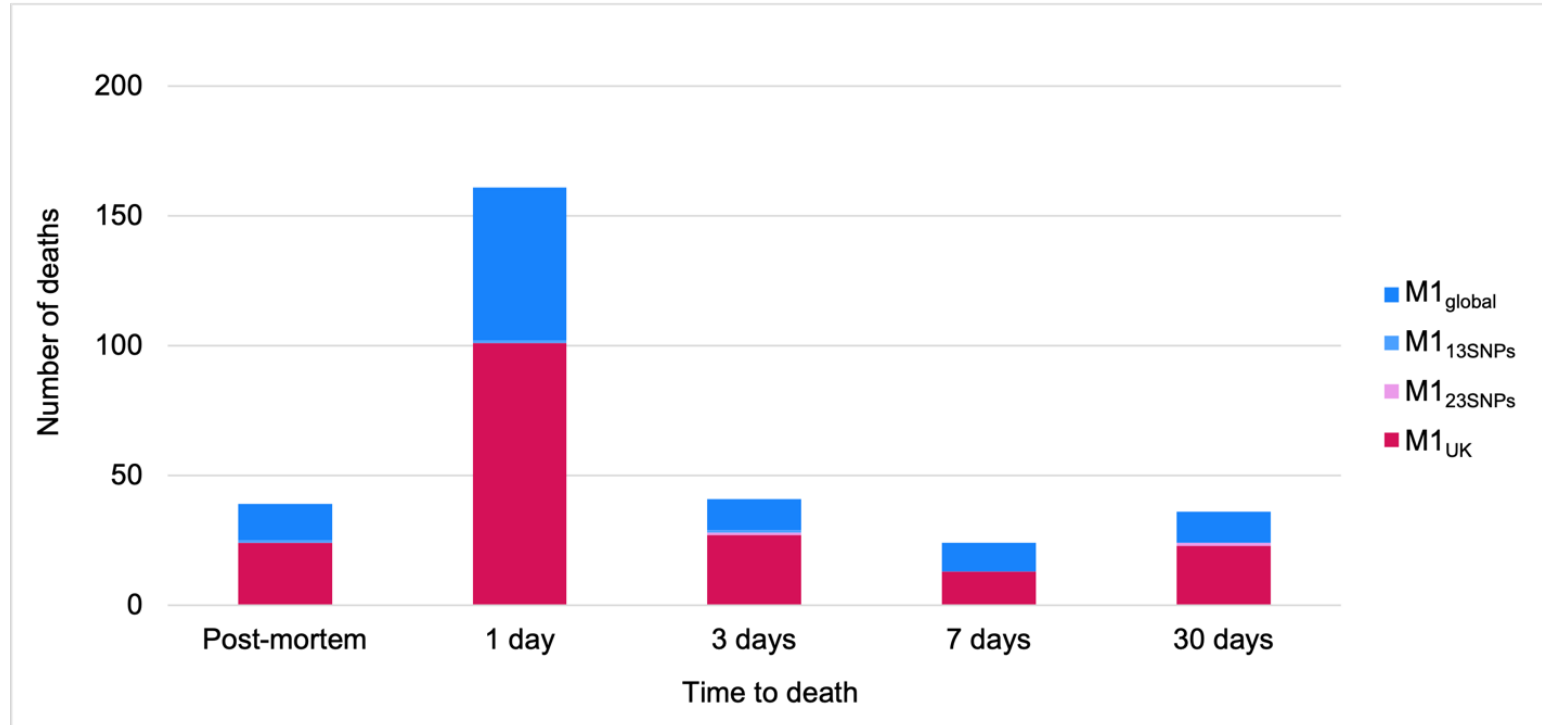
Kaplan–Meier survival estimates



Case fatality by sublineage: M1 is just dangerous



Time from first sample to death



>50% children diagnosed postmortem

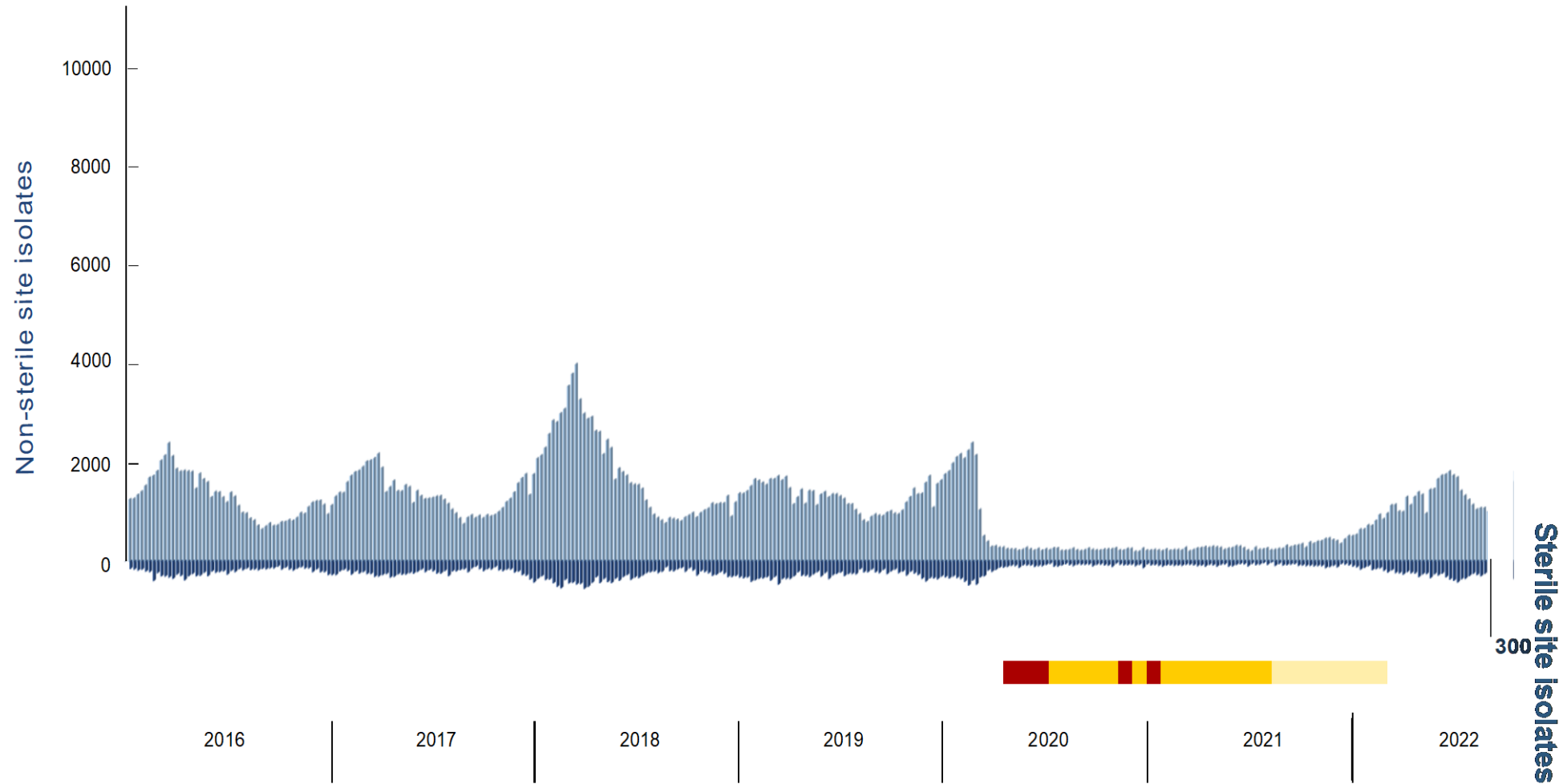
Proportion of deaths < 72h for emm1

- Children 99%
- Adults aged 15-64 78.8%
- Adults aged 65-84 70.9%
- Adults >85 69.7%

Important

- Preventable vs non preventable deaths
- Clinical trial efforts

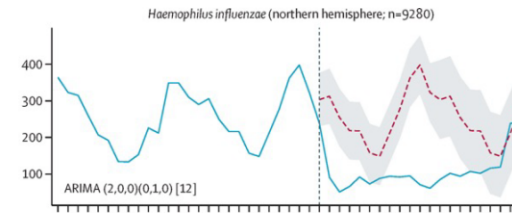
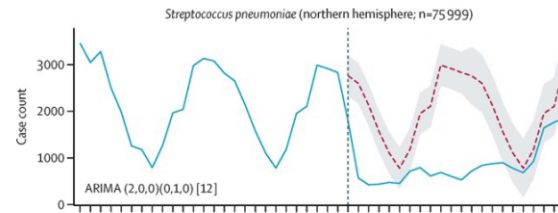
Q 2: Was reduced exposure to *S. pyogenes* important?



