Mpox gastrointestinal manifestations: a systematic review

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ABSTRACT

Introduction Mpox is a viral infection caused by the monkeypox virus, a member of the Poxviridae family and Orthopoxvirus genus. Other well-known viruses of the Orthopoxvirus genus include the variola virus (smallpox), cowpox virus and vaccinia virus. Although there is a plethora of research regarding the dermatological and influenza-like symptoms of mpox, particularly following the 2022 mpox outbreak, more research is needed on the gastrointestinal (GI) effects.

Objectives This systematic review is to outline the GI manifestations of the monkeypox virus.

Methods The authors conducted this systematic review using guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. A search was conducted through the PubMed, EMBASE and MEDLINE databases from January 1958 to June 2023. The authors selected English language papers that discussed the GI symptoms in mpox patients. A manual search was also conducted in the reference sections of these publications for other relevant papers.

Results 33 papers involving 830 patients were selected for this review. The GI manifestations in mpox patients are proctitis, vomiting, diarrhoea, rectal pain, nausea, tenesmus, rectal bleeding and abdominal pain. Although various papers explored transmission routes, one paper established a direct connection between anal-receptive sex transmission route and the development of a GI complication (proctitis). Another study reported that the mode of transmission could potentially impact the occurrence of GI symptoms and severity of the disease. The reviewed papers did not discover a relation between the severity of dermatological and influenza-like symptoms and the GI manifestations mentioned.

Conclusion This systematic review confirms that GI manifestations are observed in mpox patients. GI symptoms of mpox are crucial for gastroenterologists and other healthcare professionals to recognise in order to address patient discomfort and further understand the pathophysiology of the virus.

BACKGROUND

Mpox (monkeypox) is a viral infection caused by the monkeypox virus (MPXV), a member of the Poxviridae family and Orthopoxvirus genus. Similar to other Poxviruses, the MPXV is a double-stranded DNA virus that is linear, brick or box-shaped and enveloped. The core of the virus is described as dumbbell-shaped. Poxviruses are unique compared with other DNA viruses as they are the largest DNA virus and can replicate in the cytoplasm with other DNA viruses as they are the largest DNA virus and can replicate in the cytoplasm due to a DNA-dependent RNA polymerase. Well-known viruses of the Orthopoxvirus genus include the variola virus, cowpox virus (CPXV), camelpox virus and vaccinia virus. The naming of the Orthopoxvirus genus viruses does not represent the entire host range but rather the viruses are named based on the host where the virus was first identified. For example, the CPXV was first identified in cows, but its host range includes humans, canines, felines, rodents and other mammals. Previous papers have discussed genomic relationships in the nucleotide sequences among these Poxviridae viruses. From an immunological perspective, an infection with one Poxviridae virus would provide either partial or complete immunity to other viruses in the same genus. The smallpox and mpox vaccine, JYNNEOS, was estimated to have a vaccine effectiveness of 66% with 2
Transmission of the MPXV can occur through two pathways: human-to-human or animal-to-human. For human-to-human transmission, it can be direct or indirect contact such as through intercourse, vertical transmission, inhalation of respiratory droplets and fomites such as clothes. Animal-to-human transmission can occur from invasive forms of contact, such as scratches or bites from an infected animal, as well as non-invasive forms of contact, such as cleaning cages and being within 6 feet of an infected animal. Following either of these transmission methods, the virus will reproduce at the inoculation site and then travel to nearby lymph nodes. The virus can then spread to skin and tertiary organs. The incubation period for the virus is 1–3 weeks, and patients are not considered contagious during this period. However, patients with mpox are still recommended by physicians to isolate for 2–4 weeks.

Mpxox was first discovered in 1958 when monkeys, being shipped from Africa to Denmark, developed a pustular rash; hence the name ‘monkeypox.’ The first human mpox infection was reported in 1970 in the Democratic Republic of Congo (DRC) when an infant presented with smallpox-like blisters. Mpxox is currently endemic to West Africa and Central Africa, including the DRC, where the first human monkeypox infection was documented. The first reported case of monkeypox outside of Africa was in 2003 in USA following a shipment of exotic animals imported from Ghana. A 5-year-old girl in Wisconsin was bitten by a prairie dog and developed a fever and cellulitis. Originally, there was no sign of a pox virus. However, the patient’s mother then developed symptoms and poxviridae was found in skin lesions. Authorities then reported 72 other poxviridae cases in the Midwestern, USA from May 2003 to July 2003.

