UK Health Security Agency

Mpox: technical elements of preparedness and response for clade I

Technical briefing 10

19 December 2024

Contents

Summary

This briefing covers technical elements of risk assessment, preparedness and response activities for clade I mpox with a domestic UK focus. The Foreign, Commonwealth and Development Office (FCDO) leads on the UK's activities in support of affected countries. The briefing is produced to share data useful to other government departments, public health agencies and academic partners undertaking related work. It includes early evidence and preliminary analyses which may be subject to change.

Main points:

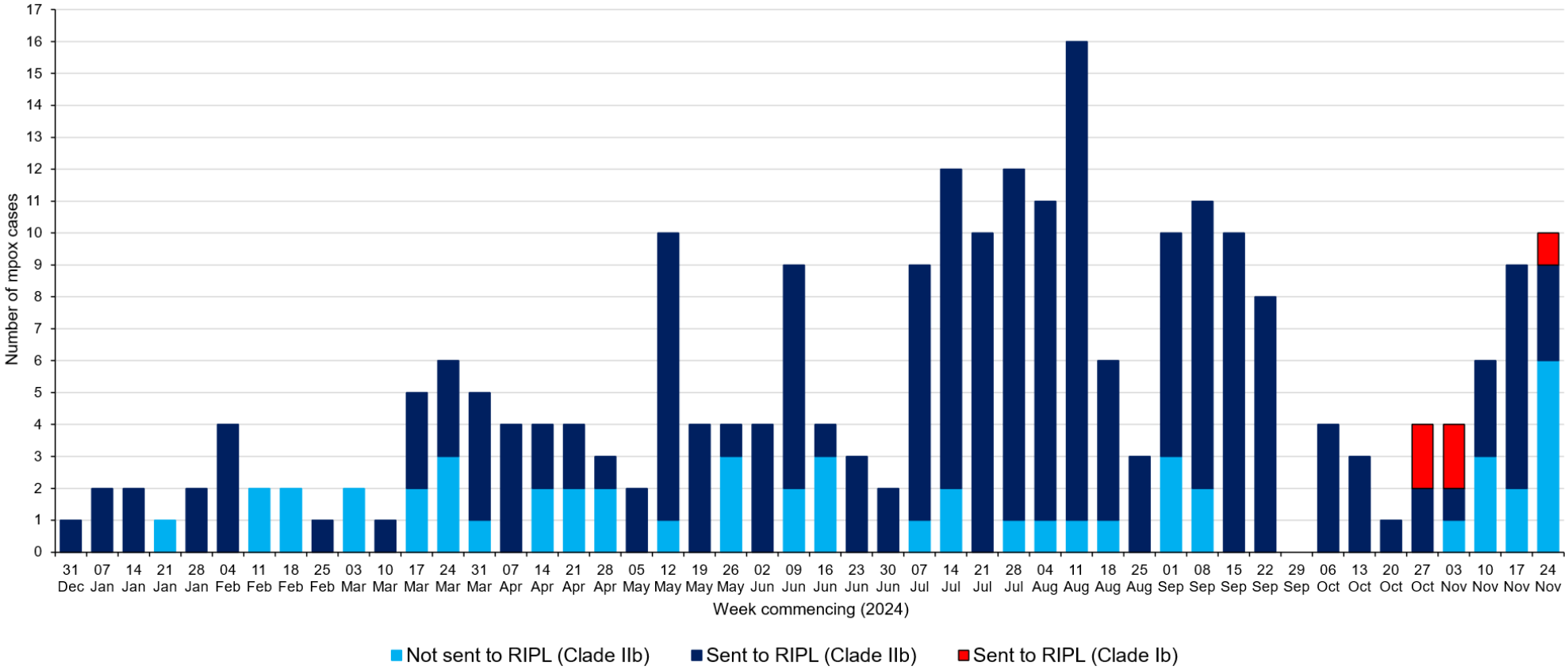
- There have now been 5 cases of mpox clade Ib detected in the UK, one imported case with onwards transmission to 3 household contacts, and one imported case without any onwards transmission to date (some contacts remain under follow up). Clade I mpox is classified as a high consequence infectious disease in the UK. A precautionary approach to contact tracing with a low threshold for post-exposure vaccination was applied.

