UK Health Security Agency

Update on the national polio incident and enterovirus surveillance webinar

Thursday 2 February

UK Health Security Agency

Update on the National Enhanced Polio Incident

Dr Vanessa Saliba

Consultant Epidemiologist, Incident Director
Immunisation and Vaccine Preventable Diseases Division, UKHSA

02/02/2023

Paralytic poliomyelitis

- common endemic infection worldwide prior to use of vaccine – mainly affected children under 5
- three types of poliovirus cause infection: 1, 2, 3
- spread through feacal-oral route
- less than 1% of all polio infections result in paralysis:
  - 1 in 200 (adults) vs 1 in 1000 (children)
- paralysis of limbs and respiratory muscles may occur
- the degree of recovery varies but residual paralysis is common
- no cure but completely preventable by vaccination

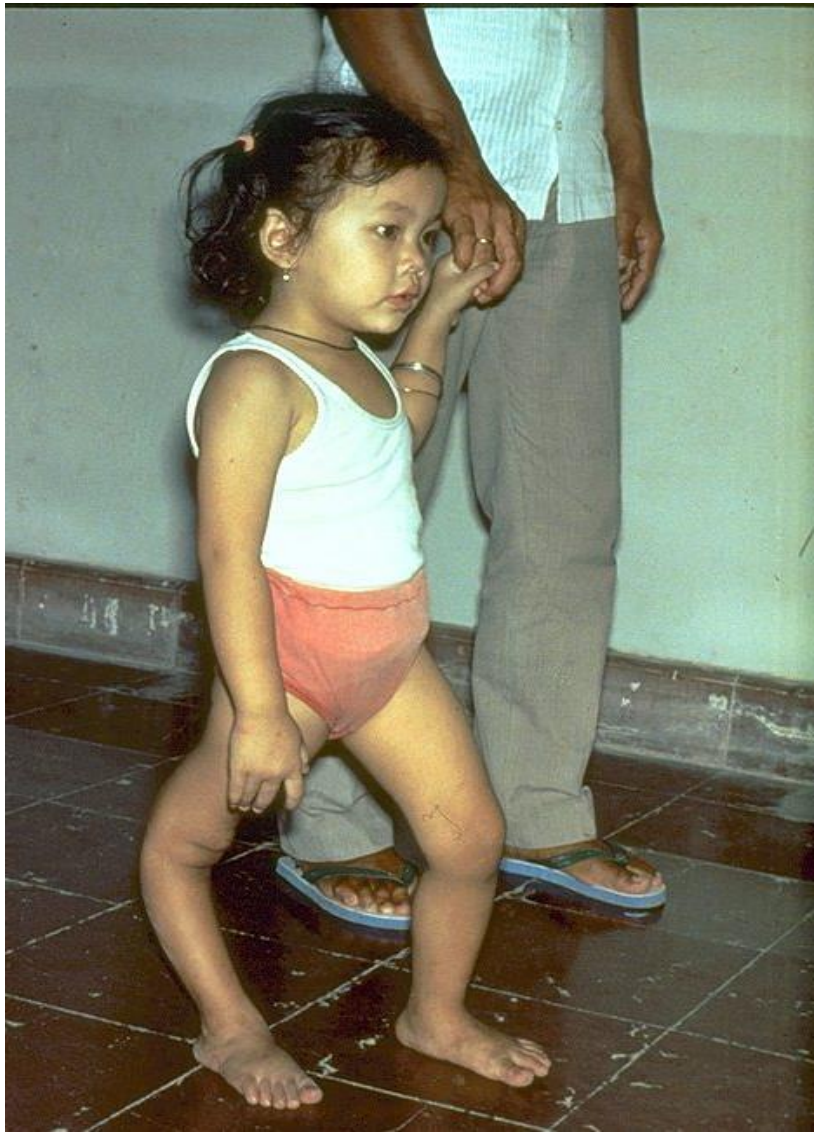
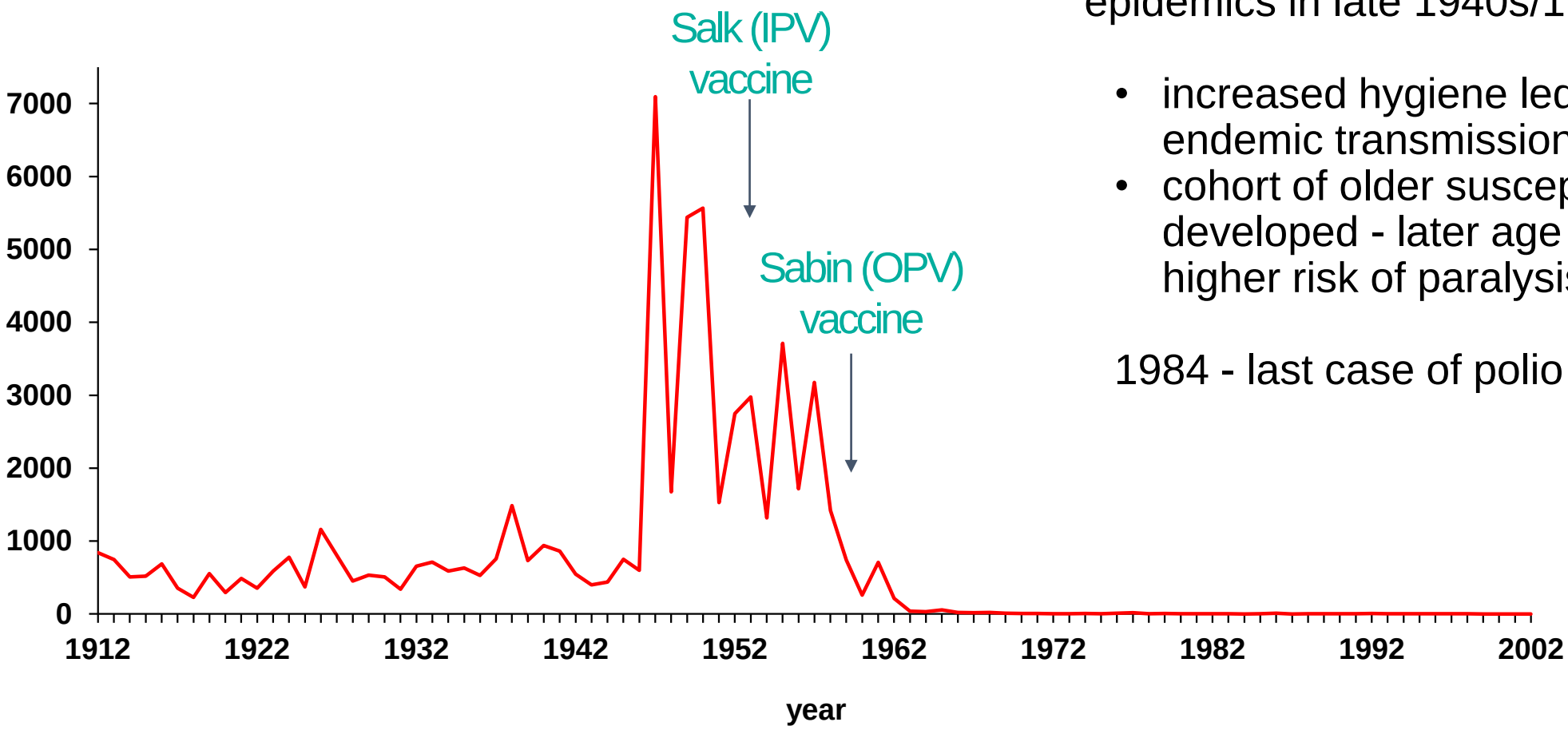


Photo courtesy of Immunization Action Coalition http://www.immunize.org/catg.d/pict001.htm

Acute paralytic poliomyelitis - England and Wales, 1912-2002*



Many developed countries had large epidemics in late 1940s/1950s:

- increased hygiene led to reduced endemic transmission
- cohort of older susceptibles developed - later age at exposure, higher risk of paralysis

1984 - last case of polio acquired in UK

* notifications to 1984, cases ascertained from any source after 1985

Polio vaccines

Sabin (live) oral polio vaccine (OPV)

- replaced IPV in the UK schedule in 1961
- contains three living viruses that have been “attenuated” so they do not cause disease
- OPV viruses grow in the human gut – high level of gut immunity
- commonly shed vaccine virus for a few weeks
- virus can spread to inadvertently immunise unvaccinated contacts
- good protection against risk of spread from imported wild virus
- very small risk of vaccine associated paralytic polio (1 case per million)

Salk (inactivated) injectable vaccine (IPV)

- introduced in UK 1955
- contains three “wild” viruses that have been inactivated (or killed)
- IPV gives good protection against paralysis
- poor gut protection, so virus circulation can occur
- so OPV continued to be used until the risk of imported virus in the UK fell
- in 2004, decision to switch to IPV in UK schedule

Polio end game – Global Polio Eradication Initiative

- Poliovirus type 1 is the only remaining wild virus (Afghanistan and Pakistan)
- Poliovirus type 2 declared eradicated in 2015
  - last case 1999
- Poliovirus type 3 declared eradicated in 2019
  - last case 2012
- Circulating vaccine derived poliovirus (cVDPV)
  - where immunisation rates are low, virus can spread and over months, mutate and **regain ability to cause paralysis**
- Immunodeficiency-related vaccine-derived poliovirus (iVDPV)
  - people with severe immunodeficiency can continue to excrete long term, acquiring more mutations
- Vaccine viruses now causing outbreaks in several countries, in communities where immunisation rates are low

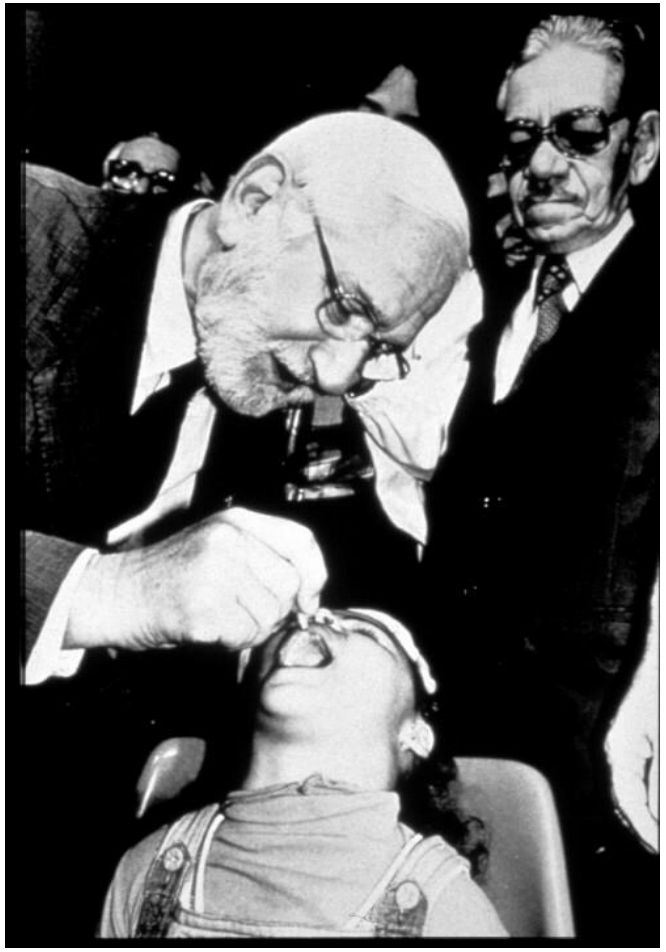
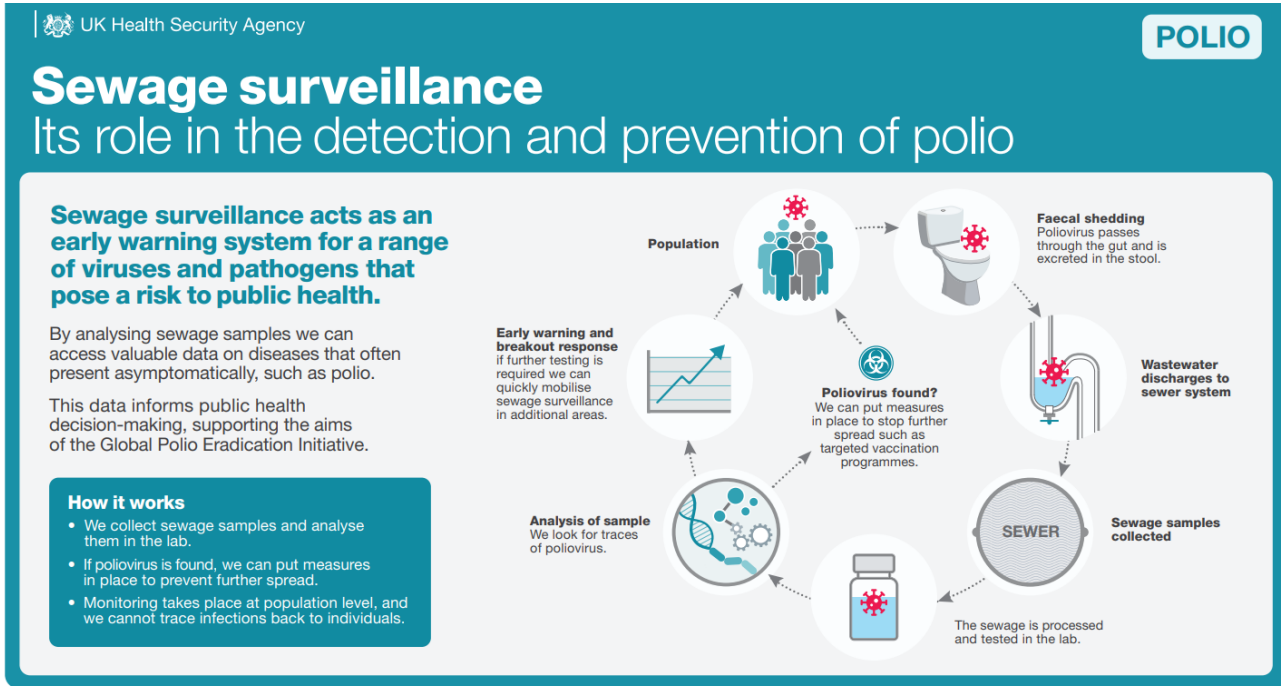


Photo courtesy of WHO
http://www.polioeradication.org/vaccines/polioeradication/all/multimedia/gallery.asp

Routine environmental surveillance for polio in UK

- Environmental surveillance for polio – a key component of our commitment to WHO global polio eradication programme
- Since 2016, bi-weekly raw sewage samples collected from London and Glasgow and sent to the National Institute for Biological Standards and Control (NIBSC, MHRA) for testing
- NIBSC is a WHO Global Specialised Laboratory for polio - perform investigations that are essential to establish the temporal and geographical transmission pathways of poliovirus circulation
- An average of 1-3 polioviruses are detected from UK sewage samples each year:
  - single detections, unrelated to each other
  - further virus characterisation has suggested that they were viruses from recent vaccinees entering the UK



Detection of poliovirus in London sewage

- vaccine-**like** poliovirus type 2 (PV2) was first identified in a sewage sample collected from London Beckton Sewage Treatment Works in February 2022
  - genetically related poliovirus was picked up again in April and has persisted since

- the most likely scenario is that an individual recently vaccinated with oral polio vaccine (OPV) entered the UK in early 2022
  - virus spread among communities in north-east and central London
  - the virus has continued to evolve and is now a vaccine-**derived** poliovirus type 2 (VDPV2)
  - VDPV2 detected for more than 2 months (**circulating** VDPV2)

- the virus has to date only been detected in sewage samples and **no associated cases of paralysis have been reported**

- **WHO confirmed that VDPV2 detected in London is genetically linked to polio viruses detected in New York state (US) and Israel**
  - case of paralytic polio confirmed in unvaccinated adult in NY state

Publication: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01804-9/fulltext

UK polio vaccination schedule

Babies

Primary course of polio vaccine consists of **three doses** given at **8, 12 and 16 weeks of age**:

6-in-1 DTaP/IPV/Hib/HepB

Toddlers

Pre-school booster at 3 years and 4 months:

4-in-1 DTaP/IPV

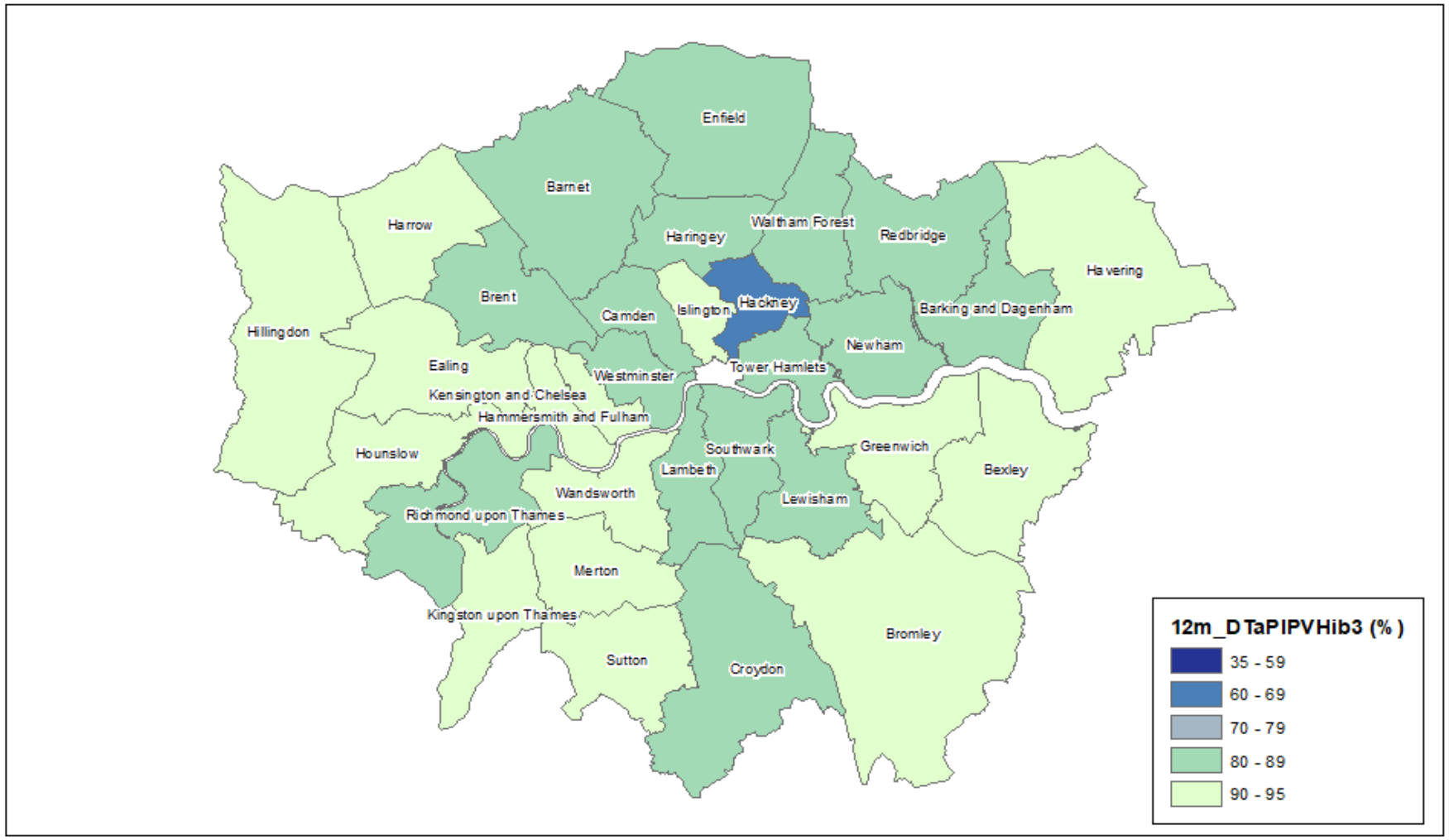
Teenagers

Teenage booster given in School Year 9 or 10, at around 14 years of age:

3-in-1 Td/IPV

Before 2004 **oral polio vaccine (OPV)** was used i.e. those aged 18 years and above

Primary vaccine course coverage at 12 months of age by London Local Authority, (October to December 2021) Source: UKHSA



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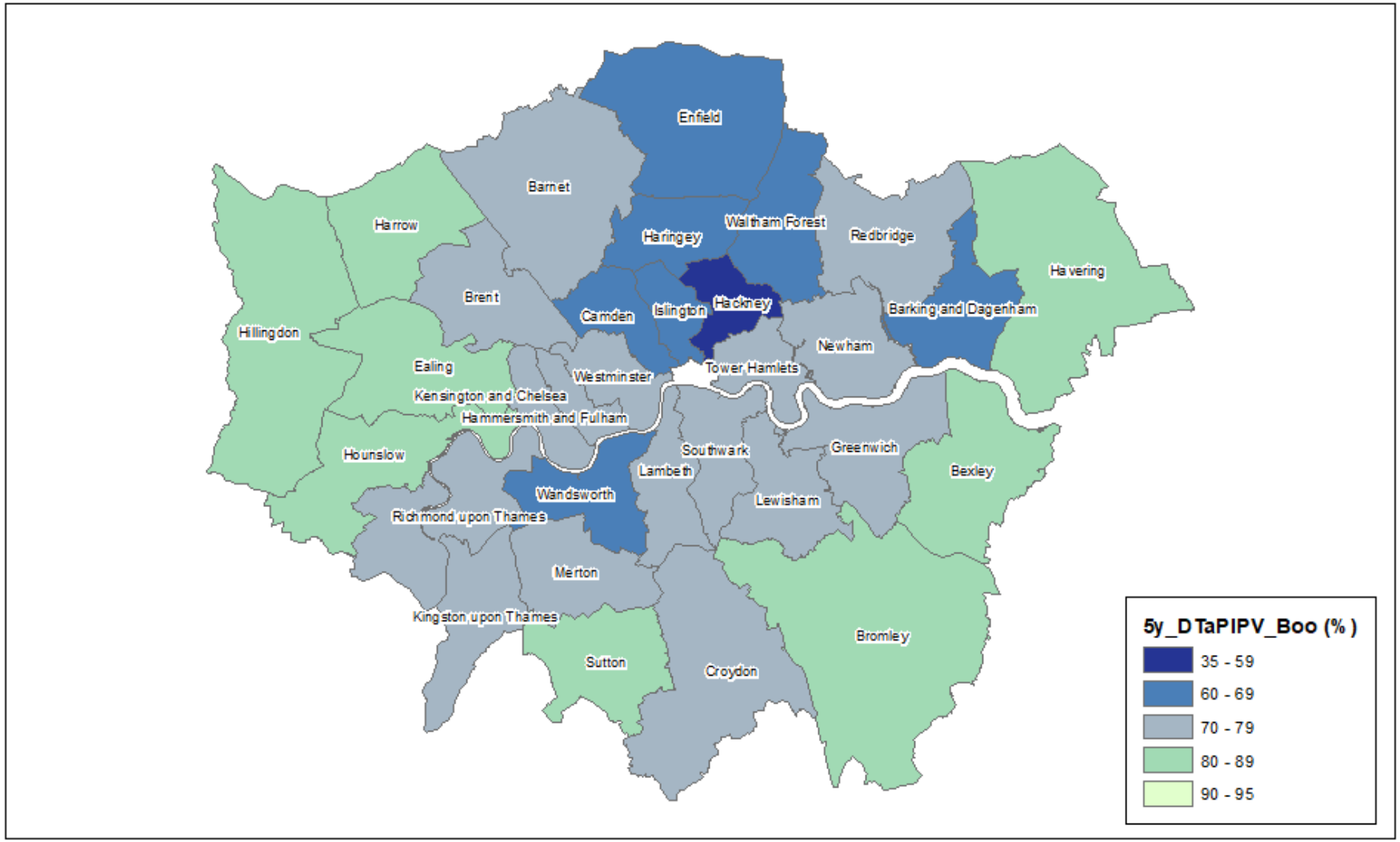
London: **86.6%**
Range: 93.4% to 61.0%

