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ScienceDirect

Journal of Nutritional Biochemistry 151 (2026) 110267

Journal of Nutritional Biochemistry

RESEARCH PAPER

Complex interactions between stress, nutrition, gut microbiota, and infectious diseases and their impact on health in global conflicts: A narrative review

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Received 16 March 2025; received in revised form 28 November 2025; accepted 13 January 2026

Abstract

Following the global recovery from the COVID-19 pandemic, wars and conflicts have escalated to levels unseen since the Cold War. It is well known that conflict is accompanied not only by significant losses among both military personnel and civilians but also by rising levels of stress and stress-related disorders within the general population. Stress is bidirectionally connected with the state of the gut microbiota through the gut–brain axis. Dietary factors and eating behaviours also play crucial roles in shaping gut microbiota composition. On the one hand, conflict negatively affects food availability and dietary patterns, leading to reduced meal frequency and potentially diminishing microbiota diversity. On the other hand, stress-induced alterations in eating behaviour, such as bulimia or anorexia, can further impair gut microbiota composition. Additionally, individuals in conflict zones face heightened risks of infectious diseases due to disrupted vaccination schedules, poor sanitation, and limited access to clean drinking water. Stress-related immune changes may increase susceptibility to infections and raise the likelihood of adverse outcomes. Moreover, the frequent use of antibiotics to treat infections during conflicts contributes to reduced gut microbiota diversity.

This review narratively examines the complex interactions among stress, immune responses, dietary patterns, infectious diseases, and gut microbiota in conflict-affected areas, and provides new perspectives on the role of artificial intelligence in modelling such comorbid pathologies.

Keywords: War; Stress; Gut microbiota; Eating disorders; Infectious diseases; Immune response.

1. Introduction

After the world started to recover from the COVID-19 pandemic, wars and conflicts have increased to levels not seen since the Cold War. The number of conflicts will likely continue to grow. Two of the biggest conflicts in recent years are Russia's full-scale invasion of Ukraine in February 2022 and the Hamas attacks in October 2023. Fighting is also happening in other parts of the world, such as Yemen, Ethiopia, and Sudan, creating serious humanitarian problems (Figs. 1–3).

According to the DSM-5, war is a strong stress factor that can cause trauma. Trauma is defined as "actual or threatened death, serious injury, or sexual violence" [1]. Experiencing war can lead to mental health problems like anxiety, depression, PTSD (post-traumatic stress disorder), and substance use disorders.

War also forces many people to leave their homes. Refugees and asylum seekers often face serious mental health challenges. For example, the war in Ukraine has created about 6 million refugees worldwide, while millions of people in Sudan are trapped in war zones [4,18]. The Middle East has also seen many forced migrations in the last 50 years, with around 16 million refugees and 60 million displaced people in the region [19]. Being a refugee can harm both physical and mental health, leading to symptoms of PTSD and major depression [20].

War also affects food availability and diet. In active war zones, people often eat simple, irregular meals that do not provide enough vitamins and minerals. In the worst cases, a lack of food can lead to starvation and death. People living outside war zones but experiencing stress may also change their eating habits. Stress affects eating behavior, and research shows that people with PTSD are more likely to eat fast food, drink sugary beverages, and have unhealthy diets (Table 1).

The gut microbiota plays an important role in the stress response, and diet during war may affect microbiota changes. This review aims to explore how war impacts stress, eating habits, and

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https://doi.org/10.1016/j.jnutbio.2026.110267

