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REVIEW PAPER

Campylobacter in Africa – A specific viewpoint

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ABSTRACT

Campylobacter infections and campylobacteriosis-associated post-infectious sequelae are a significant global health burden that needs to be addressed from a specific African perspective. We conducted a comprehensive literature search on NCBI PubMed to compile a comprehensive narrative review article on *Campylobacter* infections in Africa, focusing on key aspects in human and veterinary medicine as well as food hygiene. We specifically focused on the epidemiology of enteropathogenic *Campylobacter* spp. in sub-Saharan and North Africa considering antimicrobial susceptibility. The most significant sequela resulting from molecular mimicry to *Campylobacter* surface structures is the Guillain-Barré syndrome, which was mainly examined in the context of limited studies conducted in African populations. A dedicated subsection is allocated to the limited research on the veterinary medically important species *Campylobacter fetus*. There are significant differences in the composition of the gut microbiome, especially in rural areas, which affect the colonization with *Campylobacter* spp. and the manifestation of campylobacteriosis. There may be a problem of overdiagnosis due to asymptomatic colonization, particularly in the detection of *Campylobacter* using molecular biological techniques. To reduce the colonization and infection rate of *Campylobacter*, we propose implementing several control measures and urge further research to improve the current understanding of the peculiarities of campylobacteriosis in Africa.

KEYWORDS

Campylobacter jejuni, *Campylobacter coli*, *Campylobacter fetus*, Africa, epidemiology, antimicrobial susceptibility, control measures, Guillain-Barré syndrome, microbiome, diagnostics

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INTRODUCTION

Campylobacteriosis, the most common form of bacterial enteritis worldwide [1, 2], is responsible for a range of post-infectious complications such as reactive arthritis and, most notably, Guillain-Barré syndrome [3]. While the status of campylobacteriosis in Europe and America is well established, it exhibits several unique characteristics in Africa, including its epidemiology, habitats of origin in agriculture and environment, clinical manifestation, and the scientific study situation. Compared to other regions, the research on campylobacteriosis in Africa is still limited in many aspects. In this review article, we provide an overview on the epidemiology of enteropathogenic *Campylobacter* spp. in sub-Saharan Africa and North Africa, the antimicrobial resistance situation, and propose *Campylobacter* control measures, based on the current state of scientific literature. Additionally, we examined the significance of the microbiome in the manifestation of campylobacteriosis in Africa, particularly considering factors such as diverse dietary habits, varied water sources, and living closely with domestic animals as well as farm animals, thereby comparing urban and rural areas. Furthermore, we explore the research and experiences regarding the most significant post-infectious sequela of campylobacteriosis, the Guillain-Barré syndrome, in Africa. We also consider the role of *Campylobacter fetus*, an important microbial species in veterinary medicine, globally as well as in African countries, especially in the light of its recent subdivision into three subspecies. In the final part of this article, we address the challenges in diagnosing campylobacteriosis and the etiological relevance of positive *Campylobacter* spp. detections for human disease in the sub-Saharan African tropics. This is particularly important due to the significantly higher asymptomatic colonization rate in populations in resource-poor high-endemicity settings compared to industrialized countries.

EPIDEMIOLOGY OF *CAMPYLOBACTER* IN SUB-SAHARAN AFRICA

Prevalence of Campylobacter in farm animals and humans in sub-Saharan Africa

Campylobacteriosis is considered a significant public health problem in many parts of sub-Saharan Africa [4, 5], but the precise burden of the disease in the region is unknown due to limited surveillance. The estimated prevalence among humans in the sub-Saharan region is between 8.5% and 14.1% [5]. When examining specific risk groups, it was found that children under 5 years of age have a prevalence rate of 50.6% [5], patients with HIV of 45.0% [6], and patients with diarrhea of 20.3% [7]. The prevalence of the bacteria in farm animals varies widely, ranging from 2% in beef from Kenya to as high as 90% in sampled chicken from Cameroon [8]. Notably, certain studies have indicated particularly high rates, exceeding 50%, among pigs [9, 10] and poultry [11, 12]. *Campylobacter jejuni* and *Campylobacter coli* are the most common species isolated from both farm animals and humans [5, 6, 8]. Nonetheless, a study conducted in South Africa reported significantly more *C. jejuni* (n = 232) than *C. coli* (n = 25) among children aged 0–24 months. These two species of *Campylobacter* have adeptly evolved to survive and persist in diverse environmental settings, including high temperature zones, soil, water sources, as well as surfaces and equipment found within food processing environments [13].

The frequency and distribution of *Campylobacter* spp. in environmental samples vary significantly between different regions and countries [1]. In sub-Saharan Africa, factors such as agricultural practices, livestock management, water quality, and sanitation infrastructure have been identified to impact the transmission of *Campylobacter* spp. (Fig. 1) [14, 15]. It was observed in South Africa that free-roaming sheep and cattle spread *Campylobacter* spp. in the farm environment [14]. *Campylobacter* spp. have been detected in milk products from Tanzania [16], Ethiopia [17] and South Africa [18]. Due to the high *Campylobacter* contamination of farms, the occurrence of *Campylobacter* spp. in milk is difficult to avoid, hence effective heat treatment before consumption is highly recommended in order to reduce health risks associated with raw milk consumption [19]. Similarly, *Campylobacter* contamination of fresh vegetables has been reported in some sub-Saharan African countries [20, 21]. Contaminated irrigation water and animal manure are the main sources identified as the source of *Campylobacter* spp. contamination in vegetables (Fig. 1) [22].

Even though it is well known that *Campylobacter* infections do occur throughout the year, a few studies conducted in sub-Saharan Africa have observed a higher frequency of the bacteria in the rainy season than in the dry season [6, 23]. The authors argue that poor agricultural practices, the combination of heavy rainfall and inadequate drainage systems which are common in various areas of sub-Saharan Africa, play a role in increasing the occurrence of *Campylobacter* contamination in water sources, including drinking water. Research conducted in rural sub-Saharan Africa, involving both food-producing animals and human populations [6, 9, 11, 17], has reported rural *Campylobacter* spp. prevalence rates similar to those recorded in urban areas [7, 10, 18, 24]. However, different factors might impact the prevalence and transmission of *Campylobacter* spp. in these distinct settings. It has been suggested that the widespread involvement of rural residents in crop farming and animal husbandry activities might increase their vulnerability to *Campylobacter* spp. transmission [25]. While farming activities are less prevalent in urban areas, the higher population density can result in sanitation infrastructure challenges. Additionally, the food environment and increased levels of food processing and distribution within urban settings could also play a role in contributing to the *Campylobacter* burden [26].

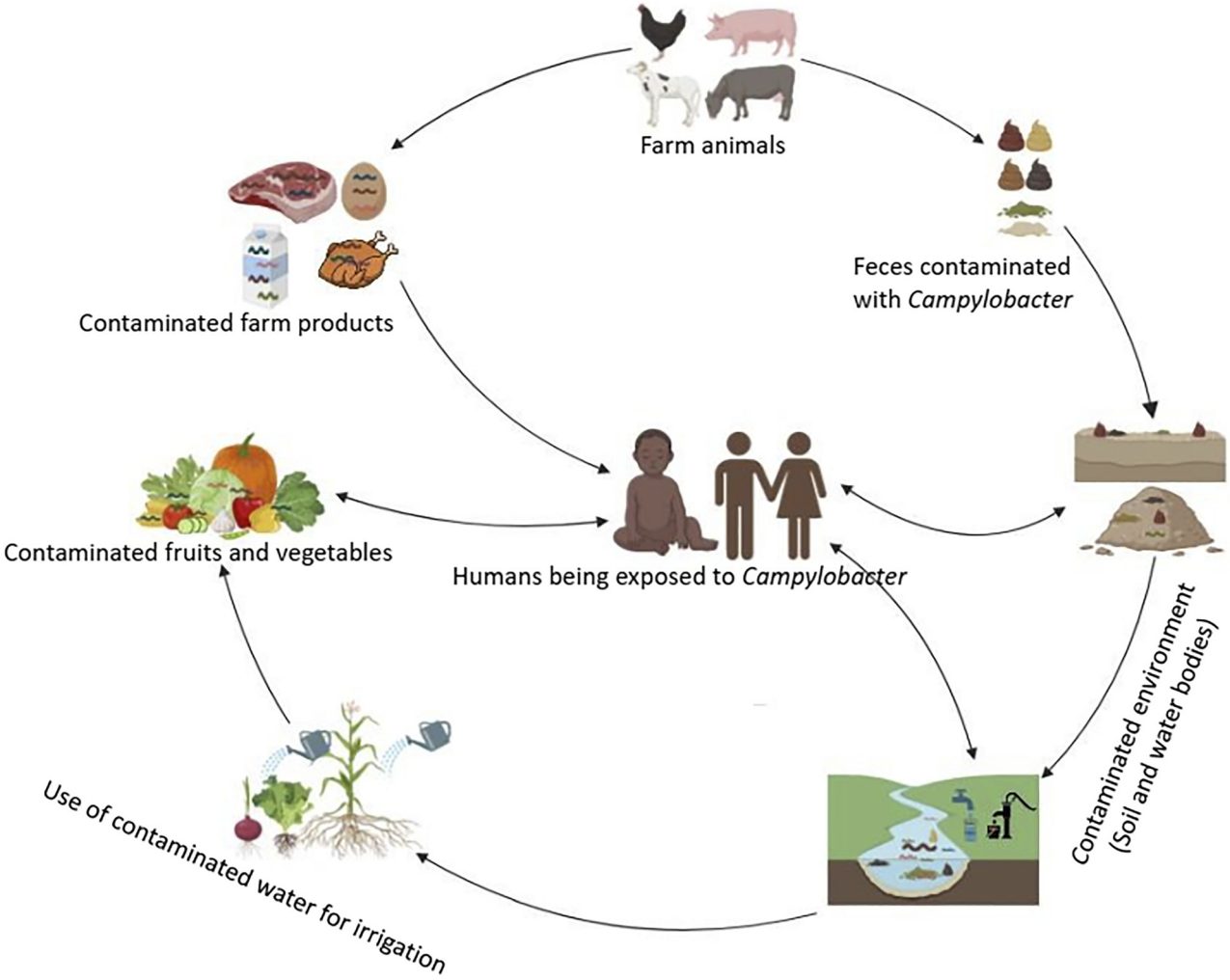

Fig. 1. Transmission routes of *Campylobacter* infection in humans. Created with Biorender.com (accessed on 15 August 2023). *Campylobacter* spp. naturally resides within the gastrointestinal tract of farm animals and primarily infects humans through the consumption of contaminated farm products. *Campylobacter* transmission can also spread through the environment via fecal contamination from reservoir hosts. Drinking contaminated water or its use for irrigation could lead to the contamination of crops that are later consumed by humans.

Antimicrobial resistance (AMR) patterns of *Campylobacter* spp. in sub-Saharan Africa

Campylobacter infections in humans are frequently self-limiting, often resolving without requiring antimicrobial intervention. However, in immunocompromised patients as well in the case of severe or prolonged diarrhea, antimicrobials may be needed. Due to the indiscriminate use of antimicrobials in humans and veterinary medicine, antimicrobial-resistant *Campylobacter* spp. strains have emerged [27]. To address the growing public health concern, it is highly recommended worldwide to decrease the use of antimicrobials in both human and veterinary medicine [28–30]. Reports of *Campylobacter* spp. isolates resistant to ciprofloxacin, erythromycin, and tetracycline have been documented in several sub-Saharan African countries [6, 7, 24, 31–34]. These antibiotics are the recommended drugs for treating campylobacteriosis, and the emergence of resistance poses challenges to ensure effective treatment within the region. Ciprofloxacin resistance in *Campylobacter* spp. isolated from poultry has been reported to be 95.4%, 71.0%, 67.3% and 40.8% in studies conducted in South Africa [32], Kenya [33], Ghana [6] and Ivory Coast [31], respectively. Similarly, high levels of erythromycin and tetracycline resistance in *Campylobacter* spp. strains isolated from poultry have been reported from Ghana [6, 7] and South Africa [32]. Compared to farm animals, lower levels (0–14%) of resistance to ciprofloxacin and erythromycin in *Campylobacter* spp. isolates from human patients have been observed in Uganda [24], Burkina Faso [34], and Nigeria [35]. The higher prevalence of antibiotic resistance in farm animals compared to humans can be attributed to several factors including dense animal populations on farms and limited regulation and oversight of antibiotic use in farm animals [27, 36].

