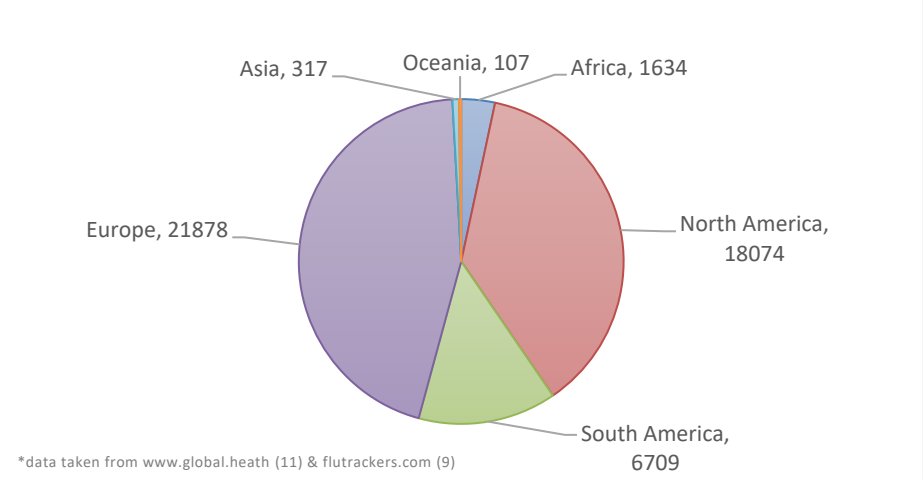
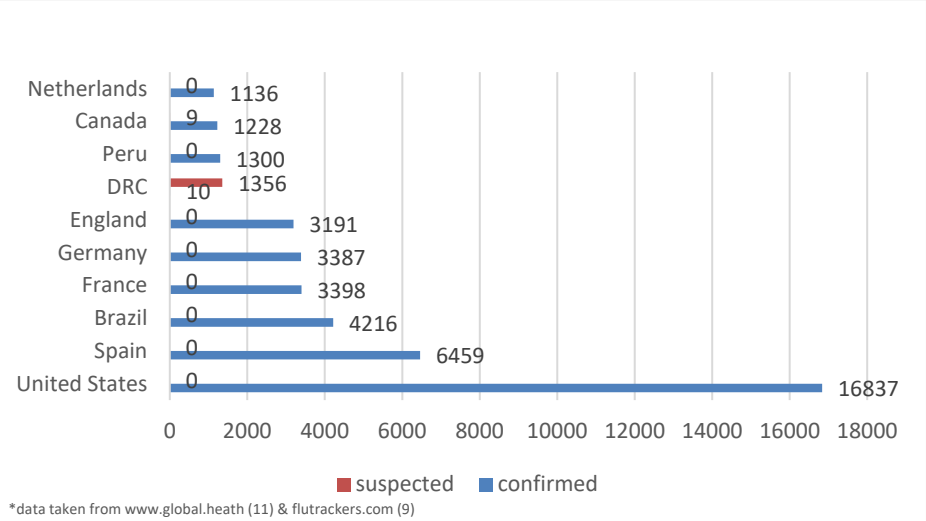
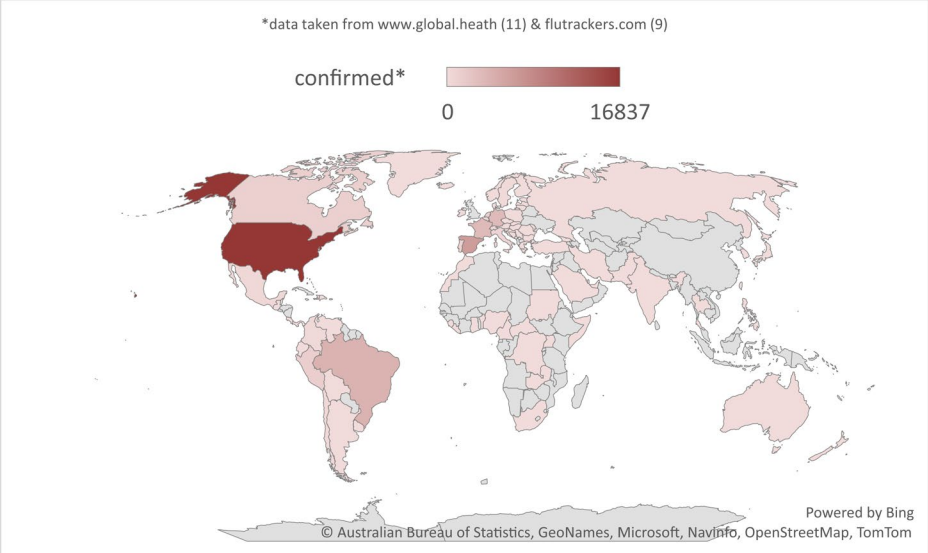
Feedback from operational stakeholders who manage or respond to outbreaks is that they are often too busy to review literature or obtain relevant background information to assist them with acute response. Unlike a traditional analytical outbreak investigation report, ***Watching Briefs*** *are intended as a rapid resource for public health or other first responders in the field on topical, serious or current outbreaks, and provide a digest of relevant information including key features of an outbreak, comparison with past outbreaks and a literature review. They can be completed by responders to an outbreak, or by anyone interested in or following an outbreak using public or open-source data, including news reports.*