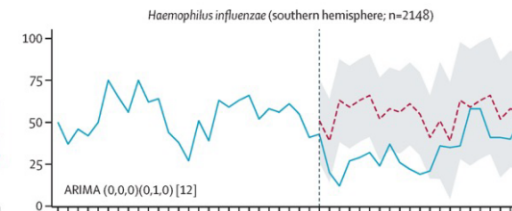
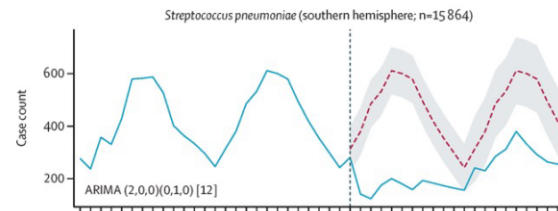
Other invasive bacterial infections 2020-2022



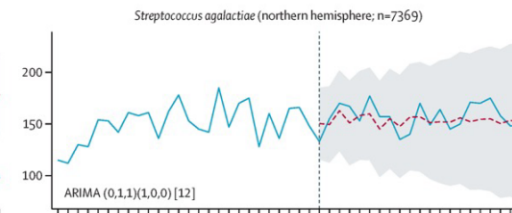
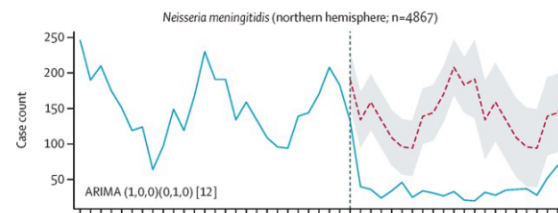
S. pneumoniae



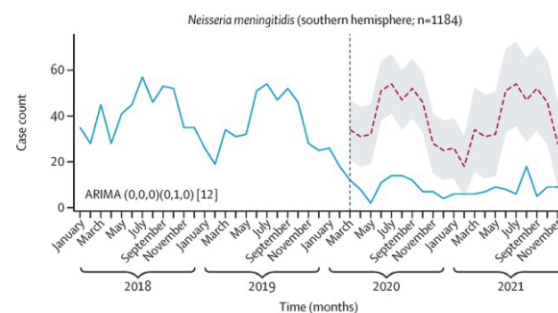
H. influenzae



N. meningitidis



S. agalactiae



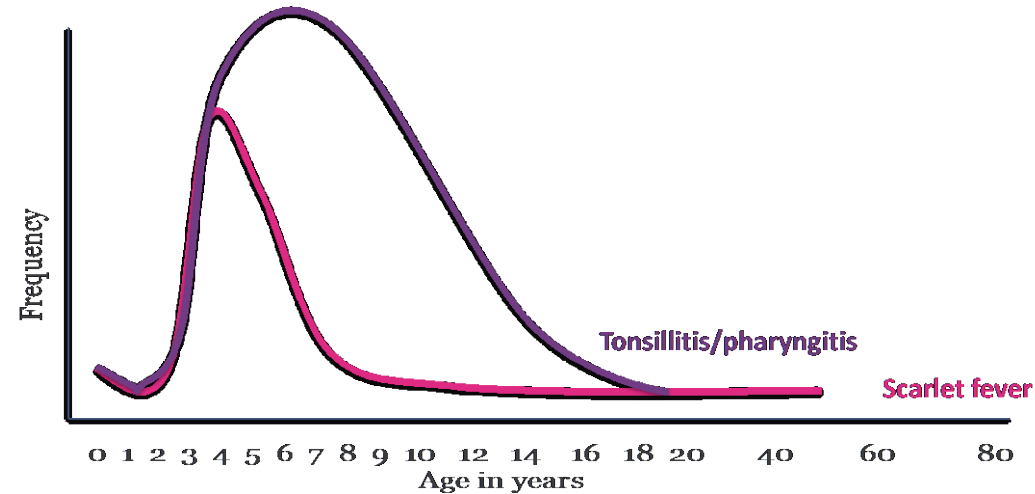
Time series
— Observed
- - - Counterfactual

