Responding to the global mpox outbreak
Ethics issues and considerations
A policy brief

19 July 2023
WHO continues to monitor the situation closely for any changes that may affect this document. Should any factors change, WHO will issue a further update. Otherwise, this document will expire 2 years after the date of publication.

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Executive Summary

In order to fulfill the strategic aim of stopping the mpox outbreak, the global response must recognize, consider and address ethical issues related to the ongoing outbreak. This is particularly relevant to achieving the objective of protecting vulnerable populations at risk of severe disease. The ethical considerations must be contextualized to the specific features of this outbreak, such as the disproportionate risks of infection and severe disease in marginalized populations and limited access to safe, effective vaccines and antiviral therapeutics.

Established ethics principles in outbreak response are: justice, beneficence, utility, respect for persons, liberty, reciprocity and solidarity (1). This policy brief provides guidance on key ethics issues that have emerged in the context of the mpox outbreak and its response, primarily: (i) stigma and discrimination, (ii) equitable access to interventions and (iii) action in the face of uncertainty, analysed with reference to the above principles. Several key considerations are highlighted to promote respect of these principles in responding to mpox outbreaks.

Stigma and discrimination are significant barriers to health care, adversely affecting achievement of the desired beneficence, respect for persons and utility in the outbreak response.

- Public health actors should understand and address multiple forms of stigmatization and discrimination which may act as barriers for outbreak control, namely, those linked to skin manifestations of infectious disease, racist stereotypes, living with HIV, a disease transmissible through sexual contact, and a disease that disproportionately affects gay, bisexual and other men who have sex with men.

- Public health actors should design and implement stigma-free pathways to access prevention, care and treatment services for mpox to support uptake of interventions (testing, vaccination, treatment and rehabilitation) by all populations at risk for mpox.

- Public health actors must conduct mpox case investigation, isolation and contact-tracing in ways that eliminate the risk of violence, abuse or criminalization of people diagnosed with mpox.

- Public health actors should ensure that personal information available from public health surveillance systems is not used to discriminate against or prosecute anyone for their sexual behaviour, orientation or identity, or in ways that are likely to stir violence against marginalized communities.
Equitable access to interventions (allocation): Vaccines, diagnostics and therapeutics must be allocated fairly to ensure justice, utility, beneficence and reciprocity in the outbreak response.

- For interventions for which supply is limited or access is difficult, such as vaccination of people at risk before exposure, public health actors should allocate and prioritize supply by following relevant ethics principles such as beneficence, utility and justice. This means offering access fairly to benefit the greatest number of people regardless of status.

- Allocation may involve prioritization of marginalized at-risk populations for outreach activities. Proactive mitigation of any potential risk of stigmatization is necessary.

Action in the face of uncertainty (evidence): Public health action is often compatible with beneficence, utility and justice when scientific evidence is limited; scientific evidence must be sought to reduce uncertainty and improve preparedness.

- Because the evidence for newer countermeasures is limited, there is an ethical and policy tension between making products considered effective and safe available in order to protect individuals (beneficence) and to help stop the outbreak (utility) and restricting use of products only to research contexts until stronger evidence emerges (respect for persons, utility).

- Investment and support are required to scale up mpox research and access to countermeasures during the outbreak response (including clinical trials of vaccines and treatments; monitoring, collating and disseminating emerging real-world evidence, and integrating it into existing guidance and policy).
This policy brief is intended to complement these documents by providing guidance on key ethical issues that have arisen in the context of the mpox outbreak response, focusing on three major areas: stigmatization and discrimination, the availability and allocation of medical interventions, and the importance and role of scientific and public health evidence. These topics are analysed with reference to established ethical principles in outbreak response: justice, beneficence, utility, respect for persons, liberty, reciprocity and solidarity. (See Definitions section)

The main intended audience of the policy brief are national governments, public health authorities and health-care institutions and providers, as well as civil-society and non-governmental organizations.

This document was prepared by a subcommittee of the WHO COVID-19 Ethics and Governance Working Group, in collaboration with the WHO Health Emergencies Programme technical team on mpox, the WHO Department of HIV, Hepatitis and Sexually Transmitted Infections and other related departments. For details, see the Annex. The subcommittee opted in the first instance to focus on ethical issues related to national or local mpox responses, which also have implications for the global response. These issues relating to mpox discussed by the subcommittee are listed in Table 1.