Watching brief	
Title	An unprecedented global resurgence of monkeypox
Authors	Fatema Kalyar, Xin Chen, Mohana Kunasekaran, Aye Moa, Abrar Chughtai, Raina MacIntyre
Date of first report of the outbreak	An outbreak started in the non-endemic United Kingdom, where the index case was reported to WHO on May 7, 2022 (1). An unprecedented outbreak started in Nigeria which is an endemic country on September 22, 2017, reported to the Nigerian Centres for Disease Control and prevention (CDC) (2). In the Democratic Republic of Congo (DRC), the disease has been endemic for the last few decades and reported a very high number of cases in 2016 (3) and is still on the rise (4).
Disease or outbreak	Monkeypox is caused by a double-stranded deoxyribonucleic acid (DNA) monkeypox virus, which is a member of the Orthopoxviruses genus in the Poxviridae family. It is a viral zoonotic disease with geographical distribution in the tropical rainforest areas of Central and West Africa and is occasionally transported to other parts of the world (5).
Origin (*country, city, region*)	United Kingdom (UK) (non-endemic countries) DRC and Nigeria (endemic countries)
Suspected Source	**Travel-related**: Outbreaks in non-endemic areas have occasionally appeared, primarily due to imported cases. On May 18, 2022, the Massachusetts Department of Public Health verified a case of monkeypox in a Canadian visitor (6). Since 2018, all outside-Africa cases have come mostly from Nigeria (6-8). The UK, Singapore, and Israel have seen travel-related importations of cases from Nigeria since 2018. In early May 2022, the UK reported a case of traveller from Nigeria, where the disease is endemic. **Community transmission**: The majority of the epidemics in endemic areas (Western and Central Africa) are due to people catching, butchering, or preparing wildlife meat for sustenance. Additionally, human-to-human transmission, spread between family clusters, and nosocomial infections are

	seen in endemic regions (9). Most of the cases in the recent 2022 outbreak in non-endemic countries is attributed to community transmission between individuals, particularly among travellers visiting the UK or Europe.
Date of outbreak beginning	May 7, 2022, in United Kingdom (1) September 22, 2017 in Nigeria (2), 2016 in DRC (10)
Date outbreak declared over	Ongoing
Affected countries & regions	The current outbreak, in May 2022, has spread to Europe, North America, South America, Asia and Australia with the surge of monkeypox in both endemic and non-endemic areas. The global distribution of confirmed and suspected cases by continent is shown in *Figure-1*, while *Figure-2* is depicting top 10 impacted countries.  ***Figure 1**. Total cases* (confirmed + suspected) from Jan 1,2022 to Aug 27, 2022*  ***Figure 2**. Top 10 monkeypox affected countries* in ascending order*