In May 2022, cases of mpox infections were reported in non-endemic countries, such as Spain, and a global outbreak was declared. The Centers for Disease Control and Prevention (CDC) reported a total of 88,549 cases globally. In November 2022, the World Health Organization (WHO) suggested renaming ‘monkeypox’ to ‘mpox.’ For 1 year following the WHO decision, as ‘monkeypox’ is phased out, both names will be used interchangeably. The virus name, however, will still be ‘monkeypox’ until the International Committee on the Taxonomy of Viruses has officially declared a name.

While the most frequently observed symptoms following monkeypox infection include rashes, fever, muscle aches and sore throat, less common complications involving secondary bacterial infections, oral ulcers and gastrointestinal (GI) manifestations have been reported. The GI complications reported in mpox patients include nausea, vomiting, diarrhoea, abdominal pain, rectal bleeding, rectal pain, rectal perforation (RPE), painful defecation, proctitis and tenesmus. Nausea is defined as the uncomfortable feeling that comes before vomiting. Vomit is the ejection of gastric contents through the mouth. Diarrhoea is when there is increased water in the stool due to either decreased reabsorption of water or increased secretion of water. Abdominal pain is discomfort that is felt below the chest and above the groin area. This pain is sometimes described by patients as being felt inside or outside the body. Rectal bleeding is the presence of blood from the anus, while rectal pain (used interchangeably with anal pain) is discomfort in the rectal region. In this paper, we placed proctalgia in a separate category from anal and rectal pain as proctalgia is defined as sudden, severe and episodic anorectal pain due to the potential involvement of anal sphincter spasms. RPE (used interchangeably with bowel perforation) is the formation of a hole in the rectal region. Painful defecation, also known as dyschezia, is discomfort related to the act of defecation. Proctitis is defined as inflammation of the anus or rectal lining, and proctitis is a broader term that can encompass rectitis in clinical contexts. In this paper, the term ‘proctitis’ is used to denote a diagnosis as established by the authors in the referenced publication. Finally, tenesmus is the painful and constant urge to defecate despite an empty colon or recent bowel movement. Potential long-term complications in untreated mpox patients include sepsis, dehydration, encephalitis, blindness, acute respiratory distress syndrome and haemorrhagic disease.

Treatment of mpxox depends on the severity of symptoms, location of the infection and immunological status of the individual. In milder cases, patients can be given supportive care such as sitz baths, stool softeners, Non-steroidal anti-inflammatory drugs (NSAIDs), oral acetaminophen or topical lidocaine for proctitis. In addition, topical lidocaine can be used for cutaneous lesions. Tecovirimat, an antiviral drug, is the drug of choice for the following categories: immunocompromised patients, severe manifestations, patients at-risk for severe complications, patients in severe pain and eye infections. The mechanism of action of tecovirimat is the inhibition of the VP37 envelope protein, an orthopoxvirus protein, which is responsible for viral formation, maturation and release. In immunocompromised individuals who may require postexposure prophylaxis, intravenous vaccinia immune globulin can be considered but its success rates are still undetermined in the literature.

To the author’s knowledge, one peer-reviewed meta-analysis has been completed and published on the topic of the GI manifestation of mpox. While the previously published systematic review and meta-analysis may appear analogous regarding research inquiries, there are many noteworthy distinctions that warrant a novel systematic review. First, many of the findings regarding clinical manifestations were different due to the methodology timeline of the previous systematic review. In our study, we determined that proctitis was a predominant manifestation among a significant majority of mpox patients presenting with GI symptoms. Conversely, the previous systematic review reported that proctitis had
a prevalence of only 11%. This difference in findings can be attributed, in part, to the fact that the previous systematic review exclusively considered publications that were published up to October 2022, while our systematic review extended to papers that were published until the summer of 2023. Consequently, the previous systematic review failed to incorporate the newest case studies, which have highlighted that proctitis is more prevalent than was initially reported. It is essential to note that the 2022 mpox outbreak, beginning in May 2022, resulted in multiple case studies and research papers that were eventually published in early 2023, all of which were not accounted for in the prior systematic review.

