<u>Abstract</u>

Introduction:

Arboviruses are a diverse group of arthropod-borne pathogens and are emerging global public health threats with no approved therapeutics. Arboviruses are spreading rapidly, posing a health threat to UK Armed Forces (UKAF) service personnel (SP) through deployment to endemic regions. There are limited data on the burden of arboviral infections in UKAF SP.

Methods:

A retrospective service evaluation of UKAF electronic healthcare records (eHRs) and statutory notifications to Defence Public Health Unit was conducted. Cases with possible/confirmed dengue, chikungunya or Zika virus infections between 2005-2023 were included. eHRs were interrogated and trends analysed.

Results:

Of 107 suspected infections between 2005-2023, 49 (45.8%) were laboratory-confirmed. Dengue fever was the most common (45/49) followed by chikungunya (3/49) and Zika (1/49) virus infections. The average yearly incidence of reported dengue infection increased from 0.51 cases per 100,000 UKAF SP per year in 2009-2011 to 3.85 cases per 100,000 SP per year in 2021-2023. 19/45 (42.2%) cases occurred during operational deployments and 24/45 (53.3%) during non-military activity. Dengue infection was most frequently acquired in Southeast Asia.

Using WHO clinical severity criteria, 33/45 (73.3%) had dengue with warning signs and 5 (11.1%) had severe dengue. 23/45 (51.1%) dengue cases were hospitalised (median length of stay 5 days, IQR 3, range 1-9). No dengue fatalities or medical discharges occurred. Occupational impact was significant, with median 11 days stood down (IQR 10, range 0-45); 3/19 (15.8%) cases on operations required aeromedical evacuation (AEROMED). 1 deployed case of chikungunya required AEROMED and 35-day downgrade.

Conclusions:

Reports of arboviral infections, particularly dengue, are increasing in UKAF personnel, presenting an emerging health threat. This has implications for UKAF provision of deployed diagnostics and dengue vaccination policy. The rapid spread of arboviruses outside their traditional geographical areas, including into Europe, necessitates further surveillance and requires diagnostic and therapeutic research.

Key Messages

What is already known on this topic

• Arboviruses are a global emerging public health threat that are spreading geographically and causing increasing morbidity and mortality worldwide.

What this study adds

 This study is the first to investigate the current burden of arboviral infections on United Kingdom Armed Forces (UKAF) service personnel. The incidence of reported dengue in the UKAF population is increasing and has significant health and occupational consequences annually.

How this study might affect research, practice or policy

- This study identifies an urgent need to develop a Defence arboviral diagnostic capability and to increase surveillance of arboviral infections in UKAF personnel.
- It underlines the importance of force health protection focused on bite avoidance and evidences the need for further research to inform Defence dengue vaccination policy, whilst highlighting the gap in arbovirus therapeutics.
- It reinforces the need for clinicians to obtain a travel history from patients presenting with nonspecific febrile illnesses which could be consistent with arbovirus infections, and to utilise Military Infectious Diseases reach-back where required.

Introduction

Arboviruses are transmitted by arthropods such as mosquitos or ticks. Of over 500 arboviruses worldwide, 150 are known to cause disease in humans, resulting in a wide variety of diseases with significant morbidity and mortality in tropical and subtropical regions [1]. The arboviruses with the highest incidence globally are dengue (96 million cases per year), chikungunya (693,000 cases per year), Zika (500,000 cases per year), yellow fever (130,000 cases per year), Japanese encephalitis (42,500 cases per year), Crimean-Congo haemorrhagic fever (10-15,000 cases per year) [2] and West Nile virus (2,588 cases per year) [3]. Many models predict that exposure to mosquito-borne viruses will be increased by climate change as a result of vector expansion towards more temperate zones. As vectors spread arboviruses into new regions, including Europe [4-6], the introduction of new strains into naïve populations can cause explosive outbreaks, with severe outcomes and arboviral coinfections [7]. Global reported cases of dengue have increased tenfold since 2010 [8] and there are increasing risks to travellers [9].

