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	Anthrax in wartime Ukraine requires increased surveillance
Authors	Joel Keep & David J Heslop School of Population Health, University of New South Wales, Sydney, Australia
Date of first report of the outbreak	14 Oct 2022, via the World Animal Health Information System (1), communicated by the International Society for Infectious Disease on Oct 15 (2).
Disease or outbreak	Anthrax (animals – goats). Disease develops when individuals are exposed to the causative agent, the spore-forming bacterium *Bacillus anthracis* (3).
Origin (*country, city, region*)	Ukraine: Vilkovets (Вільховець), Kyiv Oblast.
Suspected Source (specify food source, zoonotic or human origin or other)	This cluster is affecting goats, who may have acquired the infection while browsing vegetation. The upstream source is yet to be identified (2).
Date of outbreak beginning	The index case of this cluster was apparently infected on or around 29 September 2022 (1).
Date outbreak declared over	No official confirmation
Affected countries	The current outbreak appears to be confined to Vilkhovets, a village in Kyiv

& regions	Oblast.
Number of cases (specify at what date if ongoing)	5 confirmed, involving 5 deaths, with a further 342 animals susceptible (1).
Clinical features	Anthrax may present in goats as an acute systemic infection, with sudden death sometimes preceded by signs of staggering, tremor, dyspnoea, and seizure activity (4). Humans exposed to anthrax spores develop either cutaneous, gastrointestinal or inhalational types depending on route of exposure. The overwhelming majority (95%) of naturally occurring anthrax cases in humans are cutaneous, with an incubation period of 1 – 5 days, and exposure is usually work related. Initial papules progress to vesicles, with the ulcer base often developing a characteristic black eschar (5). Fever, malaise and headache frequently follow. If treated, mortality is normally under 1% and up to 30% if untreated (6). Gastrointestinal anthrax disease primarily affects the lower intestine, or less commonly, the oropharynx. Oropharyngeal anthrax presents with severe sore throat, oral or tonsillar ulcers, swelling of the neck and dysphagia (6,7). Acute abdominal pain involving massive ascites and bloody diarrhea is often indicative of anthrax affecting the stomach or bowel, and follows earlier signs that include anorexia, nausea, vomiting and fever (8,9). There is very high mortality despite treatment, and when untreated, it is almost invariably fatal. Inhalational anthrax is now rare and occurs after exposure to aerosolised spores. Historically, this was seen in agricultural workers handling infected hides and fur products. However, modern farming practices have almost eliminated this route of exposure. Inhalational anthrax is now almost pathognomonic of deliberate (i.e. bioterrorism or offensive biological attack) or accidental inhalation following a laboratory incident. Initial symptoms may be mild and non-specific, characterised by fever, malaise and myalgia and can be difficult to differentiate from those caused by other, more common respiratory infections. Rapid decline after the first few days of infection can be sudden, with dyspnoea, stridor and cyanosis preceding catastrophic pleural effusions, chest pain (often the only differentiating early symptom) and respiratory compromise. Rapid onset of septic shock, followed by death, can occur within 24 hours of respiratory distress becoming first apparent (10).
Mode of transmission (dominant mode and other documented	Individuals develop anthrax disease after being exposed to spores of the causative agent, *bacillus anthracis*. In this outbreak, the mode of transmission is unclear, however the gastrointestinal route is most likely, given the fact that goats often browse vegetation. Blow flies may be involved in the chain of

modes)	transmission, as they are known to feed on downed cows, before regurgitating their meal on leaves that goats exploit for their own browsing, leading to secondary infections (2). Most human cases of anthrax are cutaneous and involve contact with affected soil or livestock (6). Oropharyngeal and gastrointestinal anthrax can be caused by ingesting infected meat. Historical cases of natural inhalational anthrax were found amongst wool sorters in England (hence the eponymously named Woolsorter's Disease now rarely seen in workplaces) (12). The inhalational route has been documented in unnatural outbreaks involving aerosolised *b. anthracis* (11) following exposure to specially milled and dried spore forms of the bacterium (13).
Demographics of cases	Historically, cases of human anthrax disease in Ukraine have usually involved direct contact with livestock. Small-hold farmers, and occasionally those involved in the unregulated meat trade, have been most commonly affected. Less commonly, human cases have emerged following the purchase or consumption of contaminated meat (14). This outbreak was detected on a private farm in Kyiv Oblast, in an area just south of the capital. No human cases have been reported in relation to these cases.
Case fatality rate	Of the five animals known to have been infected in this cluster, all five have died (1). This would indicate a case fatality rate of 100% for this outbreak. In humans, cutaneous anthrax, when treated promptly, usually has a mortality rate of less than 1% (6). Gastrointestinal anthrax has a CFR of around 40% if met with timely antibiotic treatment (8). Depending on the nature of the outbreak, untreated gastrointestinal and inhalational anthrax can have a mortality of 100% (6,7).
Complications	In humans, infections via cutaneous, gastrointestinal or inhalational routes can progress to fatal systemic anthrax disease (3). Meningitis can occur as a result of any of the above forms, which is often haemorrhagic and usually only identified at autopsy as the characteristic "cardinals cap" of coagulated blood around the brain (6). Microangiopathic hemolytic anemia, coagulopathy and thrombocytopenia commonly occur and require intense clinical management (15). Goats may see complications including incoordination, respiratory distress and convulsions. As toxins released during anthrax exposure can prevent blood from clotting normally, severe haemorrhaging is often involved (4).