Campylobacter species, particularly *C. jejuni* and *C. coli*, have shown the ability to develop multidrug resistance (MDR) (here defined as resistance to the antibiotics typically

used for the treatment of campylobacteriosis, i.e., erythromycin, tetracycline, and ciprofloxacin). In sub-Saharan Africa, studies have documented MDR in *Campylobacter* spp. strains isolated from humans and poultry [6, 10, 37]. The emergence of multidrug-resistant *Campylobacter* strains is a significant public health concern as it limits the effectiveness of recommended antibiotics for treatment. Very few studies have been conducted in sub-Saharan Africa to identify antibiotic resistance genes and virulence makers. Nonetheless, the following antibiotic resistance genes: *tet*(*O*), $bla_{\text{OXA-61}}$, *aadE*, and *ermB* and the virulence makers: *ciaB*, *cdtA*, *cdtB*, *cdtC*, *cadF* have been reported by different studies in various sub-Saharan African countries [6, 10].

Proposed Campylobacter control measures in sub-Saharan Africa

According to Taha-Abdelaziz and coworkers, *Campylobacter*-specific control strategies can be categorized as pre- and post-harvest interventions [38]. The pre-harvest measures encompass: (a) implementing food hygiene measures to minimize *Campylobacter* spp. exposure in the environment, (b) enhancing avian host immunity through vaccination, and (c) employing antibiotic alternatives to reduce or eliminate the infection burden in chicken [38]. In contrast, post-harvest interventions comprise procedures like (a) cleaning and sanitizing slaughterhouses, (b) decontaminating carcasses, and (c) sanitizing eggshells [38].

Most of the *Campylobacter* studies conducted in sub-Saharan Africa have proposed pre-harvest measures, especially the enhancement of farm hygiene and improvement of infection control measures, to reduce *Campylobacter* spp. occurrence [6, 17, 21, 39]. There has been limited research conducted on utilizing vaccines, probiotics, and bacteriophages to manage the prevalence of *Campylobacter* spp. in sub-Saharan Africa. Nonetheless, some studies have been performed on employing antibiotic alternatives in order to reduce or eliminate the infection burden. Hlashwayo and coworkers have reported on the examination of 47 medicinal plants belonging to 28 families, from six sub-Saharan countries, for *in vitro* activity against *Campylobacter* spp. Out of the 47 tested plants, *Cryptolepis sanguinolenta* and *Terminalia macropter* exhibited the highest levels of antimicrobial activity against *Campylobacter* spp. [40]. Nevertheless, the persisting high prevalence of *Campylobacter* spp. infections in sub-Saharan Africa emphasizes the need for additional research in order to establish appropriate control measures within the region.

EPIDEMIOLOGY OF *C. JEJUNI* AND *C. COLI* IN NORTH AFRICA

Data from North Africa indicate that infections with *C. jejuni* and *C. coli* occur predominantly among the pediatric population. Especially in less developed rural areas, *C. jejuni* infections are widespread due to frequent contact to farm animals, particularly poultry [41, 42]. Moreover, consumption of raw chicken meat and contaminated drinking water as well as limited access to sanitation are well-recognized risk factors [43–46]. Thereby, animal-sourced foods play an important role in the decrease of undernutrition in several African regions [47, 48]. The emergence of antibiotic resistances in *C. jejuni* isolates is of high concern.

The exact prevalence rates might vary across countries and regions within North Africa. More reports about *Campylobacter* in animal-sourced foods are reported than in humans [49]. However, the WHO estimates that 70% of foodborne diseases in the Arabic and North-African region is caused by *Campylobacter* spp., but also by diarrheagenic *Escherichia coli*, *Salmonella enterica* and norovirus [2].

The majority of reports examining the prevalence of *Campylobacter* spp. in North Africa have been conducted in Egypt, while there is a limited number of studies available from other countries in this region (Table 1). One assessment from Egypt showed that *Campylobacter* spp. were isolated from 6.4% of healthy children and 16.8% of children that were suffering from diarrhea in Alexandria [50]. In Cairo, *Campylobacter* spp. were isolated from 15.2% of healthy children while it was found in 25.9% of children suffering from diarrhea [51]. Furthermore, genotyping of different *C. jejuni* isolates demonstrated that the main source for *C. jejuni* in Egypt is broiler meat [45, 46, 52]. Moreover, it was suggested that several antibiotic resistance genes are present in *C. jejuni* isolated in North Africa [46]. Especially erythromycin, nalidixic acid, streptomycin, chloramphenicol, tetracycline, ciprofloxacin, gentamicin and ampicillin-resistant strains were detected in an Egyptian assessment [53].

In Tunisia, next to several virulence factors of *Campylobacter* strains, resistances against the following antibiotics was found: quinolones (ciprofloxacin or nalidixic acid, or both), erythromycin, β-lactams (ampicillin or amoxicillin/clavulanic acid or both), tetracycline and gentamicin [54].

Table 1. Reports of *C. jejuni* or *C. coli* in northern African countries. Table adapted from Habib et al., 2021; n.d. = not detected

Country	Source (number of samples)	*C. jejuni* [%]*	*C. coli* [%]*
Egypt	broiler (101)	n.d.	4
	slaughterhouses (104)	n.d.	3.9
	fresh chicken meat (30)	46.7	46.7
	frozen chicken meat (30)	46.7	40
	raw milk (50)	20	20
	kareish cheese (50)	14	14
	yoghurt (50)	8	8
Tunisia	broiler (590)	n.d.	n.d.
	chicken meat (149)	16.1	3.4
	Turkey meat (101)	13.8	1.9
Sudan	goats (336)	5.7	69.6
Morocco	broiler (105)	n.d	40
	raw poultry (850)	n.d.	n.d.

* The percentage (%) of *Campylobacter* species was calculated from the positive samples (isolated target bacteria) by Habib et al., 2021.

Studies showed that the prevalence of *C. jejuni* and *C. coli* in Egypt is similar in chicken meat products either frozen or fresh, ranging between 40.0% and 46.7% [49, 55]. In Morocco, there is a higher reported incidence of *C. coli*, although this discrepancy may be due to a lack of comprehensive investigations [49, 56]. In Sudan, *C. jejuni* and *C. coli* were detected in goats among other facultatively pathogenic bacterial species [49, 57]. Tunisia reported a greater prevalence of *C. jejuni* in chicken and Turkey meat compared to *C. coli* [49, 58].

However, the lack of studies from North African countries other than Egypt and Tunisia makes it challenging to provide a comprehensive understanding of the *Campylobacter* spp. prevalence across the entire region.

CAMPYLOBACTER SPP. AND THE HUMAN MICROBIOME

An introduction into the topic

Once consolidated, the human gut microbiome is known to provide a robust protection against colonization with exogenous microbial agents and infections with pathogenic microorganisms [59–62]. This phenomenon has been labeled as "colonization resistance". As shown a decade ago [63], the microbiome composition can partly recover even after severe disturbances as they may be associated with infectious gastroenteritis on international travel in resource-poor settings. Discussed components of microbiome-associated colonization resistance comprise secretion of antimicrobial active components, competition for nutrients, stabilization of the integrity of the gut barrier and spreading of bacteriophages [59]. However, the gut microbiome's protective properties can be directly or indirectly compromised by disturbances due to drugs like antibiotics, proton pump inhibitors, antidiabetics and antipsychotics [59]. Further, co-evolution of entero-invasive microorganisms like *C. jejuni* has led to several virulence mechanisms which can overcome colonization resistance [59, 64]. In turn, alteration of the human gut microbiome due to severe enteric infection with microorganisms like *Campylobacter* spp. has been associated with increased odds of developing future inflammatory bowel disease [65].

The current knowledge on interactions between *Campylobacter* spp. and the gut microbiome, both based on animal studies and human assessments, is summarized in the following.

Experience with animals

In mouse experiments, rich abundance of *Escherichia coli* and *Bacteroides* spp. has been found to be associated with increased *Campylobacter* spp. colonization rates [66]. While mouse microbiomes are known to prevent *C. jejuni* infections in mice, inflammatory responses in the animals occur associated with *C. coli* challenges [67]. However, compared to mouse-specific enteric microbiota, human microbiome compositions in the animals' gut have been associated with even increased enteric inflammation in case of artificially induced colonization of the animals' guts with *C. coli* [68]. In turn as a consequence of *C. coli* infections in the gut of mice, enteric microbiome changes with an increased abundance of Enterobacterales have been recorded [69].

Antimicrobially induced depletion of enteric microbiomes in mice as well as complete lacking of enteric microbiomes facilitate both enteric and systemic inflammation in the animals in response even to *C. jejuni* challenges [70–75], but *C. jejuni*-specific colonization resistance in the gut of mice can at least partly be restored by fecal microbiota transfer (FMT) [76] and even FMT from susceptible animal donors is associated with a protective effect [77]. In case of *C. jejuni* colonization in mice with a human gut microbiome, in contrast, increased TH-2 lymphocyte and autoimmune responses as well as Guillain Barré syndrome-associated antibody induction were observed in a *C. jejuni* strain-dependent manner [78]. Toll-like receptor 4 (TLR 4) and TLR 9 have been shown to be major mediators of such *C. jejuni*-mediated inflammation [79–81]. Compared to humans, TLR 4 responses in healthy mice challenged with *C. jejuni* are 10.000× times lower, which is considered as a major factor of colonization resistance [82]. The iron-chelating compound desferoxamine reduces inflammation and promotes shifts towards asymptomatic colonization [83]. Even in mice harboring a human enteric microbiome, FMT with mouse-borne microbiota but also exposure to probiotic lactobacilli and bifidobacteria result in a decrease of *C. jejuni* colonization or infection [84, 85]. In contrast, immature mouse microbiomes which are abundant shortly after weaning in very young animals were shown to be insufficient to medicate colonization resistance in mice and even severe entero-colitis caused by *C. jejuni* was seen in such instances [86].

Focusing on wild mice, their species is considered to be of relevance for the animals' potential of harboring *Campylobacter* spp. in their gut. While *Mus minutus* was shown to carry considerable proportions of *Campylobacter* spp. DNA in its gut, enteric microbiota of *Mus musculus* were characterized by high abundance of *Lactobacillus* spp. DNA but absence of nucleic acid sequences of *Campylobacter* spp. in a Korean assessment [87].

In chicken as well, the importance of the gut microbiome for the control of *C. jejuni*-associated virulence has been shown. Chicken with lacking or antimicrobially depleted gut microbiomes were demonstrated to be more vulnerable to *C. jejuni* in terms of enteric colonization intensity, invasiveness of the pathogen and inflammation [88, 89]. Colonization of the gut of chicken with *C. jejuni* has been shown to be associated with the absence of Peptococcaceae as well as several genera of the family Ruminococcaceae. More than this, bacteria of the Christensenellaceae R-7 group and *C. jejuni* were suggested to obviously compete for the same substrate in the chicken's gut [90]. On the other hand, spontaneous decolonization of *C. jejuni* from the gut of chicken has been associated with increased detection of

Clostridiaceae, Ruminococcaceae, Lachnospiraceae, and Peptococcaceae sequences in the birds' enteric microbiomes [91]. In addition, effects on the birds' microbiomes have been shown to at least partially depend on the time of exposition to *C. jejuni* [92], while the microbiome composition is also affected by the time of infection [93]. Enrichment of the chicken's gut microbiome with presumedly protective microorganisms like lactic acid bacteria has been discussed as an option for the reduction of the colonization with *Campylobacter* spp. [94, 95]. On a mechanistic level, the application of deoxycholic acid (DCA) but not of other bile acid derivates like lithocholic acid or ursodeoxycholic acid was associated with reduced colonization of chicken guts with *C. jejuni*. DCA-associated reduced Firmicutes and increased Bacteroidetes proportions within the animals' gut microbiomes were considered as mediators of such increased colonization resistance. Also, the transplantation of DCA-modulated anaerobes made the birds less vulnerable to *C. jejuni* colonization [96]. The latter phenomenon has been confirmed for the mouse model as well [97]. Of note, the influence of bile acids on microbiome-associated colonization resistance of chicken towards *C. jejuni* has been repeatedly demonstrated [91] and microbially synthesized short-chain fatty acids have also been proven to influence gene expression patterns with relevance for persistence and virulence of *C. jejuni* [98]. Of note, short-chain fatty acids were still able to reduce *Campylobacter* spp. colonization in chicken at late stages of colonization when applied as feed additives [99]. Other compounds resulting in a decrease of *Campylobacter* spp. as part of the enteric microbiomes of chicken comprise biochar, bentonite and zeolite as 4% feed additives each [100] as well as the essential oil carvacrol [101]. In chicken pretreated either with *C. jejuni* lysate or Poly-D,L-lactide-co-glycolide polymer nanoparticles containing CpG oligodeoxynucleotides, increased microbiome diversity and increased proportions of Firmicutes and Bacteroidetes were found to be associated with reduced proportions of *Campylobacter* spp. as part of their enteric microbiomes [102].