The 2021 Integrated Review emphasised deploying UK Armed Forces (UKAF) overseas more often and for longer periods including in Southeast Asia, potentially placing more personnel at risk of arbovirus exposure [10]. UKAF continue to deploy in arbovirus endemic areas, with both permanent and temporary presences. The British Army maintains significant footprints in East Africa, Brunei and Belize. The Royal Navy maintains standing deployments in the Caribbean and Asia-Pacific and the Royal Air Force frequently deploys globally on exercise and operations.

Arboviruses typically present as non-specific febrile illnesses [11], which even when mild, have a significant economic impact through loss of productivity and overwhelming healthcare resources [12]. Dengue, chikungunya and Zika virus infections are of particular concern to UKAF. All three have global distributions, similar clinical presentations and no licensed treatments. Other arboviruses, whilst important, have relatively less impact on UKAF, either due to routine vaccination (e.g. yellow fever, Japanese encephalitis and tick-borne encephalitis), or because of a limited UKAF footprint in focally

endemic areas (e.g. Japanese encephalitis, West Nile virus), yet have the capacity for large regional outbreaks (e.g. Oropouche) [13].

Half of the world's population is at risk from dengue, with 70% of disease burden in Asia [14]. The clinical manifestation of dengue virus (DENV) infection is variable, ranging from asymptomatic disease to multi-organ failure. Up to 75% of cases may be subclinical, leading to under-reporting of cases [14,15]. Severe disease occurs in up to 5% of cases, most frequently following a second DENV infection with a differing serotype [16]. Chikungunya virus infection most commonly presents with a febrile illness typified by fever, rash and swollen, painful joints. Neurological complications such as meningoencephalitis or Guillain-Barré Syndrome may occur, and 40-80% of patients experience chronic joint pain [17]. Zika virus infection presents with a similar non-specific febrile illness to other arboviruses but can result in devastating congenital infection and neurological sequelae [18]. Congenital infections in the first trimester pose the highest risk of congenital Zika syndrome, typified by microcephaly and other abnormalities. Dengue, chikungunya and Zika virus are spread by Aedes spp. mosquitoes. Urbanisation, globalisation, climate change and reduced vector control drive expansion of these vectors into subtropical and temperate regions [3], including Western Europe [19]. Whilst candidate therapeutics are being assessed in clinical trials, no licensed treatment exists for either disease, although vaccines have been developed for dengue [20,21] and chikungunya [22,23]. Qdenga is licensed for the prevention of severe dengue in previously infected individuals and has been approved for use by the Joint Committee on Vaccination and Immunisation [24,25]; IXCHIQ chikungunya vaccine was licensed by the Medicines and Healthcare products Regulatory Agency in February 2025 [22].

The mainstay of arbovirus prevention is vector control and bite avoidance [26]. Whilst progress has been made in the control of arboviruses such as yellow fever, political instability, migration, climate change and reprioritisation of resources during the COVID-19 pandemic have challenged World Health Organisation (WHO) targets for the control of dengue and chikungunya [27].

Arboviruses pose an important public health threat to travellers including military personnel who regularly work in endemic regions [28]. Until now, the burden of arboviruses on UKAF SP and operations has not been evaluated.

Methods

A retrospective audit was conducted focussed on the most common arbovirus infections (dengue, chikungunya and Zika virus), utilising electronic health records (eHR) of military patients between January 2005 and September 2023. Patients were identified through searching eHRs for arbovirus-related coding and/or military statutory infectious diseases notification records (FMED85). eHRs were interrogated and demographic, clinical and laboratory data extracted from primary and secondary care records within the eHR. Location of infection was recorded as suspected country of acquisition per eHR review. Laboratory confirmation of infection was defined as evidence of either positive polymerase chain reaction (PCR) test, positive dengue rapid antigen-test, or positive arboviral serology with a consistent clinical presentation as per WHO recommendations [29]. Anonymised data were collected on an electronic case report form and stored in accordance with approved MOD data storage regulations and subsequently analysed using R Studio 2023.12.1+402. Normally distributed data are presented using mean and standard deviation and other data are presented using median and interquartile ranges (IQR). As a service evaluation, formal ethics approval was not required per JSP 536. It was registered with Defence Medical Services Research and Clinical Innovation department and approved by the Medical Director.