Number of cases (specify at what date if ongoing)	The epidemic has been continuing since 2017 in endemic countries, with 23,428 suspected cases and 589 fatalities reported until May 2022 (11). In 2022 alone, there are 1,599 cases in endemic areas, while in total there have been 47,491 confirmed worldwide cases with nine deaths recorded as of August 27, 2022 (12, 13). The geographic distribution of 2022 outbreak is shown in *Figure-3*.  ***Figure 3**. Worldwide distribution of monkeypox up to August 27, 2022*
Clinical features	Monkeypox has a clinical appearance comparable to smallpox in terms of symptom presentation, time of rash development, and distribution. However, it is often less severe, with a lower mortality rate and less severe scarification. **Prodromal stage or pre-eruptive stage (1-10 days)**: It is comprised of non-specific symptoms such as fever (first symptom), chills, drenching sweats, headaches, lethargy, asthenia, backache, profuse nasal discharge, ocular discharge, cough, pharyngitis, dyspnoea, and myalgia, followed by lymphadenopathy (submandibular, submental, cervical, inguinal), which is a distinguishing feature of monkeypox from smallpox and chickenpox (14). **Exanthem or eruptive stage (contagious stage)**: The mucocutaneous lesions appear and the rash often starts on the face and then spreads to the rest of the body. The rash passes through different forms of eruption (macules->papules->vesicles->pustules) to umbilication, crusting, and desquamation follow. Until all the scabs have dried and dropped off, the patient remains infectious. The typical incubation time is 12 days, with a range of 4-20 days. Symptoms last for 2-5 weeks, and the ailment resolves on its own (15). Lesions of varying sizes (3-15 mm) are common, and the face, torso, limbs, palms, soles, and scalp are affected. The features include necrosis, petechiae, and ulceration. Pain is rare and usually indicates subsequent bacterial infections and possible pruritus. 20% of unvaccinated individuals in African outbreaks had a confluent, erythematous eruption on their face and upper trunk called the septicaemic rash of monkeypox.

	However, during the May 2022 epidemic, many of the reported monkeypox cases are men who had sex with men presenting with perianal, pubic, or genital lesions as an initial symptom(16, 17). In some cases, only genital lesions were present. More details on the comparison between the epidemiological features of the outbreaks in endemic and non-endemic areas are presented in the Critical analysis section (*Table-1)*.
Mode of transmission (dominant mode and other documented modes)	Common modes of transmission are zoonotic and person-to-person. **Animal to human transmission:** Monkeypox, a zoonotic virus, is transmitted to humans by close contact with infected animals such as rodents, squirrels, monkeys, prairie dogs, rabbits, mice, squirrels, porcupines, and gazelles. In Africa, transmission has been mostly reported from animals to humans. The close contact may occur if the skin barrier is compromised by an infected animal's touch, bite, or scrape, or by consuming their undercooked meat (18, 19). Animal to human transmission has also been recorded outside of Africa. In April 2003, some infected rodents, dormice, and rope squirrels were transferred from Ghana to Texas. Some of these infected animals were housed near prairie dogs in Illinois which were sold as pets before showing symptoms. According to the findings, monkeypox transmitted to those people who were engaged in touching or getting a bite or scrape that damaged the skin. It was also noted that transmission also occurred in those people who were engaged in cleaning the infected pet's cage or touching its bedding(6). **Transmission between humans**: Monkeypox transmission in humans spreads through close, personal contact, often skin-to-skin. This includes intimate contact during sexual activity such as oral, vaginal, anal sex, touching the genitals or anus of a person infected with monkeypox (as it has been reported in the current outbreak that virus has spread mostly in men who have sex with men) (20, 21). The transmission typically occurs via direct contact with a person's rash, scabs, lesions, body fluids (serum, pus, blood), or mucous membranes (eyes, nose, and mouth). Fomite transmission occurs when individuals come into contact with surfaces and materials (such as clothes, bedding, or towels) infected with monkeypox. Additionally, transmission also occurs through large respiratory droplets during prolonged face-to-face contact.(22) Vertical transmission occurs from pregnant mother to unborn baby (23). Transmission through breast milk, and amniotic fluid is not known yet (24). Monkeypox is not yet considered as sexually transmissible infection (STI) (16, 25). Although, the virus has been found in semen in 2022 but it is still being researched whether the transmission occurs through semen and vaginal fluid (24, 26). It is also being researched if asymptomatic transmission can occur, as asymptomatic infection has been reported in vaccinated people (23). Another