Interestingly, however, experiments including reciprocal microbiota transfer suggested that the microbiome compositions only partly explain differences of *Campylobacter* spp.-specific colonization resistance in birds [103].

Experience with human individuals

A US-military medical investigation based on a controlled human infection model for *C. jejuni*, which had also provided evidence for lacking effect of rifaximin prophylaxis against *C. jejuni* infection, recently suggested a mild association between beta-diversity of the human enteric microbiome and vulnerability towards *C. jejuni*-associated gastroenteritis [104]. As shown for Swedish poultry abattoir workers with a high pre-test probability of developing *Campylobacter* spp. infection, the gut microbiome of individuals developing *Campylobacter* spp.-associated gastroenteritis was characterized by a higher abundance of *Bacteroides* spp., *Escherichia* spp., *Streptococcus* spp. and *Phascolarctobacterium* spp. but a lower abundance of sequences of Clostridiales, Lachnospiraceae and *Anaerovorax* spp., respectively, compared to a matched control population without *Campylobacter* spp. infections. In the same study, long-term effects of *Campylobacter* spp.-infections on the human microbiome were confirmed, indicating interaction in both directions [66]. Thereby, the dimension of *C. jejuni* infection-associated alteration of the human gut microbiome seems to be variable. Particularly low diversity of the human enteric microbiome after *C. jejuni* infections with high proportions of Proteobacteria, Fusobacteria and Gammaproteobacteria as well as reduced levels of several taxa of Firmicutes, especially of the order Clostridiales and the family Ruminococcaceae, were found to be associated with postinfectious bowel dysfunction. High fiber consumption seemed to have a protective effect and was associated with lower abundance of Gammaproteobacteria [105]. Even in Southern-American high endemicity settings, where *Campylobacter* spp. are often recorded as asymptomatic colonizers in the gut of local children, their abundance was associated with altered enteric microbiome compositions [106].

In low-income countries in general, *C. jejuni* infection-associated affection of the human enteric microbiome has been proposed to be associated with multiple effects on children, including malabsorption and growth reduction, but also immune impairment, cognitive reduction and even increased mortality. As admitted by the authors themselves, however, evidence is still low and future research is needed [107]. Focusing on Africa, increased abundance of *Campylobacter* spp. sequences was detected in stool samples of children from Guinea-Bissau co-infected with enteric protozoa like nonpathogenic *Entamoeba coli* and *Endolimax nana* as well as with pathogenic *Giardia duondenalis* and *Entamoeba histolytica* irrespective of clinical symptoms. It was speculated that the protozoa might shape the children's enteric microbiome in a way that colonization of *Campylobacter* spp. is facilitated [108].

Altogether, epidemiological knowledge on associations of enteric microbiome composition and enteric colonization with *Campylobacter* spp. in Africa is still extremely scarce. Future research is required to shed light on this important topic.

ASSOCIATION OF *CAMPYLOBACTER* SPP. INFECTIONS AND GUILLAIN-BARRÉ SYNDROME – EXPERIENCE FROM AFRICA

Background of Guillain-Barré syndrome-triggering by *Campylobacter* spp.

Probabilistic associations of *Campylobacter* spp. infections and the immune-mediated acute polyradiculo-neuropathy Guillain-Barré syndrome (GBS) with symmetrical flaccid paresis as a common clinical manifestation are considered as well established [109–113]. Etiologically, this association is

driven by molecular mimicry between the pathogens' surface structures and axonal or myelin components of the central nervous system. *C. jejuni*, in particular, as well as *Mycoplasma pneumoniae* and human cytomegalovirus (CMV) are believed to induce about one third of the observed GBS cases [3] with the pathogen's lipooligosaccharide (LOS) stimulating Toll-like-receptor 4 as a molecular trigger. Some authors even assume a quantitively stronger association [114, 115], with estimations of *Campylobacter*-based induction of GBS-cases ranging between 5% and 42% [116, 117]. More than this, *C. jejuni*-associated GBS-cases were reported to be characterized by particular severity [3] and sometimes irreversible courses [118], represented by predominantly axonal degeneration in the more severe cases [119, 120]. In contrast to GBS associated with respiratory infections, the clinical onset has been reported to be slightly delayed [121]. Usually, GBS onset is reported one to three weeks after the diagnosis of *C. jejuni* infections [122].

Campylobacter-associated sialylated LOS comprises ganglioside-like epitopes which have been shown to induce anti-ganglioside auto-antibodies directed against peripheral nerves [120, 123–126]. GBS-associated anti-ganglioside antibodies of the IgG_1 and IgG_3 type indicate involvement of T-cell reactivity in the disruption of the blood-nerve-barrier [127]. In addition, it has been suggested that bacterial toxins might contribute to maintaining the host's inflammatory response occurring in GBS [128] and that *C. jejuni* infection can influence innate and adaptive pro-inflammatory pathways which contribute to overcoming immune tolerance, thus supporting autoimmunity [127]. Further, several host factors including the human leukocyte antigen type are believed to play important roles as interfering factors [129]. In a strain-dependent manner and affected by peculiarities of the human host's immune system, different types of auto-antibodies can occur, triggering either demyelinating GBS, also called acute inflammatory demyelinating polyneuropathy, or axonal GBS, also called acute motor axonal neuropathy [126]. The strain-dependence affects the probability of infection-associated GBS as well. While 1 out of 1058 *Campylobacter* infections were previously shown to trigger GBS in general, even 1 out of 158 *Campylobacter* Penner:Lior serotype HS:19 (heat-stable) infections had the same outcome [118]. Penner:Lior type HS:19, which is usually a relatively rare *C. jejuni* serovar, has initially been found to be overrepresented in Japanese patients with GBS [122]. Of note, a recent meta-analysis came to a similarly low general probability of GBS triggering after *Campylobacter* infection as described by Allos [118] in the 0.07% range [130]. Nevertheless, this baseline risk of GBS after *Campylobacter* infection is still about 70-fold to 100-fold higher than the GBS risk in the general population [127].

One of the best-studied molecular mechanisms of *C. jejuni*-strain-specific differences regarding the probability of GBS triggering is a polymorphism in the sialyltransferase (*cstII*) gene. This enzyme is a key factor in the synthesis of GBS-associated ganglioside-like lipo-oligosaccharides (LOSs) [131]. If the 51st amino acid, which determines the enzymatic activity of the 291 amino acid-long peptide, is threonine (Thr), so-called GM-1-like and GD1a-like LOSs are synthesized, triggering auto-antibodies associated with limb weakness. If the 51st amino acid is asparagine (Asn), GT1a-like and GD1c-like LOSs are expressed and respectively triggered auto-antibodies have been associated with ophthalmoplegia and ataxia [131].

Of note, *Campylobacter*-induced GBS can also be accompanied by other autoimmunity-induced medical conditions. For example, concomitantly occurring GBS and focal segmental glomerulosclerosis have been recently reported associated with a *Campylobacter* infection [132].

Experience from Africa

Studies on associations of *Campylobacter* infections and GBS on the African continent are scarcely available. International comparisons, which are still based on limited case numbers, at least suggest an internationally stabile association between GBS and preceding infections. However, there are regional differences in resulting clinical phenotypes, calling for further research on a larger scale [133]. The general occurrence of *Campylobacter* spp.-associated GBS in sub-Saharan Africa is accepted, but reliable data on the local quantitative relevance of this medical condition are widely lacking [5].

From South Africa, increased proportions of GBS in both children and adults were reported in association with a *C. jejuni* biotype 2 Penner-Lior serotpye HS:41 clone and highly similar isolates in the middle of 1990s, a serotype which is regionally relatively rare [134, 135]. Clinical GBS associated with these HS:41 isolates was reported as severe, the patients required prolonged hospitalization and automated ventilation [134, 135]. Sequence data from the South African GBS-associated HS:41 isolates have been provided [136] and the *C. jejuni* integrated element 1 (CJIE1, a *Campylobacter* Mu-like prophage) was described as a genomic element of regional importance [137]. Even in clonally related HS:41 isolates, minor expression differences in the ganglioside-like lipo-oligosaccharides GM1 levels were observed [138]. In a more recent South African study on GBS, *Campylobacter* spp. were identified in about 12% of GBS patients with about 3 out of 4 cases carrying *C. jejuni*, while the other campylobacteriosis cases were due to *C. coli* or *C. jejuni*/*C. coli* co-infections [139].

In the north of the African continent, a recent Egyptian assessment focused on regional differences of *Campylobacter* infection-associated GBS compared to previous western studies. The authors reported a comparably younger age of Egyptian GBS cases after *Campylobacter* spp. infection and history of infection with a broader spectrum of *Campylobacter* serotypes, while *Campylobacter* spp.-induced anti-ganglioside auto-antibodies were broadly abundant [140]. This finding matches the results of an international assessment which was not able to identify globally applicable epidemiological markers for GBS-associated *C. jejuni* isolates in HS:19 strains and others [141, 142].

Studies on the association of *Campylobacter* infections and GBS from the middle of the African continent are widely lacking, although it is unlikely that GBS is an

irrelevant medical condition in these regions. In resource-limited Ethiopia, health-related costs of an average GBS case were calculated to be 30 times higher compared to an average diarrhea case and GBS was estimated to account for 0.2% of the total national health-related costs of the country [143]. However, detection of associations between GBS and *Campylobacter* spp.-infections is only feasible if adequate diagnostic approaches for the identification of such infections are in place [121, 144]. This is frequently not the case in resource-limited tropical settings of sub-Saharan Africa, calling for future multinational cooperative epidemiological research approaches.

THE ROLE OF *C. FETUS* IN AFRICAN COUNTRIES

Compared to other *Campylobacter* species, such as *C. jejuni*, *C. coli* and *C. lari*, *C. fetus* has received less attention from the scientific community. Nevertheless, there are quite a few publications pertaining the epidemiology and laboratory detection of this pathogen. The geography of these research efforts includes various countries of sub-Saharan and North Africa, where the health of cattle and other herd animals is essential for the well-being of local communities [145].

C. fetus comprises three subspecies: *C. fetus* subspecies *fetus* (CFF), *C. fetus* subspecies *veneralis* (CFV) - both associated with mammals - and *C. fetus* subspecies *testudinum* (CFT), which is associated with reptiles. Although CFV is mostly a bovine pathogen causing a venereal disease known as bovine genital campylobacteriosis (BGC) in cattle, there have been a few cases where it was isolated from humans, such as women with bacterial vaginosis [146]. CFV establishes a chronic infection in bulls where it is found in the penile epithelium, prepuce and urethra, without causing any obvious signs of infection [147]. A recent isolation of CFV from a fecal sample of a Rhesus monkey at a research center in the United States could suggest interspecies transmission potentially also affecting human individuals and the fact that this pathogen could be transmitted via the fecal-oral route [148]. Previously, two cases of CFF causing systemic disease and death due to liver damage of iatrogenic causes were described in immunocompromised Rhesus monkeys at another research center in the United States [149]. The human-to-animal transmission hypothesis of CFV was suggested earlier by another research group showing that CFV could have been present in humans as a pathogen in the early livestock domestication era. By jumping between species, CFV evolved solely as a venereal pathogen in cattle. In any case, many questions still remain unanswered regarding its transmission and etiological relevance [150]. Serious negative economic impact is caused each year globally for the profitability of the cattle industry due to CFV and other infectious agents causing pregnancy losses in cattle [147].

In contrast to CFV, CFF in humans is associated with extra-intestinal, systemic infections with a mortality rate up to 14% [151]. In animals, the transmission of CFF follows the fecal-oral route and, once an animal ingests the pathogen with food or water, the microorganism invades the mucosa resulting in transient bacteremia and abortion [152]. Evidently, CFF has a close affinity to blood, as in humans it often causes bloodstream-associated infections and is characterized with a hematogenous spread causing a wide range of conditions from dialysis-associated peritonitis to endocarditis and pneumonia [151]. In humans with chronic underlying illnesses, CFT has been associated with gastrointestinal and extra-intestinal disease, including bloodstream infections. Generally, the symptoms of CFT infection may include fever, cough, epigastric pain, diarrhea and fatigue [153, 154]. The major distinction between the three subspecies of *C. fetus* is that CFF and CFV affect mammals, while CFT is associated with reptiles. In fact, both CFT and CFF have been associated with cases of human *C. fetus* ssp. infections acquired from squamates [154]. Like other *Campylobacter* spp., CFF can be found in both birds and reptiles [152]. In domestic animals such as cattle and sheep, CFF infrequently causes abortions, which results in prolonged calving season [148, 151]. Besides cattle, CFF has been reported as a commensal in other animals, such as monkeys and horses, having been isolated from feces of these animals. Escher and coworkers also noted in their 2016 study the identical genotypic and phenotypic characteristics between human and bovine strains of CFF. For example, 5 human strains from two host-specific clusters in this study were identical to bovine isolates suggesting the existence of a definitive link between the two hosts [151].