Second, our systematic review extensively reported on topics from the public health perspective. This includes considerations on whether mpox should be considered a sexually transmitted infection (STI) and discussions on healthcare provisions in underserved and vulnerable communities. The inclusion of these discussions is critical as it allows healthcare professionals and public health authorities timely access to the existing literature to enable proper guidance to at-risk communities.

Third, although the previous systematic review did discuss common symptoms, the paper omitted discussions on the rarer manifestations of mpox. In marked contrast, our systematic review dedicated attention to the two rare manifestations of RPE and rectal proctalgia. This information holds significance as the reporting of rare and novel manifestations provides healthcare professionals with valuable insight for an accurate mpox identification.

Although there is a plethora of research regarding the dermatological and influenza-like symptoms reported by mpox patients, particularly following the 2022 mpox outbreak, more research is needed on documenting GI symptoms. The objective of this systematic review is to outline the GI manifestations in patients infected by mpox, which includes an investigation into the pathophysiology of GI conditions mentioned by prior studies.

METHODS
The authors conducted this systematic review using a checklist outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The authors did not prepare or register the protocol for this review.

Search strategy and eligibility criteria
The following keywords were used in the search: (monkeypox OR (monkeypox virus) OR (mpox)) AND ((gastrointestinal) OR (gastroenterology) OR (nausea) OR (vomit) OR (diarrhea) OR (proctitis) OR (rectal) OR (rectum) OR (liver) OR (abdomen) OR (pain) OR (enterocytes) OR (blood) OR (perforation) OR (stool) OR (STDs)). Additionally, the authors scanned references of relevant papers to search for other articles. The databases were PubMed, EMBASE and MEDLINE.

The screening process began through the first author (RR) who scanned through the paper’s abstract, title, exclusion criteria and inclusion criteria. The second author (AS) independently analysed the papers to ensure they met the inclusion criteria. If there was confusion or disagreement regarding whether the papers should be included, discussions were facilitated among the first three authors until a resolution was reached.

The review’s inclusion criteria were peer-reviewed English language studies that investigated or reported the GI complications of mpox. The review did not place a restriction of demographics and geography. The exclusion criteria consisted of the following: papers that were duplicated among database searches, papers that did not specifically include the GI manifestations of mpox, published systematic reviews and meta-analyses, weekly update reports from government agencies such as the CDC and European Centre for Disease Prevention and Control (ECDC), and other forms of grey literature such as conference abstracts. Specifically, papers that mentioned dermatological complications of mpox but not GI symptoms were excluded. If the papers did mention other complications, the authors analysed the paper to decide if the paper fulfilled the criteria. Refer to figure 1 for a diagram of the PRISMA used in this systematic review.

Data collection and data items
Using tools such as Microsoft Word, Microsoft Excel and a data extraction sheet, one author, RR, organised the data from various studies. Papers were carefully explored to obtain information regarding authors, objectives, methodology, GI complications, patients, demographics, strengths, limitations and study design. The extracted data were then analysed independently by author AS or RM. Disagreements regarding extracted information were discussed openly among the first three authors until a resolution was reached. The defined outcomes were the GI manifestations from the MPXV and the calculated percentages of GI complications in mpox patients.

Risk of bias assessment
Quality assessment of evidence was completed independently by two authors using the Critical Appraisal Skills Programme. Any confusion was discussed among all the authors of the review. The review only included studies with a low risk of bias. The authors did not use other assessments such as the Cochrane risk-of-bias tool as we did not include any randomised controlled trials.

Synthesis methods and analysis
The data in table 1 and the information from the studies allowed us to provide the statistics of common and rare GI manifestations in mpox patients who initially presented with GI complications. These statistics are crucial in allowing physicians and readers to easily access and observe the connection between mpox and the broad range of GI complications in mpox patients. In addition,
we did not perform a meta-analysis due to the design of included papers and defined outcomes.