	plausible route of infection is viral shedding via faeces (27). Although it is currently unestablished if monkeypox virus can be transmitted by urine or faeces, research into this mode of transmission is ongoing (28).
Demographics of cases	In the current epidemic, which has spread to both endemic and non-endemic areas, 99% of cases are males aged 0 to 65, with an average age of 37. In non-endemic countries, the majority of cases have been reported in young adult men who have sex with men, with atypical symptoms of perineum rash. In endemic areas, most cases have been reported in children presenting with typical symptoms of a centrifugal and upper trunk rash (20, 21).
Case fatality rate	The case fatality rate (CFR) is dependent on viral phylogeny, age, the availability of medical facilities, and an individual's health status. Phylogenetic analysis of the current strain (named as "clade 3") in non-endemic areas reveals its close resemblance with clade 2 (West African strain) and the CFR is less than 1% as there have been nine deaths reported until August 27, 2022 (13, 29). It has been seen from the previous outbreaks in endemic regions that most deaths occur in children and people with immunosuppression. In the previous two decades (2000-2019), children under the age of ten years accounted for 37% of all deaths (30). Meanwhile, African health officials have confirmed more than 70 deaths this year due to monkeypox. The majority of deaths were among children, with a CFR of 4.5%. Due to a lack of testing and surveillance resources, some of the cases may go undetected. overestimating the CFR value (11, 31). The two known variants of the virus are the West African strain and the Congo Basin strain, with an estimated CFR of 3.6% and 10.6%, respectively (30).
Complications	Monkeypox is often self-limiting, resolving in two to four weeks. Severe disease is more common in children, malnourished, and immunocompromised people, and severity is related to the level of virus exposure, comorbidities, and patient health conditions. Secondary bacterial infections, septicaemia, bronchopneumonia, respiratory distress, dehydration, encephalitis, corneal ulceration, and keratitis (with resultant vision loss) are all potential consequences of monkeypox (32). Furthermore, monkeypox during pregnancy may lead to postnatal problems such as congenital monkeypox or stillbirth (33).
Available prevention	Preventive strategies vary in endemic and non-endemic areas. **Endemic Areas:** In endemic areas, a rise in monkeypox cases is associated with variables such as overcrowded living quarters, poor hygiene, the cessation of smallpox vaccinations, and a subsequent loss of herd immunity (34).

	The spread of monkeypox can be prevented by increasing awareness via health education programmes and warning individuals to avoid or minimise contact with animals and infected animal products, in addition to avoiding raw meat consumption (9, 35). Focus is on strengthening access to diagnostic and treatment facilities in endemic locations and educating laboratory personnel on the proper and safe handling of specimens. Personal Protective Equipment (PPE), surgical masks, and gloves are essential for avoiding nosocomial transmission. Isolating ill individuals and keeping track of their recent contacts helps to reduce virus transmission. Patients should be screened by maintaining social distance, implementing airborne or droplet precautions, and minimizing physical contact. In addition, regardless of vaccination status, asymptomatic contacts should be observed for 21 days. When a monkeypox case is detected, the patient should be isolated until the last crust breaks off. After discharge from the medical facility, the patient's room and its belongings should be thoroughly cleaned (35, 36). Health professionals that interact with orthopoxviruses, clinical laboratory personnel, and outbreak response team members should get smallpox (vaccinia) vaccination as pre-exposure prophylaxis (PrEP). If an individual comes into contact with an infected individual, they should get post-exposure prophylaxis (PEP) vaccination (from the second or third generation) as soon as possible, preferably within 4-14 days after exposure (30, 37). In Africa, there is a need for further ecological research to better understand the animal species that aid in the transmission of monkeypox viruses(27). **Non-Endemic Areas:** Monkeypox transmission and epidemic prevention can be achieved by active case identification, contact tracing, case isolation, and the use of PrEP. In communities of men who engage in sexual activity with other men, health promotion and community participation are essential in combating the epidemic. It is also essential not to limit the case definition to men who have sex with men but to incorporate all sorts of close contacts. *Vaccinia* immunisation promotes active protection against monkeypox by producing antibodies; nonetheless, healthcare professionals and patients should be aware of the hazards connected with vaccination, particularly when using replicating vaccines. Smallpox vaccinations (which provide cross protection against monkeypox), preferably non-replicating, should be delivered as PEP to individuals who could have HIV. The patients should be given advice on how to take care of the immunisation site. Importing exotic animals should be governed by certain restrictions. Animals exhibiting respiratory distress, mucocutaneous sores, rhinorrhea, ocular discharge, or lymphadenopathy must be confined promptly to avoid contact. The "Animal Updated Interim Guidance for Veterinarians" offers the most recent CDC suggestions.