### Definitions of ethical principles in outbreak response

<table>
<thead>
<tr>
<th>Principle</th>
<th>Description</th>
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<tbody>
<tr>
<td>Justice</td>
<td>Encompasses two concepts: equity (fairness in the distribution of resources, opportunities and outcomes) and procedural justice (a fair process for making important decisions).</td>
</tr>
<tr>
<td>Beneficence</td>
<td>Acting for the benefit of others, such as relieving individuals’ pain and suffering.</td>
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<tr>
<td>Utility</td>
<td>Promoting the well-being of individuals or communities.</td>
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<tr>
<td>Respect for Persons</td>
<td>Treating individuals in ways that are fitting to and informed by recognition of our common humanity, dignity and inherent rights.</td>
</tr>
<tr>
<td>Liberty</td>
<td>Includes a broad range of social, religious and political freedoms, such as freedom of movement, freedom of peaceful assembly, and freedom of speech.</td>
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<tr>
<td>Reciprocity</td>
<td>Making a fitting, proportional return for contributions of people.</td>
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<tr>
<td>Solidarity</td>
<td>A social relation in which a group, community, nation or, potentially, a global community stands together, justifying collective action in the face of common threats and supporting efforts to overcome inequalities.</td>
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Table 1: Ethical issues regarding the mpox outbreak response discussed by the Ethics and Governance Working Group, 2022–2023

<table>
<thead>
<tr>
<th>Topic</th>
<th>Ethical issues discussed</th>
<th>Key ethical principles</th>
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<tbody>
<tr>
<td>Declaration of a public health emergency of international concern</td>
<td>Appropriate circumstances for a declaration, implications for resource allocation and international attention, consistency of determinations as a public health emergency of international concern.</td>
<td>Beneficence, utility, solidarity</td>
</tr>
<tr>
<td>Global and local allocation of mpox vaccines, diagnostics and therapeutics</td>
<td>Global justice and fairness; prioritization of health needs; lessons for future global outbreaks.</td>
<td>Justice, beneficence, utility, reciprocity, solidarity</td>
</tr>
<tr>
<td>Nomenclature</td>
<td>Addressing stereotypes and stigmatization associated with “monkeypox” and geographical references in virus clade names.</td>
<td>Respect for persons</td>
</tr>
<tr>
<td>Mpox research</td>
<td>Appropriate study design, use of placebo, prioritizing clinical trials over emergency use outside clinical trials, resource allocation for research and prevention of “neglected diseases.”</td>
<td>Beneficence, utility, respect for persons</td>
</tr>
<tr>
<td>Stigma and discrimination</td>
<td>Stigma as a barrier to health care; creating stigma-free pathways to vaccination, diagnostics and treatment; importance of community engagement.</td>
<td>Beneficence, utility, respect for persons</td>
</tr>
<tr>
<td>Allocation of vaccines, treatments and diagnostics</td>
<td>Allocative fairness; responsiveness to evidence and need; prioritization of mpox over other diseases and conditions.</td>
<td>Justice, beneficence, utility, reciprocity</td>
</tr>
<tr>
<td>Public health response</td>
<td>Balance of public and individual interests in potential responses, such as contact tracing, isolation and quarantine, case investigation, digital health surveillance, contact and travel restrictions, vaccination policies that ensure the promotion and protection of human rights globally, building the resilience of public health systems for infectious disease outbreaks.</td>
<td>Justice, beneficence, utility, reciprocity, respect for persons, liberty</td>
</tr>
<tr>
<td>Evidence</td>
<td>Uncertainty about the efficacy and safety of interventions; need for clinical trials and other sources of robust evidence.</td>
<td>Beneficence, utility, Respect for Persons</td>
</tr>
<tr>
<td>Community involvement in decision-making</td>
<td>Empowerment, participation and transparency, especially of neglected populations.</td>
<td>Respect for persons</td>
</tr>
<tr>
<td>Health communication and addressing mpox denial and belief systems</td>
<td>Respectful, sensitive communication; adaptation to social and cultural contexts; tension between public health and risk of stigmatizing communities.</td>
<td>Respect for persons, beneficence, utility</td>
</tr>
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Since the eradication of smallpox was declared by the World Health Assembly in 1980, mpox (also known as “monkeypox”(2), has become the most important orthopoxvirus threat to global health (3). The first human mpox case was detected in 1970 in the Democratic Republic of the Congo (4,5). After 1970, mpox occurred sporadically in Central and East Africa (clade I) and West Africa (clade II) (5,6). In 2003 an outbreak in the United States of America (USA) was linked to imported wild animals (clade II) (7–9). Since 2005, thousands of suspected cases are reported in the DRC every year (10–12). In 2017, mpox emerged in Nigeria (13) leading to an outbreak, with by 2021 over 226 confirmed and 550 suspected cases and a reported case fatality ratio of 4% among confirmed cases (14). Between 2018 and 2021, eight documented cases of mpox were reported to WHO from Israel, Singapore, the United Kingdom and the USA, associated with travel from Nigeria (14). The two major variant groups of the monkeypox virus are clade I, formerly known as the Congo Basin or Central African clade, and clade II, formerly known as the West African clade, which comprises subclades IIa and IIb (2).