Available prevention	Livestock can be immunised with vaccines based on the Sterne strain (21). BioThrax is licenced in the United States (16) and in Ukraine's EU neighbour, Poland, for people at increased risk (17). This Anthrax Adsorbed Vaccine (AVA) is also used in post-exposure prophylaxis, however systemic rather than mucosal immunity is induced (18). In Ukraine, compulsory vaccination of people was ceased in 1990, and was replaced by vaccination of livestock (20). Antibiotics, purified hyperimmune sera and toxin-targeting antibodies are also used in human post-exposure prophylaxis (20). Co-ordinated prevention measures based on One Health principles involving detailed geo-spatial surveillance can help prevent zoonotic anthrax infections, in addition to prophylactic vaccination of exposed people. As spores can live on in soil and skeletons for many years, addressing environmental contamination is central to anthrax control. Burial of animals infected with anthrax, which is prohibited in Ukraine, is not recommended for this reason (38). WHO guidelines recommend the incineration or rendering of carcasses, and that clear signage be used for marking the affected site, as Ukrainian authorities did in this case (21, 38). Chlorinated lime was used to disinfect the affected land thereafter (38).
Available treatment	Immunotherapy, including the use of monoclonal antibodies and immunoadhesins, has proven effective as a life-saving treatment for those in the fulminant stage of anthrax disease (20). Hemodynamic support, mechanical ventilation, adjunctive corticosteroids and surgical interventions to enable drainage of pleural effusions may be needed in severe cases (15). Antimicrobial drug combination therapy has proven successful in cases of inhalational anthrax disease, sometimes involving the use of protein synthesis inhibitors (22). Ciprofloxacin, doxycycline and levofloxacin are indicated for treatment of inhalational anthrax (15).
Comparison with past outbreaks	Anthrax was a widespread problem and endemic in Ukraine during much of the 20th Century, when Soviet collectivisation policies led to intense farming and a subsequent increase in cattle populations susceptible to infection (14). Since Ukraine gained independence from the Soviet Union in 1991, there has been a decline in both prevalence and incidence of anthrax outbreaks, with de-collectivisation and prophylactic vaccination of livestock both contributing to improvements in control. However, in 2016, 17 people were infected with anthrax after consuming contaminated pork and a further 5 people were infected in the Odesa region while slaughtering cattle. Since 2000, sporadic cases of disease have been reported in 20 regions of Ukraine, with cattle accounting for the majority of cases (71%), and sheep and goats involved in

	16.4% of cases. (23). A spatio-temporal analysis by Bezymennyi and colleagues identified four main geographic foci of enzootic anthrax in contemporary Ukraine. One of these is centred on the north-west of the country, stretching from the region (or "oblast") of Lviv, to Kyiv Oblast, in which the nation's capital is situated. The present outbreak, occurring in Vilkovets (Вільховець), a village in Kyiv Oblast, falls outside of contemporary areas of concentration identified by the Bezymennyi group, but within historical zones they have identified (14). As *b. anthracis* spores can live on in soil for 50 up to years, and far longer in the bones of infected animals, infections among grazers and browsers could occur throughout wide geographical areas that have had historical exposure. Molecular typing is thus central to identifying any foreign strains.
Unusual features	While the ultimate source of this outbreak remains unidentified, it appears to have been naturally acquired by the animals in the process of browsing vegetation (2). However, such outbreaks are a reminder of the challenges faced by Ukrainian authorities in identifying the aetiology of anthrax strains during an ongoing armed conflict. This is the first publicly reported anthrax outbreak since the Russian invasion on the 24th of February 2022. Active combat is currently taking place in areas where anthrax likely remains in the soil, placing both Russian and Ukrainian personnel at risk of infection. Anthrax is naturally occurring in many regions of the world, including Ukraine. The Russian invasion, however, brings a new context to surveillance of this pathogen. *Bacillus anthracis* has been weaponised by both established militaries and non-state actors in the past. There are documented instances of weaponised anthrax being tested and deployed against both human (24) and animal targets (25). The relative ease with which the pathogen can be acquired, weaponised and deployed provides a strong incentive for anthrax surveillance that can differentiate between natural and unnatural outbreaks (25).