	Pregnant women, neonates, children, and HIV patients who are co-infected with the virus are at the greatest risk of developing a severe illness from monkeypox and should be protected with the appropriate measures. Screening is necessary for the detection of subclinical infections; screening stations should be established to monitor and screen individuals returning from affected regions. This may be accomplished by performing an epidemiological analysis, a full medical history, and a comprehensive physical examination on each confirmed case to rule out other diagnoses. Healthcare professionals and anyone who comes into contact with asymptomatic infected individuals must monitor their symptoms and temperature for 21 days following their last known interaction with an infected individual. Everyone in healthcare settings should adhere to the monkeypox prevention and control guidelines (37-39).
Available treatment	In addition to smallpox vaccination, *vaccinia* immunoglobulin is available and can be administered in severe cases (40).The antiviral medications *tecovirimat*, *cidofivir* and *brincidofovir* can also be used for critical cases of monkeypox (41). Treatment is situation-specific; uncomplicated cases would not require specific treatment, and bedrest and supportive care is sufficient. In more grave situations, hospitalisation may be required; a negative pressure room is preferred. Supportive treatment includes: - Antipyretics for fever. - Intravenous fluid for hemodynamic stability. - Antibiotics for secondary bacterial infections - Incision and drainage for superinfection. - Topical antibiotics for exfoliating skin, oral or topical analgesics for mouth/skin sores. - Antimotility for diarrhoea. - Proton pump inhibitors for dyspepsia. - Anti-inflammatory for lymphadenopathy. - Corticosteroids for ocular infection - Treatment for crusting of vesicles. - Antihistamines for pruritis. - Vitals monitoring, hygiene advice, and psychological support. - Refer pregnant women to the obstetrician unit where a paediatrician is also available (40-42).
Comparison with past outbreaks	Monkeypox was first detected in 1958 in laboratory monkeys in Copenhagen, Denmark. The first human case of monkeypox was documented in 1970. After the elimination of smallpox, a 9-month-old child in Congo was diagnosed with a smallpox-like condition later named monkeypox. Approximately 50 cases were identified in 11 African countries between 1970 and 1979. By 1986, around 400 human cases had been documented. The attack rate in the DRC during the 1996-1997 epidemic was 22 cases per 1000 people (6). Monkeypox is considered endemic in the northern and central DRC. Disease outbreaks have been recorded sporadically in adjacent countries.

The first outbreak outside of Africa was detected in the United States (US) in 2003, and it was traced back to a pet store that sold imported pet prairie dogs from Ghana, with 47 individuals affected (6, 43). The outbreak was contained by comprehensive laboratory testing, the deployment of monkeypox vaccination and treatment, the establishment of guidelines for patients, healthcare professionals, veterinarians, and other animal handlers, the monitoring of possibly infected animals, and the investigation of suspected human cases (44). In 2005, South Sudan recorded 19 human cases of monkeypox, with no deaths documented. The DRC repeatedly reported around 2000 cases per year between 2010 and 2014 (30).

Outbreak in endemic countries since 2017

In September 2017, human monkeypox returned to Nigeria, 39 years after it was last documented. Nigeria has been coping with a large outbreak since then. In 2017, there were 2,328 suspected cases and 60 confirmed cases were reported in 24 out of 36 states (36). Nigeria has been the source of all cases reported outside of Africa since 2018 (45, 46).

In the DRC, a total of 2,850 suspected cases (CFR 2.1%) were recorded in 2018. In 2019, there were 3,794 suspected cases and 73 fatalities (CFR 1.9%). There were 4,594 probable cases of monkeypox from January 1 to September 13, 2020, with 171 fatalities (CFR 3.7%) (47).