In May 2022, WHO reported a global outbreak of mpox in previously unaffected countries, which was declared a public health emergency of international concern by WHO on 23 July 2022 (15). As of 31 May 2023, WHO had reported 87,858 confirmed cases of mpox and 143 deaths in 111 countries (16). The 10 countries that reported the largest numbers of confirmed cases as of May 2023 were Brazil, Canada, Colombia, France, Germany, Mexico, Peru, Spain, the United Kingdom, and the USA, accounting together for 83.9% of cases reported globally (16). While the current outbreak is linked primarily to clade IIb, clade I has been reported in several regions of Sudan for the first time, including an outbreak in refugee camps in eastern Sudan in mid-2022 (17).

Typical symptoms of mpox include fever, swollen lymph nodes and a rash (18–21); however, during the current global outbreak, new clinical features have been described, such as severe proctitis, urethritis and urinary retention. Mpox is usually a self-limiting disease, with symptoms lasting from 2 to 4 weeks (22). While most people with mpox recover without long-term sequelae, mpox can result in serious complications, including encephalitis (23–25), myocarditis (26,27), sepsis (28,29), bronchopneumonia (30,31), corneal ulcers and blindness (19,22,32–36). Illness can be particularly severe in people with weakened immune systems due to medication or other medical conditions, notably untreated or uncontrolled HIV infection (28,37). Infection with the monkeypox virus during pregnancy can lead to miscarriage or stillbirth (28,38–43).

Field studies showed that smallpox vaccines were approximately 85% effective in preventing mpox (44,45); however, newer vaccines have been developed that are safer and have immunogenicity similar to that of older vaccines. Before this event, the newer vaccines had not been deployed in an outbreak setting. During the outbreak, third-generation smallpox vaccines (MVA-BN, LC16-KMB) have been used in high- and middle-income countries. These vaccines were initially developed for smallpox; most countries in Africa affected by mpox had not previously had recourse to these products as in most settings, mpox outbreaks had occurred only rarely or sporadically. Conversely, in the Democratic Republic of the Congo, where the number of mpox case reports has risen steadily for decades, field studies of MVA-BN had been under way for several years (46). New mRNA-based mpox vaccines are also being developed (47). The antiviral agent tecovirimat, also developed for treatment of smallpox, is now undergoing clinical studies for use in clinical care of mpox, including in one study in the Democratic Republic of the Congo, which was planned before the global outbreak began (3,38–41,44,48).

Most of the available supply of second- and third-generation vaccines had previously been secured by a few countries for smallpox preparedness, and, in some cases, the
reserves had expired. At the beginning of the global outbreak, orders for MVA-BN were confirmed or placed by Australia, Canada, the USA and European countries. Interest in the products was also variable. For example, while the Revolving Fund of the Pan American Health Organization secured 130 000 doses for distribution in the Region of the Americas, only 12 of the 52 eligible countries placed orders (49). While there was an ample supply of LC16-KMB vaccine in Japan, this product was only licensed for the prevention of mpox in Japan in August 2022 and clinical data for this indication were also limited.

The global mpox outbreak presents features that distinguish it from previous outbreaks. In the past, clade I mpox outbreaks in central Africa initially demonstrated short chains of human-to-human transmission facilitated by close contact, usually in households (4,50). However, chains of transmission have become longer and longer and in Nigeria the role of sexual transmission in the clade II outbreak was initially under-recognized (51). In the global clade IIb outbreak, however, sustained human-to-human transmission in sexual networks resulted in rapid epidemic growth in many countries (52,53). The people most affected by mpox were men who self-identified as gay or bisexual or other men who have sex with men. While potentially effective (smallpox) vaccines, diagnostics and therapeutics were available in limited quantities in a few locations at the onset of the outbreak, their use still required data collection. Thus, combined with other public health measures, deployment of available vaccine raised policy and ethical issues regarding allocation, prioritization of access or research and discussions on research design (54). Thus, the interventions for supporting outbreak response varied widely both within and between countries with different resources, outreach strategies and prevalent attitudes to the outbreak itself.

In response to the ongoing outbreak, WHO has published five interim guidance documents on clinical and public health aspects of the mpox outbreak. They are for surveillance, case investigation and contact tracing (55); laboratory testing for the monkeypox virus (56); vaccines and immunization for mpox (44); risk communication and community engagement (57); clinical management and infection prevention and control (22); and a wide range of documents and tools with public health advice for use in risk communication and community engagement (41,58–66).
2. Ethics issues for mpox outbreak response

### 2.1 Stigma and discrimination

- A comprehensive definition of stigma and discrimination is provided by WHO public health advice on understanding, preventing and addressing stigmatization and discrimination related to mpox (58). Stigma in the context of health is ‘the negative association between a person or group of people who share certain characteristics and a specific disease. Discrimination is the behaviours that result from stigmatizing attitudes or beliefs.’ Others define stigmatization as “any attribute, trait, or disorder that marks an individual as being unacceptably different from the people with whom he or she routinely interacts, and that elicits some form of community sanction” (67,68). Stigmatization is an important public health problem in the context of many diseases, including HIV, mental health conditions and tuberculosis (22,69).