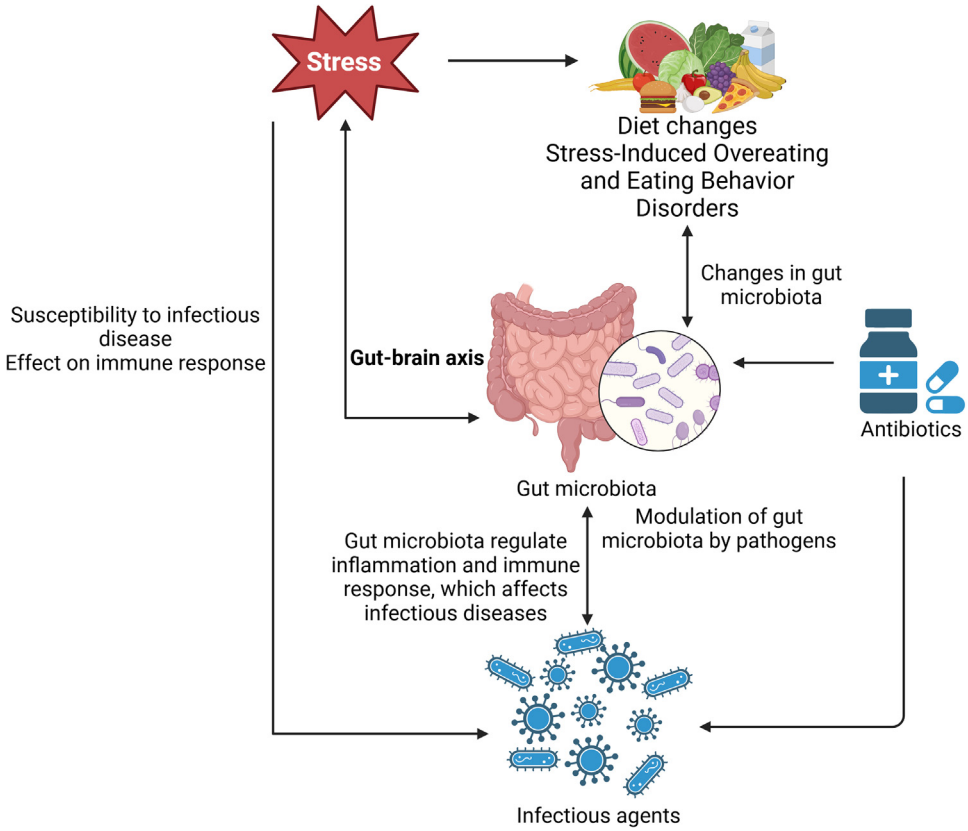

Fig. 1. Block diagram of the relationship between stress, gut microbiota, and infectious agents. This diagram illustrates how stress influences immune response, increasing susceptibility to infections. Stress can also affect eating behavior, leading to overeating (bulimia) or reduced food intake (anorexia). Additionally, the gut-brain axis plays a bidirectional role in this process. Changes in dietary habits and antibiotic use during bacterial infections can further disrupt the composition of gut microbiota, leading to an imbalance that exacerbates stress through this axis.

the gut microbiota, and how these factors are connected in conflict situations.

2. Stress and stress-related disorders during global conflicts

In recent years, the number of armed conflicts around the world has increased. Wars in Ukraine, Israel, the Middle East, Africa, and Ecuador have affected millions of people [1]. The risk of new conflicts is also rising. According to the United Nations (UN), more than 70 million people have been forced to leave their homes due to war and violence [2]. This is the highest number recorded since World War II and the Cold War [3].

The psychological effects of war are severe. The World Health Organization (WHO) estimates that one in five people in conflict-affected areas suffers from a mental disorder. These include depression, anxiety, post-traumatic stress disorder (PTSD), bipolar disorder, and schizophrenia [2]. Studies have shown that conflict-related stress can cause long-term mental health problems in both civilians and soldiers.

A study by Lushchak et al. examined the mental health of Ukrainians 9–12 months after the start of the full-scale Russian invasion. The study surveyed 3,173 participants and found that stress, anxiety, and PTSD were common. Among nondisplaced persons (NDPs), 83.7% reported moderate to high stress, while 86% of internally displaced persons (IDPs) and 89.9% of refugees experienced similar levels. PTSD symptoms (a score of 33 or higher) were observed in 32.9% of NDPs, 39.4% of IDPs, and 47.2% of refugees. More than half of the participants met the diagnostic criteria for PTSD, with 50.8% of NDPs, 55.4% of IDPs, and 62.2% of refugees affected. Only 7.2% of respondents reported low levels of stress, anxiety, and PTSD [4]. Refugees reported mental health issues in wartime more often compared to NDPs and IDPs (P=.0033).

Another study, conducted by Kurapov et al., analyzed mental health six months after the start of the war in Ukraine. The study included 706 participants from different age groups and regions. The results showed high levels of anxiety, depression, and stress. Women were more affected than men, and financial problems increased the risk of anxiety. Young people showed greater resilience to stress compared to older adults. Those who fled the country had higher levels of anxiety and depression than those who remained. Direct exposure to traumatic events increased the risk of PTSD and other mental health disorders [5].

In Latin America, war-related stress is also a concern. Mejía et al. conducted a study in 13 Latin American countries to examine the link between fear of war and mental health. They used the DASS-21 test to measure anxiety, depression, and stress. The results showed a strong connection between fear of war and severe mental health issues. Individuals who feared a large-scale armed conflict had a much higher risk of anxiety (aPR: 1.97), depression (aPR: 1.91), and stress (aPR: 2.05). The study suggested that global instability, combined with other challenges such as COVID-19 and political uncertainty, may worsen mental health in the region [6].