Research regarding *C. fetus* in Africa is scarce. In 1981, persistent infections with "*C. fetus* subspecies *jejuni*" in African children in the South African city Johannesburg were described. Whereas some of the infected children developed symptoms, others did not [155]. The actual microbial species classification "*C. fetus* subspecies *jejuni*" does not exist in the modern classification. As the bacterial isolates originated from fecal samples, the authors may have meant *C. jejuni*. Madoroba et al. identified that 1.9% of tested samples originating from South African cattle were positive for CFV [156]. Previously, Schmidt et al. described campylobacteriosis in South Africa as a significant infectious cause of reproductive disorders among cattle leading to poor calving [157].

C. jejuni and *C. fetus* were the most frequently identified *Campylobacter* spp. in a study conducted in Ethiopia in 2021 examining 519 samples originating from humans, livestock, chickens and water. *C. fetus* predominated in cattle and sheep feces, while *C. jejuni* predominated in human feces originating from Africa [158].

Various *Campylobacter* species were the object of 75 research studies originating in Africa between 1994 and 2019. South Africa, Tanzania and Nigeria were the countries where the majority of the studies took place [40]. Naturally, *C. jejuni* and *C. coli* were the most commonly researched *Campylobacter* species. However, in Nigeria — a key West African country — significant research on *C. fetus* has also been carried out. The majority of these studies (25 in total)

from the region report a high prevalence of *C. fetus* in cattle, sheep, goats, donkeys, and other farm animals. This prevalence is linked to reproductive issues within these animal populations [40]. In Tanzania and the entire region of East Africa, CFV was reported as the cause of enzootic infertility among cattle in smallholder farms. In contrast, South Africa, a representative country of the region of Southern Africa, did not identify *C. fetus* as a major problem affecting local farms [40]. Many countries from sub-saharan Africa are considerably less developed compared to South Africa, with far less allocations into research financing. For example, some reports of *C. fetus* originating from these countries were not accompanied by antimicrobial testing [40].

From a clinical point of view, differentiation between the three *C. fetus* subspecies is essential, although extremely difficult, as more than 90% of the two species' genomes are identical [159]. Sequencing of the 16S rRNA gene is ineffective in distinguishing the three species. Consequently, genotyping, amplified fragment length polymorphism (AFLP) analysis, and specific PCR analyses have been preferred. With the implementation of Next Generation Sequencing (NGS), the task of subspecies identification of *C. fetus* isolates will probably become less challenging. Furthermore, MALDI TOF MS based proteotyping allows the discrimination of CFT from CFF and CFV, but differentiation between CFF and CFV was shown to be impossible due to the lack of specific biomarkers [160]. A method for direct detection of the three *C. fetus* subspecies from clinical samples with high sensitivity and specificity but without discrimination between them is based on fluorescent *in situ* hybridization (FISH) using a combination of two DNA probes [161].

Of note, only few African clinical laboratories are equipped with the latest and expensive technology. Fortunately, 1% glycine tolerance testing is a low cost, phenotypic test to differentiate two subspecies of *C. fetus*. CFF is tolerant to glycine, while CFV is not, with occasional exceptions [162]. For the species and subspecies identification of *C. fetus* isolates, one cost effective way is coupling biochemical methods with PCR and/or genotyping. This combined approach may be successfully used in diagnostic laboratories even in low-income countries.

Immunohistochemistry (IHC) and other antibody-based assays can also be used for fairly accurate identification of CFV. For example, Campero et al. correctly identified 13 CFV cases among other *Campylobacter* spp. infections present in formalin-fixed tissues applying this technique. Thus, the *C. fetus* IHC procedure using formalin fixed tissues can be used as a practical tool for the detection of *C. fetus*-associated with ovine and bovine abortions [147, 163]. Apparently, *C. jejuni* may also cause genital infections in cattle and sheep as evidenced by Li and colleagues, thus making the application of species-level differentiation techniques necessary for the correct identification of the infectious agent [164]. IHC procedures are associated with low costs and have thus been used for the identification of *C. fetus* and other *Campylobacter* spp. in African countries [40].

Summarized, infections with *Campylobacter* spp., including *C. fetus*, in animals and especially in cattle and poultry, are common in sub-Saharan Africa. Main reasons of high prevalence rates comprise poor hygiene when handling animals, as well as unregulated open markets and animal killing practices. The public health burden of *C. fetus* needs to be seriously evaluated. Due to the difficulties in isolation and identification of this bacterium, its prevalence may be relevantly underestimated. However, worldwide, the number of patients at risk of systemic infections due to such pathogens is on the rise. Evidence suggests that *C. fetus* has a propensity of being associated with human cases having underlying conditions, such as immunodeficiency. Many African countries affected by the HIV epidemic could benefit from technological and diagnostic improvements facilitating the reliable identification of systemic infections potentially caused by *C. fetus* [165].

ETIOLOGICAL RELEVANCE OF DIAGNOSTIC *CAMPYLOBACTER* SPP. DETECTION FOR HUMAN DISEASE IN THE SUB-SAHARAN AFRICAN TROPICS

Facultative pathogenicity of *Campylobacter* spp. and its epidemiological background in sub-Saharan Africa

The term "facultative pathogenicity" describes a microorganism's ability of causing either etiologically relevant infection or harmless colonization in response to host-specific factors. Insofar, this paradigm is in partial contradiction to the third historic Henle-Koch-postulate which suggests that pure cultures of an infectious agent should be sufficient conditions for the experimental induction of an associated infectious disease [166]. Nowadays, the fulfillment of this condition would be called "obligate pathogenicity" and is quite rarely the case in infectious disease medicine.

Although large-sized studies like MAL-ED [167] have proven increased risk of diarrhea in sub-Saharan children <2 years of age in case of diagnostic detection of *Campylobacter* spp., considerable proportions of children with *Campylobacter* spp. proven in their stool samples were in the asymptomatic control group. Insofar, *Campylobacter* spp. is no exemption from the rule of predominance of facultative pathogenicity. In smaller, regional studies in Africa with a broader age spectrum of study participants like in a 40-year-old assessment from the Central African Republic [168], a recent work from Ghana [169] as well as works form other African countries like Cameroon [170] and Northern African Tunisia [171], even significance for a minor increased risk of diarrhea can get lost in comparison of individuals with and without *Campylobacter* spp. detectable in stool. Obviously, this is not solely associated with more or less virulent species within the *Campylobacter* genus, because comparable findings were observed with *C. jejuni*-specific diagnostic assays in stool samples of Ghanaian children as well [172]. Even more than this, high proportions of

asymptomatic Madagascan children showed colonization with *C. jejuni* in a previous assessment [173]. Admittedly, the above-mentioned findings were reported as results of cross-sectional assessments, while longitudinal studies on potential long-term persistence of *Campylobacter* spp. in stool samples of sub-Saharan African populations are lacking so far. Nonetheless, a colonization rate exceeding 20% in Madagascan infants, as recently reported, is indicative of a carrier state rather than the shedding of residual DNA following the successful clearance of a *C. jejuni* infection [173].

In spite of uncertain etiological relevance of *Campylobacter* spp. detection in human stool samples in sub-Saharan Africa due to asymptomatic colonization and carriage, its relevance as a causative agent of diarrhea, in particular in African children, is widely accepted [5, 174, 175]. This focus on very young infants is different in comparison to resource-rich industrialized settings, where *Campylobacter* spp.'s relevance as major causes of bacterial diarrhea remains more stable over the different age groups [176] associated with a low infection pressure. Interestingly, urban African infant populations have been associated with a later *Campylobacter* spp. infection peak compared to rural populations [177], potentially suggesting a higher transmission rate in the rural setting. Antimicrobial therapy in sub-Saharan Africa is challenged by partly high resistance levels [178, 179], e.g., up to 70% resistance against the macrolide azithromycin in Southern Africa [178].

Immune responses and microbiome effects as likely reasons for the highly variable clinical impact of *Campylobacter* spp. in sub-Saharan Africa

Various reasons are considered to influence the high variance of medical conditions following *Campylobacter* spp. transmission to human individuals in sub-Saharan Africa. Adaptive immune responses to high infection pressure are among those reasons. As early as in the late 1980s, a study in the Central African Republic on the association of *Campylobacter* spp. with diarrhea had shown that highest infection rates were observed between the first and third month of life and dropped significantly even as early as in the interval between the fourth and sixth month of life of the infants. The early switch from infections to carrier states was explained by frequent and early (re-)exposition in the tropical high endemicity setting [180]. This very early data matches with more recent observations on infectious diarrhea in infants on Zanzibar, suggesting a rapid circle of pathogen clearance and re-infection [181], leading to habituation and decreased disease severity resulting in some sort of "semi-immunity". In contrast, previous attempts have failed to produce a robust and long-lasting vaccine-induced immune-protection in humans, as infection-induced protection early wanes without repeated exposure to different *Campylobacter* spp. strains [182, 183]. The latter finding is, unfortunately, quite discouraging for early implementation steps of infection prevention and control enforcement in resource-limited tropical settings, because the waning of semi-immunity might be associated with more severe symptoms in case of re-infections due to beginning but yet insufficient infection control procedures and a resulting decreased frequency of re-exposition. This leads to the seemingly paradox situation that "a little bit" infection control might lead to worse results than both adequate infection control and no implementation of infection control at all.

The precise nature of semi-immunity induced by rapid infection cycles is complex and yet poorly understood. The induction of humoral immunity is driven by both *Campylobacter* spp. infection and carriage as early shown in the Central African Republic [184]. Later reports pointed towards a likely protective effect of gamma-type interferon [182], while multi-functional cytokine responses of $CD4^+$-type T cells triggered by campylobacteriosis were not found [185]. Epidemiological data provide further hints on the influence of an individuum's immunological state on the clinical impact of campylobacteriosis in Africa. Breastfeeding has been linked to a reduced risk of clinically apparent campylobacteriosis in infants younger than six months, even in areas where the disease is highly prevalent. This suggests that immunologically active components in breast milk, such as IgA antibodies, likely play a role in mitigating the disease [186]. In turn, malnourishment in African children and the associated immunocompromising effects were described to facilitate enteric campylobacteriosis [187].

Next to adaptive immune responses, microbiome effects have to be considered. While campylobacteriosis is known to relevantly affect the composition of the microbial flora in the human gut [104], there are also hints that specific compositions of the enteric flora show protective effects by reducing the likeliness of colonization or infection with *Campylobacter* spp. [61, 82, 94, 188, 189]. More than this, sub-Saharan African epidemiological assessments have suggested that the co-abundance of other enteric pathogens may affect the clinical courses of infection [190, 191] by the induction of immune responses and/or by specifical shaping of the enteric microbiome environment. The interplay of those factors is still poorly understood and a topic of ongoing research.

The interpretative dilemma regarding diagnostic results – when is a *Campylobacter* spp.-detection disease-associated in sub-Saharan Africa?

The uncertainty on the attribution of etiological relevance of *Campylobacter* spp. detections in human stool samples in high-endemicity settings as detailed above is a challenge for the interpretation of diagnostic results in sub-Saharan Africa. Therefore, it would be desirable to identify diagnostic strategies to overcome this challenge. As semi-quantification of pathogens in stool samples can be standardized with a realistic effort in times of real-time PCR-based diagnostics, quantitative pathogen abundance as reciprocally correlated with Ct-values in real-time PCR was early assessed for this purpose. Robust associations of the quantitative *Shigella* spp. burden in infant stool samples from sub-Saharan Africa and

East Asia with the severity of enteritis as shown by the group of Lindsay and colleagues in 2013 made this hypothesis appear promising [192]. Subsequent attempts of transferring these findings to other bacterial causative agents of diarrhea were, however, less convincing. While reciprocal association of cycle threshold (*Ct*) values in real-time PCR for diarrhea-associated pathogens with clinical diarrhea could be confirmed for *Shigella* spp./EIEC (enteroinvasive *Escherichia coli*) and additionally shown for rotavirus and astrovirus in Tanzanian infants, the authors of the respective study failed to show such an association for *Campylobacter* spp. [193]. Partly contradictory results for *C. jejuni*- and *C. coli*-specific real-time PCR were shown by Liu and colleagues, who reported evidence for etiological relevance in case of Ct-value ranges from 20 to 25 and from 25 to 30, indicative of intermediate pathogen loads, but neither for Ct-values >30, indicative of a low pathogen load, nor for Ct-values <20, indicative for a high pathogen load [194]. More than this, low Ct-values of 20 for *C. jejuni* and of 17 for *Shigella* spp./EIEC as reported for stool samples from clinically inapparent Madagascan children [173] do not necessarily indicate clinical disease and so, results obtained with study protocols which automatically attribute clinical relevance based on quantitative abundance of enteric pathogens in high endemicity settings [195] should be interpreted with care.