- Given the continued expansion of the outbreak into countries with closer links to the UK, the ongoing risk of importation of mpox clade I is now considered **medium**. Transmission has been demonstrated within the UK and the risk of acquisition in the UK is **low** for the general population but may be **medium** for those individuals and groups more closely linked to travellers from affected countries.

- The growing evidence base from the affected countries concerning the outbreak of clade Ib mpox, as well as learning from our own and other exported cases, is most compatible with our previously published **scenario B**, a moderate transmissibility scenario, with transmission driven by sexual and close contact (moderate confidence). This also means that the risk of onwards transmission should importation occur is now considered **low to medium.**

- There continue to be small numbers of both imported and domestically acquired clade II mpox in the UK (Figure 1).

Figure 1. Confirmed mpox cases in the UK, showing proportion referred to the UKHSA reference lab RIPL for clade typing



The data used in this graph can be found in the accompanying spreadsheet.

Part 1. UK clade Ib cases

There have been 5 cases of mpox clade Ib detected in the UK. All cases were confirmed using a combination of polymerase chain reaction (PCR) assays designed to identify MPXV clade Ib. Cases 1 and 5 were additionally confirmed by whole genome sequencing.

Case 1 is an imported case with travel to multiple affected countries. Cases 2 to 4 are close household contacts of case 1. Cases 2, 3 and 4 had received post-exposure vaccination at day 10 post first exposure to case 1 (vaccination was undertaken in case of further cases within the household). Cases 3 and 4 were minimally symptomatic. There was no further transmission detected in association with these cases.

Case 5 is a separate imported case with travel to Uganda. There has been no transmission detected in association with Case 5. Some contacts remain in the final stages of follow-up.

Table 1 shows the approach to contact tracing and management and the numbers of contacts in each category.

Contact tracing matrix

Table 1. UK mpox clade Ib contact classification and management summary

Exposure risk	Description	Contact management	Number of contacts associated with all UK cases (number vaccinated post exposure)	Number of contacts converting to cases [see note 1]
High (Category 3)	Unprotected direct contact or high-risk environmental contact, for example: • sexual contact • shared residence • cleaned contaminated setting without PPE • direct exposure of broken skin or mucous membranes to a case without PPE	• active monitoring • self-isolation • avoid travel for 21 days • offer MVA-BN within 4 days (up to 14 days for high-risk groups)	7 (6)	3 of 7
Medium (Category 2)	Unprotected exposure to infectious materials, droplet, or airborne potential, for example: • intact skin only contact or close proximity (less than 1m) to case without PPE • shared car • seated directly next to a case on transport	• active monitoring for 21 days • risk assessment for work or education • avoid international travel • offer MVA-BN within 4 days (up to 14 days for high-risk groups)	24 (10)	0
Low (Category 1)	Protected physical or droplet exposure, or no physical contact with unlikely droplet exposure, for example: • contact with a case or contaminated setting whilst using adequate PPE • 1 to 3m proximity to a case	Warn and inform. No restrictions if asymptomatic.	116 (0)	0

[note 1] Some contacts associated with case 5 remain in the final stages of follow-up.

Genomes and assessment

Genomic data has been generated for cases 1 and 5 and been uploaded to GenBank (Clark and colleagues). Samples from both cases were amplified with the ARTIC amplicon scheme and sequenced using nanopore technology. Case 1 was also sequenced using in-house clade IIb 1kb amplicon scheme for comparison. In both cases there is a dropout of amplicon 67 in the ARTIC scheme which appears as ambiguous bases in the consensus sequences. For case 1 (PQ628240.1), the consensus sequence was generated using a combination of de novo assembly and mapping to evaluate repeat lengths. For case 5 (PQ762586), the ARTIC pipeline was used with default settings.