- In the 2022–2023 mpox outbreak, at least five forms of stigmatization have been noted, often simultaneously: those linked to skin manifestations of infectious disease, racist stereotypes, living with HIV (48% of cases for whom such data are available), a disease transmissible through sexual contact (82% of cases for whom such data are available) and a disease that disproportionately affects gay, bisexual and other men who have sex with men (84% of cases for whom such data are available) (16). It should be noted, however, that, while gay, bisexual and other men who have sex with men constitute the majority of cases in the global mpox outbreak, anyone, regardless of sexual orientation or gender identity, can contract mpox, as the disease is transmissible by close contact with lesions, body fluids, respiratory droplets or contaminated materials such as bedding (22). Key populations at heightened risk for severe outcomes if they contract mpox include people with weakened immune systems (such as people with untreated or uncontrolled HIV infection), the elderly, children under 8 years of age, and pregnant women (28,39,43).

- Many studies have identified stigmatization as an important barrier to access to health care. Stigmatization can result in people with mpox not seeking diagnostic testing or treatment, putting their own health and the health of their communities at risk (70,71). It can also lead people not to seek information, advice or preventive measures (e.g. vaccination) against mpox. This is notably the case of gay, bisexual and other men who have sex with men who live in areas where they may fear criminalization, social exclusion or violence if such information is disclosed in any situation, including when they contact health-care services regarding mpox (72).

- WHO has issued public health advice on understanding, preventing and addressing stigmatization and discrimination related to mpox (58) and interim guidance on risk communication and community engagement for mpox outbreaks (57). In addition, the WHO Global Health Sector Strategies on HIV, viral hepatitis and sexually transmitted infections (73) and the UNAIDS Global AIDS Strategy (72) provide frameworks for addressing disease stigmatization. To complement these documents, the present policy brief focuses on key ethical issues related to stigmatization in the contexts of case investigation, contact tracing, quarantine and isolation.
Case investigation and contact tracing are important elements of the public health response to mpox. WHO rapidly issued public health interim guidance on this topic, which recommends the following measures: notification of suspected cases nationally and reporting of probable and confirmed cases to WHO, including epidemiologically relevant information; case investigation, including questioning about possible sources of infection or exposure; laboratory examination; contact identification and contact tracing (55).

A particular ethical challenge is deciding how much personal information to collect from people with suspected or confirmed mpox. In cases where transmission is likely to have occurred during sexual contact, case investigation and contact tracing would require the collection of information about people’s sex lives and history, including their sexual behaviour (e.g. oral sex, anal intercourse, condom use), the contact details of any sex partners, and relevant co-infections, including HIV, viral hepatitis and other sexually transmissible infections. This information is crucial for understanding mpox epidemiology and designing effective prevention programmes. Thus, collection of this information is in the interests not only of the individuals and affected communities but also of public health. In some contexts, however, communicating such information may put a person at risk for other reasons. Same-sex relations between consenting adults are criminalized in more than 60 countries worldwide (74). In many settings, gay, bisexual and other men who have sex with men have reason to fear social exclusion, abuse or violence if they disclose their sexual orientation and/or behaviour. In addition, disclosure of HIV or another sexually transmitted infection can result in social exclusion and violence in some communities and can put a person with mpox at risk of persecution in countries in which exposure to HIV and non-disclosure of HIV status are criminalized (72).

Policy-makers, public health professionals and health-care workers should be aware of these risks when designing and implementing case-investigation and contact-tracing programmes. To be successful, such programmes for mpox should be complemented by efforts to address stigmatization (70). Health authorities and communities should create stigma-free pathways to mpox prevention, diagnostics and treatment and should ensure that people who access health care and their contacts do not risk criminalization or violence. Health-care workers should be aware of the risks of stigmatization and criminalization that may arise when collecting, documenting or reporting information on people with an mpox diagnosis (even the mpox diagnosis itself) in some countries, and tailor their approach accordingly (e.g. not ask about a patient’s sexual history). If classic contact-tracing by public health authorities could put people with mpox at risk of criminalization, innovative solutions should be found by working with the affected community, such as identifying venues where contact may have occurred. People with mpox should be encouraged to disclose their diagnosis directly to the people with whom they were in contact, even if the contact details of those people are not provided to public health authorities. People with an mpox diagnosis should be assured of confidentiality if disclosing their diagnosis could put them at a risk of criminalization or violence by family, close contacts or other people.