**Patient involvement**
This systematic review did not require consent forms or approval from patients and the public.

**RESULTS**

**Study selection and characteristics**
A total of 2214 published articles were initially identified following methodological searches of the three databases. Prior to the screening process, 752 duplicates were removed. A total of 1462 papers were screened and 1160 of those papers were excluded based on the exclusion criteria. The eligibility of the remaining 302 papers was assessed using the criteria described in the methods section above. Based on this eligibility process, 269 articles were excluded. Thus, 33 studies were ultimately included in the systematic review. The process is outlined in the PRISMA flow diagram labelled Figure 1. Among the 33 papers, 14 studies were case studies on either one patient or a group of patients, 3 studies were prospective and 9 studies were retrospective. Seven studies did not meet the study design for the three categories. Twenty-five studies reported on patients from the 2022 mpox outbreak, while eight studies reported on patients prior to the 2022 mpox outbreak. We were able to successfully identify the GI symptoms associated with the MPXV. After our systematic database search and a thorough investigation of the included papers, we did not discover a relation between the severity of dermatological and influenza-like symptoms and the GI manifestations mentioned.

**Common GI manifestations**
Thirty-two papers discussed the common GI manifestations in mpox patients. Basgoz et al, Gandrakota et al and Lucar et al discussed four different patients from the USA who presented with rectal pain and were diagnosed with proctitis. Similarly, Gedela et al reported on two patients from the UK who presented with the same complications. Labkriman et al, who discussed one patient from Belgium and Pfafflin et al, who reported

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**Figure 1** PRISMA flow diagram of study selection process. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
on five patients from Germany, corroborated the finding of proctitis and presentation of rectal pain. de Nicolas-Ruanes et al. discussed one patient from Spain with proctitis and symptoms of rectal bleeding and tenesmus. This study is significant as it was one of the first papers to establish proctitis as an associated finding of mpox and that proctitis can occur prior to systemic symptoms of fever, myalgia and headache. Mailhe et al. examined 45 patients from France who presented with abdominal pain, anal pain, diarrhoea, and proctitis. Messina et al. studied one patient from the USA who presented with painful defecation and consequent rectal pain. The authors reached the conclusion that physicians should take into account the presence of proctitis when considering a mpox diagnosis. Thornhill et al. studied 528 cases among 16 different countries and discussed the complication of proctitis and symptoms of diarrhoea, rectal pain, and tenesmus in 61 of the patients. Palich et al. published a case series in which 50 mpox patients at the Pitié-Salpêtrière Hospital in Paris, France were analysed. Out of the 50 mpox patients, 16 patients were diagnosed with proctitis (rectitis) and had symptoms of rectal pain, rectal bleeding and diarrhoea. Yakubovsky et al. reviewed 70 mpox patients in Israel and found that 26 of these

Table 1  Summary of GI manifestations in mpox patients from 1958 to 2023

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sample size (individuals)</th>
<th>Gastrointestinal manifestations</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aguilera-Alonso et al.</td>
<td>1</td>
<td>DI, VO</td>
<td>Spain</td>
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<tr>
<td>Angelo et al.</td>
<td>33</td>
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<td>Basgoz et al.</td>
<td>1</td>
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<td>Cassir et al.</td>
<td>30</td>
<td>PR</td>
<td>France</td>
</tr>
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<td>Català et al.</td>
<td>40</td>
<td>PR, PRA</td>
<td>Spain</td>
</tr>
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<td>Escudero-Torner et al.</td>
<td>1</td>
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<td>Spain</td>
</tr>
<tr>
<td>Formenty et al.</td>
<td>6–7</td>
<td>AB, DI, VO</td>
<td>South Sudan</td>
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<td>Garcia-Piqueras et al.</td>
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<td>Spain</td>
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<td>Gedela et al.</td>
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<td>UK</td>
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<td>Heskin et al.</td>
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<td>DI</td>
<td>UK</td>
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<tr>
<td>Huhn et al.</td>
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<td>Jezek et al.</td>
<td>22</td>
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<td>Labkriman et al.</td>
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<td>Mailhe et al.</td>
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<td>Iñigo-Martinez et al.</td>
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<td>Messina et al.</td>
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<tr>
<td>Meyerowitz et al.</td>
<td>9</td>
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<tr>
<td>de Nicolas-Ruanes et al.</td>
<td>1</td>
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<tr>
<td>Ogoina et al.</td>
<td>3</td>
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<td>Oprea et al.</td>
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<tr>
<td>Patel et al.</td>
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<td>Pfafflin et al.</td>
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<td>Whitehouse et al.</td>
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<tr>
<td>Yakubovsky et al.</td>
<td>26</td>
<td>PR, RP</td>
<td>Israel</td>
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<tr>
<td>Yinka-Ogunleye et al.</td>
<td>27</td>
<td>NS, VO</td>
<td>Nigeria</td>
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</table>