Coverage is below 85% in 8 out of 33 London Local Authorities

Pre-school booster coverage at 5 years of age, by London Local Authority, (October to December 2021) Source: UKHSA



London: **71.4%**
Range: 84.7% to 54.2%

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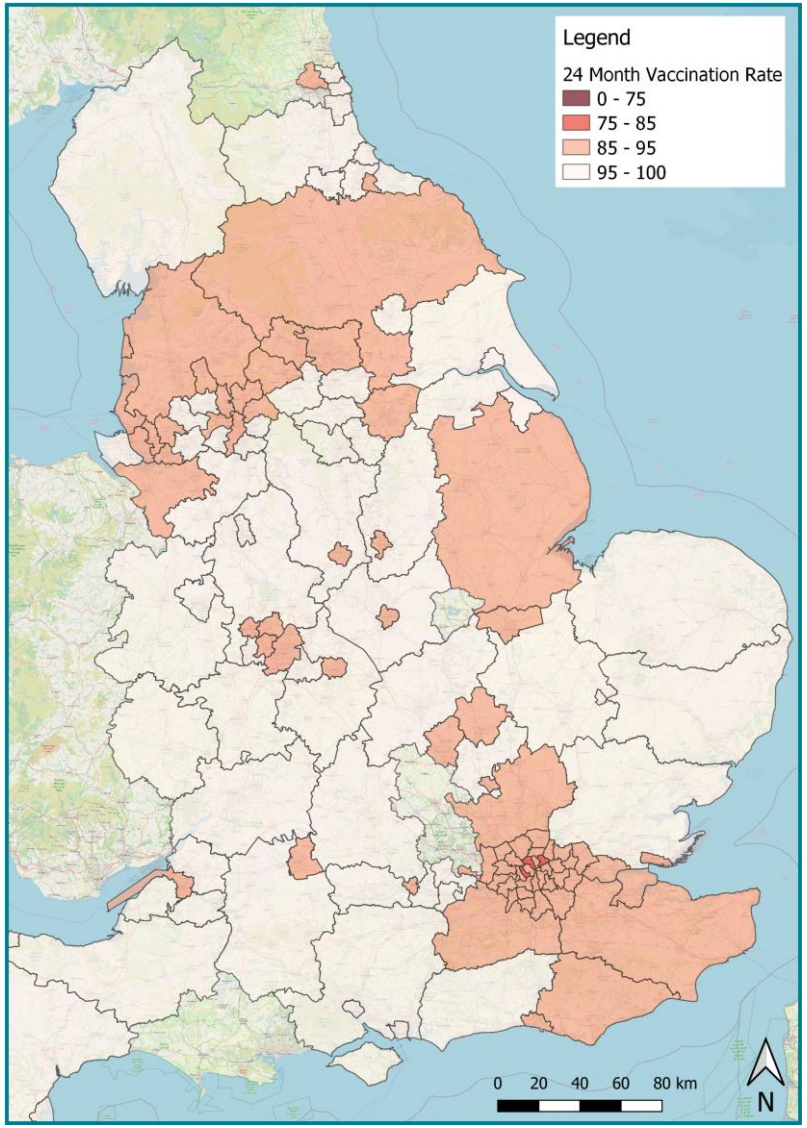
Created by UKHSA, Geospatial Team

UKHSA national enhanced in**cident response**

1. **Environmental surveillance in partnership with National Institute for Biological Standards and Control (NIBSC):**
   - sampling upstream of Beckton and Deephams and all London STWs
   - standing up 18 sites nationally (September 2022)
   - maintain for long-run to provide evidence to WHO
2. **Case finding and enhanced laboratory surveillance:**
   - public health message cascaded to health professionals via a CAS Alert and professional networks (June and November)
     - **Acute Flaccid Paralysis/Myelitis** cases due to an infectious cause should be notified to UKSHA and appropriate samples collected – 2 STOOL samples 48 hours apart + CSF + throat swabs/ nasopharyngeal aspirate (NPA)
   - Enteric Virus Unit and Polio Reference Laboratory at UKHSA Colindale: i) improving local lab data flows to SGSS and lab sample referral rates (all local EV+ samples), ii) stool survey in London, iii) polio PCR development
3. **Vaccine response:**
   - All areas – recovery of childhood programme + catch up
   - **London:**
     - June: GP-based call-recall of unimmunised/partially immunised children under 5 years
     - End August: IPV booster to all children aged 1-9 years
     - Targeted work to reach underserved communities

High risk sites identified for inclusion in national environmental surveillance



- Birmingham
- Blackburn with Darwen
- Bradford
- Brighton and Hove
- City of Bristol
- Bury
- Castle Point
- Leeds
- Leicester
- Liverpool
- Luton
- Manchester
- North Tyneside
- Newcastle upon Tyne
- Gateshead
- Nottingham
- Preston
- Salford
- Sheffield
- Watford

Criteria for inclusion:

- areas with low polio vaccination coverage (see map)
- areas with high % population with links to countries with PV / cVDPV
- areas with large pockets of under-vaccinated communities
- areas adjacent to or with links to locations in London where PV has been detected

Polio booster campaign in London

In August the Joint Committee for Vaccinations and Immunisation (JCVI) advised NHS to urgently launch polio booster campaign for children aged 1 to 9 years in London:

- for some children this is an extra dose of vaccine
- for some children this will bring them up to date

Aims of the campaign:

- provide or strengthen protection against **paralysis**
- boosting immunity should also help to interrupt **transmission**

363,972 IPV doses delivered by NHS London, September to January 2023

Evaluation: vaccine coverage and inequalities – **inform Phase 2 of the response in London**

Acknowledgments

- Polio Incident Management Team

- Dr. Mary Ramsay – UKSHA
- Dr. Maria Zambon – UKHSA
- Dr. Anita Bell - UKHSA
- Andrew Zealand, Ali Zeb – UKSHA
- Javier Martin - NIBSC MHRA
- UKSHA London and NHS London colleagues

UK Health Security Agency

Polio & Enteroviral laboratory surveillance: strengths and weaknesses

Maria Zambon

2nd February 2023

Global Polio Eradication: Annual status update

- Routine immunization coverage achieved by the National Immunization Programme at the national and sub-national levels, including coverage among known high risk sub-populations in the country (if no high risk groups in country, indicate this in statement)
- Results of supplementary polio immunization activities (SIAs) targeting high-risk territories or high-risk sub-populations, when appropriate.
- Surveillance sensitivity within the national public health system for “paralytic poliomyelitis”, assuring that health care reforms did not negatively affect delivery of health services.
- The national surveillance for Acute Flaccid Paralysis (AFP), where appropriate.
- Supplementary (enterovirus and environment) surveillance, where appropriate
- Containment activities addressing Phase I and Phase II of GAPIII with particular attention to national inventory, destruction/transfer of all PV2 materials, and national PEF certification plan
- The National Plan of Action to sustain polio-free status, particularly “outbreak preparedness Action Plan”, providing evidence that the document is up to date and in line with current global recommendations, and preferably tested
- Acknowledging a response to recommendations made by European RCC, if any.

Make sure that all elements are addressed in your statement before submitting.

Please provide, in the space below, evidence to support the NCC’s statement in 1.2.

Post certification UK laboratory surveillance approaches

Category	Surveillance stream	Strengths	Weaknesses
Clinical	Acute flaccid paralysis surveillance	• Low disease frequency • Generally high vaccination coverage	• No formal notification requirement • Poor ascertainment • Suboptimal sampling • Lack of systematic diagnostics • Lack of PID screening
Laboratory	Enhanced enteroviral surveillance	• National Referral arrangements • Geographical coverage of UK, • ~ 2,000 / year characterised	• Non systematic • Biased towards CSF testing • Lack of faecal sampling • Variable representation regions
Environmental	Wastewater surveillance	• Methodology development during COVID • Widespread sampling during COVID	• Sustainable funding • Longer term framework

Changes in clinical virology diagnostic practices since 2002 certification process

In 1990s, viral culture commonly performed

- universally available in NHS hospitals

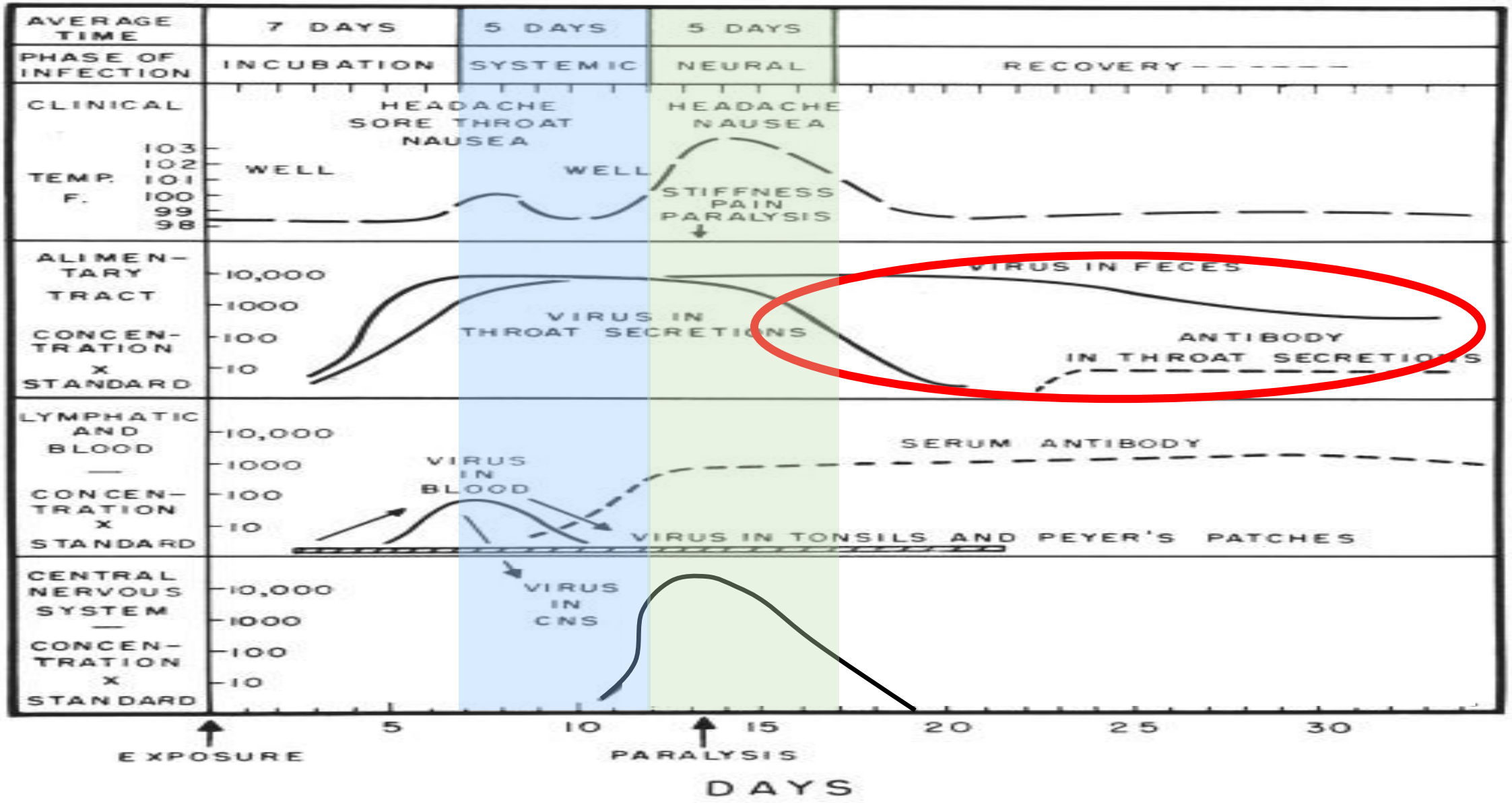
By early 2000s, reduction in typing virus isolates

- due to shortage of anti-sera and cost pressures
  - referral of untyped enterovirus isolates to national laboratory

From 2005 onwards increasing use of PCR for viral meningitis, instead of viral culture

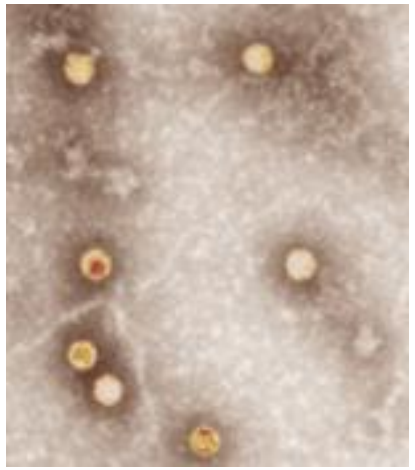
- More EV being identified than in era of viral culture
- Rarely typed beyond generic enterovirus
- CSF is main specimen type found EV PCR positive
- Lack of recognition that stool is best sample for polio or EV diagnosis
- Some new EV infections are not detected in CSF (D68)

Polio virus detection



From “Viral and Rickettsial Infections of Man”, edited by Rivers and Horsfall (1959). Polio infection.
Image available: http://www.virology.ws/2009/03/11/chronology-of-an-acute-infection/

Enterovirus surveillance

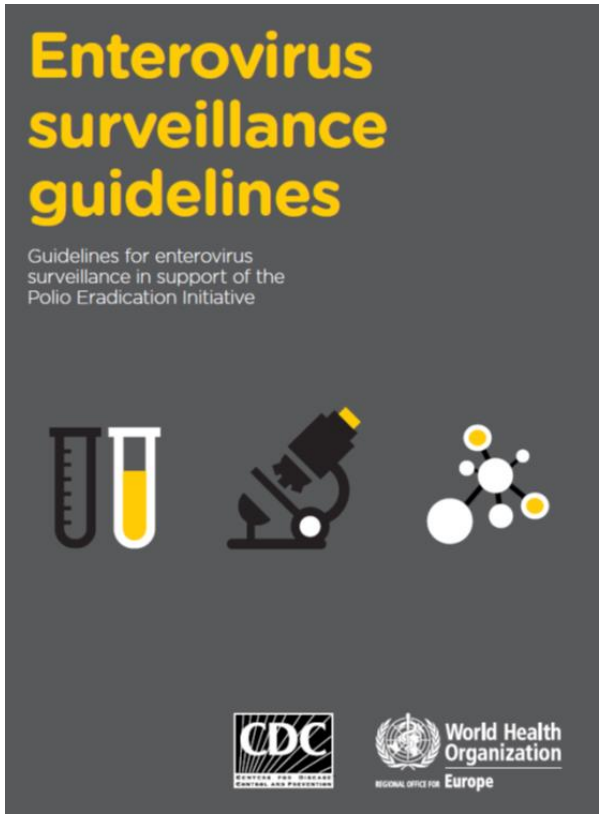


M Hannah, unpublished.

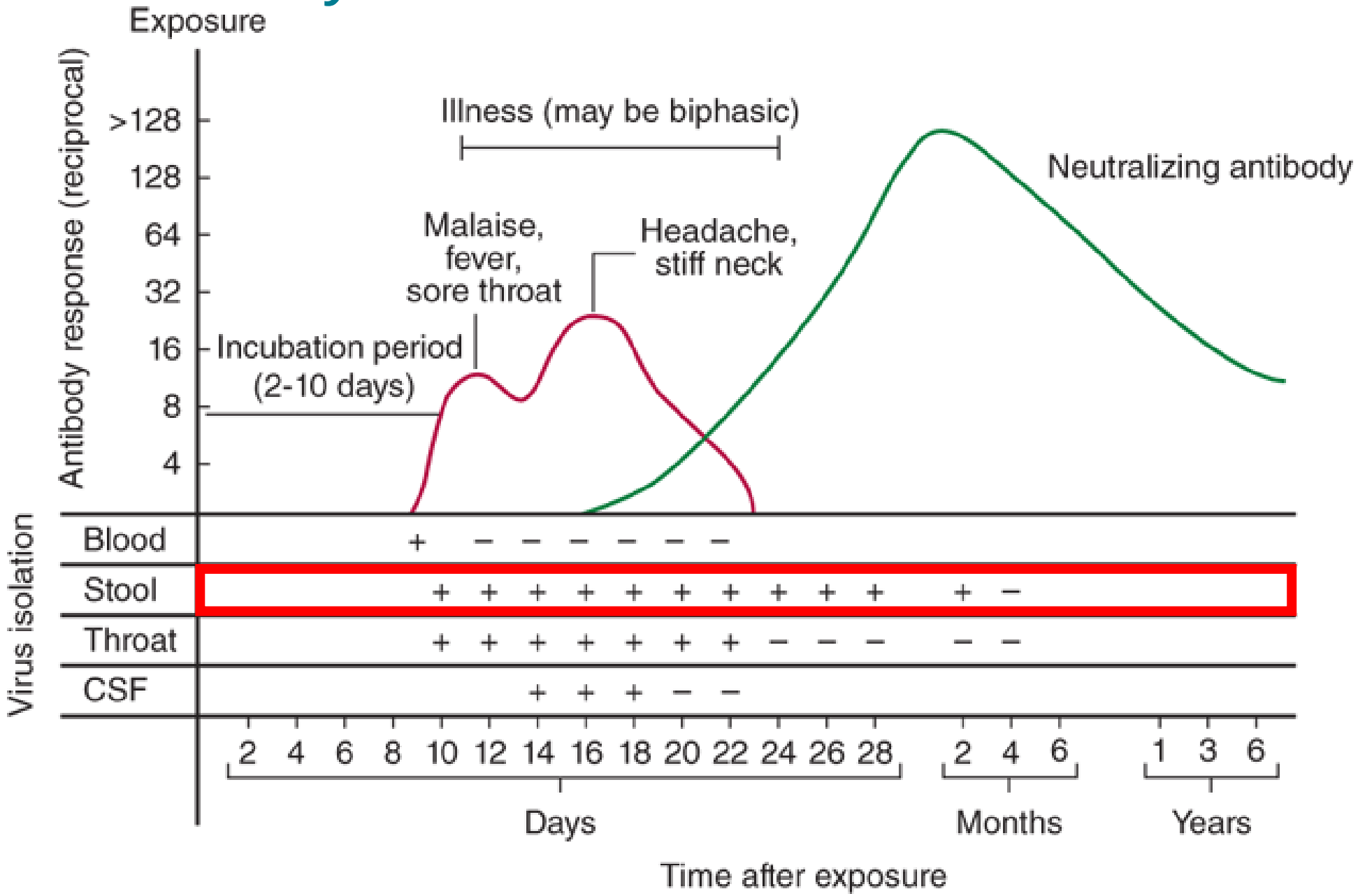
- *Picornaviridae* family
- ssRNA, +sense
- Non-enveloped
- Genome: ~7.4kb
- Genotyping based on VP1 sequence
- Classified in species: A to D relevant

- Mild to severe symptoms
- Genotypes of concern: E-D68 and EV-A71
- Related to Poliovirus that can induce acute flaccid paralysis and poliomyelitis
- Similarities with Rhinoviruses (HRV)

WHO Enterovirus surveillance guidelines to support the Global Polio Eradication Initiative, to monitor EV strain circulation and characterise emerging strains.