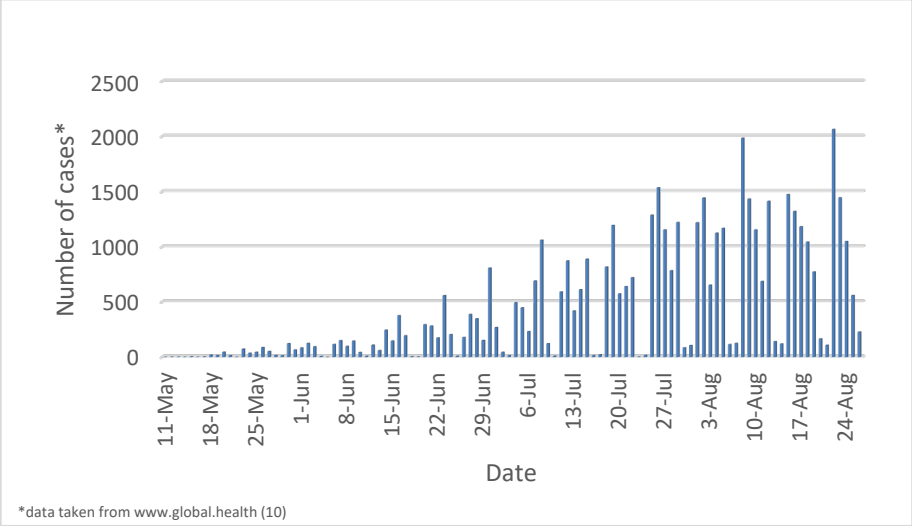
The Nigerian CDC has been managing the outbreak by sending fast response teams to all states with confirmed cases. Ongoing activities include surveillance, case research, and contact tracking. The *Surveillance and Outbreak Response Management System* has been implemented and is now being used to improve data management and real-time mapping of cases and contacts. In addition to palliative care, case management facilities and isolation units have been developed. Moreover, healthcare professionals have been educated in case management, and the danger of monkeypox has been conveyed to the public through media campaigns (48).

Importations of cases to non-endemic countries from 2018 to 2021

In 2018, there were two confirmed imported, unconnected cases in the UK (49), and one in Singapore in 2019. In 2021, there were three cases reported in the UK and one in the US (50).

Current outbreak in non-endemic countries

The outbreak of May 2022 has spread primarily through the UK, Europe, and North America. So far, as of August 27, 2022 over 47,000 cases have been reported in more than 95 countries (12) , As in *Figure-4* the global outbreak is still on the rise. This is unprecedented when compared with the previous outbreaks with rare cases having documented travel linkages to endemic regions.

	For the current outbreak, intensive surveillance and robust health promotion are being put in place, but ring vaccination and antivirals are being used varyingly (51).  *Figure-4 Time trend of confirmed cases* of monkeypox reported in non-endemic countries, May 5, 2022- August 27, 2022*
Unusual features	Over the past five years, only tourists returning from endemic areas have been infected. This year, though, people who have never been to the endemic parts of Africa have been infected with monkeypox (52). There seems to be little connection between many of the clusters, which raises the possibility of undocumented local viral transmission (52). Although animals afflicted with a disease may not show the same symptoms as humans, their infection might result in superspreading events (53). Most of the cases were identified among men who had sex with other men. It appears that the virus has spread via very intimate social networks (52). In the 2022 outbreak, sexual activities at two raves in Spain and Belgium were possible drivers of monkeypox transmission, raising the possibility that the virus has evolved to become more adept at sexual transmission. Several mutations are described in the epidemic strain in Europe, suggestive of continuous and rapid evolution, which is unusual for a stable DNA virus (54).The phenotypic expressions of these changes are not well understood yet. However, it may explain the different clinical presentations and pattern of the spread. Many patients in this epidemic are not exhibiting the typical clinical picture of monkeypox but rather are presenting with a perineal rash (55).