In view of these risks, ensuring the confidentiality of all data collected in surveillance systems of any kind in the context of case investigation and contact tracing is crucial. Identifiable data must not be used for any purposes other than identifying and informing potential contacts of people with mpox and monitoring and preventing the spread of the virus. Health authorities and institutions must also take sufficient precautions to ensure data safety, to prevent unauthorized access to and use of such data, and to ensure that the data are accessible only to institutions and people entrusted with public health and not with other public bodies, such as the police for criminal investigations.

Full data safety can never be absolutely ensured, even with these precautions. There always remains a risk of misuse of or unauthorized access to such data. Authorities have an obligation to minimize this risk. The potential public health benefits must be
Isolation and quarantine and prevention of stigmatization

National guidelines for case investigation, surveillance and contact tracing should be based on an assessment of these risks for people with an mpox diagnosis and their contacts. In addition, public health authorities and health-care workers should be sensitized to the importance of confidentiality in such matters and to the potentially devastating consequences of not respecting it. Particular caution should be exercised if vulnerable groups (e.g., children and young people, women, refugees, and men who have sex with men in some settings) are involved, or if case investigation and contact tracing must be conducted in a setting of violence (e.g., a person living in an abusive relationship with a record of being a victim of domestic violence). Concerned communities or, in contexts where there are no official community representatives, social workers, physicians and other activists should be involved in developing such guidance. In situations where official contact-tracing and reporting may put people with mpox and their contacts in serious danger of criminalization or violence, people with mpox must be adequately informed of their right to decide on how to inform their contacts.

WHO interim guidance recommends isolation of persons with confirmed or suspected mpox during the presumed and known infectious periods (prodromal and rash stages of the illness), and of contacts who develop prodromal symptoms or lymphadenopathy, even without a rash. It does not recommend quarantine or exclusion from work for contacts as long as no symptoms develop (55). It also does not require isolation for any fixed period, emphasizing rather the importance of the time to healing of skin lesions. WHO also acknowledges that where isolation cannot be maintained for any reason, affected persons should cover their lesions and avoid physical contact with others (60). For contacts of cases, a period of self-monitoring or supervised monitoring is recommended for a period of 21 days, generally accepted to be the maximum incubation period (55). In response to early evidence that transmission may occur before symptoms become apparent (75–78), contacts of persons with mpox are also advised to refrain from sexual activity for 21 days, which is generally accepted to be the maximum incubation period for mpox (55).

2.1.2 Isolation and quarantine and prevention of stigmatization

Isolation and quarantine are often important for protecting public health and containing infectious disease outbreaks. In 2016, WHO issued ethics guidance for managing infectious disease outbreaks that includes a discussion of ethical issues in restricting freedom of movement, isolation and quarantine (1). In view of its epidemiological characteristics, however, mpox presents specific ethical challenges with regards to isolation. It should be noted that quarantine of contacts is not required or recommended for mpox.

First, the infectious period for mpox is variable and may therefore be difficult to communicate (52,53,75,78). The infectious period may be significantly longer than those for other diseases because of the high infectiousness of the rash lesions until they heal by crusting over and falling off. Healing can take days but may take 2–4 weeks (or longer in severe cases) (22). As emerging evidence suggested that the infectious period may also begin earlier than previously documented, before symptoms appear, perhaps due to the mode of transmission through direct contact with mucosa or body fluids, as noted this led WHO to recommend that contacts, and particularly sexual contacts, avoid sexual activity during the potential incubation period to avoid passing on the infection, even if they have no
or few symptoms or visible lesions (55). This precaution is neither isolation nor quarantine but represents a period of restraint similar to that usually recommended to a contact of a person with a sexually transmissible infection. Nonetheless, this may require effort, behaviour change and, for sex workers, loss of income.

- Secondly, changing public health policies with respect to isolation may have unintended consequences. In the global outbreak, many patients diagnosed with mpox have had less severe lesions only in areas of the body that can be covered. This has raised the question of whether the isolation period could be shortened even though the rash or lesions persist, as long as the lesions can be covered. Some jurisdictions have considered relaxing isolation measures in favour of such new provisions. Indeed, there may be less incentive for individuals to avoid testing and diagnosis if isolation is not an absolute requirement. Conversely, lifting an isolation requirement as a public health policy may be based on overestimation of the ability of individuals to assess their condition adequately and thereby introduce infectious disease risks to others in the community. Lifting a requirement to isolate may also provide an incentive to health authorities, clinicians, social services, employers and insurance companies to reduce the standard of care and services available to patients or clients. This could occur when an already marginalized individual or community requires more support rather than less. It is also critical for global and national health authorities to consider whether changing core public health policies would have unintended consequences for communities other than those for whom the policies were written. For example, when considerable extra effort must be made to organize isolation facilities for an outbreak of mpox, such as for under-resourced communities or families, in refugee camps or in any context in which the modes of transmission are not well understood, the risk to the community of lifting an isolation requirement may exceed the perceived or actual benefit to the individual or actually cause harm if care and support are withheld or not available. WHO has therefore recommended that any relaxation of isolation measures during the infectious period be carefully considered by health authorities and clinical teams in the light of the local context and individual circumstances (59,60).