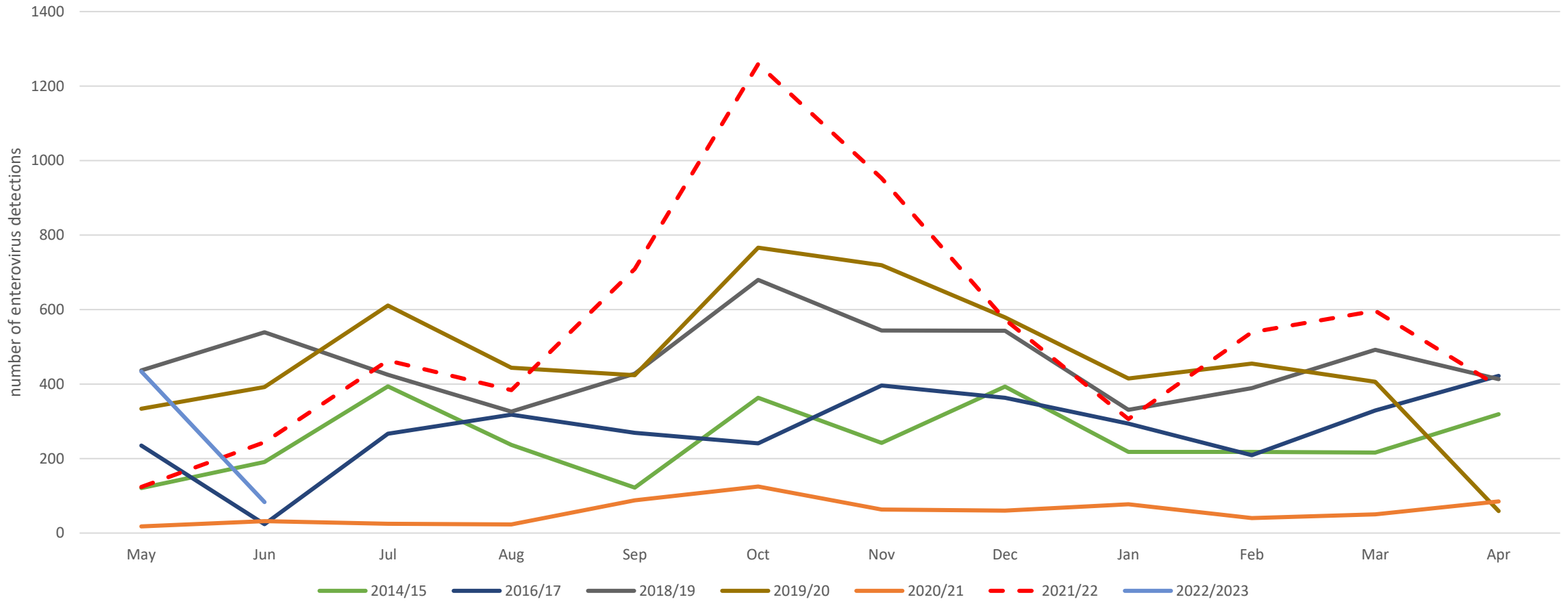


Natural History of enteroviral infection

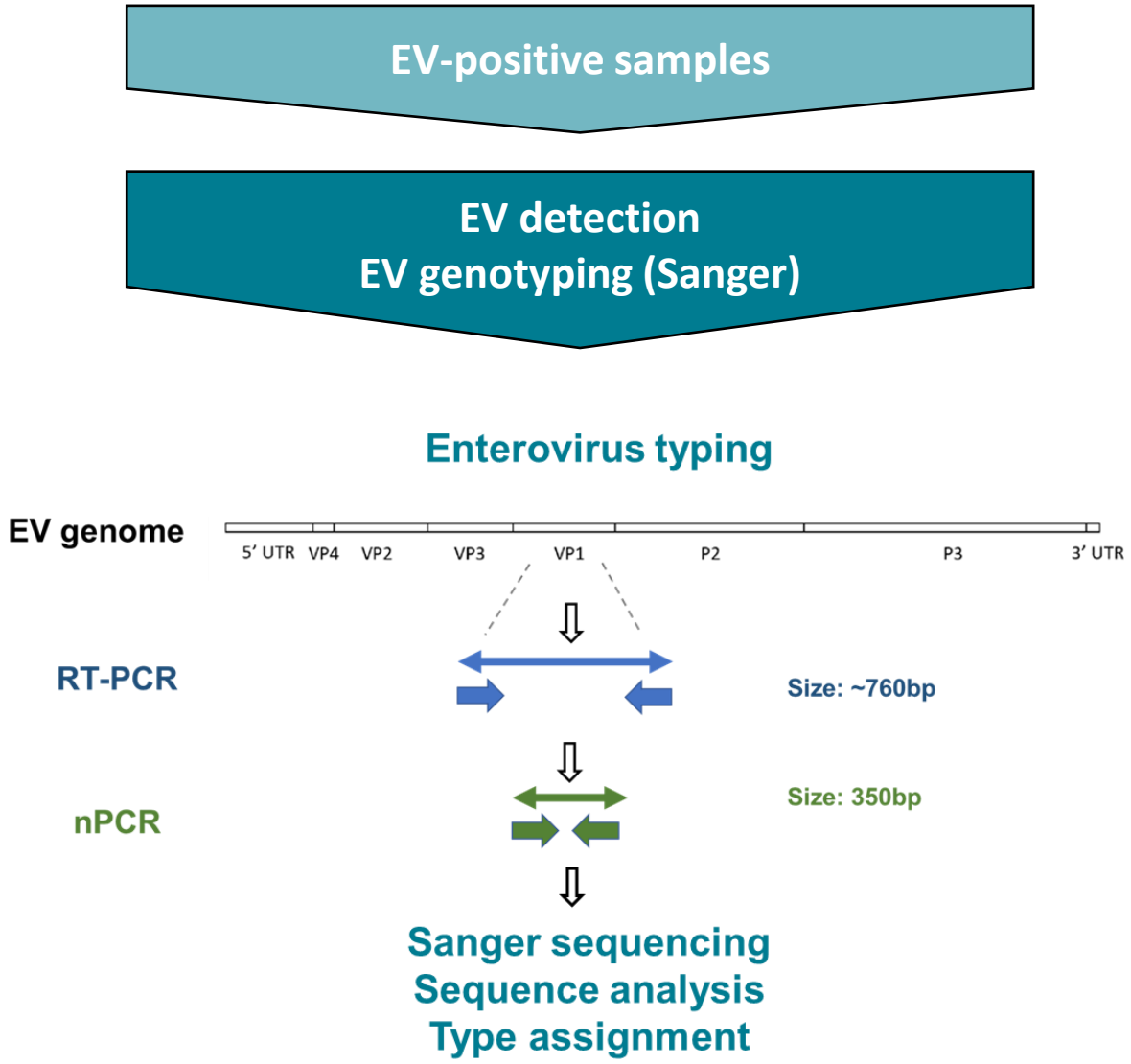


Kenneth, R. Sherris
Medical Microbiology,
7th Ed. 2018.

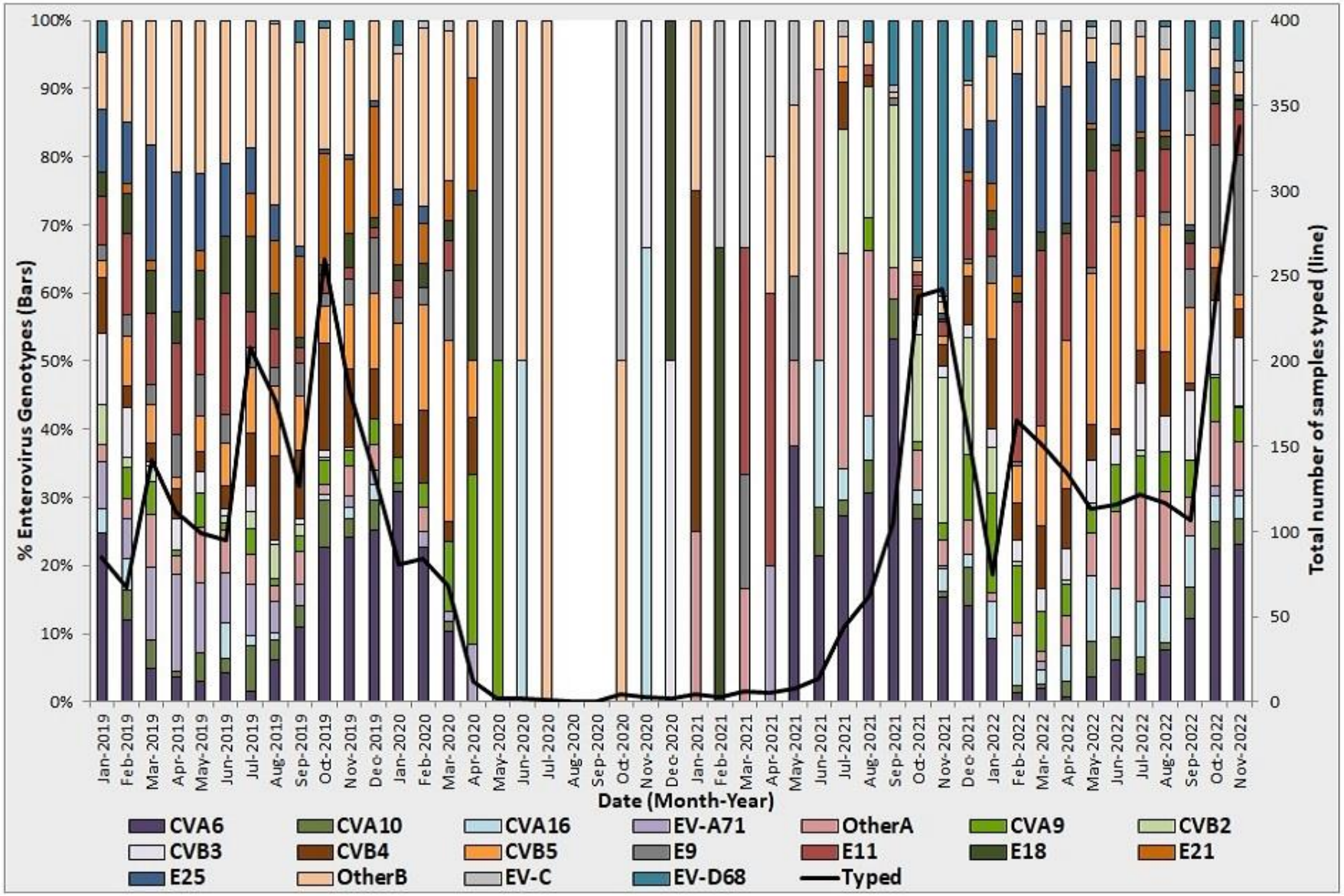
Number of enterovirus positive samples (all ages) reported through SGSS, 2014 - 2022



Enterovirus molecular typing for surveillance



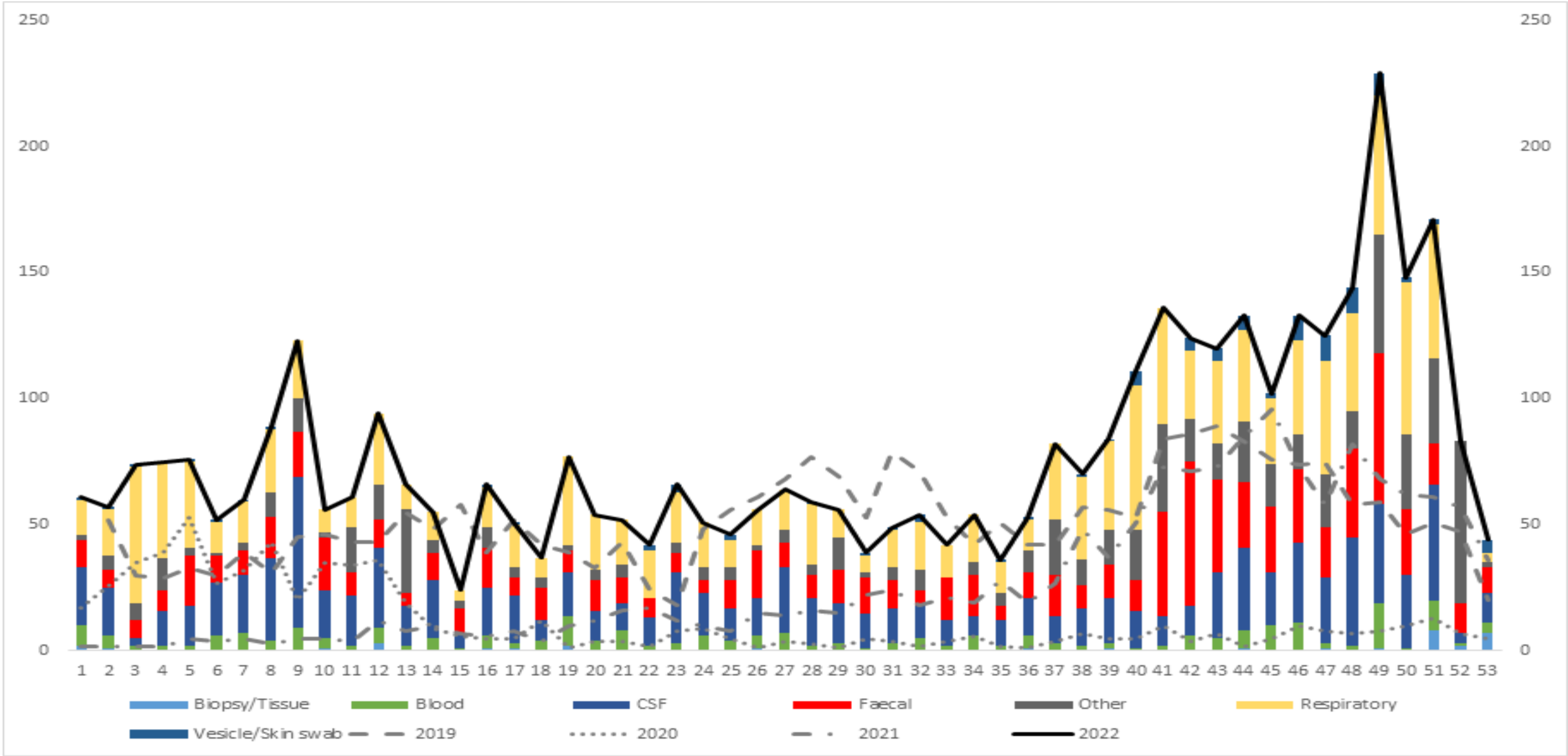
EV surveillance: genotyping results



UKHSA. Enterovirus: summary of strain characterisation. 10 January 2023. https://www.gov.uk/government/publications/enterovirus-strain-characterisation/enterovirus-summary-of-strain-characterisation [accessed 27 January 2023]

Enteroviral typing 2023
Different sample types

80% of referred material is typed



RESEARCH & SURVEILLANCE CENTRE

UK Health Security Agency

Virology Dashboard

Virology swabs by week at my practice

Go to vaccine coverage

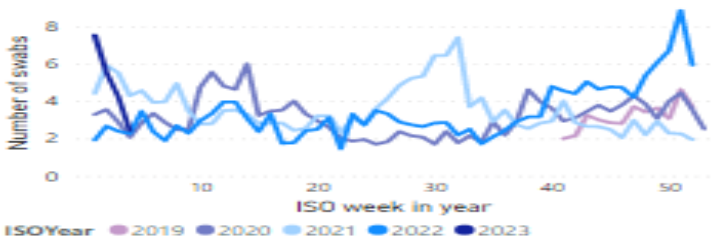
UNIVERSITY OF OXFORD

Practice Key (+Enter) : Search | Year: Multipl... | Patient Group: All | Age Band: All | Swab Source: All | Coded Swabs*: All

Number | Comparator

Number of swabs by week

Average number of swabs per practice, by week



Total this ISO week

100

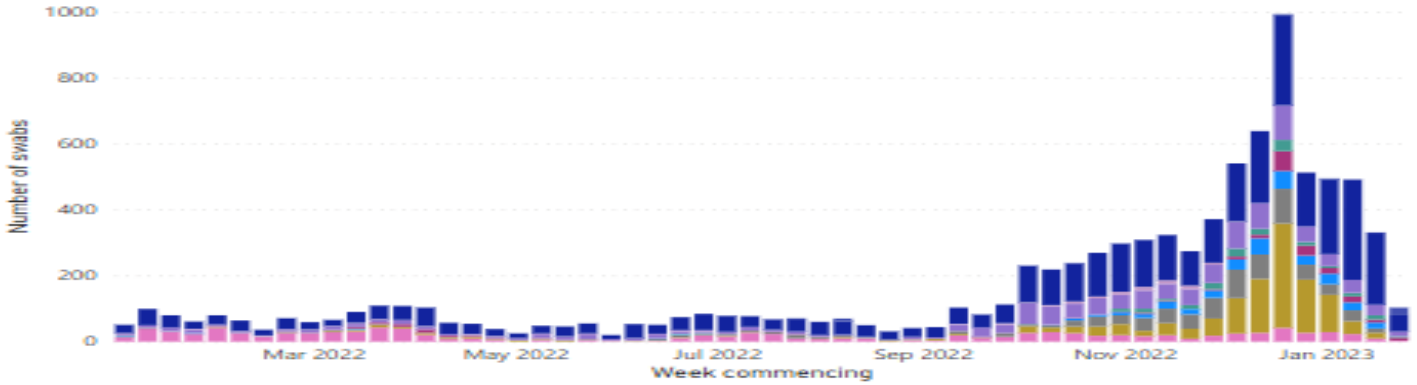
Total last ISO week

323

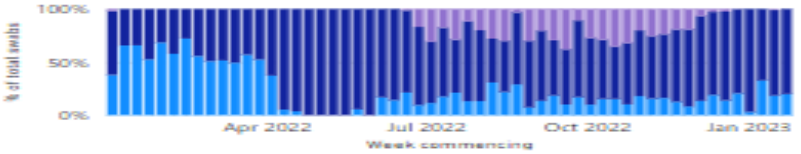
Number of swabs to date

NHS Region	Number of swabs
South East	1996
London	1505
North East and Yorkshire	1498
Midlands	1189
South West	1033
North West	806
East of England	574
Unknown	50
Total	**8651**

Number of positives by virus by week

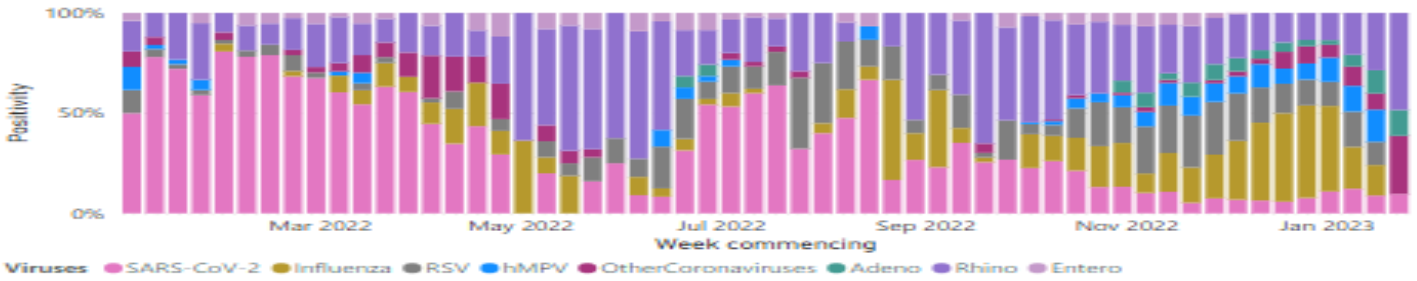


Number of swabs by swab source



Strain

Positivity by week



This dashboard presents:

The number of swabs (top left); the average number of swabs per practice (top middle).

The number of positives by virus (middle left).

Positivity by virus and a toggle button to view by viral strain (bottom left).
B: Influenza B, H1: Influenza A (H1N1)
H3: Influenza A (H3N2); Adeno: Adenovirus
Rhino: Human Rhinovirus; Entero: Enterovirus

A snap-shot of the total number of swabs this week and last week (top right).

The number of swabs to date by NHS region (middle right).

The number of swabs by swab source (bottom right).

*A filter which allows you to identify whether or not swabs have been recorded in the extract of patient electronic health records.

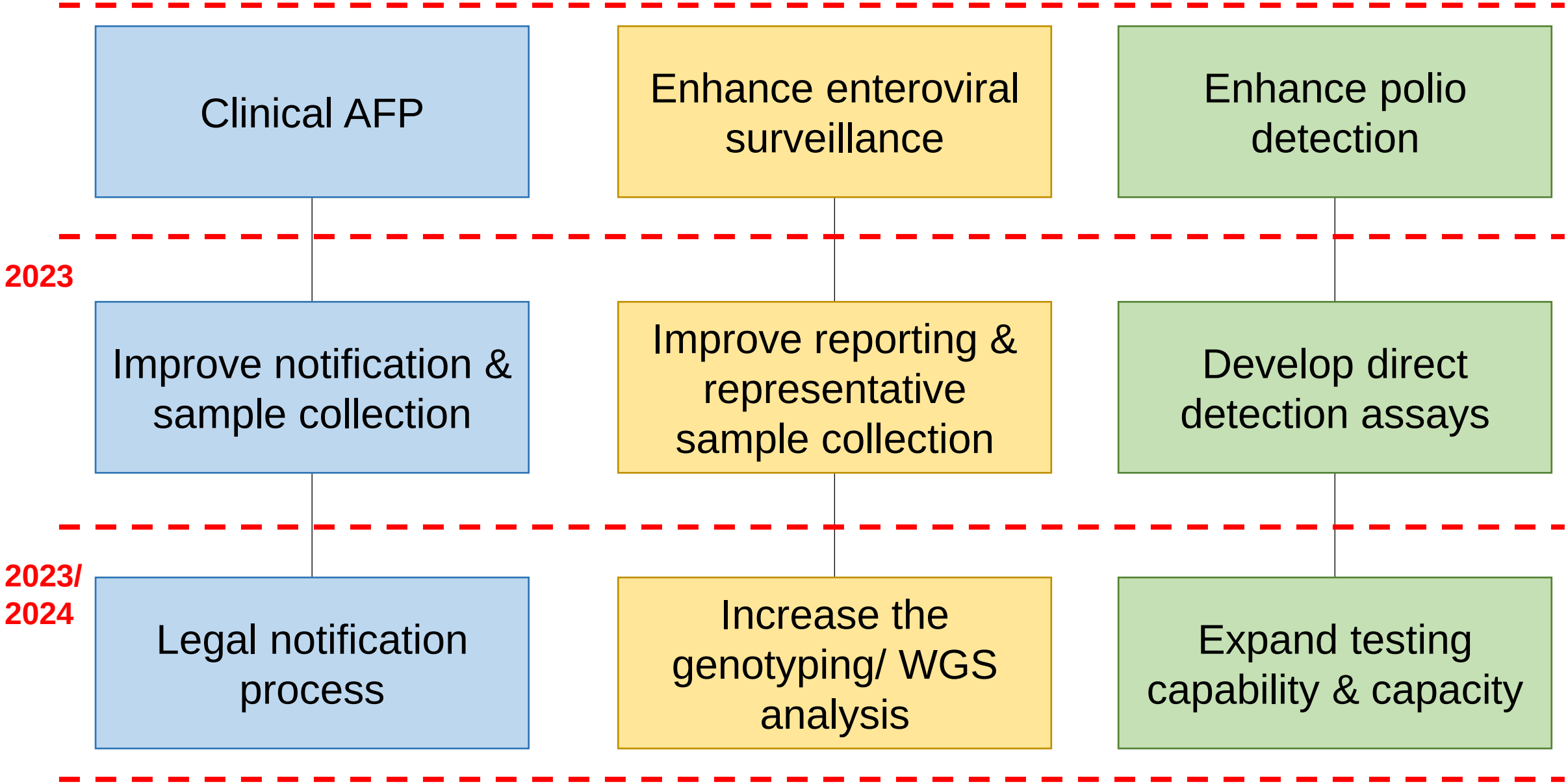
Further swabbing resources and support to increase swab numbers:
https://orchid.phc.ox.ac.uk/index.php/all-year-virology-and-serology-surveillance/

Contact: E: practiceenquiries@phc.ox.ac.uk, T: 01865 617284.

Summary of Issues for polio detection assurance

- Follow up of AFP cases to get appropriate samples collected
- Guidance on clinical specimen collection from AFP is already clear and part of national guidance
  - Refreshed in 2018
- Need to raise clinical awareness of stool as an important sample for detection of EVs, even if CSF is negative (MISSED DIAGNOSIS)
- Faecal samples for viral culture based work need to be original material (LABORATORY OPERATIONAL ISSUE)

Laboratory Enteroviral surveillance Improvement plan



Conclusions

- Enteroviral surveillance in UK can be further optimised
- Several areas for improvement
- Opportunity for enhancing clinical awareness, relevant for non polio enterovirus infections (D68, A-71)
- Focus on clinical sample collection pathways

Thanks to

- **Enteric virus Unit** VRD (Cristina Celma, Stuart Beard)
- **Polio reference Unit** VRD (Robin Gopal, Monika Patel, Claudia Rosenow, Julian Hand)
- **Respiratory Virus unit** VRD (Janice Baldeverona, Katja Hoschler)
- Sample reception team (Fiona Clode)
- All London laboratories, especially Barts health
- Jonathan Turner & Melanie Amphlett
- RCGP & Simon de Lusignan

Poliovirus, and non-polio enteroviruses

- What sort of clinical presentations are of interest?
- What questions should be asked during clinical assessment?