Virus isolates have been cultured from samples from cases 1 and 5.

Part 2. Risk assessment

The risk assessment uses the framework in Table 2. Since the last technical briefing published on 12 September 2024, the risk of importation into the UK has increased from **low to medium** to **medium.** This is based on the eastwards spread of the outbreak into countries with stronger travel and diaspora connections to the UK, with substantially more travel to the UK from Uganda than from other more seriously affected countries, and increasing numbers of exported cases from the African region to Europe and North America (Table 2a).

The risk of onwards transmission in the UK should importation occur is considered **low to medium** as indicators suggest that the outbreak is most consistent with scenario B, but at low numbers of cases control measures may influence transmission (Table 2a).

The risk of acquisition in the UK is now considered **low to medium.** For the population generally, exposure is unlikely, however we expect continued importation and have demonstrated the potential for transmission to close contacts within the UK. Exposure is possible within the UK in contacts of travellers, or communities or occupational groups where there are strong travel links to affected countries (Table 2b).

The risk to travellers depends on their activities in country and for most travellers will range from **low to medium** (Table 2b).

Travel patterns change over the year, and it is highly likely that there will be increased air travel between some countries of interest in December and January. This includes Kenya, Zimbabwe, and Tanzania which, whilst highly connected to the UK, pose an overall low risk of importation. It also includes Uganda, which is moderately connected (with an estimated 37,000 total annual arrivals to the UK, compared to 168,000 for Kenya). Increases to average travel from other less-connected countries of interest are expected, but at a lower level than the annual high in travel in late summer. Over December to January total arrivals from Uganda will likely increase by around a third over October to November volumes, and Uganda is likely to pose the greatest risk of importation to the UK due to prevalence of disease in country and overall passenger volumes.

Table 2. Situational assessment framework: future risk to the UK from an overseas outbreak and current risk to UK population (cells highlighted in green indicate the current level)

Table 2a. Risk to the UK from an overseas outbreak: mpox-specific risk assessment, clade Ib outbreak

Risk level	Very low	Low	Medium	High
Probability of Importation	A single case or localised outbreak in another country, well defined and monitored, with no evidence of sustained community transmission.	Community transmission in another country or countries – these countries have limited travel links to the UK.	Community transmission in another country or countries, including countries with stronger travel and diaspora links to the UK – and/or cases exported to intermediate locations that may increase the risk to the UK.	Community transmission in multiple countries; strong travel links to the UK.
Potential for spread in the UK once introduced	N/A	Disease is likely to be contained at a small, localised outbreak (for example, household), see scenario A.	Disease is likely to cause transmission in the UK in specific risk groups, see scenario B.	Disease is likely to cause widespread population transmission in multiple groups, see scenario C.
Severity of disease	Similar to clade IIb.	Intermediate between clades IIb and Ia.	Similar to clade Ia.	Higher than clade Ia.
Countermeasures	There are effective vaccines and/or treatments, which are available.	There are effective vaccines and/or treatments – there is limited availability.	There are vaccines and treatments of limited or unproven effectiveness.	There are no effective countermeasures.

Table 2b. Current risk to the UK population

Risk level	Very low	Low	Medium	High
Risk of acquisition in the UK	Human exposure to the pathogen in the UK is very unlikely. There is no suggestion that importation or transmission are occurring.	Human exposure to the pathogen in the UK is unlikely – it is possible that importation is occurring.	Human exposure to the pathogen in the UK is possible, limited to a specific risk groups.	Human exposure to the pathogen in the UK is possible and not limited to a specific risk groups.
Risk of acquisition to UK population travelling to affected areas	Infection is limited to a single localised outbreak – travellers can avoid any exposure.	Infection is spreading in clearly delineated areas outside the UK with known modes of transmission – it is generally easy for travellers to avoid exposure.	Infection is transmitting widely in some groups or with multiple or unknown modes of transmission – it is difficult to avoid exposure, or some activities undertaken by travellers may have exposure risks.	It is not possible to avoid exposure.