AB, abdominal pain; DI, diarrhoea; DRC, Democratic Republic of Congo; GI, gastrointestinal; N/A, not applicable; NS, nausea; PD, painful defecation; PR, proctitis/rectitis; PRA, proctalgia; RB, rectal bleeding; RP, rectal/anal pain; RPE, rectal perforation; TE, tenesmus; VO, vomit.
patients had proctitis and presented with rectal pain. The authors explained that the diagnosis of mpox remains a plausible consideration even in the absence of mucosal or skin lesions. These 12 studies discussed 162 patients among 18 countries with the diagnosis of proctitis.

While mpox can result in multiple GI symptoms, in some studies the authors only discussed the diagnosis of proctitis. Escudero-Tornero et al.\(^6\) examined proctitis in a mpox patient from Spain following unprotected sexual intercourse 5 days prior. Inigo Martinez et al.\(^3\) published a study on 503 mpox patients from Spain and discovered that 81 patients had proctitis. Along with this GI complication, patients also may have presented with exanthema, fever, or lymphadenopathy. Català et al.\(^3\) analysed 185 mpox patients throughout Spain and found that 40 patients either presented with proctalgia or were diagnosed with proctitis. A particular finding was that 0 patients presented with abdominal pain or vomiting. Meyerowitz et al.\(^6\) studied the efficacy of anorectal testing as a tool for mpox diagnosis and discovered that in nine patients with proctitis, all nine patients had positive rectal mpox DNA. García-Piqué et al.\(^6\) and Cassir et al.\(^6\) studied 19 patients and 30 patients, respectively, with the diagnosis of proctitis. The papers discussed topics such as how asymptomatic patients can further the spread of mpox during symptomatic quarantine measures as well as the importance of tapering prednisone to treat severe proctitis. Due to the broad range of countries and diversity of patients with different demographics, it can be confirmed that proctitis is a typical GI manifestation of the MPXV.

While the majority of the aforementioned studies reported proctitis as a primary GI manifestation of mpox infection, a few studies identified mpox patients with diarrhoea and nausea. Angelo et al.\(^1\) examined 211 patients among various countries and found 33 patients with a broad range of GI manifestations including abdominal pain, diarrhoea, nausea, rectal bleeding, rectal pain and tenesmus. Reed et al.\(^5\) outlines 11 patients in the Midwestern, USA who contracted mpox following direct contact with prairie dogs. Two of these patients experienced diarrhoea and nausea.