Critical analysis

1.Monkeypox in endemic area

Since 2017, seven countries in the endemic region (Cameroon, Central African Republic, DRC, Republic of Congo, Liberia, Nigeria, Sierra Leone) have reported the majority of the cases. The DRC alone has reported 96% of the total number of suspected cases (22,379) (11). Although no cases of monkeypox were reported in Nigeria between the years 1978 and 2017, this might be due to the high frequency of smallpox vaccination, which provided cross-protection against monkeypox among 1970s cohorts. However, there is a possibility that mild or asymptomatic infections might have occurred but gone unreported because monkeypox was not on the *Integrated Disease Surveillance and Response System* list of reportable diseases in Nigeria (56). In endemic areas, the problem is most acute due to underdeveloped health infrastructure and limited financial resources. As a result, there are gaps in surveillance systems, early identification, and reporting (57). Another barrier to accurate diagnosis is access to polymerase chain reaction (PCR) testing and a lack of adequate lab facilities. Furthermore, vaccines have not been provided owing to their expensive cost, and even if vaccines are delivered, individuals have a high refusal rate for immunizations (58). Outside of Africa, the incidence of monkeypox has been extremely low in the last 50 years (55).

2. Monkeypox in non-endemic area

There have been sporadic travel-related cases in non-endemic countries outside Africa until May 2022. Since then, multiple unrelated cases and isolated outbreaks have been detected in several non-endemic countries, which is unusual for previous epidemic patterns. As of August 27, 2022, there are over 47,000 laboratory-confirmed cases of monkeypox from around 100 countries. The US has the highest number of cases (so far) and has declared a public health emergency on August 11, 2022(12).

Even though WHO has already declared a *Public Health Emergency of International Concern* on July 23, 2022 (59) the number of infections still continues to rise as more cases are anticipated globally. Ironically, epidemiological links between most cases are currently unclear (52).

The comparison of epidemiological features of monkeypox between endemic and non-endemic areas is shown in *Table 1*.

Table 1. Epidemiological features of monkeypox outbreaks

Factor under consideration	Endemic	Non-Endemic
Age group	Majority cases are children with average age between 4-21 years (30)	Majority cases are 31-40 years old (60). 5 children infected in USA (61, 62)
Gender	69% male (36)	99% cases have males gender (12, 60) [24% cases reported with gender]
Distribution of rash	Centrifugal, face, oropharynx, tongue, and limbs (36)	Perianal, genital, and pubic (60). Confused with STI.

Affected Population	Most children and young adults with immunocompromised; HIV, varicella, syphilis (57).	Men having sex with Men (60), multiple sex partners, condomless sex (63), comorbid patients with HIV or other STI (17).
CFR	Median 8.7% with deaths almost all in children (30).	<1% as 9 deaths reported so far (12, 60).
Affected areas	African countries **1.** Nigeria's outbreaks started in 2017 and is still on-going. Since Jan 2022 1536 suspected cases (and 57 confirmed cases) reported with 72 deaths (64). **2.** Congo: In first half of 2018, 2845 suspected cases with 36 deaths reported (65).	Mainly European countries. Since outbreak started 86% cases reported from Europe, 12% cases from North America (12).
Secondary attack rate	Up to 50% in household contacts. Also include prisons and nosocomial (30, 57).	0% so far with no data of epi-links (30).
Variants	2 clades (West African and Central African) (30).	West African clade (66). Genomic sequencing shows two different strains are circulating(67)now its referred as "clade 3" (29).
Basic reproduction number - R_0	R_0>1 (68)	R_0 unknown, West African clade has R_0<1 (43)
Vaccination status of cases	80 – 96 % not vaccinated against smallpox (30).	Cases remains asymptomatic if vaccinated (69).
Drivers of Epidemic	Mostly zoonotic, human-to-human(H2H) transmission either direct contact, respiratory droplets (32).	Mostly imported cases from endemic locations(30). H2H transmission among homosexual men (60). 83% reported cases in men who have sex with other men (52).