- Thirdly, stigmatization poses particular challenges. In many countries, mpox is viewed as a disease that primarily affects gay, bisexual and other men who have sex with men (indicating the importance of public education and messaging about different possible modes of mpox transmission). People with suspected or confirmed mpox might have to disclose the reason for being isolated from their social environment (e.g. family, friends, employers), which may place them at a risk of violence, discrimination and social exclusion, which may be important source of social stress and lead to significant deterioration of their mental and physical health.

- Isolation in health-care facilities rather than at home could benefit individuals who are at risk of violence or stigmatization by providing an opportunity to recover and be treated in a safe place. For others, isolation at home might be preferable, particularly if they live alone, do not fear social isolation and can continue remote employment (in settings where they are not stigmatized for mpox infection or do not have to disclose their medical condition), or if they can be supported by family members, who can safely provide care if properly informed and resourced.

- WHO has not recommended quarantine for contacts of persons with mpox, as the risk of infecting others during daily activities, such as attending work or school, is very low. Ward et al. (75) estimated that a quarantine period of 16–23 days would be required to detect 95% of people with a potential infection. As the risk to an individual contact of such an extended quarantine period would probably far exceed any benefits to the community, quarantine for contacts would violate the principle of proportionality, except under very exceptional circumstances.

- Thus, in general, the potential benefits for public health of compulsory or voluntary isolation must be proportionate to the potential harm to isolated persons. Potential benefits of isolation for the individual and their family must also be considered. “Proportionality” means that these measures fill a legitimate public health purpose, are adequate and necessary to achieve that purpose and strike a fair balance between the interests of public health and of
the individuals concerned. Because of the low risk to others, quarantine is not recommended for contacts of people with mpox, for whom self-monitoring is recommended; if deemed useful, supportive health monitoring by local health authorities can be offered or added for persons who may be contacts of a case.

National guidelines should provide a clear framework for isolation based on: (i) the epidemiological characteristics of the respective mpox outbreak, including information on modes of transmission; (ii) the importance of isolation to contain the respective outbreak; (iii) potential benefits or risks for people with mpox and/or their contacts as a consequence of mpox isolation; and (iv) specific circumstances under which isolation could be lifted even if skin lesions are not yet healed, and mitigation measures that can be put in place (e.g. covering lesions, wearing a mask as lesions may occur in the mouth or throat). Information should be directed to the public as well as to individuals affected or at risk in clear, culturally appropriate language. In line with WHO technical guidance (55), quarantine of contacts or exclusion from work would be disproportionate, as long as no symptoms develop.

Public health authorities should be sensitized to any (potential) risks to the physical, mental and social well-being of people with mpox and/or their contacts before they issue mpox isolation orders, in order to mitigate those risks. Affected and at-risk communities should be included in decision-making. Caution should be exercised with regard to vulnerable groups (e.g. children and young people, women, refugees, and in settings in which men have sex with men) and for people living in a setting of violence (e.g. living in an abusive family relationship). As a general principle (and not only in the context of mpox), adequate mental health care and financial support to meet basic needs (e.g. nutrition, clean water, shelter) should be ensured for all people with mpox and/or their contacts if necessary throughout isolation. Provision of sufficient financial support for basic needs is imperative according to the principles of justice, solidarity and reciprocity: every effort should be made to support people who contribute to protecting public health by isolating themselves, through locally appropriate means to cover their living expenses during this period.

2.2 Availability and allocation of medical interventions

- When vaccines, therapeutics and/or diagnostics are in short supply or prohibitively expensive, pressing ethical questions emerge about equitable distribution. The 2016 WHO guidance for allocation of scarce resources during infectious disease outbreaks applied general principles to generate a list of considerations: balancing utility and equity; defining utility; attending to vulnerable populations; and reciprocating to those who contribute to outbreak response (1).

- In the mpox outbreak, the unequal international distribution and the principle of solidarity suggest that, even while studies of effectiveness are under way, countries with access to a supply should consider sharing their supply with countries that might also have populations in need during such an outbreak, so that vaccines can be deployed more equitably, even if in limited quantities appropriate for use in research or for compassionate use based on experience with that class of vaccines. While such inequity persists, supply will probably remain constrained in many places, and countries may have to make difficult decisions about which populations to prioritize for vaccination (79). WHO has continued to support and broker bilateral vaccine donation agreements.