Results

A total of 162 patients were initially identified, and 55 records excluded because of either incorrect coding (13/162 [8.0%]); arbovirus infection prior to UK military service (16/162 [9.9%]); or the patient not being in UK uniformed regular or reserve service (26/162 [16.0%]). Of the remaining 107 cases, 49 (45.8%) had laboratory-confirmed arboviral infection, including 45/49 (91.8%) with dengue, 3 (6.1%) chikungunya and 1 (2.0%) with Zika virus.

Dengue

Most (35/45; 77.8%) dengue cases were acquired in Southeast Asia, with 21/45 (46.7%) cases occurring in Nepal [Table 1]. Army personnel were more commonly affected (84.4% of cases compared to 54.5% of wider UKAF). There were no differences observed across age groups or ranks. Dengue cases were seen year-round, with peaks in the Northern Hemisphere summer months. In Nepal, cases were exclusively seen between June-November, relating to the local monsoon season. 24/45 (53.3%) dengue cases occurred during non-military activity (e.g. travelling or visiting friends or relatives – VFR) and 19/45 (42.2%) dengue cases occurred during military activity. The most common locations of acquisition of dengue during military activity were Brunei and Nepal (6/19 - 31.6% each), Belize (3/19 - 15.8%) and Kenya (2/19 - 10.5%).

—	Arbovirus		
-	Dengue	Zika	Chikungunya
Number of laboratory	45 (91.8%)	1 (2.0%)	3 (6.1%)
confirmed cases			
Countries of Acquisition	Nepal: 21 (46.7%)	Belize: 1 (100%)	Colombia: 1 (33.3%)
·	Brunei: 6 (13.3%)		Ghana: 1 (33.3%)
	Thailand: 6 (13.3%)		Senegal: 1 (33.3%)
	Belize: 3 (6.7%)		
	Bangladesh: 2 (4.4%)		
	Kenya: 2 (4.4%)		
	Barbados: 1 (2.2%)		
	Fiji: 1 (2.2%)		
	India: 1 (2.2%)		
	Jamaica: 1 (2.2%)		
	Nicaragua: 1 (2.2%)		
Service			
Air Force	3 (6.7%)	0	0
Army	38 (84.4%)	1 (100%)	1 (33.3%)
Navy	1 (2.2%)	0	2 (66.6%)
Unknown	3 (6.7%)	0	0
Rank ¹			
Junior Ranks (OR1-OR4)	29 (64.4%)	0	1 (33.3%)
Senior Ranks (OR5-OR9)	11 (24.4%)	1 (100%)	2 (66.6%)
Officer (OF1-OF10)	5 (11.1%)	0	0
Unknown	0	0	0
Mean age (standard deviation)	31.8 (7.9)	39 (-)	33.3 (4.9)
Country of Birth			
Unknown	27 (60.0%)	1 (100%)	1 (33.3%)
Nepal	12 (26.7%)	0	0
United Kingdom	3 (6.7%)	0	1 (33.3%)
Hong Kong	2 (4.4%)	0	0
Fiji	1 (2.2%)	0	0
Ghana	0	0	1 (33.3%)
Activity at time of infection			
Non-military*	24 (53.3%)	0	1 (33.3%)
Firm base†	8 (17.8%)	0	0
Deployment ‡	6 (13.3%)	1 (100%)	2 (66.6%)
Exercise§	5 (11.1%)	0	0
Unknown	2 (4.4%)	0	0
Bite Avoidance Briefed			_
Yes	1 (2.2%)	1 (100%)	0
No or Unknown	44 (97.8%)	0	3 (100%)

 Table 1. Demographic details of 49 UKAF personnel with a confirmed arbovirus virus infection between

 2005 and 2023. Number of cases with percentages provided. ¹ as per NATO ranking system, OR5 equates to

 Sergeant (Army, Air Force) or Petty Officer (Navy). *: defined as leave in a different country from duty station.