Dr Anika Singanayagam

Clinical Lecturer, Infectious Diseases, Imperial College London

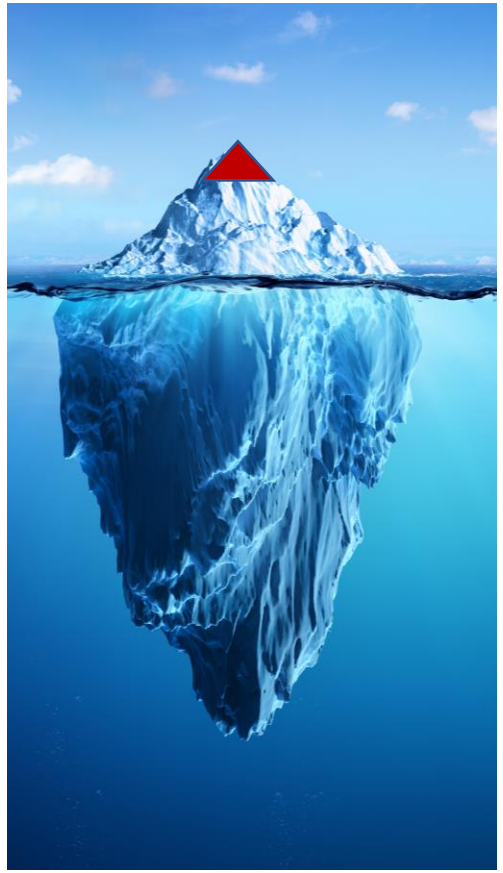
Imperial College London

UK Health Security Agency

Polio: clinical presentations

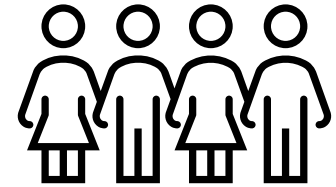
~1/4 will have a flu like illness (e.g. sore throat, fever, tiredness, GI disturbance, headache) for 2-5 days

~3/4 of poliovirus infections are asymptomatic

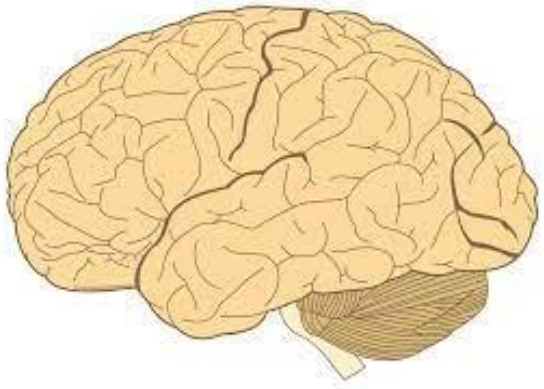


0.5% paralytic poliomyelitis (acute flaccid paralysis)

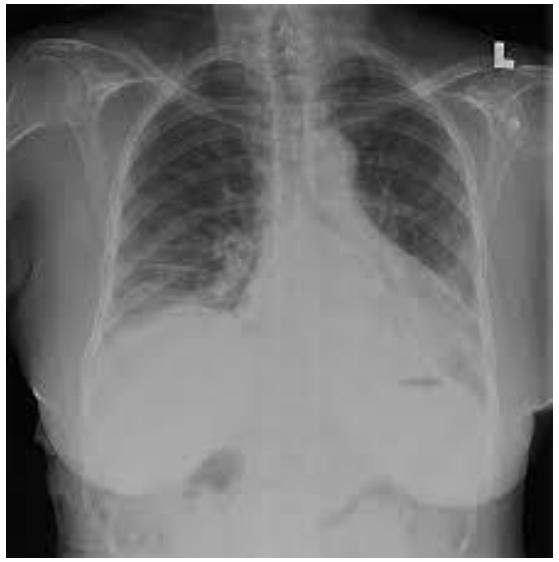
1-5% aseptic meningitis



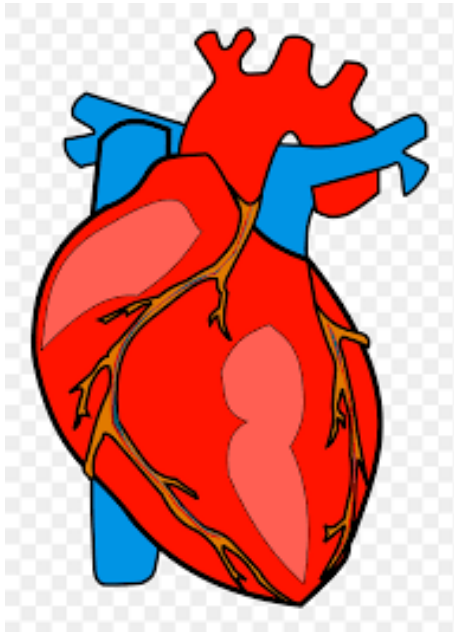
Non-polio enteroviruses: severe presentations



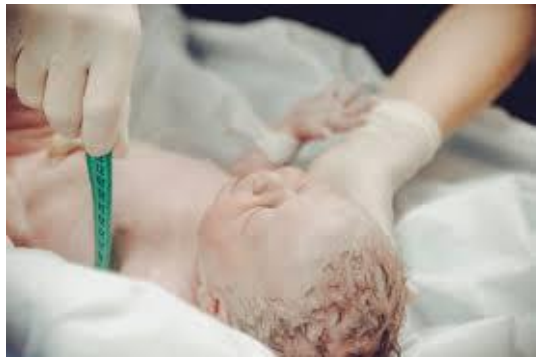
Neurological presentations:
AFP
Aseptic meningitis



Severe respiratory infection



Myocarditis



Neonatal infection

Infections in the immunocompromised

When should you have a higher index of suspicion for poliovirus infection?

Acute flaccid paralysis

Aseptic meningitis

EV positive sample with a neurological condition

e.g. paralytic symptoms, encephalitis, meningism, irritability, headache, convulsions, apnoea, sudden death

EV positive sample from a person with a primary immunodeficiency

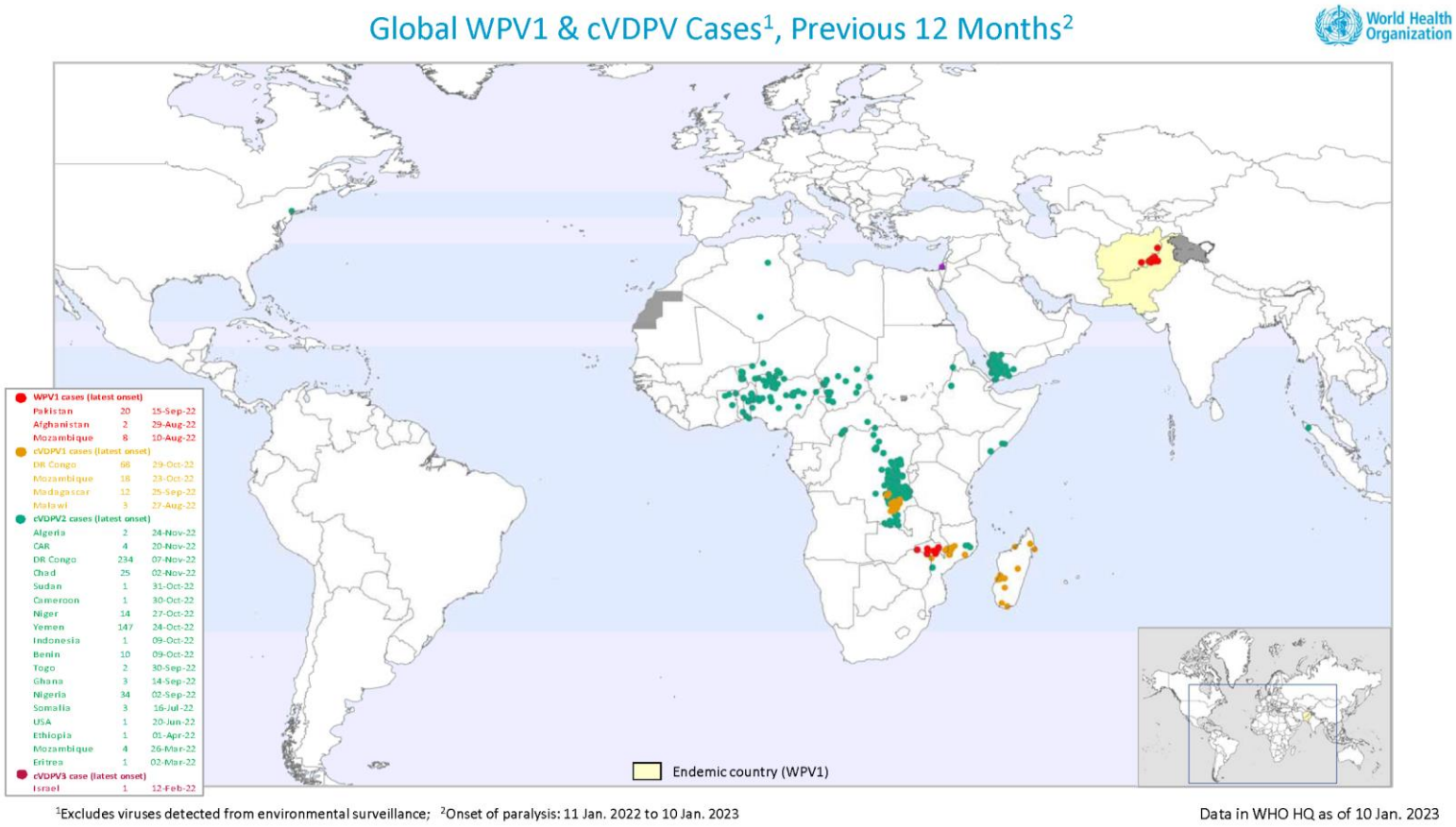
Geographical risk

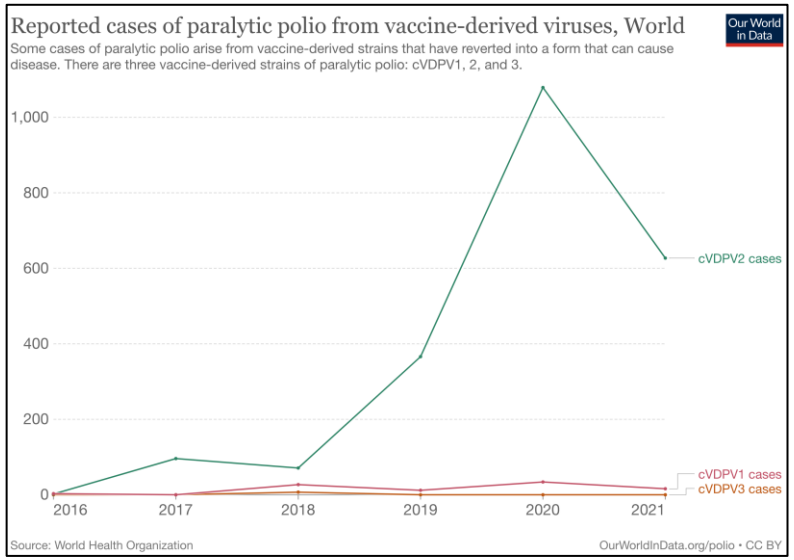
Recent travel to an area where polioviruses are circulating

Vaccination status

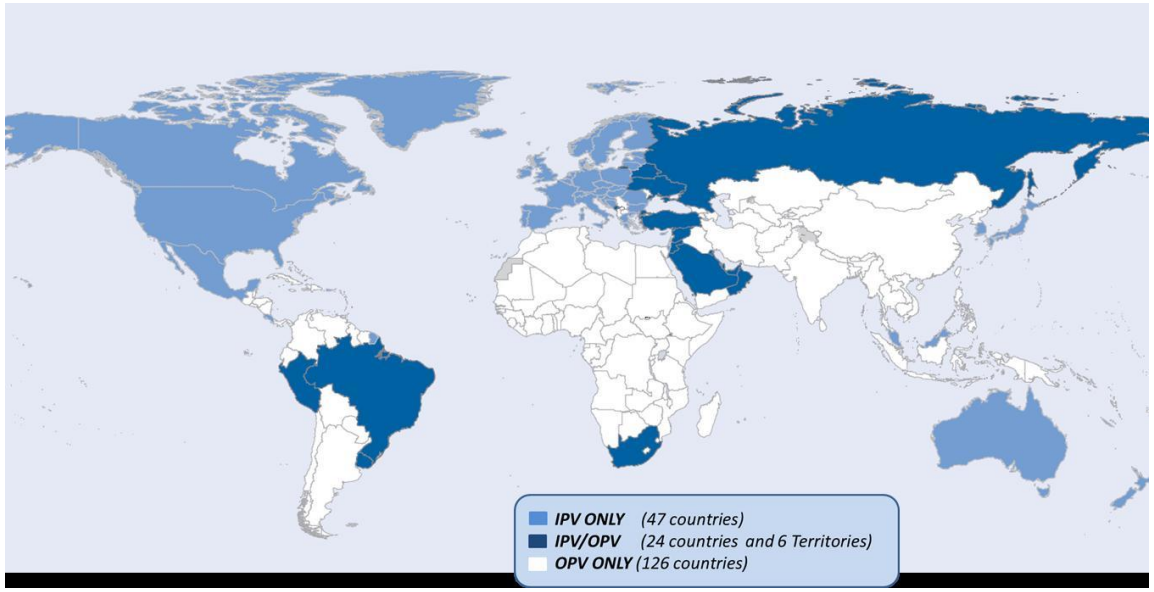
Geographical risk

https://polioeradication.org





Primary immunodeficiency

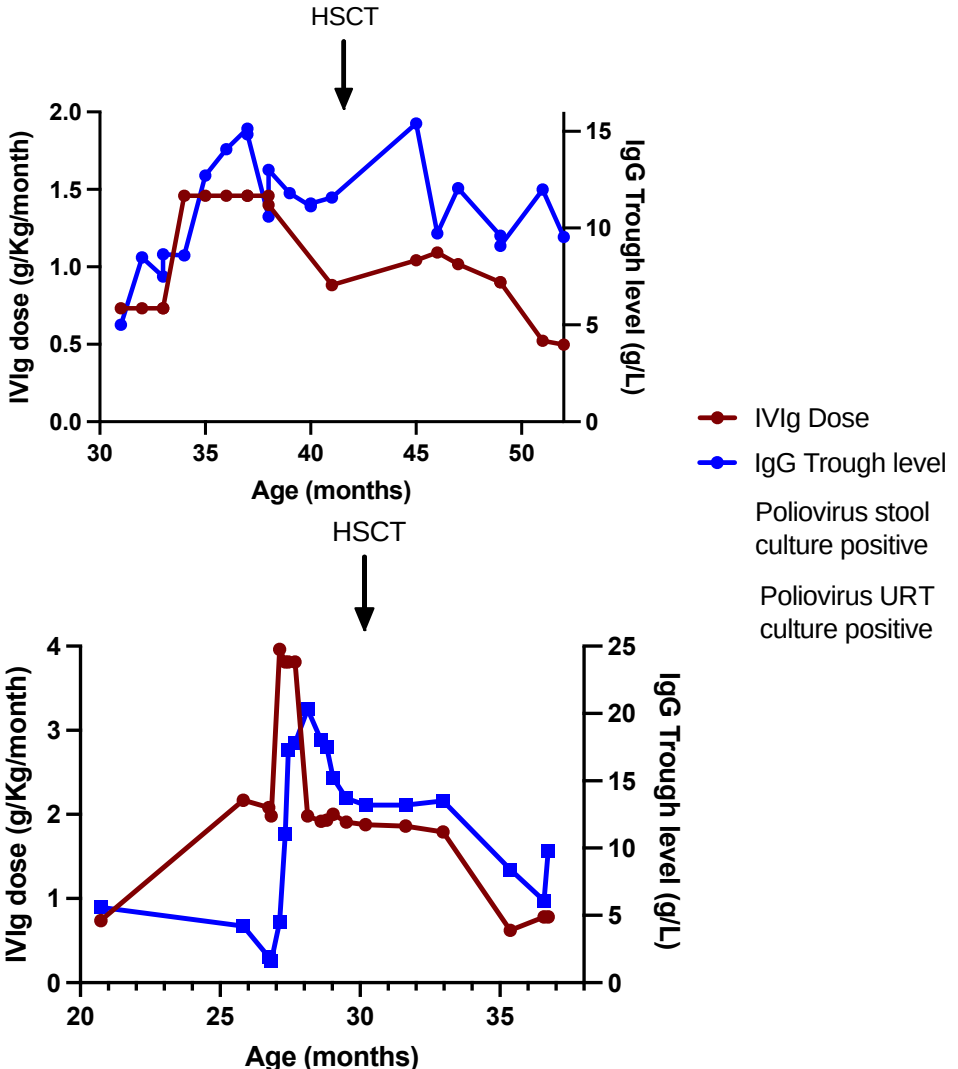


polioeradication.org

- Healthy people excrete OPV for ~3-6 weeks in stool
- PID patients (B cell or combined B+T cell deficiencies) may excrete PV for longer (months-years)
- Virus can evolve, becoming an iVDPV
  - increased risk of paralytic poliomyelitis (VAPP)
- iVDPVs are rarely reported, but may be under detected via current surveillance
- **2 iVDPV excreting PID patients were detected in the UK in 2019**

iVDPV detection in the UK

- iVDPV detected from 2 children with primary immunodeficiency (CD40 ligand and MHC class 2 deficiency) in 2019
- Previous travel/residence in the Middle East (where OPV is used)
- First child detected through national EV surveillance
- Second child detected because the same clinicians had a higher index of suspicion and requested testing
- PV shed for 3 and 4 months respectively, and evolved over time to a more neurovirulent phenotype
- No neurological symptoms
- Clearance of PV shedding after increased dose of IVIG (child 1) or HSCT (child 2)

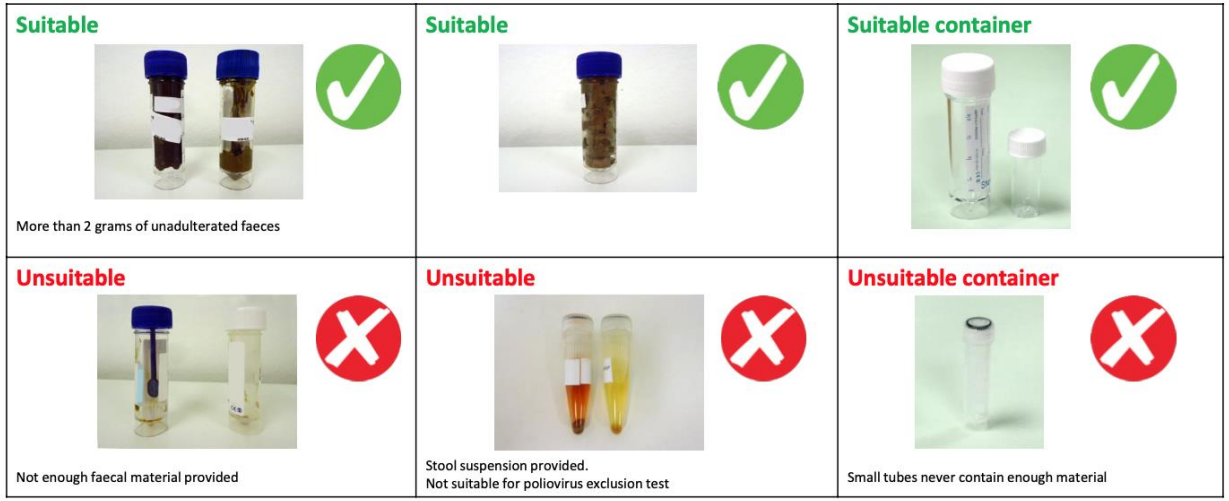


Clinical assessment

- Side room with droplet and contact precautions
  - PV can spread in droplets from URT and feco-orally
- History and Examination
  - Rapid progression of weakness, progressing to max severity within 10 days
  - Often asymmetric, proximal>distal
  - Reduced tone, absent or diminished reflexes
  - Can affect muscles of respiration and swallowing
  - Preceding flu-like symptoms e.g. fever, myalgia, GI disturbance
  - Incubation period – 3-6 days for non-paralytic symptoms, 7-21 days for paralysis
  - Take a vaccination history
  - Travel history, including close contacts
- Investigations e.g. MRI, EMG, LP
- AFP with possible infectious cause is notifiable

Optimum diagnostic test requests

- **The greatest yield for poliovirus is from viral culture of stool specimen**
  - 2x fresh unadulterated stool specimens (>2g 48h apart) with 14 days of onset of symptoms
- Respiratory sample
  - Oropharyngeal swab, NPA
  - EV-D68 less well detected in stool
- CSF (if available)
  - detection of PV/EV-D68 is uncommon
  - negative CSF does not exclude
- Serum/plasma



Send to **Virus Reference Department, UKHSA Colindale**

Can be discussed with Duty Virologist

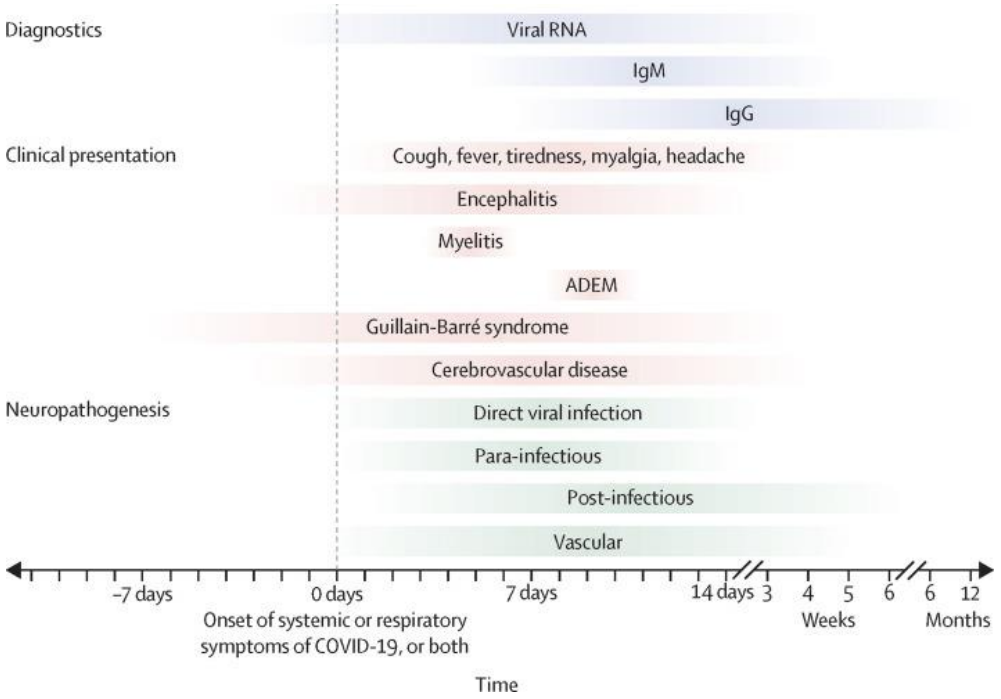
Conclusions

- Think of poliovirus and non-polio enteroviruses in neurological presentations such as AFP, aseptic meningitis and others
- Factor in GEOGRAPHICAL RISK and vaccination status
- Notify all AFP cases with a possible infectious cause
- Consider sending EV positive samples (e.g. stool) [particularly where recent travel to an area with polio circulating] for typing and polio exclusion
- STOOL is the optimum sample for polio exclusion (>2g unadulterated, 2x samples 48h apart)