- Just as the WHO SAGE working group on coronavirus disease (COVID-19) vaccine allocation applied these principles to approaches for allocating COVID-19 vaccine (80), an ethically principled approach is
necessary for distribution of vaccines for mpox. Allocation in an outbreak of mpox must be based on its unique epidemiology, in particular the risk factors that increase the likelihood of being affected, suffering and/or dying from mpox (81). For example, as noted earlier, evidence has emerged that people with untreated or uncontrolled HIV infection are at high risk of severe mpox disease. The principles of beneficence and utility align with ensuring scarce resources reach the individuals who would benefit most, and prevention and control programmes can strengthen each other by integrated action to reach people at risk with necessary interventions. Some countries have opted to use their scarce vaccine first for post-exposure prophylaxis for individuals with known contacts with someone with mpox (82). In some contexts, however, wider distribution may be more efficient because of practical challenges in contact tracing, as noted. Over time and as the issue of supply eased, more countries offered vaccines to protect more people at risk before exposure.

- Trade-offs may be necessary when those at greatest risk face substantial stigmatization. WHO has recommended that, in contexts where men who have sex with men are at high risk of contracting mpox, they should be a priority for pre-exposure vaccination within carefully designed immunization programmes (44). While reaching these populations will maximize the benefits to those who are most vulnerable, care must also be taken to avoid further stigmatization by requiring individuals to reveal their at-risk status to unfriendly entities or media outlets, for example. Nevertheless, concern about stigmatization should not be used as a reason for not prioritizing at-risk communities. In such circumstances, injustice may be compounded if risk factors associated with stigmatization during allocation are ignored. Instead, efforts should be made to ensure the privacy of individuals receiving interventions and proactively counteract stigmatization through public health outreach. Specifically, provision of vaccination in the same way as other health services may reduce “recognition” of the reason for seeking health care and thereby reduce the fear of stigmatization and avoidance of care.

- Resolving such tensions requires careful consideration of ethics trade-offs and inclusive engagement of affected communities and relevant stakeholders. In particular, key populations should be involved, such as men who have sex with men, particularly those who may be further marginalized and for whom access to services may be limited (83). Other groups who may be at risk in different contexts, such as health workers or workers whose livelihood depends on hunting and the sale of bushmeat, whose voices may not be heard without deliberate attention, should also be engaged. As noted previously in WHO guidance, “In addition to being ethically important in its own right, community engagement is essential to establishing and maintaining trust and preserving social order” (1). This is true for all communities that may be at risk, wherever they may be.
As noted, deployment of mpox medical countermeasures is complicated by the limited evidence of their effectiveness in the context of this outbreak, which has ethical ramifications. Decades of development have led to a unique situation in which older vaccines shown to be effective in the eradication of smallpox have been superseded by newer products in the same class that are safer than their forebears but for which there is no evidence of effectiveness in the context of an outbreak of either smallpox or mpox. There is therefore an ethical tension, whereby products considered to be safe and likely to be effective based on pre-clinical and clinical data should be deployed to protect individuals (beneficence) and help stop the outbreak (utility), while uncertainty suggests that more evidence should be collected on their effectiveness in the new circumstances (respect for persons, utility).

The current vaccines were originally developed for use against smallpox, and evidence for their effectiveness in mpox is based on studies in experimental animals, studies of immunogenicity and safety in humans, use for laboratory personnel at occupational risk of exposure and, more recently, emerging observational data on people who were vaccinated during the global outbreak (44,84,85). While observational studies provide valuable real-world evidence, they are subject to selection bias (e.g. individuals who seek vaccination may be more likely to take other precautions against infection), which clinical trials are designed to obviate.

Because of the vaccine shortfall early in the outbreak, some countries opted for dose-sparing approaches, whereby one-fifth of the standard dose is given in order to increase the number of people who can be vaccinated (86). As evidence for the efficacy of fractional dosing is limited and mixed (87,88) and intradermal administration may more often cause injection-site reactions, more research is being conducted to fully establish the efficacy and side-effects of dose-sparing approaches. Previous guidance on fractional vaccine dosing for other infectious diseases, such as polio (89) and yellow fever (90), may be relevant to decisions in relation to mpox.

Similarly, current evidence for the effectiveness of antiviral treatments such as tecovirimat, brincidofovir and the compound most recently approved for mpox, NIOCH-14 (with a mechanism of action similar to that of tecovirimat), comes from studies in experimental animals, assessment of pharmacokinetics, studies of clinical safety and a growing body of observational clinical data (22,91). Clinical trials of vaccines and therapeutics are underway (92–94).