If, however, sole quantity is not the whole story, the question arises which auxiliary parameters could be included in the diagnostic interpretation with realistic effort. As neither specific immunological profiles indicative of clinically apparent campylobacteriosis nor both specific and easy-to-obtain microbiome and/or co-infection profiles are available, the achievement of a high pre-test probability by considering clinical parameters prior to diagnostic testing seems most promising. In case of clinically apparent infection, *Campylobacter* spp. have been associated with invasive courses of enteritis with either visible blood [5] or increased numbers of red and white blood cells [196] in stool samples in Sub-Saharan African assessments. Also, dehydration of African children with enteric campylobacteriosis is common [186]. While specificity and predictive value of such clinical signs are admittedly still low, their lacking abundance might, however, provide more confidence to clinicians when denying likely etiological relevance of molecular *Campylobacter* spp. detections in stool samples due to insufficient matching with clinical findings.

CONCLUSIONS

The number of studies on *Campylobacter* spp. in Africa, both in the field of human medicine and veterinary medicine, is still limited to date. Such studies should be conducted more frequently in the near future, as they provide a basis for, e.g., drinking water and food hygiene procedure as well as other preventive medical approaches. This is particularly important due to the relatively high mortality rate of gastrointestinal infections in newborns and young children in Africa. Due to the different microbiome composition within the human intestine in African individuals living in rural areas compared to inhabitants of industrialized regions and due to the considerably higher *Campylobacter* spp.-colonization rate without patho-etiological significance, the diagnosis of campylobacteriosis remains a challenge, with culture-based methods, but also with highly sensitive molecular biological techniques. This challenge needs to be addressed in medical microbiology laboratories in African countries, calling for ongoing implementation research.

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REFERENCES

1. Kaakoush NO, Castaño-Rodríguez N, Mitchell HM, Man SM. Global epidemiology of *Campylobacter* infection. Clin Microbiol Rev. 2015;28:687–720.
2. World Health Organization. WHO estimates of the global burden of foodborne diseases: foodborne disease burden epidemiology reference group 2007-2015. World Health Organization; 2015. Available: https://apps.who.int/iris/handle/10665/199350.
3. Finsterer J. Triggers of Guillain-Barré syndrome: *Campylobacter jejuni* predominates. Int J Mol Sci. 2022;23:14222.
4. Gahamanyi N, Mboera LEG, Matee MI, Mutangana D, Komba EVG. Prevalence, risk factors, and antimicrobial resistance profiles of thermophilic *Campylobacter* species in humans and animals in Sub-Saharan Africa: a systematic review. Int J Microbiol. 2020;2020:2092478.
5. Hlashwayo DF, Sigaúque B, Noormahomed EV, Afonso SMS, Mandomando IM, Bila CG. A systematic review and meta-analysis reveal that *Campylobacter* spp. and antibiotic resistance are widespread in humans in sub-Saharan Africa. PLoS One. 2021;16:e0245951.
6. Paintsil EK, Ofori LA, Akenten CW, Zautner AE, Mbwana J, Jaeger A, et al. Antibiotic-resistant *Campylobacter coli* and

Campylobacter jejuni in commercial and smallholder farm animals in the Asante Akim North municipality of Ghana. Front Microbiol. 2022;13:983047.
7. Karikari AB, Obiri-Danso K, Frimpong EH, Krogfelt KA. Antibiotic resistance of *Campylobacter* recovered from Faeces and carcasses of healthy livestock. BioMed Res Int. 2017;2017:4091856.
8. Asuming-Bediako N, Parry-Hanson Kunadu A, Abraham S, Habib I. *Campylobacter* at the human-food interface: the African perspective. Pathog Basel Switz. 2019;8:87.
9. Mdegela RH, Laurence K, Jacob P, Nonga HE. Occurrences of thermophilic *Campylobacter* in pigs slaughtered at Morogoro slaughter slabs, Tanzania. Trop Anim Health Prod. 2011;43:83–7.
10. Sithole V, Amoako DG, Abia ALK, Perrett K, Bester LA, Essack SY. Occurrence, antimicrobial resistance, and molecular characterization of *Campylobacter* spp. in intensive pig production in South Africa. Pathog Basel Switz. 2021;10:439.
11. Nonga HE, Muhairwa AP. Prevalence and antibiotic susceptibility of thermophilic *Campylobacter* isolates from free range domestic duck (*Cairina moschata*) in Morogoro municipality, Tanzania. Trop Anim Health Prod. 2010;42:165–72.
12. Nzouankeu A, Ngandjio A, Ejenguele G, Njine T, Ndayo Wouafo M. Multiple contaminations of chickens with *Campylobacter, Escherichia coli* and *Salmonella* in Yaounde (Cameroon). J Infect Dev Ctries. 2010;4:583–686.
13. Bolton DJ. *Campylobacter* virulence and survival factors. Food Microbiol. 2015;48:99–108.
14. Espunyes J, Cabezón O, Dias-Alves A, Miralles P, Ayats T, Cerdà-Cuéllar M. Assessing the role of livestock and sympatric wild ruminants in spreading antimicrobial resistant *Campylobacter* and *Salmonella* in alpine ecosystems. BMC Vet Res. 2021;17:79.
15. Machdar E, van der Steen NP, Raschid-Sally L, Lens PNL. Application of Quantitative Microbial Risk Assessment to analyze the public health risk from poor drinking water quality in a low income area in Accra, Ghana. Sci Total Environ. 2013;449:134–42.
16. Kashoma IP, Kassem II, John J, Kessy BM, Gebreyes W, Kazwala RR, et al. Prevalence and antimicrobial resistance of *Campylobacter* isolated from dressed beef carcasses and raw milk in Tanzania. Microb Drug Resist Larchmt N. 2016;22:40–52.
17. Admasie A, Eshetu A, Tessema TS, Vipham J, Kovac J, Zewdu A. Prevalence of *Campylobacter* species and associated risk factors for contamination of dairy products collected in a dry season from major milk sheds in Ethiopia. Food Microbiol. 2023;109:104145.
18. Mabote KI, Mbewe M, Ateba CN. Prevalence of *Campylobacter* contamination in fresh chicken meat and milk obtained from markets in the north-west province, South Africa. J Hum Ecol. 2011;36:23–8.
19. Taghizadeh M, Nematollahi A, Bashiry M, Javanmardi F, Mousavi M, Hosseini H. The global prevalence of *Campylobacter* spp. in milk A systematic review and meta-analysis. Int Dairy J. 2022;105423.
20. Kougblénou SD, Jerrold Agbankpé A, Béhanzin JG, Victorien Dougnon T, Aniambossou AV, Baba-Moussa L, et al. Microbiological safety of leafy vegetables produced at Houeyiho and Sèmè-Kpodji vegetable farms in Southern Benin: risk factors for *Campylobacter* spp. Int J Food Sci. 2019;2019:8942608.
21. Ssemanda JN, Reij MW, Middendorp G van, Bouw E, Plaats R van der, Franz E, et al. Foodborne pathogens and their risk exposure factors associated with farm vegetables in Rwanda. Food Control. 2018;89:86–96.
22. Farhadkhani M, Nikaeen M, Hadi M, Gholipour S, Yadegarfar G. *Campylobacter* risk for the consumers of wastewater-irrigated vegetables based on field experiments. Chemosphere. 2020;251:126408.
23. Adam MA, Wang J, Enan K-A, Shen H, Wang H, El Hussein AR, et al. Molecular survey of viral and bacterial causes of childhood diarrhea in Khartoum state, Sudan. Front Microbiol. 2018;9:112.
24. Mshana SE, Joloba M, Kakooza A, Kaddu-Mulindwa D. *Campylobacter* spp. among children with acute diarrhea attending Mulago hospital in Kampala–Uganda. Afr Health Sci. 2009;9:201–5.
25. LeJeune J, Kersting A. Zoonoses: an occupational hazard for livestock workers and a public health concern for rural communities. J Agric Saf Health. 2010;16:161–79.
26. Nadimpalli ML, Marks SJ, Montealegre MC, Gilman RH, Pajuelo MJ, Saito M, et al. Urban informal settlements as hotspots of antimicrobial resistance and the need to curb environmental transmission. Nat Microbiol. 2020;5:787–95.
27. Paintsil EK, Ofori LA, Akenten CW, Fosu D, Ofori S, Lamshöft M, et al. Antimicrobial usage in commercial and domestic poultry farming in two communities in the Ashanti Region of Ghana. Antibiot Basel Switz. 2021;10:800.
28. Ford L, Healy JM, Cui Z, Ahart L, Medalla F, Ray LC, et al. Epidemiology and antimicrobial resistance of *Campylobacter* infections in the United States, 2005–2018. Open Forum Infect Dis. 2023;10:ofad378.
29. Shen Z, Wang Y, Zhang Q, Shen J. Antimicrobial resistance in *Campylobacter* spp. Microbiol Spectr. 2018;6:10.
30. Portes AB, Panzenhagen P, Pereira dos Santos AM, Junior CAC. Antibiotic resistance in *Campylobacter*: a systematic review of South American isolates. Antibiotics. 2023;12:548.
31. Goualié GB, Akpa EE, Kakou-N'gazoa ES, Guessennd N, Bakayoko S, Niamké LS, et al. Prevalence and antimicrobial resistance of thermophilic *Campylobacter* isolated from chicken in Côte d'Ivoire. Int J Microbiol. 2012;2012:150612.
32. Bester LA, Essack SY. Observational study of the prevalence and antibiotic resistance of *Campylobacter* spp. from different poultry production systems in KwaZulu-Natal, South Africa. J Food Prot. 2012;75:154–9.
33. Nguyen TNM, Hotzel H, Njeru J, Mwituria J, El-Adawy H, Tomaso H, et al. Antimicrobial resistance of *Campylobacter* isolates from small scale and backyard chicken in Kenya. Gut Pathog. 2016;8:39.
34. Sangaré L, Nikiéma AK, Zimmermann S, Sanou I, Congo-Ouédraogo M, Diabaté A, et al. *Campylobacter* spp. epidemiology and antimicrobial susceptibility in a developing country, Burkina Faso (West Africa). Afr J Clin Exp Microbiol. 2012;13:110–7.
35. Samuel SO, Aboderin AO, Akanbi AA, Adegboro B, Smith SI, Coker AO. *Campylobacter* enteritis in Ilorin, Nigeria. East Afr Med J. 2006;83:478–84.
36. Hedman HD, Vasco KA, Zhang L. A review of antimicrobial resistance in poultry farming within low-resource settings. Anim Open Access J MDPI. 2020;10:1264.
37. Kashoma IP, Kassem II, Kumar A, Kessy BM, Gebreyes W, Kazwala RR, et al. Antimicrobial resistance and genotypic