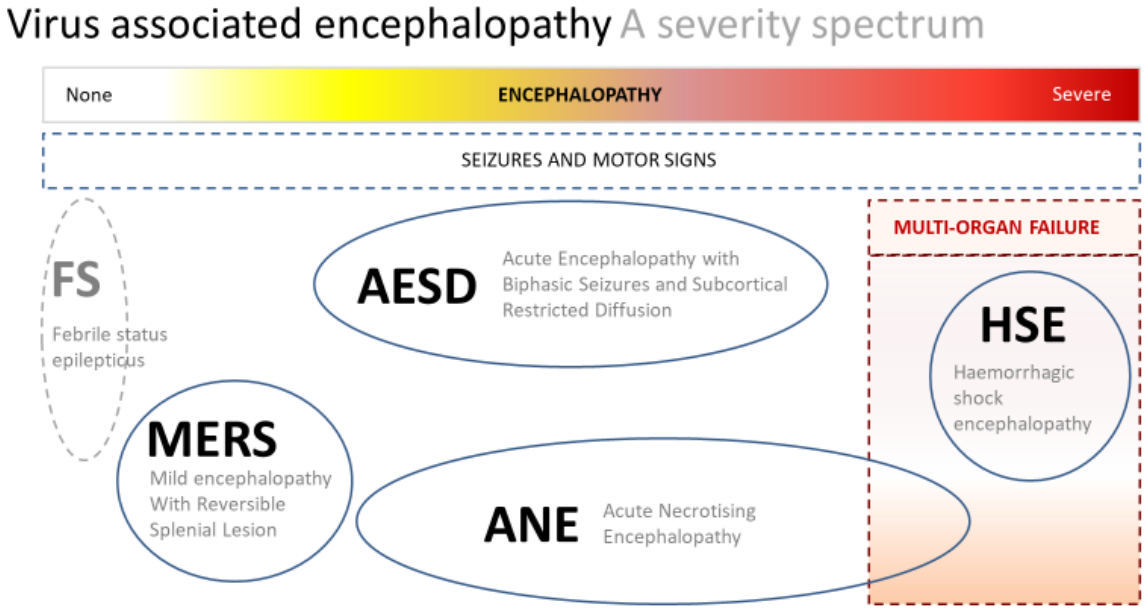
Severe enterovirus CNS disorders

Dr Ming Lim
Consultant and Reader in Paediatric Neurology
Head of Service Children's Neurosciences
Evelina R&D and Paediatric CRF Lead
Children's Neurosciences, Evelina London Children's Hospital, Kings Health Partners Academic Health Science Centre
Women & Children's Health, Faculty of Life Sciences and Medicine, Kings College London
Ming.lim@gstt.nhs.uk

The spectrum of virus associated CNS syndromes



Courtesy of Dr Terence Thomas, Singapore



Lancet Neurol. 2020 Sep; 19(9): 767–783

Outbreaks of enterovirus infections

	1973	1980	1986	1990	1993	1994	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Singapore	..	..	..	..	..	..	B3, B4	B3, C1	B3	B4*	B4	C1, B4	B4	-	-	B5	-	B5
Peninsular Malaysia	..	..	..	..	..	..	B3*, B4*, C1†, C2†	C1	B4, C1	B4*, C1*	-	-	-	-	B5*, C1	-	-	-
Sarawak, Malaysia	..	..	..	..	..	..	B3*	C1	None‡	B4*, C1	None‡	C1	B5, C1	None‡	B5	B5		
Perth, Australia	..	..	..	..	..	..	..	..	B3, C2	C1	None‡	None‡	-	-	-	-	-	-
Japan	B1	..	..	B2, C1	B2	C3	B3, B4, C2	C2	C2	B4	C2	B4, C2	C4, B5	C4	-	C4	C4	-
Taiwan	..	B1	B1	..	..	..	..	C2*, B4†	B4	B4*	B4	B4, C4†	B4, B5†	C4*	C4*, C5†	C5	C5, B5	B5*
Korea	..	..	..	..	..	..	..	..	..	C3*	None‡	None‡	C4	-	-	-	-	-
Brunei	..	..	..	..	..	..	..	..	..	-	-	-	-	-	-	B5	-	-
Vietnam	..	..	..	..	..	..	..	..	..	-	-	-	-	-	C1, C4, C5	-	-	-
Thailand	..	..	..	..	..	..	..	..	..	-	-	C1	C1	C1	-	B5, C1, C2, C4	B5, C1, C2, C4, C5	B5†, C1, C2†, C4*
China	..	..	..	..	..	..	C3	C4	..	C4	C4	C4	C4	C4	-	-	C4	C4

*Genotypic subgroups caused large outbreaks. †Genotypic subgroup isolated in a small number of patients. ‡No enterovirus 71 detected, despite active surveillance.

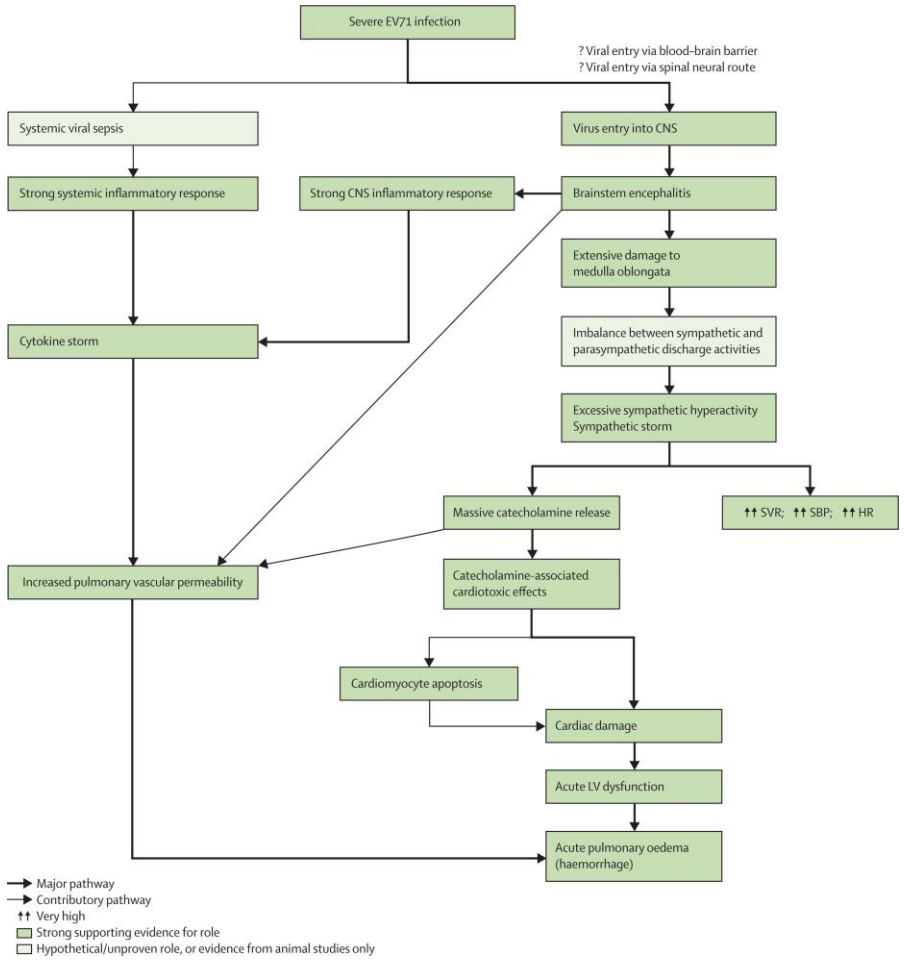
Table 2: Enterovirus 71 genotypic subgroups reported to be circulating in the Asia-Pacific region between 1973 and 2008, by year[8-14,45-53]

2013

Lancet Infect Dis. 2010 10(11):778-90

JAMA Neurol 2016 73(3):300-7

Clinical Classification of Patients With EV71 Neurological Disease



Lancet Infect Dis. 2010 10(11):778-90

WHO case definition

• Encephalitis	**11%**	
• Brainstem encephalitis	**35%**	**35-40%**
• Encephalomyelitis	**40%**	
• Acute Flaccid paralysis	**7%**	**95-100%**
• Autonomic instability	**7%**	**10%**
• Neurogenic pulmonary oedema		

JAMA Neurol 2016 73(3):300-7

Lancet. 2021 397(10271):334-346

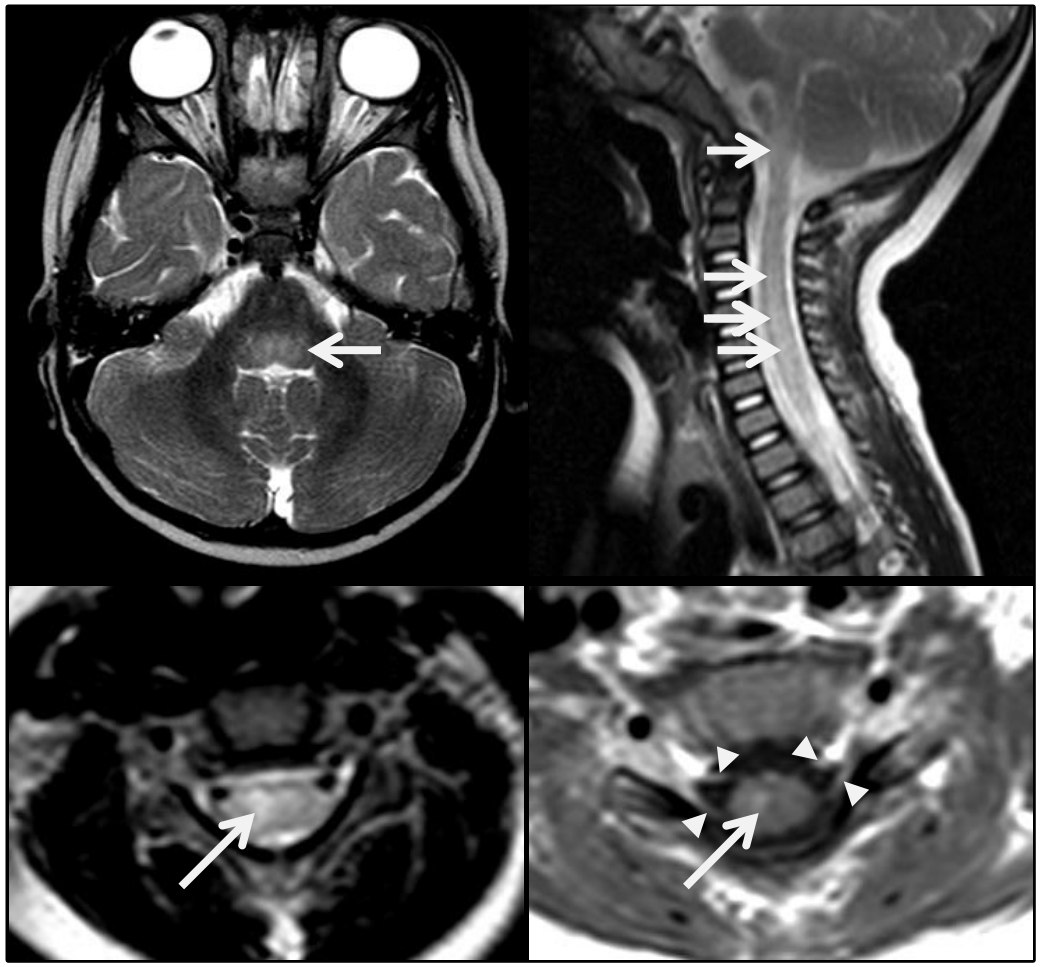
Case 1 18m F

- Previously fit and well
- 48 hour febrile prodrome,
  - Onset of drowsiness, neck stiffness and right arm weakness.
  - Her neurological examination revealed weakness of the right arm with lower motor neuron signs, but no other neurological signs.

Case 1 18m F

- CSF 181 cells/uL (predominantly lymphocytes)
- EMG/NCV revealed a motor axonopathy (reduced CMAP) with normal sensory studies.
  - In addition, there is evidence of partial denervation in the right upper limb

Enterovirus 71 identified in the stool



Case 1 18m F

- D4 treated IVIG
- D 15 days she was discharged with an improvement of her cognitive skills and her communicative function but still being unable to move her right arm properly (weak with incomplete swing).
- At latest follow-up (3 months) she currently fully ambulant but still with low tone in her right arm, with deltoid atrophy and no reflexes.

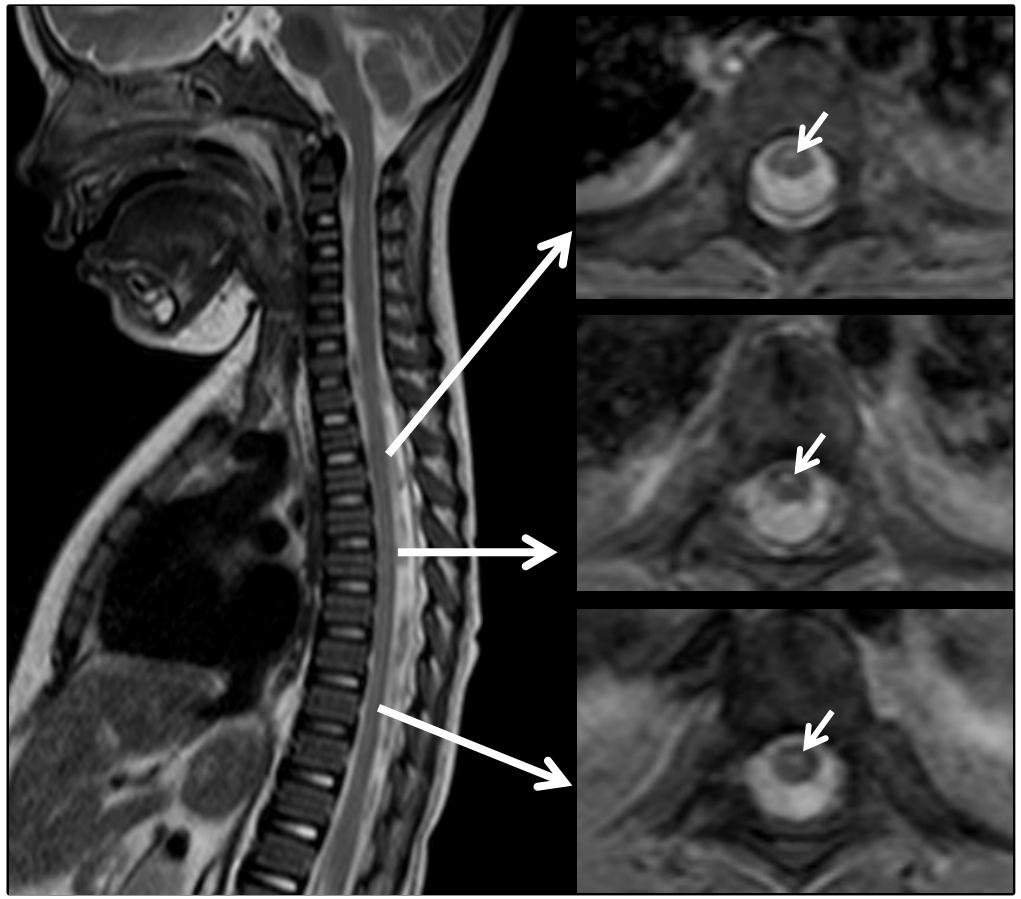
Case 2 3yr F

- Three day febrile prodrome
- Decreased oral intake, vomiting, being lethargic and without any evidence of diuresis for the last 24 hours.
- She presented in the emergency room with a septic shock, with poor peripheral perfusion, tachycardia and hypotension requiring 130 ml/kg of fluids and inotropic support, she was intubated and admitted to the PICU

Case 2 3yr F

- IVIG for treatment, there she spent 15 days.
- During her admission, she developed with profound global flaccid paralysis in all four limbs with no anti-gravity movements

➢ EMG/NCV revealed generalized axonal motor neuropathy, with sensory sparing



Case 2 3yr F

- Plasmapheresis was started
  - Sat up with support and head control
  - Upper limbs remained the same some anti-gravity movements in lower limbs were seen with return of deep tendon reflexes
- D23 Discharge
- 2 month- no deficit

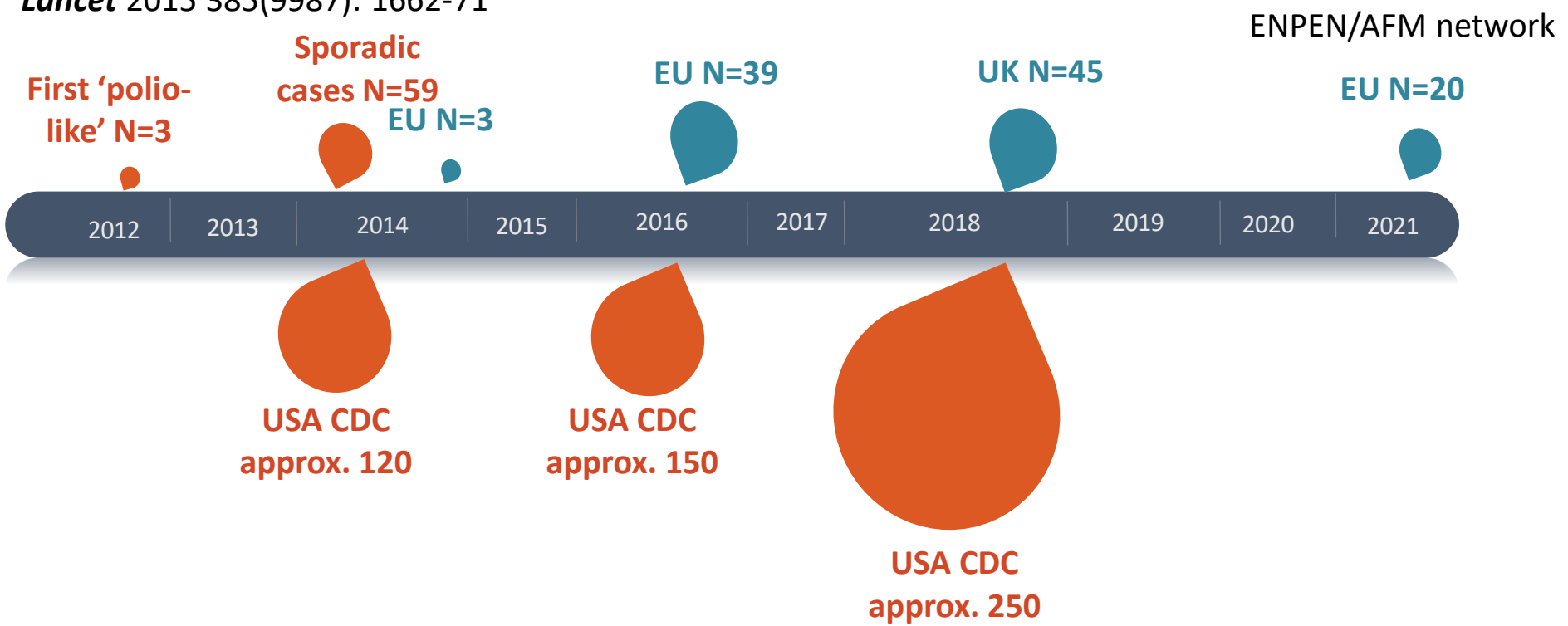
No viral isolates

“Novel” outbreak of acute flaccid paralysis

Lancet Infect Dis 2015 15(6):671-82

Lancet 2015 385(9987): 1662-71

Euro Surveill 2019 24(6):1900093



https://www.cdc.gov/acute-flaccid-myelitis/afm-cases.html

Clinical surveillance

- Polio is a notifiable infection – so if you suspect polio please notify to your local Health Protection Team
- Health professionals are strongly encouraged to fully investigate and report any suspected case of Acute Flaccid Paralysis or Acute Flaccid Myelitis (AFP/AFM) that may be due to an infectious cause
- For any patient presenting with AFP/AFM:
  - Report to UKHSA national duty doctor (020 8200 4400) 9am – 5.30pm 7 days per week
  - Complete an enhanced surveillance questionnaire (by responsible clinician)

- *AFP or AFM is characterised by rapid onset of weakness of an individual's extremities, often including weakness of the muscles of respiration and swallowing, progressing to maximum severity within 10 days. The term 'flaccid' indicates weakness accompanied by hyporeflexia or areflexia in the affected limb(s)*

[PHE document (publishing.service.gov.uk)]

Summary of clinical symptoms reported in *suspected* AFP cases (n=66)

- 67% reported respiratory symptoms preceding AFP symptoms
- 15% reported an underlying Illness
- 32% admitted to ITU

- Limbs affected:
  1 limb- 11%
- 2 limbs- 36% (62% lower limbs)
- 3 limbs- 6%
- 4 limbs- 47%

-

Clinical/epidemiological feature	Estimated frequency
Age<21	80-90%
Prodromal fever or viral illness	85-95%
Neurological onset to nadir <10 days	100%
Headache or neck stiffness at onset	12-60%
Asymmetric onset of weakness	65-95%
Limb weakness	85-95%
Upper limb weakness	60-85%
Flaccidity and/or hyporeflexia of affected limbs	95-100%
Neck, face, extraocular, and/or bulbar weakness	20-60%
Trunk weakness	30-70%
Requirement for mechanical ventilation	10-40%
Bladder or bowel dysfunction	5-40%
Non-specific sensory symptoms e.g. paresthesia	10-20%
Cardiovascular autonomic dysfunction	<10%
CSF pleocytosis (with testing <5 days after onset)	85-95%
Gray-matter predominant spinal cord lesion(s) on MRI	95-100%
Brainstem lesion(s) on MRI	35-45%
Cerebral deep gray matter lesion(s) on MRI	<5%

Lancet. 2021 397(10271):334-346

Clinical presentation

- Many of us have not seen an acute presentation of polio for quite some time!
- Viral prodrome
  - URTI and gastrointestinal
- The key neurological presentation is
  - Limb weakness often asymmetric
    Flaccid and/or hypoflexic
    Upper limbs versus lower limbs
  - Head and neck involvement
  - Trunk involvement
  - Sensory symptoms
  - Can start off with a headache or neck stiffness
  - Bladder and bowel dysfunction

Lancet. 2021 Jan 23;397(10271):334-346

Initial clinical assessments

- Consider AFM in patients presenting with rapid-onset weakness, particularly when occurring during or shortly following a suspected viral illness.
- Complete neurological examination should include specific tests for proximal muscle weakness (such as standing up from a seated position on the floor), axial weakness (neck and trunk flexion and extension), and cranial nerve abnormalities.
- Clinical features atypical for AFM include encephalopathy unrelated to metabolic disturbance, seizures, extensive sensory abnormalities, or evolution to nadir over more than 10 days.
- Neurology and infectious disease specialists should be consulted (where available) to help with diagnosis, evaluation, and treatment.
- Admission to intensive care unit should be considered when indicated, and close monitoring for respiratory or autonomic deterioration, or both, is essential.