Because of resource constraints, infrastructural capacity and other factors, it will not be feasible to set up a randomized controlled trial or even other appropriate clinical studies for every population that would require a given mpox intervention. In such circumstances, WHO has developed an ethical framework for “monitored emergency use of unregistered and experimental interventions” to guide use of interventions for which there are no formal clinical trials (95). The framework is intended to benefit recipients of medical products when clinical trials are not feasible, while ensuring that data from interventions are systematically recorded and shared for future research and practice (95). Nevertheless, even such a process may itself delay access to interventions if not implemented expeditiously in the interests of public health during a multi-country outbreak.

Uncertainty about the effectiveness of vaccines and therapeutics for preventing and treating mpox is an important consideration during a public health emergency. Delaying distribution until clinical trials are completed could result in exposure of large numbers of people to substantial, preventable harm. As there are several similar vaccine products (44) and different therapeutics proposed, securing effectiveness data on all will take time. While emerging evidence suggests vaccines are an effective adjunct to other public health
interventions in the context of outbreak response, and there have been no adverse safety signals for the use of tecovirimat for treatment, caution is warranted, especially as some interventions may carry a risk of adverse events in certain population groups. Moreover, as a matter of respect for persons, the uncertainty of the evidence concerning mpox interventions should be made transparent to individuals and communities before they are administered. While uncertainty could fuel scepticism about interventions and reluctance to receive them, respect for individuals and communities implies that recipients of interventions should be in a position to determine whether they accept the uncertainty of the benefits or risks involved in accepting or not accepting the intervention, through informed consent. It is therefore also of critical importance to ensure that the use of evidence in drafting interim recommendations rely on as robust an assessment as possible of the values and preferences of affected communities regarding access to and use of interventions for which evidence is evolving.

The GRADE approach to reviewing evidence accounts for such preferences to be taken into consideration in the process of systematic review. In addition, transparent, culturally appropriate communication of risks and benefits can promote trust in public health entities in the long run (57).

- The evolving evidence base highlights the importance of continuing support for clinical trials of mpox countermeasures in various settings in order to generate a standard of evidence that can ensure that safe, effective interventions are used where necessary and that any interventions found to be unsafe and/or ineffective are taken out of distribution. This is not only a scientific imperative but an ethical one. The obligation of beneficence through public health extends into the future, and a more robust evidence base from well-designed clinical trials and best-in-class observational studies (54) will help prevent infection, suffering and death from mpox in the long run.
As stressed above, ethics considerations play a major role in the design and implementation of policies for mpox outbreak response. This policy brief is intended mainly for national governments, public health authorities and health-care providers as well as civil society organizations, and thus focuses on ethical issues raised by the global mpox outbreak response and national and local implications, in particular: stigmatization and discrimination, the availability and allocation of medical interventions, and the role of and search for evidence on countermeasures during an emergency. Due consideration of ethics principles and how they support decision-making can help public health authorities to ensure that mpox response policies balance the urgent need for response with the rights and needs of individuals.

This policy brief outlines several universal principles that should guide the mpox response at national level, with due consideration of local cultural, social and legal contexts. The universal principles are justice, beneficence, utility, respect for persons, liberty, reciprocity and solidarity. WHO Member States should ensure that ethics considerations are given due weight in the design and implementation of public health measures, including responses to infectious disease outbreaks.

3. Conclusion
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Annex

Methods

This document was developed by consensus and a review of existing guidance and recommendations. For this purpose, WHO formed a multi-disciplinary subcommittee of the WHO COVID-19 Ethics and Governance Working Group, consisting of 17 experts from all WHO regions who met fortnightly for approximately four and a half months. The subcommittee received information from the WHO technical team for mpox and from other WHO departments on the current status of the international response to the mpox outbreak. This was used to compile a preliminary set of ethical issues arising from the outbreak, which was refined to identify the ethical issues most pertinent to countries that are responding to the current outbreak.

The subcommittee decided that sustained analysis of a small group of key issues would be of more value to decision-makers than a broader overview with only superficial ethical reflection. In conducting this analysis, the working group identified several distinctive features of mpox that require sustained ethical attention (see Background). Given the intended readership, this document focuses on issues faced domestically (nationally) and locally, although these issues also intersect with international guidance and globally coordinated response. The issues included stigmatization and discrimination in certain affected communities, the scarcity of interventions, and the limited evidence base. Table 1 provides an indicative list of the broader ethical issues raised by various aspects of the mpox response considered by the subcommittee, all of which are not addressed in this document. Further ethical reflection would be necessary in setting policy in those domains.

When possible, the document cites existing WHO guidance and recommendations either directly related or applicable to the mpox outbreak (such as on other infectious diseases such as HIV, COVID-19, tuberculosis and influenza). When such guidance or recommendation was not available, guidance and recommendations from other entities deemed to be relevant and useful were used.
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