diversity of *Campylobacter* isolated from pigs, dairy, and beef cattle in Tanzania. Front Microbiol. 2015;6:1240.
38. Taha-Abdelaziz K, Singh M, Sharif S, Sharma S, Kulkarni RR, Alizadeh M, et al. Intervention strategies to control *Campylobacter* at different stages of the food chain. Microorganisms. 2023;11:113.
39. Carron M, Chang Y-M, Momanyi K, Akoko J, Kiiru J, Bettridge J, et al. *Campylobacter*, a zoonotic pathogen of global importance: prevalence and risk factors in the fast-evolving chicken meat system of Nairobi, Kenya. PLoS Negl Trop Dis. 2018;12: e0006658.
40. Hlashwayo DF, Sigaúque B, Bila CG. Epidemiology and antimicrobial resistance of *Campylobacter* spp. in animals in Sub-Saharan Africa: a systematic review. Heliyon. 2020;6:e03537.
41. Berndtson E, Danielsson-Tham M-L, Engvall A. *Campylobacter* incidence on a chicken farm and the spread of *Campylobacter* during the slaughter process. Int J Food Microbiol. 1996;32:35–47.
42. Medley S, Ponder M, Alexander KA. Anthropogenic landscapes increase *Campylobacter jejuni* infections in urbanizing banded mongoose (*Mungos mungo*): a one health approach. PLoS Negl Trop Dis. 2020;14:e0007888.
43. Izat AL, Gardner FA, Denton JH, Golan FA. Incidence and level of *Campylobacter jejuni* in broiler processing. Poult Sci. 1988;67: 1568–72.
44. Skarp CPA, Hänninen M-L, Rautelin HIK. Campylobacteriosis: the role of poultry meat. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2016;22:103–9.
45. Awad A, Elkenany R, Sadat A, Ragab W, Elhadidy M. Multilocus sequence typing (MLST) of *Campylobacter jejuni* isolated from broiler meat in Egypt. Pak J Biol Sci PJBS. 2019;22:574–9.
46. Moawad AA, Hotzel H, Awad O, Tomaso H, Neubauer H, Hafez HM, et al. Occurrence of *Salmonella enterica* and *Escherichia coli* in raw chicken and beef meat in northern Egypt and dissemination of their antibiotic resistance markers. Gut Pathog. 2017;9:57.
47. Iannotti LL, Lutter CK, Stewart CP, Gallegos Riofrío CA, Malo C, Reinhart G, et al. Eggs in early complementary feeding and child growth: a randomized controlled trial. Pediatrics. 2017;140: e20163459.
48. Headey D, Nguyen P, Kim S, Rawat R, Ruel M, Menon P. Is exposure to animal feces harmful to child nutrition and health outcomes? A multicountry observational analysis. Am J Trop Med Hyg. 2017;96:961–9.
49. Habib I, Mohamed M-YI, Khan M. Current state of *Salmonella, Campylobacter* and *Listeria* in the food chain across the Arab countries: a descriptive review. Foods Basel Switz. 2021;10:2369.
50. Pazzaglia G, Bourgeois AL, Araby I, Mikhail I, Podgore JK, Mourad A, et al. *Campylobacter*-associated diarrhoea in Egyptian infants: epidemiology and clinical manifestations of disease and high frequency of concomitant infections. J Diarrhoeal Dis Res. 1993;11:6–13.
51. Pazzaglia G, Bourgeois AL, el Diwany K, Nour N, Badran N, Hablas R. *Campylobacter* diarrhoea and an association of recent disease with asymptomatic shedding in Egyptian children. Epidemiol Infect. 1991;106:77–82.
52. Ahmed HA, El Hofy FI, Ammar AM, Abd El Tawab AA, Hefny AA. ERIC-PCR genotyping of some *Campylobacter jejuni* isolates of chicken and human origin in Egypt. Vector Borne Zoonotic Dis Larchmt N. 2015;15:713–7.
53. Hassanain N. Antimicrobial resistant *Campylobacter jejuni* isolated from humans and animals in Egypt. Glob Veterina. 2011; 6(2):195–200.
54. Gharbi M, Béjaoui A, Ben Hamda C, Ghedira K, Ghram A, Maaroufi A. Distribution of virulence and antibiotic resistance genes in *Campylobacter jejuni* and *Campylobacter coli* isolated from broiler chickens in Tunisia. J Microbiol Immunol Infect Wei Mian Yu Gan Ran Za Zhi. 2022;55:1273–82.
55. El-Aziz DMA, Abd-Allah SM. Incidence of *Campylobacter* species in wholesale chicken carcasses and chicken meat products in Assiut city, Egypt. Int Food Res J. 2017;24:2660–5.
56. Asmai R, Karraouan B, Es-Soucratti K, En-Nassiri H, Bouchrif B, Karib H, et al. Prevalence and antibiotic resistance of *Campylobacter coli* isolated from broiler farms in the Marrakesh Safi region, Morocco. Vet World. 2020;13:1892–7.
57. Elbrissi A, Sabeil YA, Khalifa KA, Enan K, Khair OM, El Hussein AM. Isolation, identification and differentiation of *Campylobacter* spp. using multiplex PCR assay from goats in Khartoum State, Sudan. Trop Anim Health Prod. 2017;49:575–81.
58. Jribi H, Sellami H, Mariam S, Smaoui S, Ghorbel A, Hachicha S, et al. Isolation and identification of *Campylobacter* spp. from poultry and poultry by-products in Tunisia by conventional culture method and multiplex real-time PCR. J Food Prot. 2017;80: 1623–7.
59. Ducarmon QR, Zwittink RD, Hornung BVH, van Schaik W, Young VB, Kuijper EJ. Gut microbiota and colonization resistance against bacterial enteric infection. Microbiol Mol Biol Rev MMBR. 2019;83:e00007–19.
60. Worley MJ. Immune evasion and persistence in enteric bacterial pathogens. Gut Microbes. 2023;15:2163839.
61. Herzog MK-M, Cazzaniga M, Peters A, Shayya N, Beldi L, Hapfelmeier S, et al. Mouse models for bacterial enteropathogen infections: insights into the role of colonization resistance. Gut Microbes. 2023;15:2172667.
62. Stecher B. The roles of inflammation, nutrient availability and the commensal microbiota in enteric pathogen infection. Microbiol Spectr. 2015;3(3):MBP-0008-2014.
63. David LA, Materna AC, Friedman J, Campos-Baptista MI, Blackburn MC, Perrotta A, et al. Host lifestyle affects human microbiota on daily timescales. Genome Biol. 2014;15:R89.
64. Masanta WO, Heimesaat MM, Bereswill S, Tareen AM, Lugert R, Groß U, et al. Modification of intestinal microbiota and its consequences for innate immune response in the pathogenesis of campylobacteriosis, modification of intestinal microbiota and its consequences for innate immune response in the pathogenesis of campylobacteriosis. J Immunol Res J Immunol Res. 2013;2013: e526860.
65. Axelrad JE, Olén O, Askling J, Lebwohl B, Khalili H, Sachs MC, et al. Gastrointestinal infection increases odds of inflammatory bowel disease in a nationwide case-control study. Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc. 2019;17: 1311–22.
66. Dicksved J, Ellström P, Engstrand L, Rautelin H. Susceptibility to *Campylobacter* infection is associated with the species composition of the human fecal microbiota. mBio. 2014;5(5):e01212–14.
67. Genger C, Kløve S, Mousavi S, Bereswill S, Heimesaat MM. The conundrum of colonization resistance against *Campylobacter* reloaded: the gut microbota composition in conventional mice

does not prevent from *Campylobacter coli* infection. Eur J Microbiol Immunol. 2020;10:80–90.
68. Heimesaat MM, Genger C, Kløve S, Weschka D, Mousavi S, Bereswill S. The host-specific intestinal microbiota composition impacts *Campylobacter coli* infection in a clinical mouse model of campylobacteriosis. Pathog Basel Switz. 2020;9:804.
69. Heimesaat MM, Genger C, Biesemeier N, Kløve S, Weschka D, Mousavi S, et al. Inflammatory immune responses and gut microbiota changes following *Campylobacter coli* infection of IL-10-/- mice with chronic colitis. Pathog Basel Switz. 2020;9:560.
70. Heimesaat MM, Mousavi S, Bandick R, Bereswill S. *Campylobacter jejuni* infection induces acute enterocolitis in IL-10-/- mice pretreated with ampicillin plus sulbactam. Eur J Microbiol Immunol. 2022;12:73–83.
71. Shayya NW, Foote MS, Langfeld LQ, Du K, Bandick R, Mousavi S, et al. Human microbiota associated IL-10−/− mice: a valuable enterocolitis model to dissect the interactions of *Campylobacter jejuni* with host immunity and gut microbiota. Eur J Microbiol Immunol. 2023;12:107–22.
72. Bereswill S, Fischer A, Plickert R, Haag LM, Otto B, Kuhl AA, et al. Novel murine infection models provide deep insights into the "menage a trois" of *Campylobacter jejuni*, microbiota and host innate immunity. PLoS One. 2011;6:e20953.
73. O'Loughlin JL, Samuelson DR, Braundmeier-Fleming AG, White BA, Haldorson GJ, Stone JB, et al. The intestinal microbiota influences *Campylobacter jejuni* colonization and extraintestinal dissemination in mice. Appl Environ Microbiol. 2015;81:4642–50.
74. Brooks PT, Bell JA, Bejcek CE, Malik A, Mansfield LS. An antibiotic depleted microbiome drives severe *Campylobacter jejuni*-mediated Type 1/17 colitis, Type 2 autoimmunity and neurologic sequelae in a mouse model. J Neuroimmunol. 2019; 337:577048.
75. Wymore Brand M, Sahin O, Hostetter JM, Trachsel J, Zhang Q, Wannemuehler MJ. *Campylobacter jejuni* persistently colonizes gnotobiotic altered Schaedler flora C3H/HeN mice and induces mild colitis. FEMS Microbiol Lett. 2020;367:fnaa163.
76. Heimesaat MM, Mrazek K, Bereswill S. Murine fecal microbiota transplantation lowers gastrointestinal pathogen loads and dampens pro-inflammatory immune responses in *Campylobacter jejuni* infected secondary abiotic mice. Sci Rep. 2019;9:19797.
77. Heimesaat MM, Plickert R, Fischer A, Göbel UB, Bereswill S. Can microbiota transplantation abrogate murine colonization resistance against *Campylobacter jejuni*? Eur J Microbiol Immunol. 2013;3:36–43.
78. Brooks PT, Brakel KA, Bell JA, Bejcek CE, Gilpin T, Brudvig JM, et al. Transplanted human fecal microbiota enhanced Guillain Barré syndrome autoantibody responses after *Campylobacter jejuni* infection in C57BL/6 mice. Microbiome. 2017;5:92.
79. Kløve S, Genger C, Mousavi S, Weschka D, Bereswill S, Heimesaat MM. Toll-like receptor-4 dependent intestinal and systemic sequelae following peroral *Campylobacter coli* infection of IL10 deficient mice harboring a human gut microbiota. Pathog Basel Switz. 2020;9:386.
80. Otto B, Haag L-M, Fischer A, Plickert R, Kühl AA, Göbel UB, et al. *Campylobacter jejuni* induces extra-intestinal immune responses via Toll-like-receptor-4 signaling in conventional IL-10 deficient mice with chronic colitis. Eur J Microbiol Immunol. 2012;2:210–9.
81. Haag LM, Fischer A, Otto B, Plickert R, Kühl AA, Gobel UB, et al. *Campylobacter jejuni* induces acute enterocolitis in gnotobiotic IL-10-/- mice via Toll-like-receptor-2 and -4 signaling. PLoS One. 2012;7:e40761.
82. Heimesaat MM, Mrazek K, Bereswill S. Murine fecal microbiota transplantation alleviates intestinal and systemic immune responses in *Campylobacter jejuni* infected mice harboring a human gut microbiota. Front Immunol. 2019;10:2272.
83. Bereswill S, Mousavi S, Weschka D, Buczkowski A, Schmidt S, Heimesaat MM. Iron deprivation by oral deferoxamine application alleviates acute campylobacteriosis in a clinical murine *Campylobacter jejuni* infection model. Biomolecules. 2023; 13:71.
84. Mousavi S, Bereswill S, Heimesaat MM. Novel clinical *Campylobacter jejuni* infection models based on sensitization of mice to lipooligosaccharide, a major bacterial factor triggering innate immune responses in human campylobacteriosis. Microorganisms. 2020;8:482.
85. Wagner RD, Johnson SJ, Kurniasih Rubin D. Probiotic bacteria are antagonistic to *Salmonella enterica* and *Campylobacter jejuni* and influence host lymphocyte responses in human microbiota-associated immunodeficient and immunocompetent mice. Mol Nutr Food Res. 2009;53:377–88.
86. Haag LM, Fischer A, Otto B, Grundmann U, Kühl AA, Göbel UB, et al. *Campylobacter jejuni* infection of infant mice: acute enterocolitis is followed by asymptomatic intestinal and extra-intestinal immune responses. Eur J Microbiol Immunol. 2012;1: 2–11.
87. Song H, Kim J, Guk J-H, Kim W-H, Nam H, Suh JG, et al. Metagenomic analysis of the gut microbiota of wild mice, a newly identified reservoir of *Campylobacter*. Front Cell Infect Microbiol. 2020;10:596149.
88. Han Z, Willer T, Li L, Pielsticker C, Rychlik I, Velge P, et al. Influence of the gut microbiota composition on *Campylobacter jejuni* colonization in chickens. Infect Immun. 2017;85(11): e00380–17.
89. Han Z, Li L, Willer T, Baumgärtner W, Rautenschlein S. Adhesion and invasion of *Campylobacter jejuni* in chickens with a modified gut microbiota due to antibiotic treatment. Vet Microbiol. 2020; 240:108504.
90. Hankel J, Kittler S, Chuppava B, Galvez E, Strowig T, Becker A, et al. Luminal and mucosa-associated caecal microbiota of chickens after experimental *Campylobacter jejuni* infection in the absence of *Campylobacter*-specific phages of group II and III. Microb Genomics. 2022;8:mgen000874.
91. Asakura H, Nakayama T, Yamamoto S, Izawa K, Kawase J, Torii Y, et al. Long-term grow-out affects *Campylobacter jejuni* colonization fitness in coincidence with altered microbiota and lipid composition in the cecum of laying hens. Front Vet Sci. 2021;8: 675570.
92. Connerton PL, Richards PJ, Lafontaine GM, O'Kane PM, Ghaffar N, Cummings NJ, et al. The effect of the timing of exposure to *Campylobacter jejuni* on the gut microbiome and inflammatory responses of broiler chickens. Microbiome. 2018;6: 88.
93. Awad WA, Mann E, Dzieciol M, Hess C, Schmitz-Esser S, Wagner M, et al. Age-related differences in the luminal and mucosa-associated gut microbiome of broiler chickens and shifts