Part 3. Scenarios and indicators for mpox clade Ib

Early in the clade Ib outbreak, it was difficult to assess whether the outbreak was driven by intrinsically high transmissibility of the virus or by contextual factors, or both. UKHSA published 3 global scenarios to help inform planning assumptions that illustrate how an outbreak in the UK might develop with a high, moderate or low transmissibility virus, where transmissibility is considered as the probability of any given susceptible contact becoming infected (see Appendix 1).

Since the last technical briefing, published on 12 September 2024, when indicators were assessed as being most compatible with Scenario A, there has been an increasing evidence base on several key points:

1. Sustained person-to-person transmission and deteriorating epidemiology in the outbreak in some parts of the outbreak in Africa poorly compatible with scenario A (WHO situation report 42 and 43).
2. Preprinted or published literature describing contact tracing analysis in affected Africa countries, indicating a high proportion of cases acquired through sexual and very close contact, compatible with scenario B. (Malembi and colleagues, Brosius and colleagues).
3. An increasing number of cases imported to new countries outside the African region, with limited onwards transmission despite substantial numbers of contacts, which does not suggest an intrinsically very high transmissibility virus and is poorly compatible with scenario C.

The indicators are currently **most compatible with scenario B** – a virus with moderate transmissibility (similar to or slightly exceeding the transmissibility of the clade II outbreak).

Indicator assessment

Assessments of global epidemiology and limited laboratory data are available to support determining which scenario we are in. A set of indicators has been developed to support assessment of this data. On the basis of this data the indicator assessment has been revised as shown in Table 3.

Indicators are signals or signs that certain conditions or events are present, but their occurrence can often result from multiple causes or align with various scenarios, not solely the scenario under consideration. An indicator may be necessary for a scenario but is rarely sufficient on its own to confirm it. Indicators must be analysed in context, alongside other information, to determine which scenario is most likely to be occurring.

A confidence rating is assigned to the assessment of each indicator. High confidence means that uncertainties remaining should have negligible or no effect on the indicator assessment. Moderate confidence means that uncertainties remaining could expose the indicator assessment to change. Low confidence means that critical uncertainties remain which could invalidate the indicator assessment.

Table 3. Indicator monitoring and assessment

Indicator	Supports scenario	Current assessment	Confidence
Importation to new countries, without onwards transmission	A	Met, exceeded	High
A high proportion of cases are in defined risk groups with very high contact connections	A	Met in some parts of the outbreak	Low
A high proportion of cases are in sexual networks	B	Met in some parts of the outbreak	Low
There is a high growth rate in sexual networks which is not demonstrated outside these networks	B	Unclear	Low
New cases do not have detectable link to known outbreak (for example, travel)	B	Met in some parts of the outbreak in Africa	High
In vitro, in vivo or case characterisation data demonstrating characteristics related to transmissibility with findings similar to clade IIb.	B	Not met	Low
A higher overall growth rate than the maximum in 2022 or very high growth in population groups linked by touch (for example, young children)	C	Unclear	Low
A high secondary attack rate in households with an ability to reduce touch and clean environment	C	Unclear	Low
Epidemiological evidence of non-sexual, non-household transmission (an early signal may be the route of exposure of exported cases)	C	Unclear	Low
Evidence of respiratory transmission outside households	C	Not met	Low
In vitro, in vivo or case data demonstrating characteristics compatible with higher transmissibility than clade IIb.	C	Not met	Low
Frequent outbreaks in settings without close touch or sexual contact	C	Not met	Low

Part 4. Research, evaluation and enhanced surveillance

Research and evaluation coordination

UKHSA continues to contribute to the cross-government research funders groups in the context of the UK Government's health and care research and innovation framework for pandemic preparedness, prevention and response, to articulate emerging knowledge and evidence gaps and assess the routes under which those need to be addressed (Mpox technical briefing 9). The groups (national, led by DHSC and international, led by FCDO) coordinate the domestic and international research response including agreeing routes for funding.