 †: defined as long-term posting. ‡: defined as short-term operational posting. §: defined as short-term posting within a

 defined exercise.

No data were recorded about previous dengue infections. When data were available, Nepal was the most common place of birth (12/18 - 66.6%).

The incidence of reported laboratory-confirmed dengue infection, as a proportion of total UKAF personnel in that year, has increased year on year, from 0.51 cases per 100,000 SP per year in 2009-2011 to 3.85 cases per 100,000 SP per year in 2021-2023 [Figure 1]. 18/21 (85.7%) cases in Nepal have occurred since 2019, with 10/21 (47.6%) cases occurring in 2022 alone, when a national dengue outbreak occurred [30].

All 45 dengue cases had clinical data recorded [Table 2]. 43 (95.6%) had recorded fever and 38 (84.4%) met the WHO 2009 criteria for probable dengue. Overall, 33 (73.3%) had a recorded clinical picture compatible with dengue with warning signs (DWS), but 9 (20.0%) met the DWS criteria when lethargy was excluded. 5 (11.1%) cases had severe dengue by WHO criteria, with 2 cases of severe haemorrhage, 2 cases of severe organ dysfunction and 1 case of fluid third space loss with respiratory distress. All five patients fully recovered. One patient suffered from persistent lethargy, requiring a long-term downgrade for 133 days. Cases occurring during military activity had similar rates of complicated disease, with 15/19 (78.9%) meeting DWS criteria, 5/19 (26.3%) meeting DWS criteria when lethargy was excluded, and 4/19 (21%) meeting severe dengue criteria.

Symptom or sign	Number of Patients	
Probable Dengue criteria met	38/45 (84.4%)	
Fever	43/45 (95.6%)	
Nausea and Vomiting	23/45 (51.1%)	
Rash	8/45 (17.8%)	
Aches and Pain	35/45 (77.8%)	
Positive Tourniquet Sign	1/45 (2.2%)	
Leucopenia	21/45 (46.7%)	
Dengue with Warning Signs criteria met*	33/45 (73.3%)	
Lethargy	24 (53.3%)	
Abdominal Pain	5 (11.1%)	
Hepatomegaly	1 (2.2%)	
Mucosal bleeding	2 (4.4%)	
Persistent vomiting	2 (4.4%)	
Rising haematocrit with falling platelet count	2 (4.4%)	
Nil	12 (26.7%)	
Severe dengue criteria met	5/45 (11.1%)	
Severe haemorrhage	2 (4.4%)	
Organ involvement: central nervous system	1 (2.2%)	
Organ involvement: hepatitis	1 (2.2%)	
Fluid accumulation	1 (2.2%)	

 Table 2. Clinical features recorded in 45 laboratory-confirmed dengue cases in UKAF personnel. * Patients

 may have more than one warning sign.

Serological diagnosis, in addition to a compatible clinical picture, was the most common method of diagnosis (25/45, 55.6%), followed by NS1 antigen detection (14, 31.1%) and PCR (6, 13.3%). Data for dengue serotype and prior serostatus were not available. 29 (64.4%) of patients were managed in secondary care, 23/45 (51.1%) as inpatients and 6 (13.3%) as outpatients. 16/45 (35.6%) patients were managed in primary care, with 9/19 (47.3%) cases occurring during military activity being managed in military primary care.

There was an occupational impact of those with dengue. Patients admitted to hospital stayed for a median of 5 days (IQR 3 days, range 1-9 days). Time at less than full duty was a median of 11 days (IQR 10 days, range 0 to 45 days). Three cases occurring during military activity required aeromedical evacuation from theatre (AEROMED). There were few long-term sequelae from dengue, with only 1/45 (2.2%) patient requiring medical downgrade for 133 days, due to persistent lethargy. No patients died or were medically discharged from service.