Lancet. 2021 Jan 23;397(10271):334-346

Key investigations

Neuroimaging

- The **characteristic MRI abnormality** is grey-matter predominant T2 hyperintensity of the spinal cord with associated spinal cord oedema; lesion(s) are usually longitudinally extensive and non-enhancing. Nerve root enhancement might be present.
- Repeat MRI can be considered after further clinical evolution in patients with a suggestive clinical presentation but in whom early MRI of the spinal cord is apparently normal

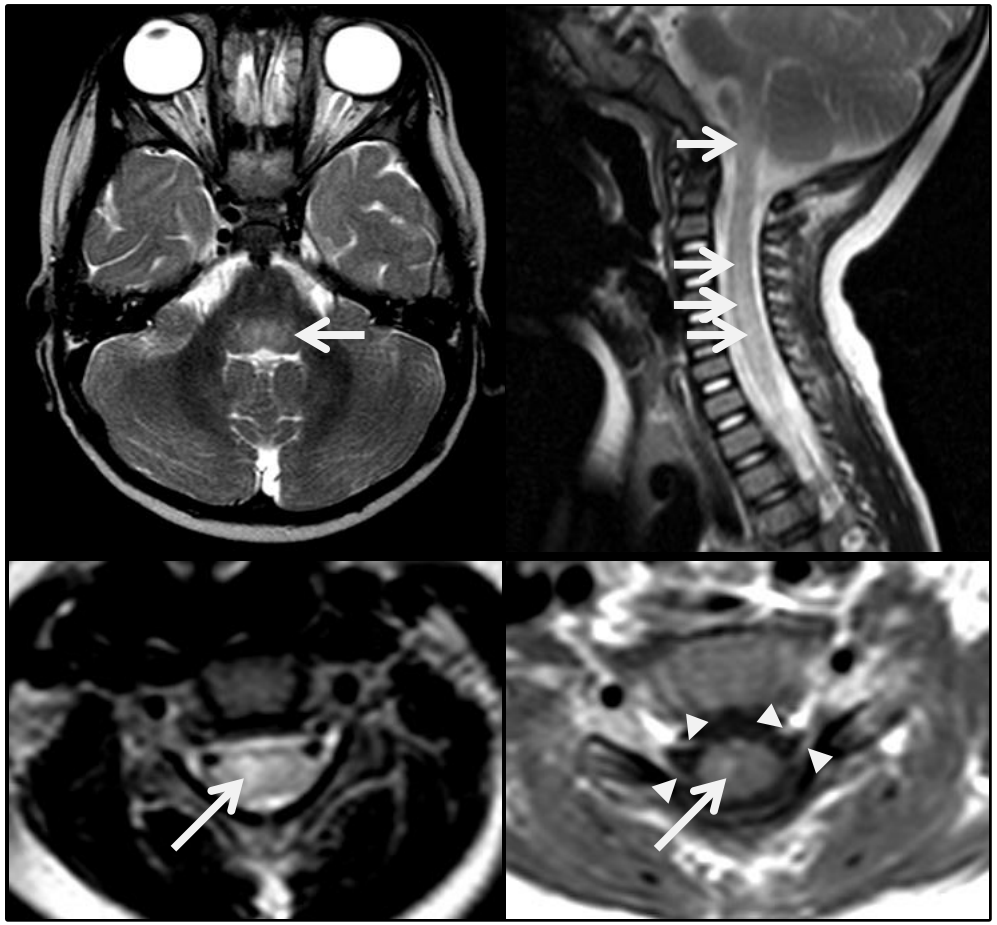
Neurophysiology

Lumbar puncture

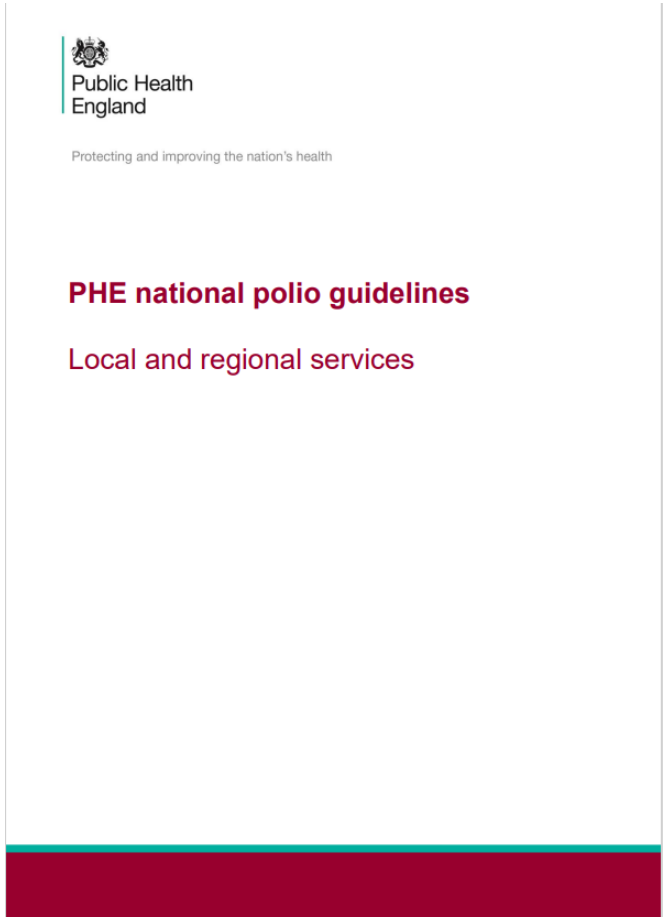
- CSF **pleocytosis**
- Specific diagnostic investigations

Laboratory evaluations

Respiratory, stool, serum, and CSF samples



Laboratory surveillance



- AFM/AFP cases - collect the following samples for poliovirus isolation and characterisation:
  - 2 stool samples 48 hours apart
  - Throat swabs/naso-pharangyeal aspirate (NPA) and
  - Cerebro-spinal fluid (CSF) (if collected)
- Stool samples are encouraged for all acute neurological illness presentations including meningitis
- Local and regional laboratories should refer all local enterovirus positive samples to the Enteric Virus Unit (EVU) – *need to increase referral of samples to the ref laboratory*
- PHE National Polio Guidelines - Local and regional services (publishing.service.gov.uk)

UK Health Security Agency

Notification Requirements

National Guidance


GOV.UK Menu

Home > Infectious diseases

Collection

Polio: guidance, vaccination, data and analysis

The diagnosis, vaccination, management and epidemiology of polio (poliomyelitis).

From: UK Health Security Agency
Published 23 October 2013
Last updated 10 August 2022 — See all updates

Contents
— Diagnosis
— Clinical management
— Data collection
— Immunisation programme and resources

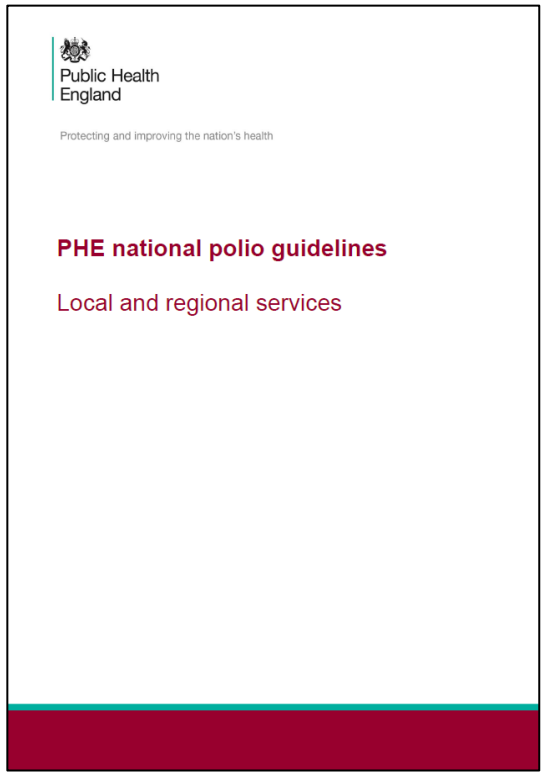
Related content
Inactivated polio vaccine (IPV) booster: information for healthcare practitioners
Polio vaccination campaign letter
Polio: national guidelines
Polio booster campaign resources
Polio: surveillance form

Poliomyelitis (polio) is a highly infectious vaccine preventable disease. It is a notifiable disease in England and Wales.

Polio invades the nervous system and can cause total paralysis in a matter of hours (see acute flaccid paralysis). It can strike at any age but affects mainly children under 3 years old. Most people infected with the poliovirus have no signs of illness. Symptomless people can spread the infection to thousands of others before the first case of polio paralysis emerges.

See enterovirus infections for further information.

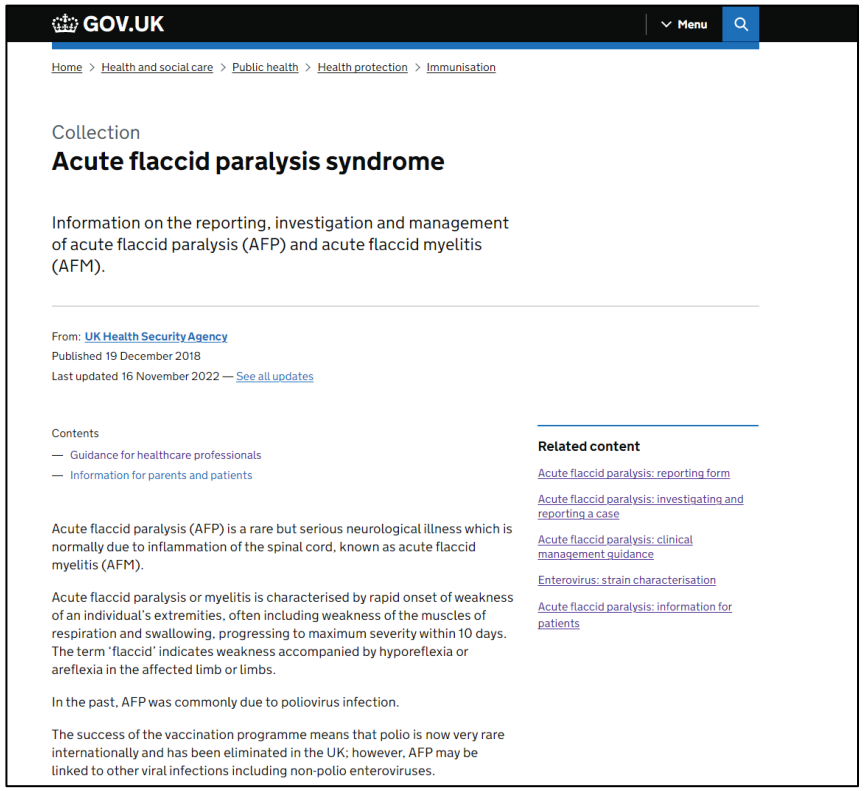
For the latest international news on polio see statements from the World Health Organization (WHO) and news from the National Travel Health


Public Health England

Protecting and improving the nation's health

PHE national polio guidelines

Local and regional services


GOV.UK Menu

Home > Health and social care > Public health > Health protection > Immunisation

Collection

Acute flaccid paralysis syndrome

Information on the reporting, investigation and management of acute flaccid paralysis (AFP) and acute flaccid myelitis (AFM).

From: UK Health Security Agency
Published 19 December 2018
Last updated 16 November 2022 — See all updates

Contents
— Guidance for healthcare professionals
— Information for parents and patients

Related content
Acute flaccid paralysis: reporting form
Acute flaccid paralysis: investigating and reporting a case
Acute flaccid paralysis: clinical management guidance
Enterovirus: strain characterisation
Acute flaccid paralysis: information for patients

Acute flaccid paralysis (AFP) is a rare but serious neurological illness which is normally due to inflammation of the spinal cord, known as acute flaccid myelitis (AFM).

Acute flaccid paralysis or myelitis is characterised by rapid onset of weakness of an individual's extremities, often including weakness of the muscles of respiration and swallowing, progressing to maximum severity within 10 days. The term 'flaccid' indicates weakness accompanied by hyporeflexia or areflexia in the affected limb or limbs.

In the past, AFP was commonly due to poliovirus infection.

The success of the vaccination programme means that polio is now very rare internationally and has been eliminated in the UK; however, AFP may be linked to other viral infections including non-polio enteroviruses.

https://www.gov.uk/government/collections/polio-guidance-data-and-analysis

https://www.gov.uk/government/collections/acute-flaccid-paralysis-syndrome

Health Protection Regulations 2010

- Regulation 2(1)(b) of the Health Protection (Notification) Regulations 2010 place a duty on registered medical practitioners (RMPs) to report any suspected infections that present or could present significant harm to human health.
- This covers reporting of acute flaccid paralysis and acute flaccid myelitis (AFP/AFM) not explained by a non-infectious cause.
- In addition, under Schedule 1 of the Health Protection (Notification) Regulations 2010, suspected cases of acute poliomyelitis are notifiable.
  - This situation is extremely rare. The last UK acquired case of polio was notified in 1984.
- Appropriate testing of AFP or AFM cases not explained by a non-infectious cause, to exclude polio as a causative agent, is an integral component of clinical management and polio surveillance.

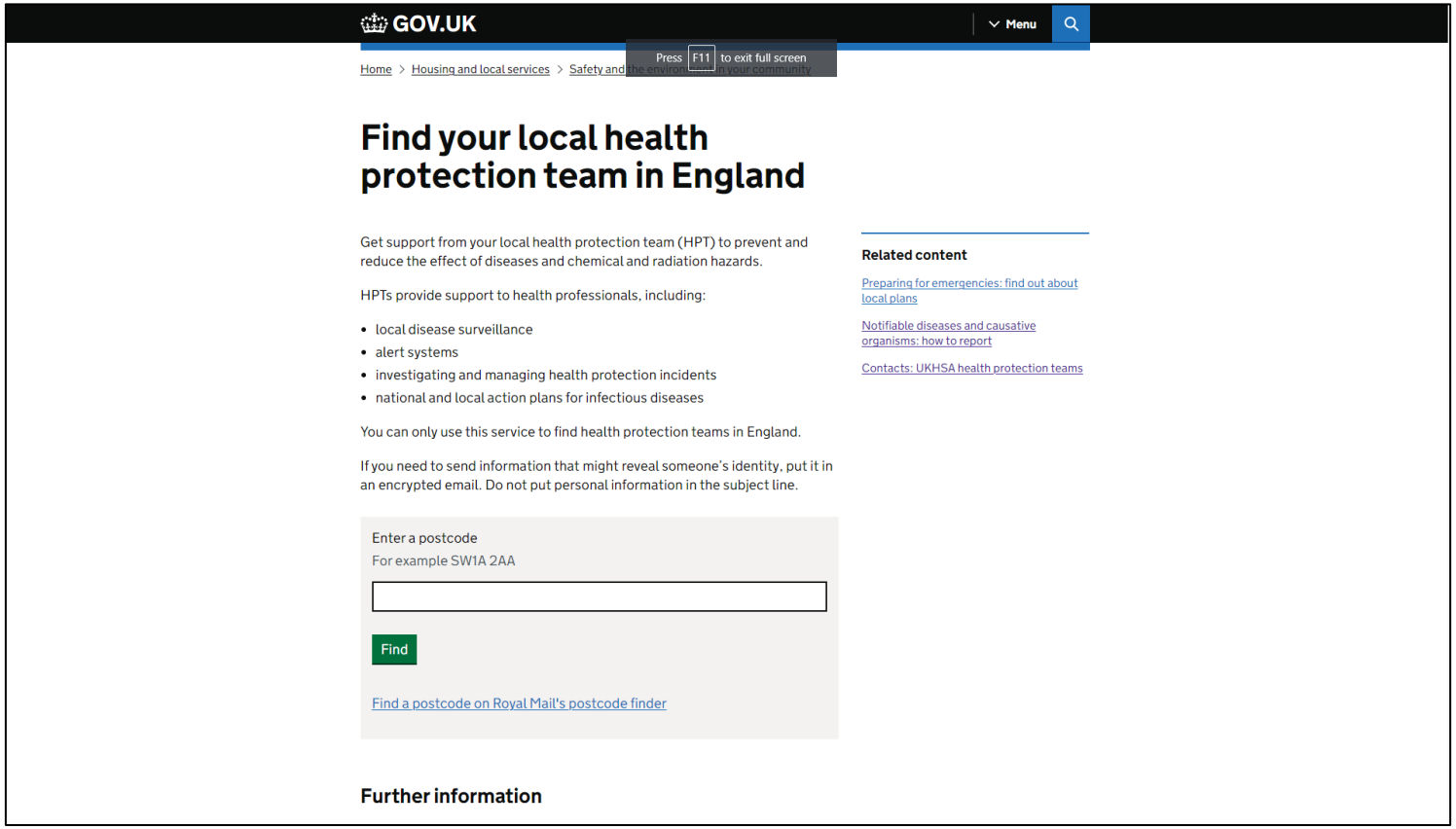
Acute flaccid paralysis syndrome

- **Case definition**: acute flaccid paralysis/myelitis is characterised by rapid onset of weakness of an individual's extremities, often including weakness of the muscles of respiration and swallowing, progressing to maximum severity within 10 days. The term 'flaccid' indicates weakness accompanied by hyporeflexia or areflexia in the affected limb or limbs

- Clinicians should perform the following actions for patients meeting the above case definition:

1. Report the case of AFP/AFM to your local Health Protection Team by telephone during working hours (same day or next day)

Find your local Health Protection Team



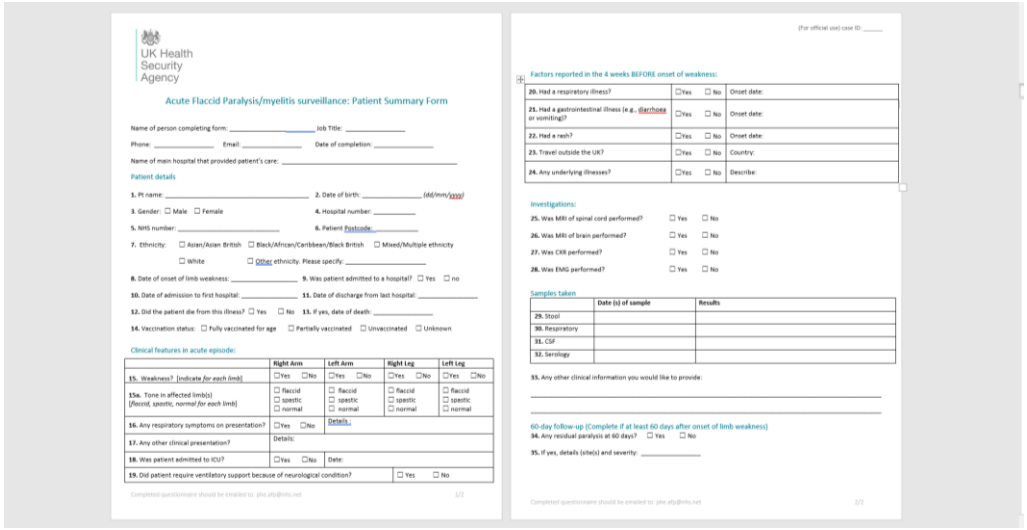
https://www.gov.uk/health-protection-team

Notification of AFP/ AFM

2. Inform your local virology or microbiology on call clinician
3. Collect the following samples and send to the UKHSA Virus Reference Department for poliovirus isolation and further characterisation via your local laboratory
   a) 2 stool samples 48 hours apart
   b) throat swabs or nasopharyngeal aspirate (NPA) and
   c) cerebrospinal fluid (CSF) (if collected)
4. Complete an enhanced surveillance questionnaire

Enhanced Surveillance Questionnaire

- Patient details
- Presenting symptoms, particularly neurological and respiratory symptoms
- Investigations performed to date, including virology, and results
- Details and results of any neuroradiological investigations
- Polio vaccination history, if available
- Recent overseas travel history, if available



UK Health Security Agency

Acute Flaccid Paralysis/myelitis surveillance: Patient Summary Form

Name of person completing form: _____ Job Title: _____

Phone: _____ Email: _____ Date of completion: _____

Name of main hospital that provided patient's care: _____

Patient details

1. Pt name: _____ 2. Date of birth: _____ (dd/mm/yyyy)

3. Gender: ☐ Male ☐ Female 4. Hospital number: _____

5. NHS number: _____ 6. Patient Postcode: _____

7. Ethnicity: ☐ Asian/Asian British ☐ Black/African/Caribbean/Black British ☐ Mixed/Multiple ethnicity ☐ White ☐ Other ethnicity. Please specify: _____

8. Date of onset of limb weakness: _____ 9. Was patient admitted to a hospital? ☐ Yes ☐ no

10. Date of admission to first hospital: _____ 11. Date of discharge from last hospital: _____

12. Did the patient die from this illness? ☐ Yes ☐ No 13. If yes, date of death: _____

14. Vaccination status: ☐ Fully vaccinated for age ☐ Partially vaccinated ☐ Unvaccinated ☐ Unknown

Clinical features in acute episode:

	Right Arm	Left Arm	Right Leg	Left Leg
15. Weakness? (Indicate for each limb)	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
15a. Tone in affected limb(s) (flaccid, spastic, normal for each limb)	☐ flaccid ☐ spastic ☐ normal	☐ flaccid ☐ spastic ☐ normal	☐ flaccid ☐ spastic ☐ normal	☐ flaccid ☐ spastic ☐ normal
16. Any respiratory symptoms on presentation?	☐Yes ☐No	Details:		
17. Any other clinical presentation?	Details:			
18. Was patient admitted to ICU?	☐Yes ☐No	Date:		
19. Did patient require ventilatory support because of neurological condition?	☐ Yes ☐ No			

Completed questionnaire should be emailed to: phe.afp@nhs.net 1/2

(For official use) case ID: _____

Factors reported in the 4 weeks BEFORE onset of weakness:

20. Had a respiratory illness?	☐Yes ☐ No	Onset date:
21. Had a gastrointestinal illness (e.g., diarrhoea or vomiting)?	☐Yes ☐ No	Onset date:
22. Had a rash?	☐Yes ☐ No	Onset date:
23. Travel outside the UK?	☐Yes ☐ No	Country:
24. Any underlying illnesses?	☐Yes ☐ No	Describe:

Investigations:

25. Was MRI of spinal cord performed? ☐ Yes ☐ No

26. Was MRI of brain performed? ☐ Yes ☐ No

27. Was CXR performed? ☐ Yes ☐ No

28. Was EMG performed? ☐ Yes ☐ No

Samples taken

	Date (s) of sample	Results
29. Stool		
30. Respiratory		
31. CSF		
32. Serology		

33. Any other clinical information you would like to provide:

_____

_____

60-day follow-up (Complete if at least 60 days after onset of limb weakness)

34. Any residual paralysis at 60 days? ☐ Yes ☐ No

35. If yes, details (site(s) and severity: _____

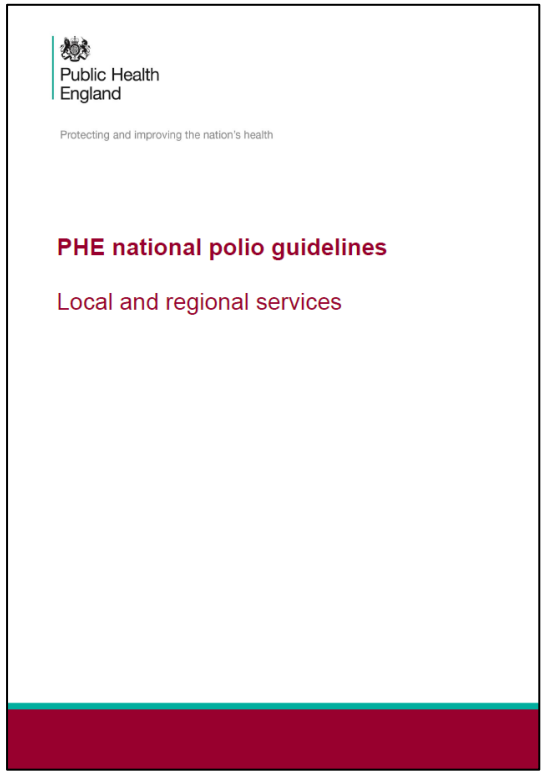
Completed questionnaire should be emailed to: phe.afp@nhs.net 2/2

Aims of Surveillance

- Investigate and exclude poliovirus infection
- Investigate the potential contribution of other enteroviruses, especially enterovirus D68
- Systematically characterise the illness and document long-term sequelae
- Increase awareness of guidance on investigation and management of cases
- Act as a focal point for national and international collaboration

Suspected acute poliomyelitis

- Clinical suspicion of acute paralytic poliomyelitis
  - Case definition: a patient with clinical features compatible with paralytic poliomyelitis from whom either vaccine derived or wild poliovirus has been isolated from a clinical specimen
- Laboratory report of poliovirus detected in stool, respiratory or other sample
- Clinical, laboratory and epidemiological details (e.g. travel, vaccination status) will determine level of subsequent public health response.