Critical analysis	This outbreak is most notable for the socio-political context in which it has emerged, and the fact that bacterial culture and sensitivity analysis, rather than genomic sequencing, was used to identify the pathogen (2). While this method remains the gold standard for identifying anthrax, genomic tools may be more useful for alerting authorities to any future outbreaks of unknown aetiology in an expeditious manner. Brangsch and colleagues published the most detailed study of molecular typing of anthrax in Ukraine to date, in which the investigators identified four endemic strains subsequently assigned to the Tsiankovskii subgroup of the Trans-Eurasia clade (27). Similar whole genome sequencing techniques could help identify the origin of the current strain and alert investigators to any anomalies. Those supporting disease control in Ukraine would benefit from maintaining an awareness of the potential for both natural and unnatural outbreaks of anthrax in the context of the current armed conflict. The Russian Federation is known to have inherited a large-scale bioweapons programme from the Soviet Union that involved bulk weaponised anthrax production (28). Russian officials have since maintained an ambiguous posture as to its present status (29). It is worth highlighting that the largest recorded outbreak of inhalational anthrax was the result of accidental release from a biological weapons facility in the Soviet city of Sverdlovsk, now known as Yekaterinburg, in 1979 (11). Ukrainian officials have voiced increasing concern that the Kremlin will make use of unconventional weapons as the Russian military faces repeated setbacks on the battlefield (30). Key personalities in the Russian military command structure responsible for offensive operations in Ukraine have shown a willingness to oversee the deliberate targeting of civilians in Syria (31), where chemical weapons were deployed against the population on several occasions (32). Furthermore, Russian military and intelligence operatives are also known to have deployed unconventional weapons against political targets in Ukraine and elsewhere in Europe (33, 34, 35). Russian military planners have also used long-range munitions to indirectly threaten or directly target chemical plants and nuclear sites in Ukraine (36, 37). International concern over the use of unconventional weapons in the current conflict should encourage donors to support Ukrainian authorities in their efforts to detect not only potential chemical and radiological signatures, but also bacteriological threats such as weaponised anthrax. Future clusters occurring outside of expected areas would warrant further investigation in determining whether they are of natural origin or otherwise. Intentional deployment against animal populations could serve as a precursor attack against humans, as a means of degrading food sources, or as a vector for infecting civilian populations. Any future cases of inhalational anthrax should be given priority for urgent investigation.

	Surveillance and control of anthrax, regardless of its origin, faces serious impediments amidst Russia's ongoing invasion. As mentioned above, Bezymennyi and colleagues identified four loci of enzootic anthrax in contemporary Ukraine (14). Notably, two of these foci fall in areas that are currently zones of intense armed combat: one in the north-east, on the Kharkiv-Luhansk regional border; and another falling on the border of the Donetsk and Zaporizhzhia oblasts. It should be noted that surveillance of these regions will be exceedingly challenging, if not impossible, for Ukrainian health authorities while they remain under Russian occupation, or the site of active warfighting. In late November 2022, the WHO and the United States government provided Ukrainian authorities with a mobile laboratory capable of identifying anthrax strains and other pathogens that pose a danger to human health (39). Broader support of a similar nature is urgently needed for Ukraine, as the Russian military intensifies its attacks on civilian infrastructure, and local health authorities contend with profound public health impacts of the invasion.
Key questions	1. Do Ukrainian authorities have in place procedures for differentiating between natural and unnatural outbreaks of anthrax in the current context? 2. Is there functioning capacity for genomic sequencing to identify novel strains, or must samples be transported to neighbouring countries? 3. How best can international donors support disease surveillance in conflict-affected areas of the country? 4. Which international donors are best positioned to supply medical countermeasures in the event of a bacteriological attack? 5. Is there evidence of using anthrax against humans or livestock in current Russian military doctrine? 6. How can Ukrainian authorities extend disease surveillance to areas under Russian military occupation?

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Author contributions

Authors made equal contributions. JK conceived of the report and wrote the initial manuscript. DH made substantial amendments and additions, while providing essential guidance throughout.

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