Other arboviruses

There were only three laboratory-confirmed cases of chikungunya and one of Zika virus infection. 3/4 (75%) chikungunya and Zika virus infections were acquired during military activity; the chikungunya infections were acquired in West Africa and South America and the Zika virus infection was acquired in Belize. One chikungunya patient required local inpatient admission, subsequent AEROMED from operations and a medical downgrade for 35 days due to arthralgia.

Discussion

This is the first study to review the burden of arbovirus infection in UKAF. It shows that arboviruses, mainly dengue, are being increasingly reported and represent an increasing threat to UKAF personnel and operations. Dengue, even in non-severe form, is a debilitating disease that results in frequent hospitalisation and a median of 11 days at less-than-full duty. It is resource-intensive, requiring daily laboratory and clinical review. This may not be possible in Role 1 settings, necessitating casualty evacuation to a higher level of care. Despite this, 47.3% of cases occurring during military activity were managed in military primary care. The WHO 2009 guidelines allow for management of uncomplicated dengue in primary care, but patients must have a daily clinical review and point-of-care full blood count testing if same-day laboratory tests are not available.

Severe dengue occurred in this population with haemorrhage, respiratory distress and severe organ dysfunction being observed, resulting in 3/19 deployed cases requiring AEROMED back to the UK. Only 2/45 had high risk medical co-morbidities [26], both asthma. A surprisingly high number of cases (73.3%) were recorded as having DWS. This may be due to investigators overstating the degree of lethargy, as in 72.7% of cases, DWS criteria was met due to the presence of lethargy.

This study shows that UKAF contains a cohort of personnel who have previously been infected with dengue and could be at risk of severe dengue infection from a second dengue infection. The size of this cohort is likely underestimated due to undetected subclinical infection, under-reporting of cases, and unknown infections that may have been acquired prior to military service. Primary infections may have

occurred through residence or recreational and/or occupational travel to dengue-endemic areas. Importantly, UKAF recruits heavily from Nepal, Fiji and West African and Caribbean nations, which are all dengue-endemic. The incidence in these nations is poorly characterised, but this should improve with increasing surveillance networks as part of the WHO Global Arbovirus Initiative [31]. Globally, an estimated 59.3-81.1% of dengue infections are asymptomatic [14,15], and of those that are symptomatic, only 30% attend healthcare facilities [14]. Many personnel travelling or residing in endemic areas will have developed sub-clinical disease and mounted an adaptive immune response to primary infection, that could place them at higher risk of severe disease following a second dengue infection.

UKAF have a permanent presence in dengue-endemic areas through static installations in Belize, Kenya, Singapore, Brunei and Nepal, in addition to permanent Royal Navy patrols through the Caribbean and Asia Pacific. Many smaller, short-term exercises, deployments and contingency operations also occur through dengue-endemic regions. The geographic spread of these locations, in addition to the high throughput of training locations such as Belize, Kenya and Brunei, increases the potential occupational exposure of SP to differing serotypes, as individual countries may have differing dominant circulating serotypes. As dengue continues to emerge globally, due to both geographical spread and increasing case numbers in endemic areas, the number of UKAF personnel at risk of dengue will likely increase.

Currently, the primary method of dengue prevention is through vector control and bite avoidance. Military activity often involves working in remote and austere environments, potentially with limited infrastructure and healthcare resources. Military public and environmental health measures to prevent dengue may have a limited impact in austere environments. Even when well-resourced health protection measures are instituted, dengue outbreaks and infections may still occur [32]. The incidence of reported dengue in UKAF has increased 755% between 2009-2023, which is in line with global trends [8]. This increase may be due to increased exposure of UKAF SP to endemic regions or increased incidence in host nations. Conversely, it may be due to increased clinician awareness, increased remote Infectious