associated with *Campylobacter jejuni* infection. Front Cell Infect Microbiol. 2016;6:154.
94. Wyszyńska AK, Godlewska R. Lactic acid bacteria - a promising tool for controlling chicken *Campylobacter* infection. Front Microbiol. 2021;12:703441.
95. Mañes-Lázaro R, Van Diemen PM, Pin C, Mayer MJ, Stevens MP, Narbad A. Administration of *Lactobacillus johnsonii* FI9785 to chickens affects colonisation by *Campylobacter jejuni* and the intestinal microbiota. Br Poult Sci. 2017;58:373–81.
96. Alrubaye B, Abraha M, Almansour A, Bansal M, Wang H, Kwon YM, et al. Microbial metabolite deoxycholic acid shapes microbiota against *Campylobacter jejuni* chicken colonization. PLoS One. 2019;14:e0214705.
97. Fu Y, Almansour A, Bansal M, Alenezi T, Alrubaye B, Wang H, et al. Microbiota attenuates chicken transmission-exacerbated campylobacteriosis in Il10-/- mice. Sci Rep. 2020;10:20841.
98. Luethy PM, Huynh S, Ribardo DA, Winter SE, Parker CT, Hendrixson DR. Microbiota-derived short-chain fatty acids modulate expression of *Campylobacter jejuni* determinants required for commensalism and virulence. mBio. 2017;8:e00407–17.
99. Guyard-Nicodème M, Keita A, Quesne S, Amelot M, Poezevara T, Le Berre B, et al. Efficacy of feed additives against *Campylobacter* in live broilers during the entire rearing period. Poult Sci. 2016;95: 298–305.
100. Prasai TP, Walsh KB, Bhattarai SP, Midmore DJ, Van TTH, Moore RJ, et al. Biochar, bentonite and zeolite supplemented feeding of layer chickens alters intestinal microbiota and reduces *Campylobacter* load. PLoS One. 2016;11:e0154061.
101. Kelly C, Gundogdu O, Pircalabioru G, Cean A, Scates P, Linton M, et al. The *in vitro* and *in vivo* effect of carvacrol in preventing *Campylobacter* infection, colonization and in improving productivity of chicken broilers. Foodborne Pathog Dis. 2017;14:341–9.
102. Taha-Abdelaziz K, Yitbarek A, Alkie TN, Hodgins DC, Read LR, Weese JS, et al. PLGA-encapsulated CpG ODN and *Campylobacter jejuni* lysate modulate cecal microbiota composition in broiler chickens experimentally challenged with *C. jejuni*. Sci Rep. 2018;8:12076.
103. Chintoan-Uta C, Wisedchanwet T, Glendinning L, Bremner A, Psifidi A, Vervelde L, et al. Role of cecal microbiota in the differential resistance of inbred chicken lines to colonization by *Campylobacter jejuni*. Appl Environ Microbiol. 2020;86: e02607–19.
104. Stamps BW, Kuroiwa J, Isidean SD, Schilling MA, Harro C, Talaat KR, et al. Exploring changes in the host gut microbiota during a controlled human infection model for *Campylobacter jejuni*. Front Cell Infect Microbiol. 2021;11:702047.
105. Jalanka J, Gunn D, Singh G, Krishnasamy S, Lingaya M, Crispie F, et al. Postinfective bowel dysfunction following *Campylobacter* enteritis is characterised by reduced microbiota diversity and impaired microbiota recovery. Gut. 2023;72:451–9.
106. Rouhani S, Griffin NW, Yori PP, Olortegui MP, Siguas Salas M, Rengifo Trigoso D, et al. Gut microbiota features associated with *Campylobacter* burden and postnatal linear growth deficits in a Peruvian birth cohort. Clin Infect Dis. 2020;71:1000–7.
107. Schnee AE, Petri WA. *Campylobacter jejuni* and associated immune mechanisms: short-term effects and long-term implications for infants in low-income countries. Curr Opin Infect Dis. 2017; 30:322–8.
108. von Huth S, Thingholm LB, Kofoed P-E, Bang C, Rühlemann MC, Franke A, et al. Intestinal protozoan infections shape fecal bacterial microbiota in children from Guinea-Bissau. PLoS Negl Trop Dis. 2021;15:e0009232.
109. Isaäcson M. Guillain-Barré syndrome and *Campylobacter* infection. J Travel Med. 1998;5:160.
110. Hadden RD, Gregson NA. Guillain–Barré syndrome and *Campylobacter jejuni* infection. Symp Ser Soc Appl Microbiol. 2001;30:145S–54S.
111. Smith JL. *Campylobacter jejuni* infection during pregnancy: long-term consequences of associated bacteremia, Guillain-Barré syndrome, and reactive arthritist. J Food Prot. 2002;65:696–708.
112. Hughes R. *Campylobacter jejuni* in Guillain-Barré syndrome. Lancet Neurol. 2004;3:644.
113. Moore JE, Corcoran D, Dooley JSG, Fanning S, Lucey B, Matsuda M, et al. *Campylobacter* Vet Res. 2005;36:351–82.
114. Allos BM. *Campylobacter jejuni* infection as a cause of the Guillain-Barré syndrome. Infect Dis Clin North Am. 1998;12:173–84.
115. Poropatich KO, Walker CLF, Black RE. Quantifying the association between *Campylobacter* infection and Guillain-Barré syndrome: a systematic review. J Health Popul Nutr. 2010;28:545–52.
116. Scallan Walter EJ, Crim SM, Bruce BB, Griffin PM. Incidence of *Campylobacter*-associated Guillain-Barré syndrome estimated from health insurance data. Foodborne Pathog Dis. 2020;17:23–8.
117. Zautner AE, Johann C, Strubel A, Busse C, Tareen AM, Masanta WO, et al. Seroprevalence of campylobacteriosis and relevant post-infectious sequelae. Eur J Clin Microbiol Infect Dis. 2014;33:1019–27.
118. Allos BM. Association between *Campylobacter* infection and Guillain-Barré syndrome. J Infect Dis. 1997;176 Suppl 2:S125–8.
119. Rees JH, Gregson NA, Griffiths PL, Hughes RA. *Campylobacter jejuni* and Guillain-Barré syndrome. Q J Med. 1993;86:623–34.
120. Nyati KK, Nyati R. Role of *Campylobacter jejuni* infection in the pathogenesis of Guillain-Barré syndrome: an update. BioMed Res Int. 2013;2013:852195.
121. Sovilla JY, Regli F, Francioli PB. Guillain-Barré syndrome following *Campylobacter jejuni* enteritis. Report of three cases and review of the literature. Arch Intern Med. 1988;148:739–41.
122. Mishu B, Blaser MJ. Role of infection due to *Campylobacter jejuni* in the initiation of Guillain-Barre syndrome. Clin Infect Dis. 1993; 17:104–8.
123. Vriesendorp FJ. Insights into *Campylobacter jejuni*-induced Guillain-Barré syndrome from the Lewis rat model of experimental allergic neuritis. J Infect Dis. 1997;176 Suppl 2:S164–8.
124. Yuki N. Molecular mimicry between gangliosides and lipopolysaccharides of *Campylobacter jejuni* isolated from patients with Guillain-Barré syndrome and Miller Fisher syndrome. J Infect Dis. 1997;176 Suppl 2:S150–3.
125. Yuki N. Pathogenesis of Guillain-Barré and Miller Fisher syndromes subsequent to *Campylobacter jejuni* enteritis. Jpn J Infect Dis. 1999;52:99–105.
126. Nachamkin I, Allos BM, Ho T. *Campylobacter* species and Guillain-Barré syndrome. Clin Microbiol Rev. 1998;11:555–67.
127. Latov N. *Campylobacter jejuni* infection, anti-ganglioside antibodies, and neuropathy. Microorganisms. 2022;10:2139.
128. Tsang RSW. The relationship of *Campylobacter jejuni* infection and the development of Guillain-Barré syndrome. Curr Opin Infect Dis. 2002;15:221–8.

129. Kaida K, Ariga T, Yu RK. Antiganglioside antibodies and their pathophysiological effects on Guillain-Barré syndrome and related disorders–a review. Glycobiology. 2009;19:676–92.
130. Keithlin J, Sargeant J, Thomas MK, Fazil A. Systematic review and meta-analysis of the proportion of *Campylobacter* cases that develop chronic sequelae. BMC Public Health. 2014;14:1203.
131. Yuki N. *Campylobacter* sialyltransferase gene polymorphism directs clinical features of Guillain-Barré syndrome. J Neurochem. 2007;103 Suppl 1:150–8.
132. Lim A, Lydia A, Rim H, Dowling J, Kerr P. Focal segmental glomerulosclerosis and Guillain-Barre syndrome associated with *Campylobacter* enteritis. Intern Med J. 2007;37:724–8.
133. Leonhard SE, van der Eijk AA, Andersen H, Antonini G, Arends S, Attarian S, et al. An international perspective on preceding infections in Guillain-Barré syndrome: the IGOS-1000 cohort. Neurology. 2022;99:1299–313.
134. Lastovica AJ, Goddard EA, Argent AC. Guillain-Barré syndrome in South Africa associated with *Campylobacter jejuni* O:41 strains. J Infect Dis. 1997;176 Suppl 2:S139–43.
135. Goddard EA, Lastovica AJ, Argent AC. *Campylobacter* 0:41 isolation in Guillain-Barré syndrome. Arch Dis Child. 1997;76: 526–8.
136. Parker CT, Huynh S, Heikema AP, Cooper KK, Miller WG. Complete genome sequences of *Campylobacter jejuni* strains RM3196 (233.94) and RM3197 (308.95) isolated from patients with Guillain-Barré syndrome. Genome Announc. 2015;3: e01312–15.
137. Quinones B, Guilhabert MR, Miller WG, Mandrell RE, Lastovica AJ, Parker CT. Comparative genomic analysis of clinical strains of *Campylobacter jejuni* from South Africa. PLoS One. 2008;3:e2015.
138. Wassenaar TM, Fry BN, Lastovica AJ, Wagenaar JA, Coloe PJ, Duim B. Genetic characterization of *Campylobacter jejuni* O:41 isolates in relation with Guillain-Barré syndrome. J Clin Microbiol. 2000;38:874–6.
139. Thobela MS, Smith AM, Moonsamy S, Du Plessis H, Govender N, Keddy KH. Detection of *Campylobacter* species in stool specimens from patients with symptoms of acute flaccid paralysis in South Africa. J Infect Dev Ctries. 2018;12:542–9.
140. Wierzba TF, Abdel-Messih IA, Gharib B, Baqar S, Hendaui A, Khalil I, et al. *Campylobacter* infection as a trigger for Guillain-Barré syndrome in Egypt. PLoS One. 2008;3:e3674.
141. Engberg J, Nachamkin I, Fussing V, McKhann GM, Griffin JW, Piffaretti JC, et al. Absence of clonality of *Campylobacter jejuni* in serotypes other than HS:19 associated with Guillain-Barré syndrome and gastroenteritis. J Infect Dis. 2001;184: 215–20.
142. Nachamkin I, Engberg J, Gutacker M, Meinersman RJ, Li CY, Arzate P, et al. Molecular population genetic analysis of *Campylobacter jejuni* HS:19 associated with Guillain-Barré syndrome and gastroenteritis. J Infect Dis. 2001;184:221–6.
143. van Wagenberg CPA, Delele TG, Havelaar AH. Patient-related healthcare costs for diarrhoea, Guillain Barré syndrome and invasive non-typhoidal salmonellosis in Gondar, Ethiopia, 2020. BMC Public Health. 2022;22:2091.
144. Nachamkin I. Microbiologic approaches for studying *Campylobacter* species in patients with Guillain-Barré syndrome. J Infect Dis. 1997;176 Suppl 2:S106–14.
145. Thomas KM, de Glanville WA, Barker GC, Benschop J, Buza JJ, Cleaveland S, et al. Prevalence of *Campylobacter* and *Salmonella* in African food animals and meat: a systematic review and meta-analysis. Int J Food Microbiol. 2020;315:108382.
146. Kalka-Moll WM, Van Bergen M a. P, Plum G, Krönke M, Wagenaar JA. The need to differentiate *Campylobacter fetus* subspecies isolated from humans. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2005;11:341–2.
147. Campero CM, Anderson ML, Walker RL, Blanchard PC, Barbano L, Chiu P, et al. Immunohistochemical identification of *Campylobacter fetus* in natural cases of bovine and ovine abortions. J Vet Med B Infect Dis Vet Public Health. 2005;52: 138–41.
148. Kim SG, Summage-West CV, Sims LM, Foley SL. Complete genome sequence of *Campylobacter fetus* subsp. *venerealis* P4531 from a rhesus monkey. Microbiol Resour Announc. 2021;10: e0073921.
149. Clemmons EA, Jean SM, Machiah DK, Breding E, Sharma P. Extraintestinal campylobacteriosis in rhesus macaques (*Macaca mulatta*). Comp Med. 2014;64:496–500.
150. Iraola G, Forster SC, Kumar N, Lehours P, Bekal S, García-Peña FJ, et al. Distinct *Campylobacter fetus* lineages adapted as livestock pathogens and human pathobionts in the intestinal microbiota. Nat Commun. 2017;8:1367.
151. Escher R, Brunner C, von Steiger N, Brodard I, Droz S, Abril C, et al. Clinical and epidemiological analysis of *Campylobacter fetus* subsp. *fetus* infections in humans and comparative genetic analysis with strains isolated from cattle. BMC Infect Dis. 2016; 16:198.
152. Dworkin J, Blaser MJ. Molecular mechanisms of *Campylobacter fetus* surface layer protein expression. Mol Microbiol. 1997;26: 433–40.
153. Patrick ME, Gilbert MJ, Blaser MJ, Tauxe RV, Wagenaar JA, Fitzgerald C. Human infections with new subspecies of *Campylobacter fetus*. Emerg Infect Dis. 2013;19:1678–80.
154. Masila NM, Ross KE, Gardner MG, Whiley H. Zoonotic and public health implications of *Campylobacter* species and squamates (lizards, snakes and Amphisbaenians). Pathog Basel Switz. 2020;9:799.
155. Richardson NJ, Koornhof HJ, Bokkenheuser VD. Long-term infections with *Campylobacter fetus* subsp. *jejuni*. J Clin Microbiol. 1981;13:846–9.
156. Madoroba E, Gelaw A, Hlokwe T, Mnisi M. Prevalence of *Campylobacter foetus* and *Trichomonas foetus* among cattle from Southern Africa. Afr J Biotechnol. 2011;10:10311–4.
157. Schmidt T, Venter EH, Picard JA. Evaluation of PCR assays for the detection of *Campylobacter fetus* in bovine preputial scrapings and the identification of subspecies in South African field isolates. J S Afr Vet Assoc. 2010;81:87–92.
158. Chala G, Eguale T, Abunna F, Asrat D, Stringer A. Identification and characterization of *Campylobacter* species in livestock, humans, and water in livestock owning Households of Peri-urban Addis Ababa, Ethiopia: a one health approach. Front Public Health. 2021;9:750551.
159. Silva MF, Pereira AL, Fraqueza MJ, Pereira G, Mateus L, Lopes-da-Costa L, et al. Genomic and phenotypic characterization of *Campylobacter fetus* subsp. *venerealis* strains. Microorganisms. 2021;9:340.