Thank you for listening.

- Any questions?

UK Health Security Agency

National Enterovirus Survey Key Findings

Alexander Allen
19/01/23

Uptake

In total, 41 labs responded. The breakdown by NHS region:

North West:	**7**
North East & Yorkshire:	**3**
Midlands:	**6**
East of England:	**3**
South West:	**2**
South East:	**9**
London:	**11**

The most common respondents were lab managers followed by virologists and biomedical scientists.

Lab manager	**15**
Biomedical scientist	**8**
Clinical Scientist	**2**
Virology/Molecular Service Manager	**1**
Principal Healthcare Scientist	**1**
Consultant Microbiologist	**4**
Consultant Virologist	**8**

Testing across regions

Variation across regions:

Unsurprisingly higher testing in London. In most regions, respiratory sample testing was the highest, with most regions (outside of London) testing around **200** samples per week, about double that of CSF samples.

In particular, there are very low rates of stool testing across every area except London.

Most regions reported testing less than **25** stool samples per week, with the North West and South East reporting less than **10**.

London reported **381** stool samples test, with the great majority coming from **2** labs.

Capacity for testing

There is potential capacity within the lab systems across the country, with most labs currently utilising **50%** or less of their theoretical maximum weekly capacity.

In particular, there is a large capacity to scale up testing on stool samples if needed, with most regions reporting using less than 10% of their maximum weekly capacity.

On the labs that reported this, this would to approximately lead to a spare capacity of around **400** respiratory sample tests, **300** stool samples tests, and **200** CSF tests per week in each region, with London labs having the capacity for around double that.

Assays used for testing

The majority of labs use commercial screening PCR tests for their enterovirus testing. **12** labs conducted testing for the three major sample types (respiratory, CSF and stool). **10** labs only tested CSF samples.

47% (15/32) of responding labs reported that they could not distinguish between enterovirus and rhinovirus on their commercial respiratory sample assays, with the Biomeriuex – Biofire and the AusDiagnostics assays being unable to distinguish between the two.

Three labs reported that while they could not distinguish between the two on respiratory samples, they could on CSF and stool samples

The use of these assays is seen across all regions with at least one lab in each region using them. Biomeriuex – Biofire is more commonly used in the South East, and AusDiagnostics in London.

Referral to Colindale

- **12 l**abs reported sending all enterovirus samples to the Virus Reference Department (VRD) at Colindale
- **9** labs sent only CSF samples
- **5** sent samples that came from suspected Acute Flaccid Paralysis cases
- **3** referred to other (UKHSA) labs
- **5** reported sending no samples to the VRD
- **1** lab sent all samples with a cycle threshold ≤ 30 to Colindale

The most common reason given for not sending samples to Colindale was insufficient resources to pick and send samples or the cost or financial burden, with **18** labs reporting this.

3 labs reported that a significant barrier was an insufficient sample to send, particularly in paediatric cases.

4 labs reported that they were unsure of what samples to send, with one respondent expressing disbelief that we would want all their enterovirus-positive samples

What next?

- Better understand the rationale for the use of the given commercial assays
- Understand the performance characteristics of selected assays and differences in referral patterns
- Understand the barriers to more widescale testing of stool samples
- Understand the widespread differences in testing patterns between regions, and reasons for this
- Investigate any potential inequalities regarding widespread variation in testing patterns

And as part of the WHO requirements for the use of nOPV2, understand any arrangement for Primary Immunodeficiency Disorders (PID) testing

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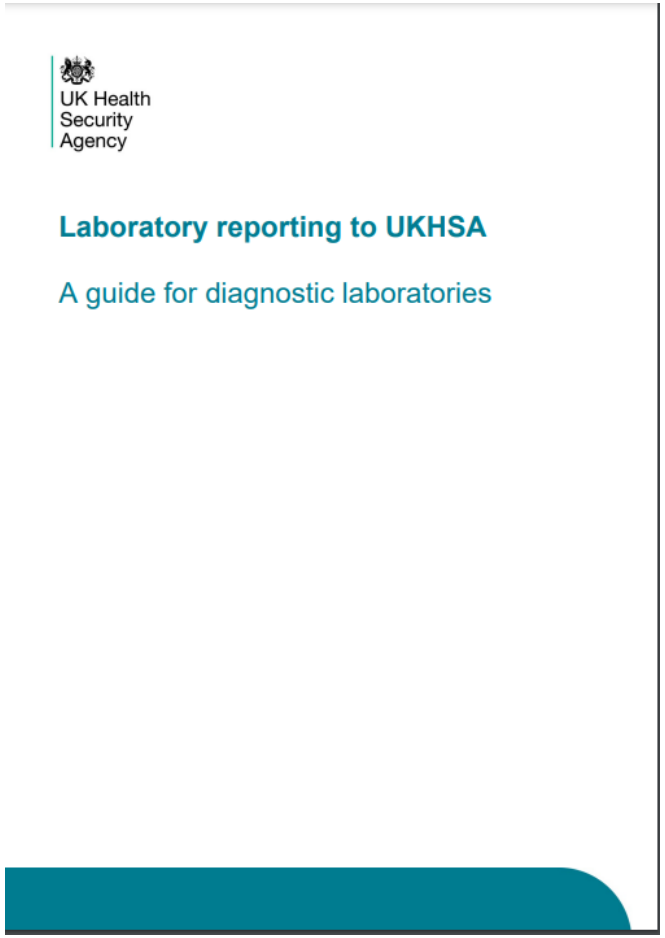
Improving data capture in London: Implications for other regions

Thomas Ma - Field Service South East and London

Dr Karthik Paranthaman - Field Service South East and London

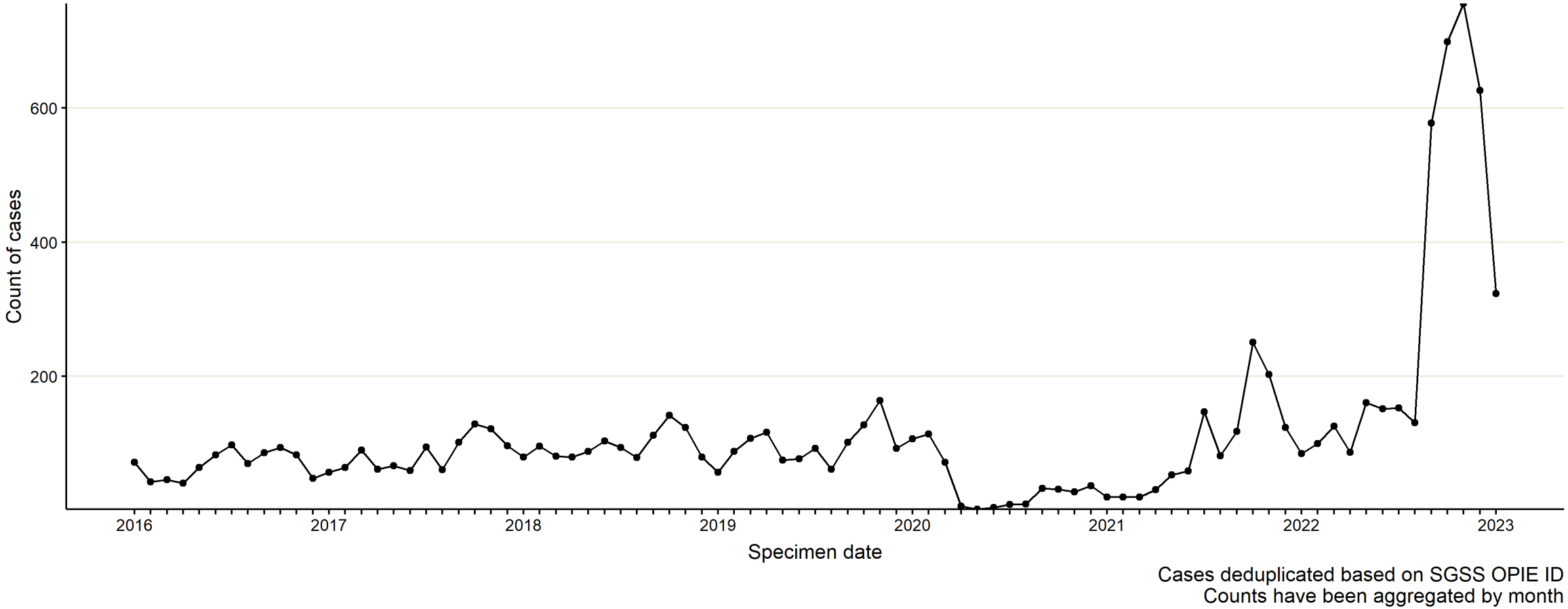
Background

- Diagnostic laboratories have legal obligations to report certain organisms https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1108438/UKHSA_Laboratory_reporting_guidelines__1_.pdf
- Organisms under surveillance by UKHSA are covered by Regulation 3, The Health Service (Control of Patient Information) Regulations 2002
- Work to strengthen laboratory reporting of enterovirus since summer 2022
  - Letter to all DsIPC in London requesting reporting
  - Work with individual laboratories to enable reporting



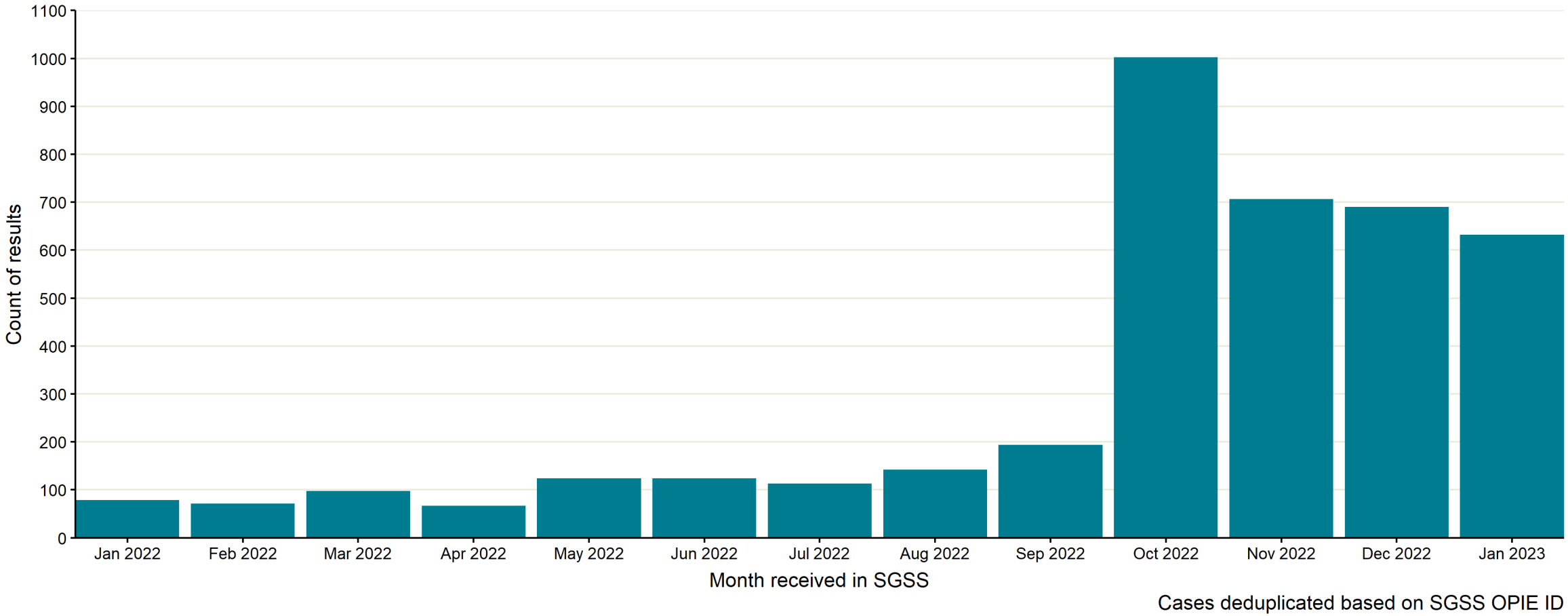
Data as of 27/01/2023

Enterovirus results reported to SGSS, London



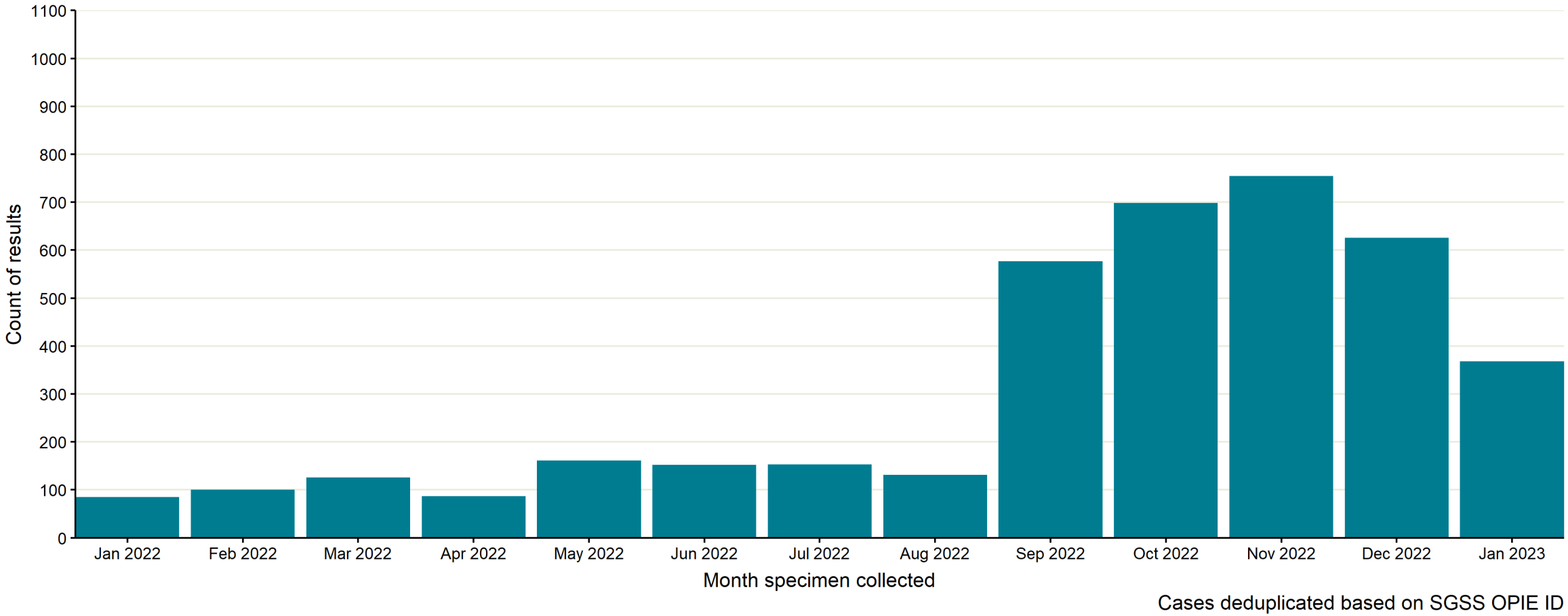
Data as of 27/01/2023

Enterovirus cases in SGSS, London, received date



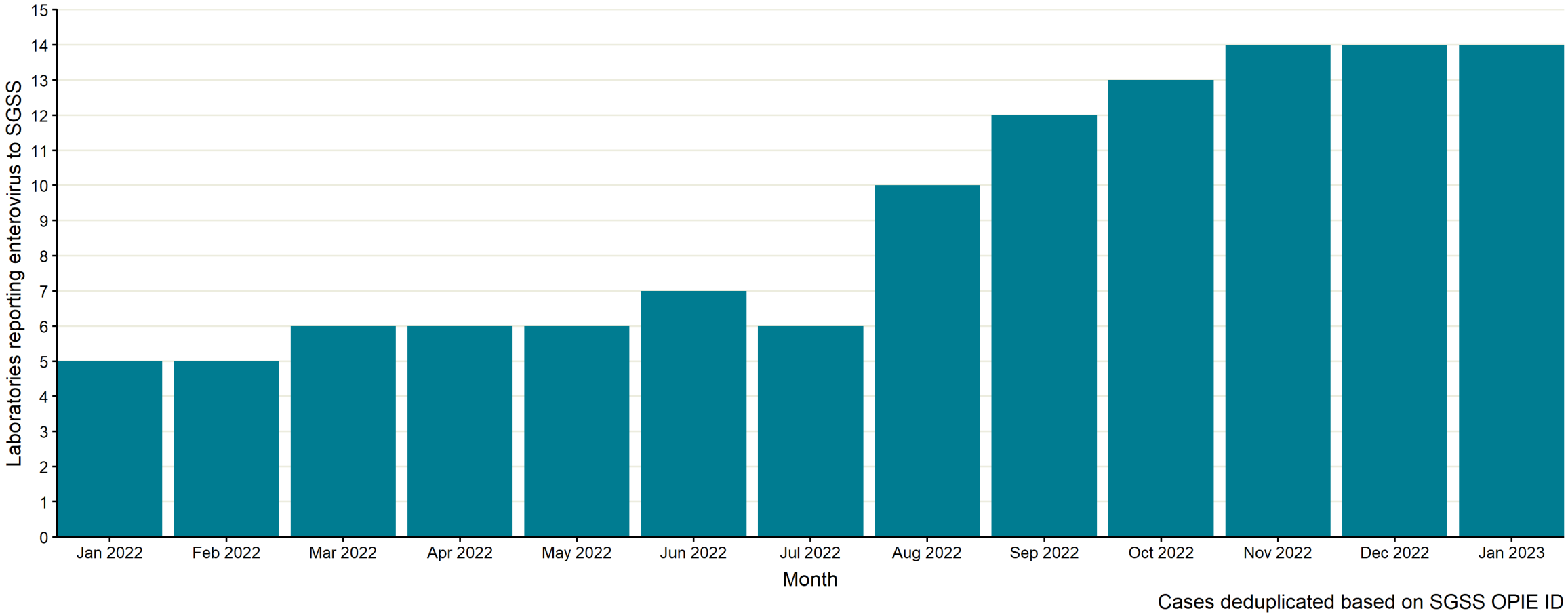
Data as of 30/01/2023

Enterovirus cases in SGSS, London, specimen date



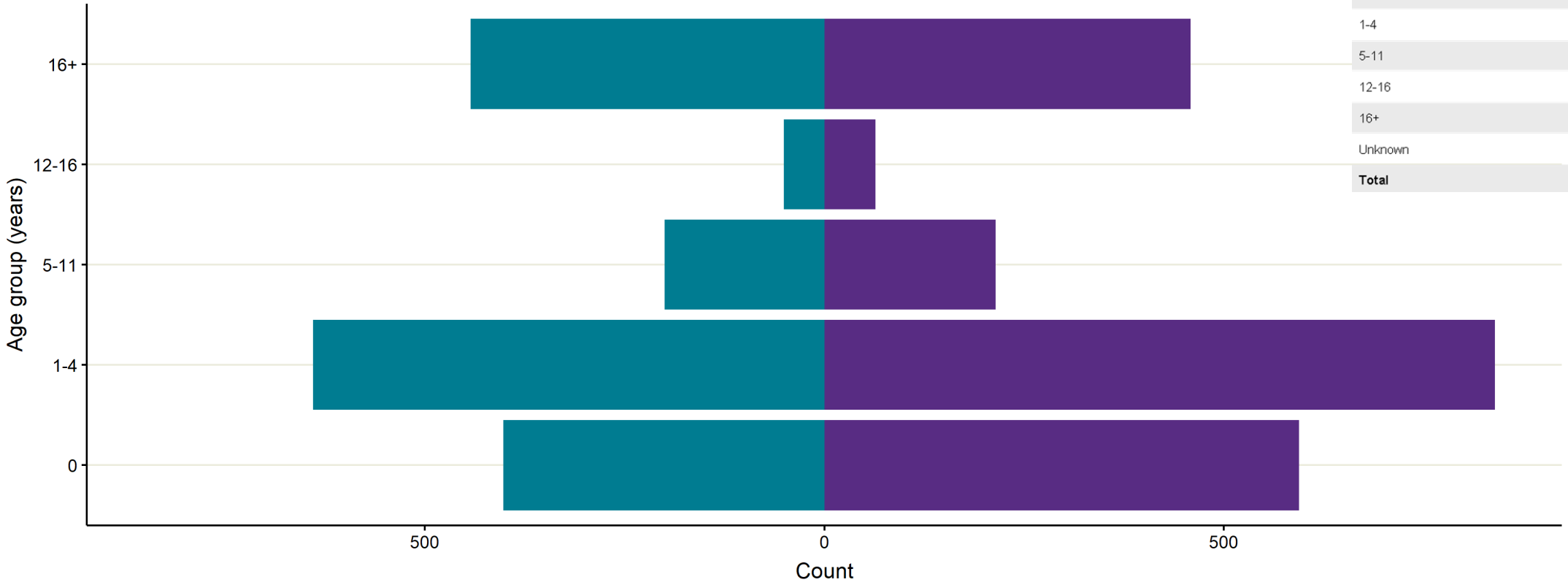
Data as of 30/01/2023

Number of laboratories reporting enterovirus to SGSS, London



Data as of 30/01/2023

Age and sex distribution of enterovirus cases, London



Age Group (Years)	Total
0	1,028
1-4	1,497
5-11	418
12-16	115
16+	915
Unknown	1
Total	**3,974**