In the UK, research and scientific evaluation priorities have been identified by UKHSA in collaboration with academic partners and chief scientific advisors across government. UKHSA has identified 75 knowledge and evidence gaps across all the pillars of the above framework (Understand, Prevent, Detect, Respond) and many of the related science and research areas (transmission dynamics, biological characterisation, clinical characterisation, surveillance methods, vaccines, public health and social measures, diagnostics, therapeutics, understanding attitudes and behaviours, and health inequalities and risk for vulnerable groups).

The 75 gaps were prioritised with input from UKHSA experts and academics. This resulted in 27 priority gaps that were relevant to the current UK situation and preparedness scenarios, and may require additional funding. Listed below are the topic areas and the research questions for each of those areas.

Clinical characterisation, virulence, population risk stratification

1. How does mpox clade I present clinically in UK cases, what is the course of the disease?
2. Does clade I affect children more than clade II in the UK population?
3. Mpox clade I incubation, infectiousness and severity by different groups
4. Which groups are at highest risk of severe infection from clade I?
5. Impact of infections in pregnancy and congenital infections
6. Proportion or frequency of asymptomatic and pre-symptomatic infection and propensity for transmission
7. Is there pre-symptomatic shedding of virus?
8. What are the clinical characteristics of those who have been infected following previous vaccination?

Diagnostics development and evaluation

9. Development of rapid point of care tests, improving consistency of performance of tests.

Public health and social measures development and evaluation

10. Evaluation of effectiveness of co-production and engagement (for example, in comms and guidance production) for increasing uptake of recommended behaviours.
11. What is the effectiveness of contact tracing to prevent secondary cases of mpox among household and close contacts?

Therapeutics development and evaluation

12. Cell-based evaluation of antivirals, for example Tecovirimat compared with Brincindofovir, combinations of licensed antiviral to identify potential treatment routes.
13. Identifying candidate therapeutics and evaluating potential therapeutics.

Transmission dynamics

14. Risk of onward transmission in contaminated environments: for example, risk to healthcare workers treating patients, and risk of transmission in homes, workplaces, and schools.
15. What is the period and duration of infectivity
    a. before rash/symptoms?
    b. after rash appears – and how does this vary for different modes of transmission (for example, sexual, touch)? How long does infectiousness persist in humans?
16. Level of population immunity and how this protects against clade Ib rather than clade IIb (immunity from vaccines, exposure to mpox and residual vaccination to smallpox).

Vaccines development and evaluation

17. Development and evaluation of new candidate vaccines.
18. Does previous vaccination confer immunity for clade Ib and what is the duration of immunity from previous vaccines?
19. What is the efficacy of current vaccines against clade I?
20. Developing tools and optimizing in vitro and in vivo capabilities for vaccine evaluation.

Understanding attitudes and behaviours, and health inequalities and risk for vulnerable groups

21. What messages and communications strategies can most effectively address barriers to uptake of interventions (for example, Test, Trace and Isolate; vaccination) and boost facilitators among at risk populations? Including co-production.
22. How can we raise awareness of mpox among the public, particularly at-risk populations, and increase engagement, including clearly communicating the risks of different clades or variants of mpox?
23. What is the acceptability of interventions to different groups at risk? Can interventions be co-produced with at risk populations to improve acceptability?
24. What is Central and East African diaspora communities engagement with health services and what are the barriers and facilitators to increase engagement in the context of mpox?

25. Tracking public understanding and behaviours over time. Among the public and at risk populations, how are perceptions of risk, effectiveness of interventions and the government response, as well as self-reported health protective behaviours changing over time and what psychological factors are associate with uptake of behaviours?
26. How do we effectively and appropriately target communications and engagement with at risk populations without stigmatising?
27. Barriers and facilitators to recent travellers from affected countries coming forward for testing. What factors influence the decision to self-declare symptoms for example, stigma, economic, language barriers?