30 country analysis

Shaw et al, *The Lancet Digital Health* 2023 5e582-e593 DOI: (10.1016/S2589-7500(23)00108-5)

Scarlet fever susceptibility and pool of susceptibles

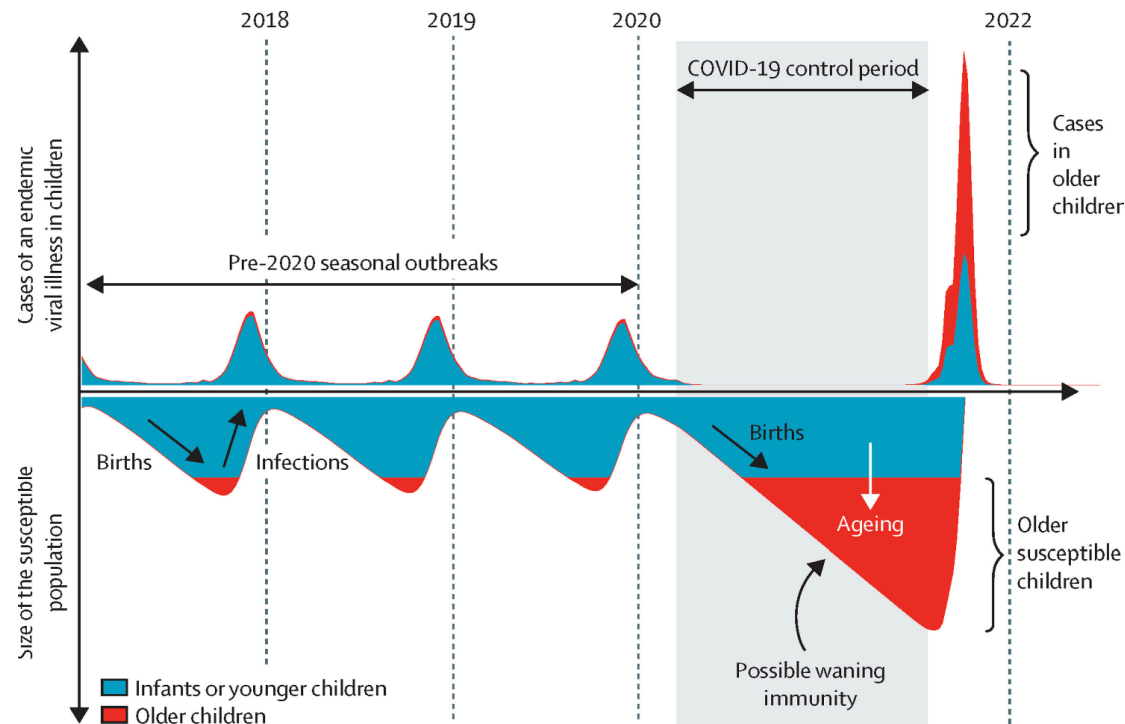
Disease incidence
by age



- Most scarlet fever happens in first school year (Herdman et al, BMJ Open, 2021)
- Did size of susceptible cohort expand during pandemic and could that be enough to explain fold increase in cases? ??3-fold

Predicting upsurges after NPI e.g. RSV

Preparing for uncertainty: endemic paediatric viral illnesses after COVID-19 pandemic disruption