Cases deduplicated based on SGSS OPIE ID
1 case removed due to missing age
68 cases removed due to missing sex

Data as of 27/01/2023

Conclusions

- Substantial improvement in laboratory reporting of enterovirus results in London; our thanks to all reporting laboratories for their cooperation
- Next phase is to review completeness of reporting
- Likely that similar approach required in other regions to strengthen reporting
- Laboratory data is critical to track enterovirus trends closely
- Able to identify gaps in surveillance, e.g. compare reported data to samples received at Enteric Virus Unit (EVU) at Colindale

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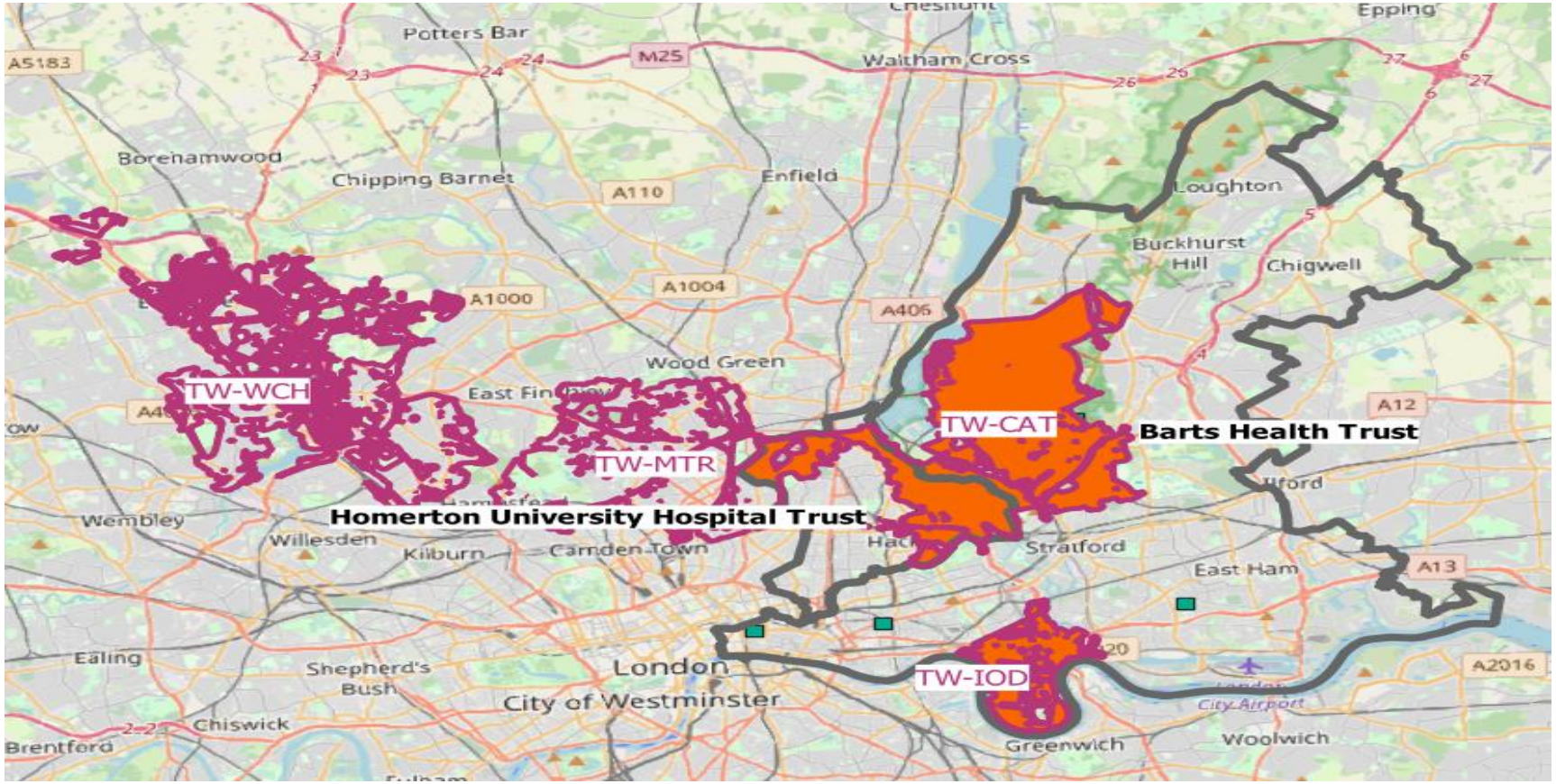
UKHSA Briefing 2022 Stool survey

Dr Kamil McClelland

NICC72 Laboratory surveillance cell

Relationship of hospital catchment areas to wastewater surveillance

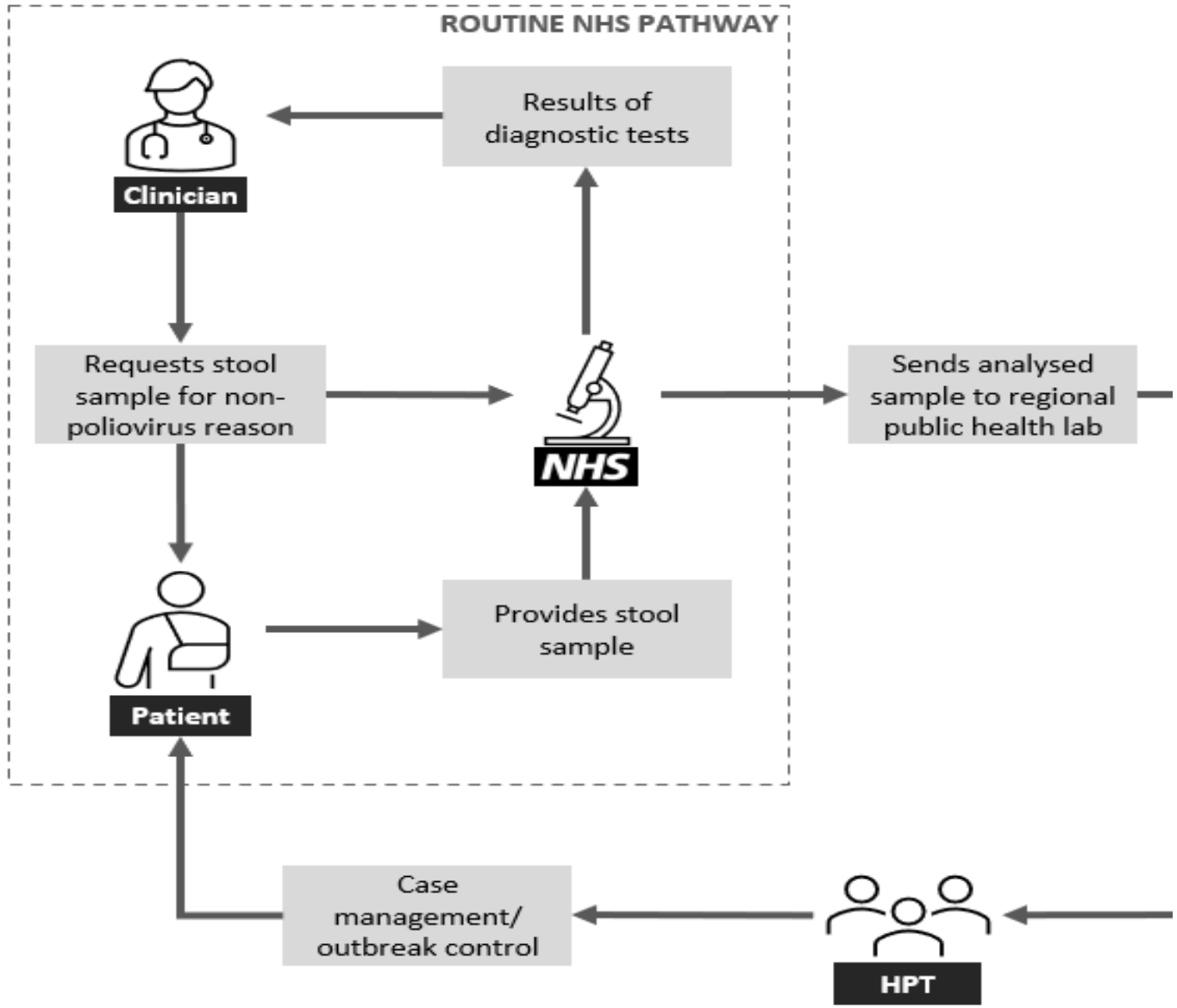


Stool survey design

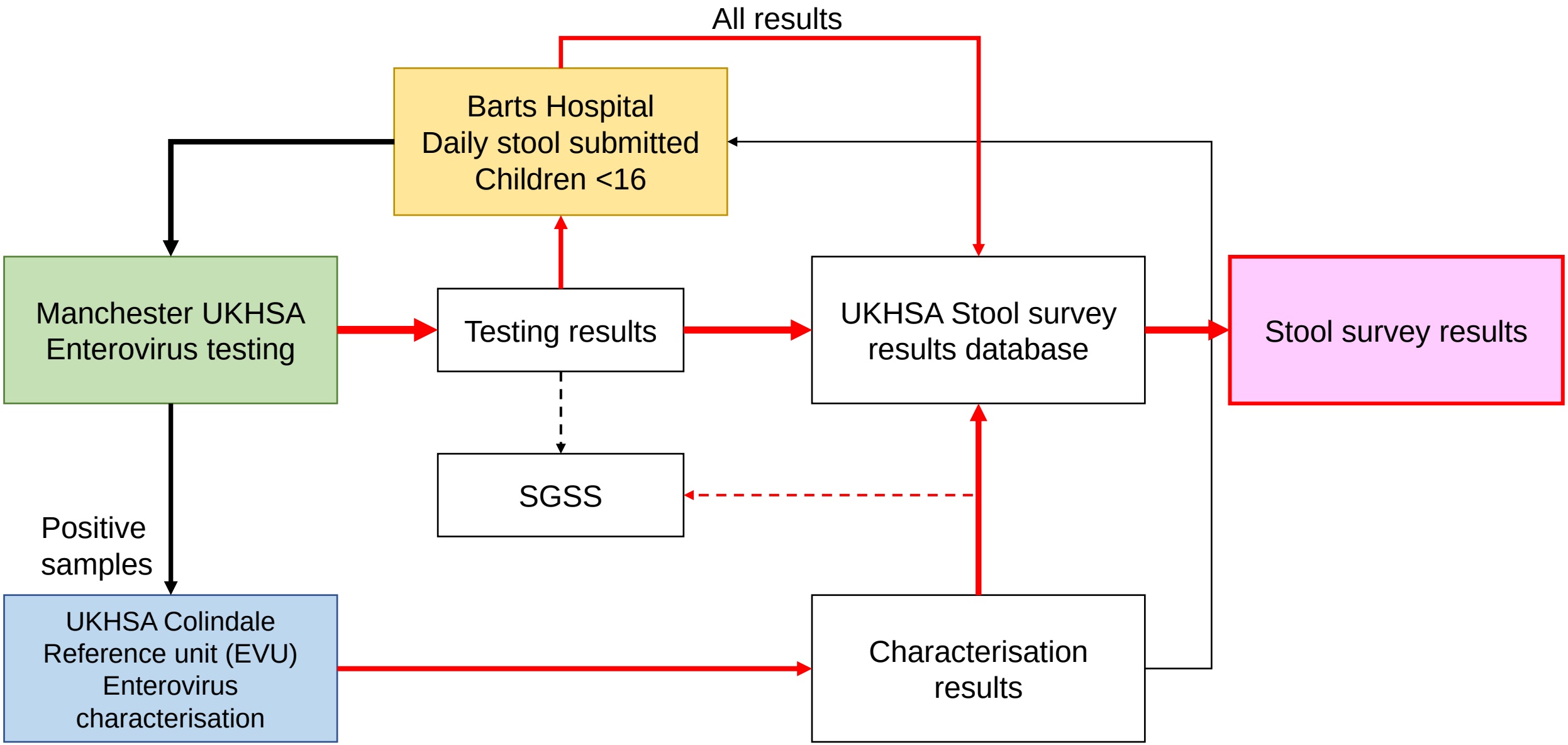
- Opportunistic, pragmatic approach
- Feasibility discussion with clinical & operational teams
- Protocol development August
- UKHSA Ethics approval September
- Data Protection Impact Assessment (DPIA) September
- Operational briefings
- Implementation 4th October 2022
- Some funding for continuation

Clinical Protocol:

- Stool sample submitted from child <16 years
- Sample originating from any hospital within Barts Heath Trust and Homerton Healthcare Foundation Trust
- Samples consolidated at central pathology triage location
- No screening of clinical conditions, but typically admission for sepsis/GI illness
- Samples would not otherwise have had virology testing performed
- Sample referrals capped at 40/day
- Funding within existing resources
- Results back to patients – no anonymisation

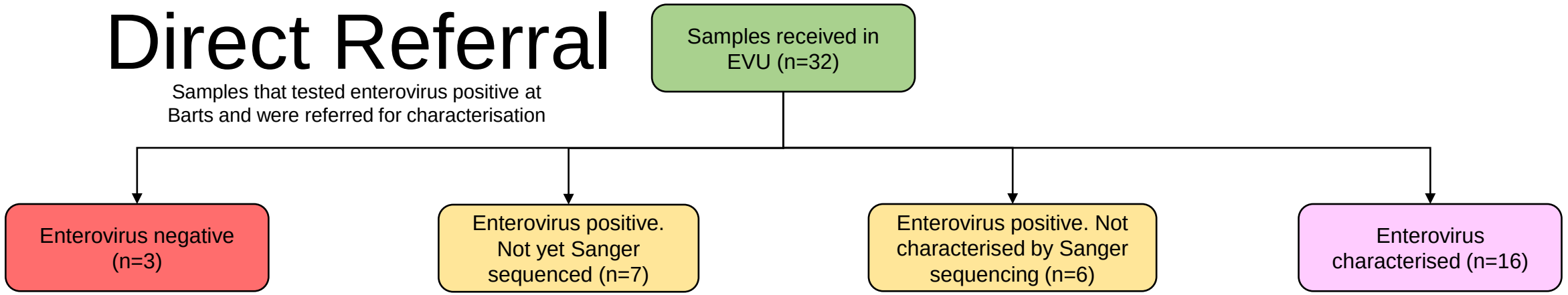

ROUTINE NHS PATHWAY
Clinician
Results of diagnostic tests
Requests stool sample for non-poliovirus reason
NHS
Sends analysed sample to regional public health lab
Patient
Provides stool sample
Case management/ outbreak control
HPT

London Hospital Stool Survey 2022
Data & Sample Flows



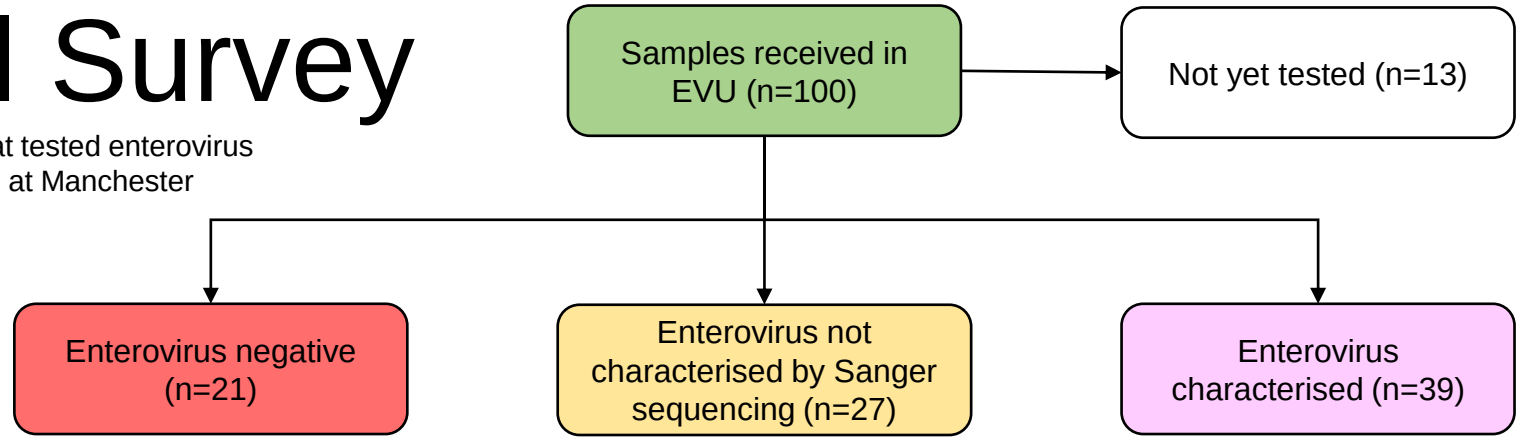
Direct Referral

Samples that tested enterovirus positive at Barts and were referred for characterisation



Stool Survey

Samples that tested enterovirus positive at Manchester



Manchester Enterovirus Testing

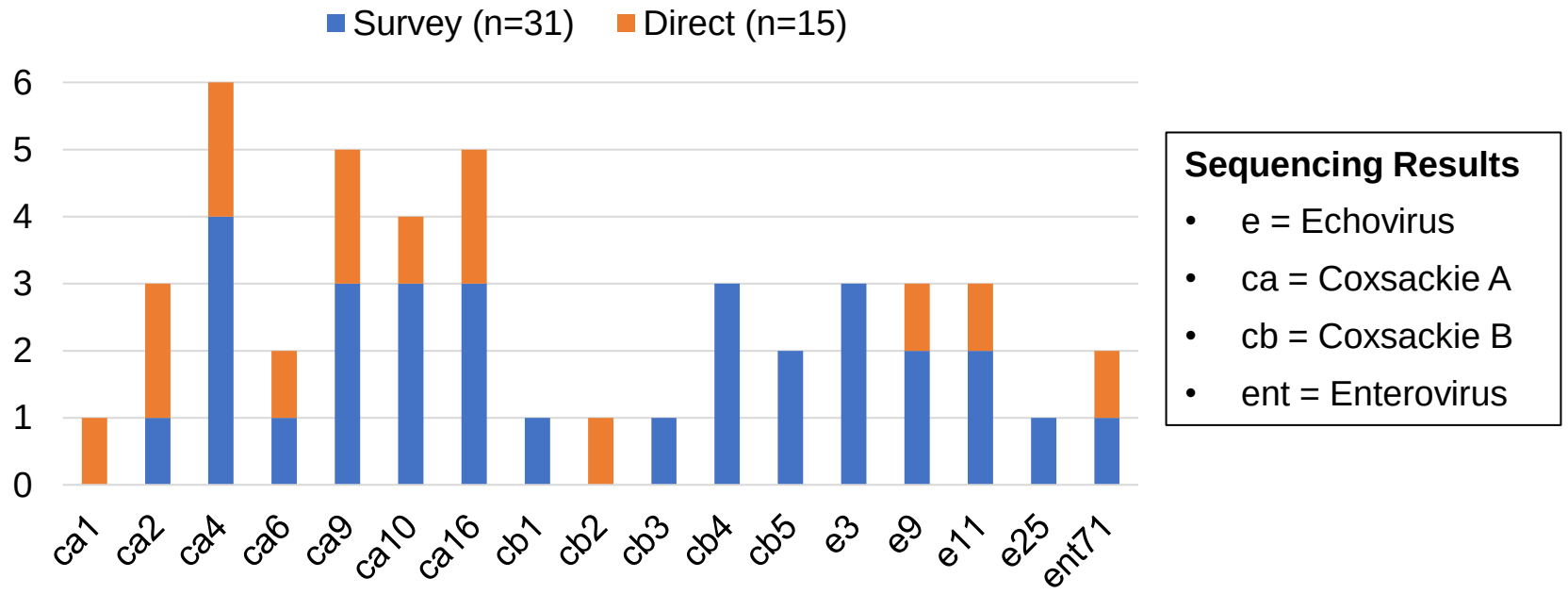
- 5th Oct - 23rd Nov 738 samples had been referred from Barts to Manchester
- 733 (from 620 patients) tested
- Any sample with a Ct value <45 was called as positive by Manchester
- 12.4% (91/733) tested positive for enterovirus.
- However, Ct values were often very high
- 96 individuals had more than one sample submitted as part of the stool survey
- Deduplication …11.6% (71/610) samples tested positive

EVU Data up to Dec 5th

- Paediatric faecal samples referred directly from Barts or via Manchester
- As of 2nd December, 32 enterovirus (+) samples had been referred directly from Barts.
- As of 5th December, 100 samples that tested positive in Manchester had been referred
- 29 duplicate or untested samples removed, giving 103 samples for analysis. There were no discordant results among the duplicate patient samples

EVU Deduplicated Sample Analysis (n=103)

- 71% (51/72) of stool survey samples were confirmed to be enterovirus positive.
- 90% (28/31) of direct referral samples were confirmed enterovirus positive
- Only 44% (31/71) of stool survey samples that underwent Sanger sequencing were successfully typed as enterovirus, compared to 71% (15/21) of direct referrals
- 73% (11/15) of direct referral samples were Coxsackie A compared to 48% (15/31) of survey samples
- Samples that failed Sanger sequencing but were positive on enterovirus detection PCR are undergoing whole genome sequencing regardless of the Ct value on detection PCR



Conclusions so far

- Study working as envisaged (sample and data flows are fully operational)
- No polio detected – mix other of enterovirus viruses found
- Significant proportion of enteroviral detection found in samples which would not otherwise have been tested (11%).
- Significant number of Manchester detections cannot be typed due to low viral load.
- Continued requirement for stool survey as Polio detection capabilities improve

Next steps

1. Develop lab algorithm for untypeable samples for assurance that these are not polio (Intratypic differentiation testing)
2. Clinical data follow up
3. Continue study to meet requirements from WHO
4. Add virus isolation work to study samples. Develop lab algorithms further
5. Report summary Phase 1 (Oct - Dec) due end February
6. Restart survey in January with some protocol changes

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Thanks to…

- Barts Hospital Trust especially Spiro Pereira, clinical and laboratory teams
- Manchester UKHSA laboratory teams
- Enteric Virus Unit Colindale, especially Stuart Beard & Cristina Celma
- Jonathan Turner & Melanie Amphlett UKHSA

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- Kamil McClelland - UKHSA Virology for data analysis
- Stuart Beard & Praveen SebastianPillai for LIMS data support
- Vanessa Saliba and NICC72 Incident team

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Update on the national polio incident and enterovirus surveillance webinar

Thursday 2 February