An interesting aspect of the MPXV includes the emergence of vomiting as an additional symptom in patients. Aguilera-Alonso et al.\(^5\) discussed a paediatric patient in Spain who presented with vomiting and diarrhoea. This paper was crucial when initially published in September 2022 as the authors concluded that paediatric cases could signify broader transmission risks within schools. This reinforces the idea that primary care providers and paediatricians should be aware of the various mpox complications in order to provide the proper treatment regimens to patients of all ages. Huhn et al.\(^5\) retrospectively studied the clinical manifestations in 10 mpox patients from the Midwestern, USA during the 2005 outbreak and reported symptoms of vomiting, abdominal pain, diarrhoea and nausea. The authors reported that the identification of unusual GI symptoms, such as vomiting, coupled with a comprehensive patient history, can lead to an accurate diagnosis of mpox. Reynolds et al.\(^1\) studied 47 mpox patients in the USA and found that 14 patients had various GI manifestations including nausea, vomiting, diarrhoea and abdominal pain. An interesting finding by the research team was that individuals who had direct contact with infected animals through bites and scratches had a higher probability of having GI manifestations such as vomiting. Ogoina et al.\(^6\) performed a retrospective study of 40 hospitalised mpox patients and found that 3 patients presented with GI symptoms of nausea and vomiting. The research team concluded their study by emphasising the importance of continuing research regarding the interactions between mpox and HIV as many hospitalised patients had both infections. Whitehouse et al.\(^6\) outlined 1057 cases of mpox in the Tshuapa Province of the DRC and found that 250 patients presented with vomiting. This research team did note in their study that there was missing data, so the sample sizes may not be fully representative of the actual proportion of patients with GI manifestations. Overall, of the 33 studies included in the systematic review, vomiting was present in about 40% of the 830 mpox patients.

In addition to discussing GI symptoms in mpox patients, several authors have explored various aspects of mpox, including routes of transmission, difficulties in accessing care in certain communities and strategies for public health officials to address the concerns of mpox patients. Yinka-Ogunleye et al.\(^6\) described 122 mpox patients in Nigeria and discovered that 27 patients had vomiting or nausea. In South Sudan, Formenty et al.\(^4\) studied 19 mpox patients and discovered that 7 patients had complications of abdominal pain, diarrhoea and vomiting. The authors hypothesised that in this community, the infections may have been spread by healers and dentists who performed teeth extraction rituals and other procedures.

In the DRC, Jezek et al.\(^1\) identified 338 mpox patients from 1981 to 1986 and noted that 22 patients presented with vomiting and diarrhoea. The researchers discovered that most of the affected patients were males living near and within dense tropical forests who were often exposed to infected rodents and deceased monkey carcasses.

In Spain, Tarín-Vicente et al.\(^2\) performed a prospective observational cohort study of 181 patients and reported 45 cases of proctitis. Furthermore, Tarín-Vicente et al. found that males who engaged in anal-receptive sex (ARS) were more likely to develop proctitis. The authors also stated that males with mpox who engaged in ARS may have ‘higher rates of distant dissemination’ compared with males who did not.

In the UK, Heskin et al.\(^1\) investigated two patients who presented with diarrhoea and confirmed that both patients were infected through sexual contact. The authors emphasised the importance of educating the public in an open and careful manner to prevent discrimination against certain groups and communities.

Viguié et al.\(^5\) reported on one patient from France who presented with diarrhoea and rectal pain, which
improved following treatment with tecovirimat. Viguer’s team argued that the MPXV should be considered an STI based on transmission; the authors suggested that mpox patients should also be screened for other STIs such as HIV.

This statement regarding STI screening is reaffirmed by a study from Oprea et al. 2024 who reported on a patient from Romania who presented with abdominal pain and nausea following sexual contact. According to the authors, this patient was the first documented case of an individual with simultaneous infections of HIV, mpox, syphilis and hepatitis A due to sexual encounters. These findings reinforce the conclusion by Heskin et al. 2024 that sexually active individuals are at risk, emphasising the need for proper education of the public and awareness. Although these included papers did not report transmission routes through shared contaminated objects such as clothing and sex toys, it is worth noting this potential transmission route. 48

Rare GI manifestations
One study outlined a rare GI manifestation of RPE, a formation of a hole due to damage in the mucosal rectal wall. Patel et al. 2024 investigated 197 male mpox patients in the UK and reported that one of the patients presented with RPE. The other patients had proctitis and presented with painful defecation and rectal pain. A treatment regimen of metronidazole and ceftriaxone, administered intravenously, was given to the patient. This study provides insight into the serious GI complications associated with mpox infection and how it was addressed by the treating physicians. To the author’s knowledge, RPE has never been described before in relation to the MPXV as this is an unusual complication of mpox. Although the authors of the research paper did not suggest an explanation for the progression of the complication, RPE can develop in response to trauma and ulcerations due to rectal wall strain. Proctalgia is another rare complication that was mentioned above in the study by Català et al. In our systematic review of the 830 patients, RPE occurred in 0.09% of the patients while proctalgia presented in 4.8% of patients.