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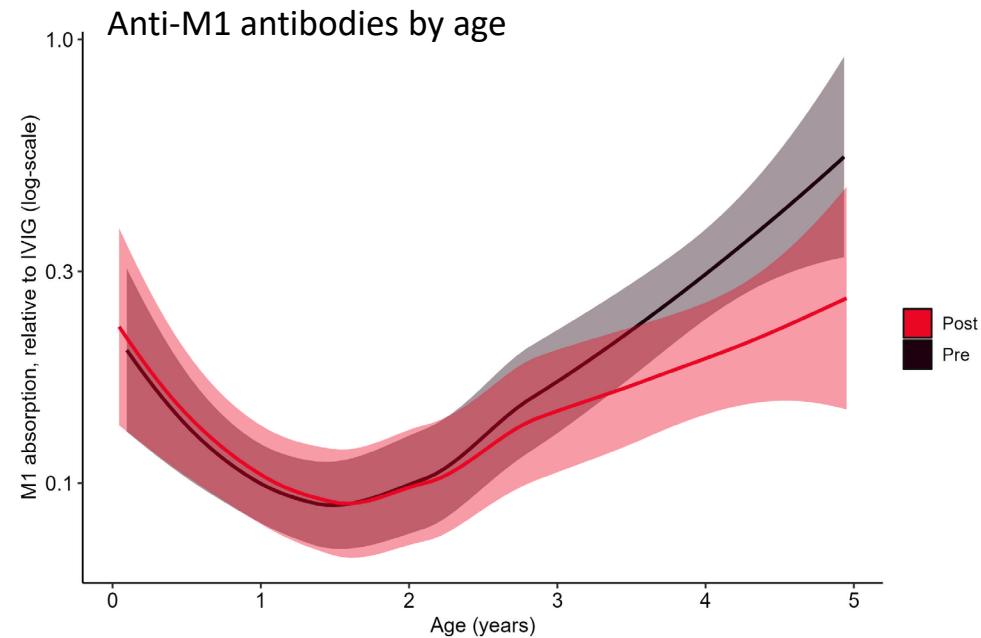
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Preparing for uncertainty: endemic paediatric viral illnesses after COVID-19 pandemic disruption

[Kevin Messacar](#)^{a,b} · [Rachel E Baker](#)^c · [Sang Woo Park](#)^c · [Hai Nguyen-Tran](#)^a · [Jessica R Cataldi](#)^{a,b} · [Bryan Grenfell](#)^{c,d}

July 2022

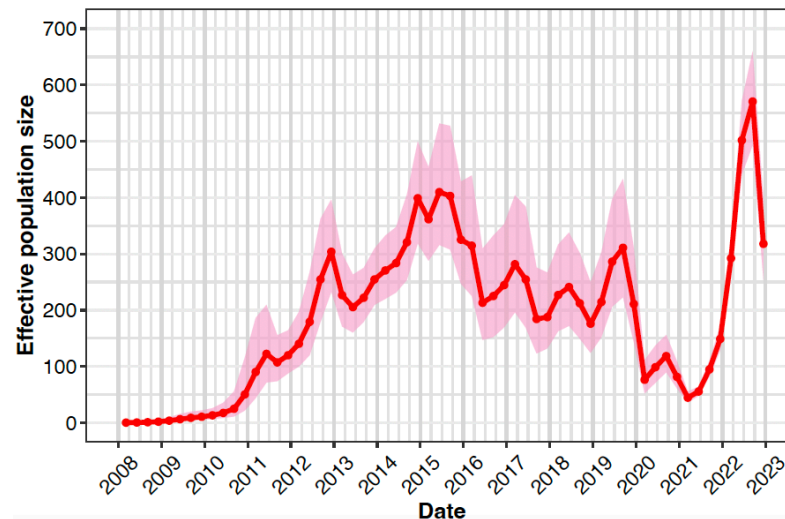
244 children under 5y pre-March 2020,
247 children under 5y after March 2020
(Perform and Diamonds cohorts)



Dokal, Channon-Wells et al, 2024, unpublished

Why is this case interesting?

- First case of invasive GAS recognized to be part of new subclone “M1_{UK}”
- Suggested new subclone to be important
- Prompted local then national genomic investigation
- M1_{UK} emerged 2008 but expanded rapidly 2010-2015
- Makes more SpeA (scarlet fever toxin) and appears fitter than older strains



Model of effective population size (N_e) through time based on the dated tree.

- N_e is the number of bacterial genealogies contributing to the next generation through transmission.

Transmission bottleneck during COVID-19 lockdowns in 2021.

Putting it all together – the 2022/23 upsurge



Thank you.....




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