Diseases support to clinicians and increased reporting of cases. Incidence of infection in UKAF SP will in part reflect local host nation incidence, with UKAF SP indirectly reliant on host nation disease control. This was seen in Nepal in 2022, where a large increase in UKAF cases mirrored a wider, national outbreak. Additionally, the majority (24/45 – 53.3%) of recorded dengue cases in this study occurred during non-military activity, such as those Visiting Friends and Relations (VFR), a pattern that is also seen in UKAF malaria cases. Military public and environmental health measures will have limited ability to prevent infection in individuals VFR. However, free pre-travel advice is available via Defence Primary Healthcare to UKAF SP and should continue to be promoted through clinician advocacy and patient awareness. With increasing levels of Defence activity in dengue endemic regions, it is likely there will remain a cohort of at-risk individuals in the UKAF who have acquired primary infection and continue to be at risk of acquiring second dengue infections, independent of military health protection measures.

Vaccination may reduce the risk of severe disease to UKAF personnel who have previously been exposed to a primary infection. Two dengue vaccines currently exist: QDenga [20] and Dengvaxia [21]. Only QDenga is licenced in the UK and it has good efficacy against dengue infection and hospitalisation across all 4 DENV serotypes in seropositive individuals, but no clear benefit to seronegative individuals against DENV3 and DENV4. In 2024 the Joint Committee on Vaccination and Immunisation approved QDenga vaccination in individuals with a history of dengue infection and who continue to remain at risk of dengue infection, with dengue serology used to inform decision making [24]. Further work is required to establish the UKAF at-risk population for dengue to inform future vaccination policy.

This study does not support chikungunya and Zika viruses having a significant impact on UKAF, however such cases are likely underestimated due to sub-clinical disease, lack of clinician awareness and lack of access to diagnostics. It is surprising that no cases were reported during significant outbreaks in the Americas and Caribbean (2014-2017), despite UKAF SP operating and travelling in these regions. The lack of UKAF deployable arbovirus diagnostics, represents a significant capability gap and must be addressed for ongoing surveillance as these arboviruses continue to spread. The risk from

chikungunya was evident with one patient experiencing marked polyarthralgia, a potentially careerlimiting complication. The role for chikungunya vaccine will need to be determined.

The retrospective study design, combined with poor data quality (only 47.5% of patient records met pre-defined criteria for data completeness [Supplementary Appendix 1]) could result in bias. To mitigate these limitations, strict inclusion criteria for laboratory-confirmation and data quality were used. Some true cases may have been excluded, leading to under-reporting. The use of arboviral serology for laboratory-confirmation in UKAF SP is complicated as UKAF has universal yellow fever vaccination, which often causes cross-reaction with diagnostic assays for flaviviruses such as dengue. Requiring laboratory-confirmation likely missed a large proportion of cases. The true number of arbovirus cases in UKAF is likely higher given that ~75% of dengue are subclinical, and those symptomatic cases must have presented to a medical treatment facility with access to suitable diagnostics for inclusion in this study. Retrospective extraction of data from eHRs risks significant bias and missing data, which could not be addressed in this study.

This study provides insight into the increasing impact of arboviruses on UKAF. Dengue poses a significant health threat to UKAF SP as cases surge globally. Clinicians need to consider arboviruses in patients presenting with fever travelling or resident in endemic regions and take a thorough travel history. Appropriate diagnostics should be available to those deployed to high-risk areas to support decision making, in collaboration with Military Infectious Diseases reach-back support. Surveillance is required to monitor the impact of arboviruses on UKAF as they emerge globally. Further work is required to quantify the UKAF personnel at highest risk of severe dengue infection. Policy on the vaccination of high-risk UKAF personnel with a demonstrable history of dengue infection should be considered to mitigate the future risk of severe infection in those who continue to live or travel in high-risk areas.

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Figure Legends

Figure 1: 3-year rolling average incidence of laboratory-confirmed dengue cases amongst UKAF between

2010 and 2023.