The priority gaps have been shared with UK Research and Innovation (UKRI), National Institute for Health and Care research (NIHR) and the Department for Environment, Food and Rural Affairs (DEFRA). Government funders are reviewing their existing portfolios of work to consider how existing programmes can be pivoted to incorporate work on mpox or directly funding new programmes. Funders will also utilise these prioritisation exercises to prepare to mount a rapid domestic research response if any further escalation of the mpox situation occurs in the UK.

The research and scientific evaluation priorities were used to inform the launch of a combined responsive funding call from the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections (HPRU EZI) and The Pandemic Institute (TPI). Funding was awarded to 7 research studies in the areas of:

- understanding attitudes and behaviours
- diagnostics development and evaluation
- vaccines development and evaluation
- transmission dynamics
- biological characterisation

UKHSA is undertaking research and scientific evaluation studies on vaccine candidates and vaccination strategies, assay development, evaluation of therapeutics, and behavioural sciences.

Case and contacts study

UKHSA has deployed an enhanced investigation of contacts for clade I mpox. This enhanced surveillance study will provide an assessment of the epidemiological features of the early laboratory confirmed cases and their close contacts. The investigation is implemented alongside the public health management for cases and their close contacts. Protocol publication will follow.

Appendix 1. Scenarios

These scenarios are an update to those previously published in mpox technical briefing 9.

Scenario A. Incursions and small clusters of cases

- Clade Ib MPXV is transmissible enough to spread effectively within very close contact settings and some highly connected sexual networks. This allows it to propagate in its current location and potentially other areas of the world where there are equivalent conditions. At this level of transmissibility, international sexual and close contact networks will not be sufficient to sustain a widespread global outbreak.
- It is highly likely that imported cases will occur in the UK, but they will be detected, and the low transmissibility of the virus means that they can be controlled by isolation of cases, contact tracing, post-exposure vaccination and quarantine of contacts. Where index cases are not detected, there may be small transmission clusters that would not be sustained.
- UK population immunity will not factor into this scenario as transmission will terminate regardless of immunity.
- A package of advice at the border to travellers from affected areas, aircraft declaration, and general messaging in immigration may help to identify imported cases or to facilitate their presentation to healthcare. This supports containment and reduces small clusters.
- Pre-travel advice and vaccination of deployed healthcare workers reduces the number of importations to a lesser extent.
- The commissioned High Consequence Infectious Disease (HCID) NHS system cares for imported cases of clade Ib mpox, reducing risk of poor outcomes through expert infectious diseases input, while clinical and epidemiological information emerges.

Scenario B. A controllable epidemic in high contact sexual networks

Globally:

- Clade Ib is as transmissible or slightly more transmissible than clade IIb, which caused the 2022 outbreak.
- It spreads efficiently within high-contact sexual networks but is not transmissible enough to spread more widely into other population groups. The outbreak is not self-sustaining without a sexual transmission component.
- Transmission is primarily through gay, bisexual and other men who have sex with men (GBMSM) and heterosexual individuals with high numbers of sexual partners

including sex workers. There are superspreader events internationally at sex tourism destinations.
- Non-sexual transmission does occur sporadically, for example in households or other settings with close contact (schools, prisons). Most cases are adults, although limited onwards transmission means that small numbers of children are affected, largely due to household transmission.