160. Emele MF, Karg M, Hotzel H, Bloois LG, Groß U, Bader O, et al. Differentiation of *Campylobacter fetus* subspecies by proteotyping. Eur J Microbiol Immunol. 2019;9:62–71.
161. Karg M, Frickmann H, Hotzel H, Lugert R, Groß U, Hagen RM, et al. Identification of *Campylobacter fetus* by fluorescence *in situ* hybridization (FISH). J Microbiol Methods. 2018;151:44–7.
162. Schulze F, Bagon A, Müller W, Hotzel H. Identification of *Campylobacter fetus* subspecies by phenotypic differentiation and PCR. J Clin Microbiol. 2006;44:2019–24.
163. Morrell EL, Barbeito CG, Odeón CA, Gimeno EJ, Campero CM. Histopathological, immunohistochemical, lectinhistochemical and molecular findings in spontaneous bovine abortions by *Campylobacter fetus*. Reprod Domest Anim Zuchthyg. 2011;46: 309–15.
164. Li X, Tang H, Xu Z, Tang H, Fan Z, Jiao X, et al. Prevalence and characteristics of *Campylobacter* from the genital tract of primates and ruminants in Eastern China. Transbound Emerg Dis. 2022;69: 1892–8.
165. Meier PA, Dooley DP, Jorgensen JH, Sanders CC, Huang WM, Patterson JE. Development of quinolone-resistant *Campylobacter fetus* bacteremia in human immunodeficiency virus-infected patients. J Infect Dis. 1998;177:951–4.
166. Löffler F. Untersuchungen über die Bedeutung der Mikroorganismen für die Entstehung der Diphtherie beim Menschen: bei der Taube und beim Kalbe. Mitt Kais Gesundheitsamt. 1884;2: 421–99.
167. Platts-Mills JA, Babji S, Bodhidatta L, Gratz J, Haque R, Havt A, et al. Pathogen-specific burdens of community diarrhoea in developing countries: a multisite birth cohort study (MAL-ED). Lancet Glob Health. 2015;3:564–75.
168. Georges MC, Roure C, Tauxe RV, Meunier DM, Merlin M, Testa J, et al. Diarrheal morbidity and mortality in children in the Central African Republic. Am J Trop Med Hyg. 1987;36:598–602.
169. Eibach D, Krumkamp R, Hahn A, Sarpong N, Adu-Sarkodie Y, Leva A, et al. Application of a multiplex PCR assay for the detection of gastrointestinal pathogens in a rural African setting. BMC Infect Dis. 2016;16:150.
170. Koulla-Shiro S, Loe C, Ekoe T. Prevalence of *Campylobacter* enteritis in children from Yaounde (Cameroon). Cent Afr J Med. 1995;41:91–4.
171. Gueddana N, Saffen S, Ben Aissa R, Khemiri F, Chaker A, Arouji A, et al. [Etiological study of acute gastroenteritis in children in Tunisia]. Arch Fr Pediatr. 1988;45:207–11.
172. Krumkamp R, Sarpong N, Schwarz NG, Adlkofer J, Adelkofer J, Loag W, et al. Gastrointestinal infections and diarrheal disease in Ghanaian infants and children: an outpatient case-control study. PLoS Negl Trop Dis. 2015;9:e0003568.
173. Frickmann H, Schwarz NG, Rakotozandrindrainy R, May J, Hagen RM. PCR for enteric pathogens in high-prevalence settings. What does a positive signal tell us? Infect Dis Lond Engl. 2015;47: 491–8.
174. Loening WE, Coovadia YM, van den Ende J. Aetiological factors of infantile diarrhoea: a community-based study. Ann Trop Paediatr. 1989;9:248–55.
175. Cassel-Beraud AM, Morvan J, Rakotoarimanana DR, Razanamparany M, Candito D, Ravaomanarivo AM, et al. [Infantile diarrheal diseases in Madagascar: bacterial, parasitologic and viral study]. Arch Inst Pasteur Madagascar. 1990;57:223–54.
176. Guerrant RL, Hughes JM, Lima NL, Crane J. Diarrhea in developed and developing countries: magnitude, special settings, and etiologies. Rev Infect Dis. 1990;12 Suppl 1:S41–50.
177. Simango C, Nyahanana M. *Campylobacter* enteritis in children in an urban community. Cent Afr J Med. 1997;43:172–5.
178. Chibwe M, Odume ON, Nnadozie CF. A review of antibiotic resistance among *Campylobacter* species in human, animal, and water sources in South Africa: a One Health Approach. J Water Health. 2023;21:9–26.
179. Mulatu G, Beyene G, Zeynudin A. Prevalence of *Shigella, Salmonella* and *Campylobacter* species and their susceptibility patters among under five children with diarrhea in Hawassa town, south Ethiopia. Ethiop J Health Sci. 2014;24:101–8.
180. Georges-Courbot MC, Beraud-Cassel AM, Gouandjika I, Georges AJ. Prospective study of enteric *Campylobacter* infections in children from birth to 6 months in the Central African Republic. J Clin Microbiol. 1987;25:836–9.
181. Andersson ME, Elfving K, Shakely D, Nilsson S, Msellem M, Trollfors B, et al. Rapid clearance and frequent reinfection with enteric pathogens among children with acute diarrhea in Zanzibar. Clin Infect Dis Off Publ Infect Dis Soc Am. 2017;65: 1371–7.
182. Kirkpatrick BD, Lyon CE, Porter CK, Maue AC, Guerry P, Pierce KK, et al. Lack of homologous protection against *Campylobacter jejuni* CG8421 in a human challenge model. Clin Infect Dis Off Publ Infect Dis Soc Am. 2013;57:1106–13.
183. Tribble DR, Baqar S, Scott DA, Oplinger ML, Trespalacios F, Rollins D, et al. Assessment of the duration of protection in *Campylobacter jejuni* experimental infection in humans. Infect Immun. 2010;78:1750–9.
184. Martin PM, Mathiot J, Ipero J, Georges AJ, Georges-Courbot MC. Antibody response to *Campylobacter coli* in children during intestinal infection and carriage. J Clin Microbiol. 1988;26:1421–4.
185. Fimlaid KA, Lindow JC, Tribble DR, Bunn JY, Maue AC, Kirkpatrick BD. Peripheral CD4+ T cell cytokine responses following human challenge and re-challenge with *Campylobacter jejuni*. PLoS One. 2014;9:e112513.
186. Zaki AM, DuPont HL, el Alamy MA, Arafat RR, Amin K, Awad MM, et al. The detection of enteropathogens in acute diarrhea in a family cohort population in rural Egypt. Am J Trop Med Hyg. 1986;35:1013–22.
187. Kakai R, Wamola IA, Bwayo JJ, Ndinya-Achola JO. Enteric pathogens in malnourished children with diarrhoea. East Afr Med J. 1995;72:288–9.
188. Mousavi S, Bereswill S, Heimesaat MM. Murine models for the investigation of colonization resistance and innate immune responses in *Campylobacter Jejuni* infections. Curr Top Microbiol Immunol. 2021;431:233–63.
189. Kampmann C, Dicksved J, Engstrand L, Rautelin H. Composition of human faecal microbiota in resistance to *Campylobacter* infection. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2016;22:61.e1–8.
190. Andersson M, Kabayiza J-C, Elfving K, Nilsson S, Msellem MI, Mårtensson A, et al. Coinfection with enteric pathogens in East African children with acute gastroenteritis-associations and interpretations. Am J Trop Med Hyg. 2018;98:1566–70.
191. Moyo SJ, Kommedal Ø, Blomberg B, Hanevik K, Tellevik MG, Maselle SY, et al. Comprehensive analysis of prevalence,

epidemiologic characteristics, and clinical characteristics of monoinfection and coinfection in diarrheal diseases in children in Tanzania. Am J Epidemiol. 2017;186:1074–83.
192. Lindsay B, Ochieng JB, Ikumapayi UN, Toure A, Ahmed D, Li S, et al. Quantitative PCR for detection of *Shigella* improves ascertainment of *Shigella* burden in children with moderate-to-severe diarrhea in low-income countries. J Clin Microbiol. 2013;51:1740–6.
193. Platts-Mills JA, Gratz J, Mduma E, Svensen E, Amour C, Liu J, et al. Association between stool enteropathogen quantity and disease in Tanzanian children using TaqMan array cards: a nested case-control study. Am J Trop Med Hyg. 2014;90:133–8.
194. Liu J, Kabir F, Manneh J, Lertsethtakarn P, Begum S, Gratz J, et al. Development and assessment of molecular diagnostic tests for 15 enteropathogens causing childhood diarrhoea: a multicentre study. Lancet Infect Dis. 2014;14:716–24.
195. Platts-Mills JA, Liu J, Rogawski ET, Kabir F, Lertsethtakarn P, Siguas M, et al. Use of quantitative molecular diagnostic methods to assess the aetiology, burden, and clinical characteristics of diarrhoea in children in low-resource settings: a reanalysis of the MAL-ED cohort study. Lancet Glob Health. 2018;6:e1309–18.
196. Ohanu ME, Offune J. The prevalence of *Campylobacter* in childhood diarrhoea in Enugu state of Nigeria. J Commun Dis. 2009;41:117–20.