	There are a few peculiar, unexpected, and intriguing aspects to these epidemics that need consideration. Transmission in non-endemic regions has been related to sexual activities (52). Although monkeypox is not a sexually transmitted disease, it may be passed on via intimate contact during sex if someone has an active rash. The clusters have appeared among men who have sex with men, which is not a known trend. Suspectedly, events like summer festivals, gay bars, and saunas could become superspreading events (70). The unexpected development of monkeypox in multiple non-endemic areas suggests previously undiscovered transmission and recent amplification events. The majority of the reported cases were detected in the UK, Spain, Germany, and Portugal (71). The virus has never been identified in Spain or Portugal previously. The majority of reported cases had no known travel ties to an endemic area and were presented to general care or sexual health providers (72). As predicted by WHO earlier, "The public health danger might become serious if this virus takes advantage of the opportunity to establish itself as a human pathogen and spreads to people at greater risk of severe disease, such as young children and immunocompromised adults," (73). The majority of monkeypox cases are recorded in high-income countries, which may be attributable to improved surveillance and health-care systems in developed countries and underreporting or misdiagnosis in poor or undeveloped countries. For instance, in India, there is a mystery epidemic of tomato fever, which causes a rash like monkeypox (74). On the other hand, several countries are experiencing an epidemic of hand-foot-mouth disease (75). Misdiagnosis and other difficulties with surveillance are plausible. Moreover, improving patient awareness of this illness, reporting honesty, and accessing diagnostic capabilities are critical actions for obtaining the data needed for a better knowledge of and stronger protection against monkeypox. Since the monkeypox rash is visible and is the first sign that brings an infected patient to any healthcare setting like an emergency department, general practice, or sexual clinics. Therefore, there is a need for multidisciplinary cooperation among doctors (GPs), nurses, virologists, and public health professionals that can swiftly detect monkeypox infection, adopt preventive measures, and begin public health reporting to form a bulwark against this ever-rising epidemic. Additionally, epidemics may be controlled with efficient monitoring and contact tracing. Isolation of confirmed patients, as well as identification and immunisation of all close contacts, will form a protective circle around them, breaking the transmission chain (76). The majority of the monkeypox cases have occurred in men (99% of cases). There is a fear of stigmatization among men who have sex with men, which may hinder the timely reporting of the infection, contact tracing, and potentially challenge the public health response. This needs to be addressed by raising awareness of the disease and ensuring the privacy of the patients and their contacts (52). To reduce stigma, the WHO is contemplating renaming the monkeypox variant and has established a forum to discuss the matter (77). Initially, only men who have sex with men were thought to be infected. However,

	monkeypox has been observed to spread in close quarters, including households and dormitories. This requires revising the case definition (78). The recurrence of monkeypox might be attributed to a decline in smallpox immunity in the population. The smallpox vaccine, which also protects against monkeypox, has not been used in 40 years, and most mass vaccination campaigns stopped in the 1970s, so few individuals under the age of 50 have been immunised. Moreover, in countries where everyone was vaccinated against smallpox, over 20% of the population may still have vaccine-induced immunity, but its strength and efficacy are unknown (79). Furthermore, the immunisation gives protection for 5-20 years or more, although its effectiveness may drop at a rate of 1-2% each year (80). The 'ring vaccination' technique used to eliminate smallpox (in which only confirmed patients' close contacts are immunised), can be used to control the monkeypox outbreak (81). Meanwhile, globally, public health interventions such as vaccinations and antivirals should be given to affected communities and other relevant communities on an equal basis (82). It is unknown if domesticated cats and dogs may serve as vectors for the monkeypox virus. A dog has recently been found to have monkeypox, which was passed from a person to the dog (83). There is concern that if the virus continues to spread among domestic animals such as pets, the sickness might spiral out of control. Therefore, collaboration on interventions between humans and animals is important (53). Pets such as cats, dogs, and rabbits should go through regular vet checks. In a nutshell, the cessation of smallpox vaccination, which leads to waning immunity, increased exposure to animal reservoirs and spill over events as a result of deforestation and climate change, enhanced human-to-human transmission, and increased surveillance and reporting, all seem to be contributing factors to the global increase in monkeypox cases.
Key questions	1. Why is a formerly rare virus now becoming more prevalent and what is the relationship to lack of past smallpox immunity, COVID-19 related immune dysfunction and HIV co-infection? 2. Is monkeypox an illness that recurs? 3. What interventions and control methods can be currently used in the United Kingdom and other non-endemic nations? 4.What is the R_0 for the virus in this current outbreak in non-endemic countries and how does it compare to past outbreaks? 5. What are the phenotypic expressions of the multiple mutations in the European epidemic strain? 6. Could the current epidemic be under-reporting cases or misdiagnosed as other illnesses with rash and fever? 7.Is the case definition of probable cases too narrow? 8. Has the human-to-human transmission route changed in this epidemic? 9. Is this a natural occurrence or a bio-attack?

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