In the UK:

- By the time cases are detected in the UK, importation will be occurring and some degree of transmission may have occurred depending on context (updated from original scenario to take account of current understanding of transmission).
- A high proportion of GBMSM with high numbers of sexual partners have natural or vaccine-mediated immunity from the clade IIb outbreak. While this level of immunity is likely to allow some breakthrough infections, it will reduce severe disease in this population.
- There is very little prior immunity in heterosexuals with high numbers of partners, including sex workers. There will be some older individuals vaccinated against smallpox (pre-1971) who are also likely to retain some protection against severe disease if not immunosuppressed by other conditions.
- There are clusters of infections in closed settings including schools and early years settings, care homes, prisons and places of detention that can be effectively controlled by contact tracing, quarantine of contacts, and post-exposure vaccination.
- Most cases are adults, although limited onwards transmission means that small numbers of children are affected with potential for severe disease in young children.
- It is reasonable to assume that a similar-sized outbreak would occur in the UK compared to the global clade IIb outbreak with a potential increase in severity. It is likely that this would need to be managed more widely in the NHS than within infectious diseases services. If there were larger numbers of children affected, paediatric services may have pathway and capacity challenges; consideration will also need to be given to clinical pathways for pregnancy and the immunocompromised.
- Vaccination of sex workers and heterosexuals with high number of sexual partners, in addition to GBMSM, reduces transmission, however targeting vaccination at these individuals will be significantly more difficult than the GBMSM community who are engaged with sexual health services through regular sexually transmitted infection (STI) testing, HIV PrEP (Pre-Exposure Prophylaxis) and other regular vaccination programmes.
- Contact tracing is enhanced and ring vaccination of close contacts of cases, and potentially contacts of contacts, occurs around clusters identified in schools, hospitals, care homes and other closed settings, limiting onwards spread.
- Highly accessible testing which allows individuals to access diagnosis conveniently, rapidly, and potentially remotely (for example postal polymerase chain reaction (PCR) kit) helps to reduce transmission. Rapid diagnostic home sampling kits with

sufficient sensitivity may have a role in control if they can be developed and are acceptable for use.

Scenario C. Community transmission in general population through close contact

Globally:

- There is considerable uncertainty on whether it is possible for mpox to be more transmissible than experienced in 2022, however this possibility should not be discounted as a future scenario in this or other potential emergent mpox outbreaks.
- Clade Ib has substantially increased transmissibility compared to the 2022 outbreak clade IIb virus. It spreads not only through very close contact including sexual contact but can also establish long chains of transmission through touch and possibly respiratory transmission in some circumstances.
- There is non-sexual transmission that is sufficiently effective to drive multiple outbreaks in household and other close-contact settings and groups (for example, early years childcare and some school settings, care homes, hospitals, prisons). Sexual transmission may remain an important driver of the outbreak, or touch borne transmission may be successful enough to drive the outbreak entirely.
- Wider community transmission occurs. Chains of transmission would be difficult to control through close contact isolation and post-exposure vaccination. Depending on the level of transmissibility and the ease with which infections can be identified, this may result in anything from difficulty to control outbreaks in specific settings such as schools and hospitals, or more widespread community transmission in population groups with high degree of touch contact, such as early years school age children and the elderly in care settings.

In the UK:

- In many countries, including the UK, chains of transmission are established before the identification of the first cases. A wide demographic group is affected early.
- Existing population immunity has little effect on transmission. In the UK 0.14% of the population were vaccinated in response to the 2022 outbreak. Outside this group there is almost no immunity in those born after 1971. Older adults may have some residual immunity through smallpox vaccination, of uncertain effect.
- Standard public health measures such as contact tracing, and quarantine may have limited impact particularly if there is a high level of asymptomatic or pre-symptomatic transmission. Vaccination will need to be prioritised to those at risk of severe disease and healthcare workers until a global supply is available. Alternative vaccines using different technology will require large scale clinical trials and production. Response in the NHS and public health will require large scale surge plans, especially if there is a significantly higher case fatality rate in children and adults than is observed with

clade IIb. Where there is significant morbidity or mortality, public health and social measures to reduce spread may be required while pharmaceutical (for example, new vaccines or increased vaccine supply of current vaccines; effective therapeutics to use as treatment and post exposure prophylaxis) and non-pharmaceutical interventions (for example rapid diagnostic home tests) are scaled for a global response.

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UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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