DISCUSSION
Interpretation and implications
Our review discusses an important topic as members of the public and healthcare professionals may continue to view mpox only as a dermatological and influenza-like infection. Multiple papers discussed how the virus could potentially bind and infiltrate cells through cell-surface receptors such as chondroitin sulfate or heparan sulfate that bind to viral proteins such as MPXV A29 protein. 75 76

Although the general pathophysiology of the MPXV is documented in the literature, there is a gap in knowledge regarding how the MPXV can specifically infect cells in the GI tract. An understanding of the MPXV and its relationship to the GI symptoms can aid physicians in not only diagnosing affected patients but also exploring the most effective treatment options.

The presence of multiple patients from a diverse range of backgrounds and demographics is promising as this confirms a consistency in how mpox can present from a GI perspective. Although the cases of mpox have significantly diminished following the 2022 outbreak, this review reinforces the idea that physicians throughout the world should be prepared to recognise these GI symptoms in the case of another outbreak. Furthermore, the travel history and sexual history of suspected patients should be thoroughly reviewed. This would allow for accurate diagnosis, immediate treatment options and crucial information regarding close contacts and countries that should be monitored closely. Tools and screening measures such as a proctoscopy and rectal swab are imperative for screening an at-risk patient. Additionally, laboratory orders such as a comprehensive metabolic panel (CMP) and complete blood count (CBC) can help determine individuals who have a severe mpox infection and will need immediate treatment and management.

Limitations
Although the systematic review strictly followed the PRISMA guidelines, there were some limitations. First, the criteria for the inclusion of papers excluded non-English studies that may have provided information regarding other GI complications. Second, the majority of included papers were case reports and case studies of mpox patients that may have had additional limitations. Furthermore, some patients presented with other health conditions and infections such as hepatitis or syphilis. It cannot be fully determined whether these additional diseases played a significant role in the pathogenesis and presence of GI abnormalities in mpox patients. However, one paper did determine that mpox patients with HIV were more likely to have complications such as proctitis. 77 Furthermore, as the topic matter is sensitive, patients may provide inaccurate responses or non-responses to questions related to transmission routes or symptoms such as rectal bleeding.

Additionally, anorexia was not included as a GI complication in our search and results section. It is unclear whether anorexia is a direct complication of the mpox virus or a result of other mpox manifestations such as nausea and vomiting. Finally, considering these papers discussed patients that immediately presented to the medical setting following symptoms such as diarrhoea and were treated appropriately, we are unable to discern whether there are long-term GI complications that could occur in mpox patients. Our systematic review attempted to address these limitations through various measures such as relevant keywords, strong inclusion and exclusion criteria, thorough review process, and a large group of patients from various backgrounds.
CONCLUSION

In the majority of mpox patients with GI manifestations, the finding of proctitis and symptoms of rectal pain, diarrhoea, vomiting and tenesmus were prevalent. Most mpox patients who experience GI symptoms will exhibit at least one of these complications. In contrast, the less common GI complications in mpox patients experiencing GI symptoms included RPE and proctalgia. GI symptoms of mpox are crucial for gastroenterologists and other healthcare professionals to recognize in order to address patient discomfort and further understand the pathophysiology of the virus. Moreover, it is crucial to identify and consider GI symptoms as they can play a key role in the early detection of a mpox infection, as some patients may exclusively or primarily present with these symptoms.

Further research of patient complications would promote a better understanding of mpox, the optimal treatment regimens, and how the GI manifestations may vary based on aspects such as patient demographics and comorbidities.

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Contributors

RR is the guarantor who initiated and conducted the systematic review and search strategy. RR and AS reviewed the literature for eligibility criteria. RM and DM reviewed the selected articles for eligibility. RR wrote the main manuscript with RS and AS completing the PRISM checklist. RM and DM reviewed and made final edits to the manuscript with RR serving as the corresponding author.

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