The psychological effects of war have also been studied in Israel. Palgi et al. examined the mental health of 375 Israelis during the Israel-Hamas war. The study found that 35.7% of participants had probable PTSD, while 41.6% showed significant signs of subjective traumatic outlook (STO). Although PTSD and STO were closely

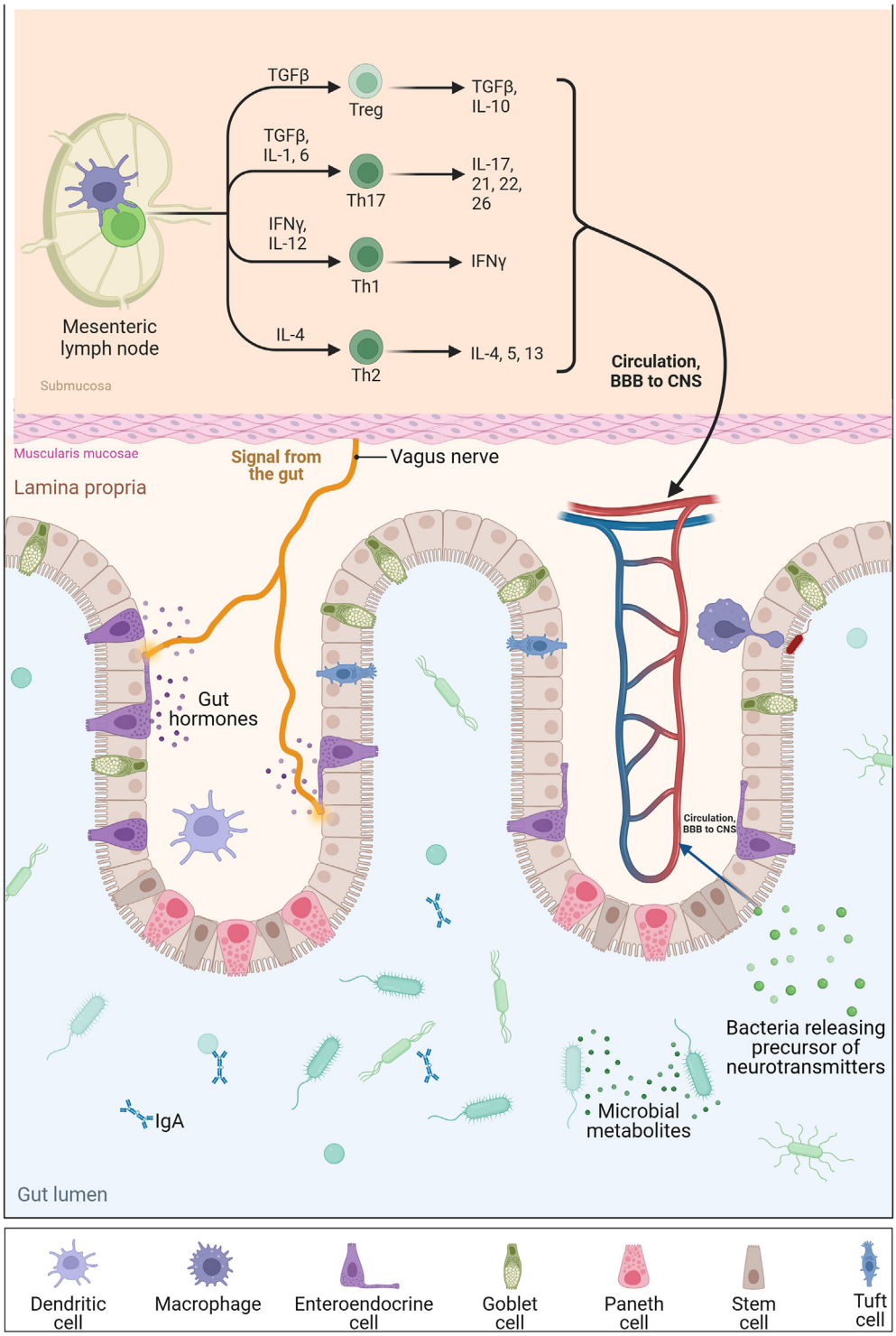

Fig. 2. Gut-brain axis signaling pathways and their influence on stress. This figure depicts the interaction between the gut lumen, gut microbiota, and the central nervous system through pathways such as the vagus nerve, immune cells, and neurotransmitter signaling. Various gut-derived signals, including neurotransmitters (dopamine, serotonin, glutamate, and gamma-aminobutyric acid [GABA]), tryptophan metabolites, and short-chain fatty acids (SCFAs), regulate stress responses by transmitting signals to the brain. These interactions occur via the vagus nerve, immune modulation, and the hypothalamic-pituitary-adrenal (HPA) axis, which controls the release of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol. Dysregulation in these pathways can negatively affect mood and emotional stability, contributing to stress-related disorders.

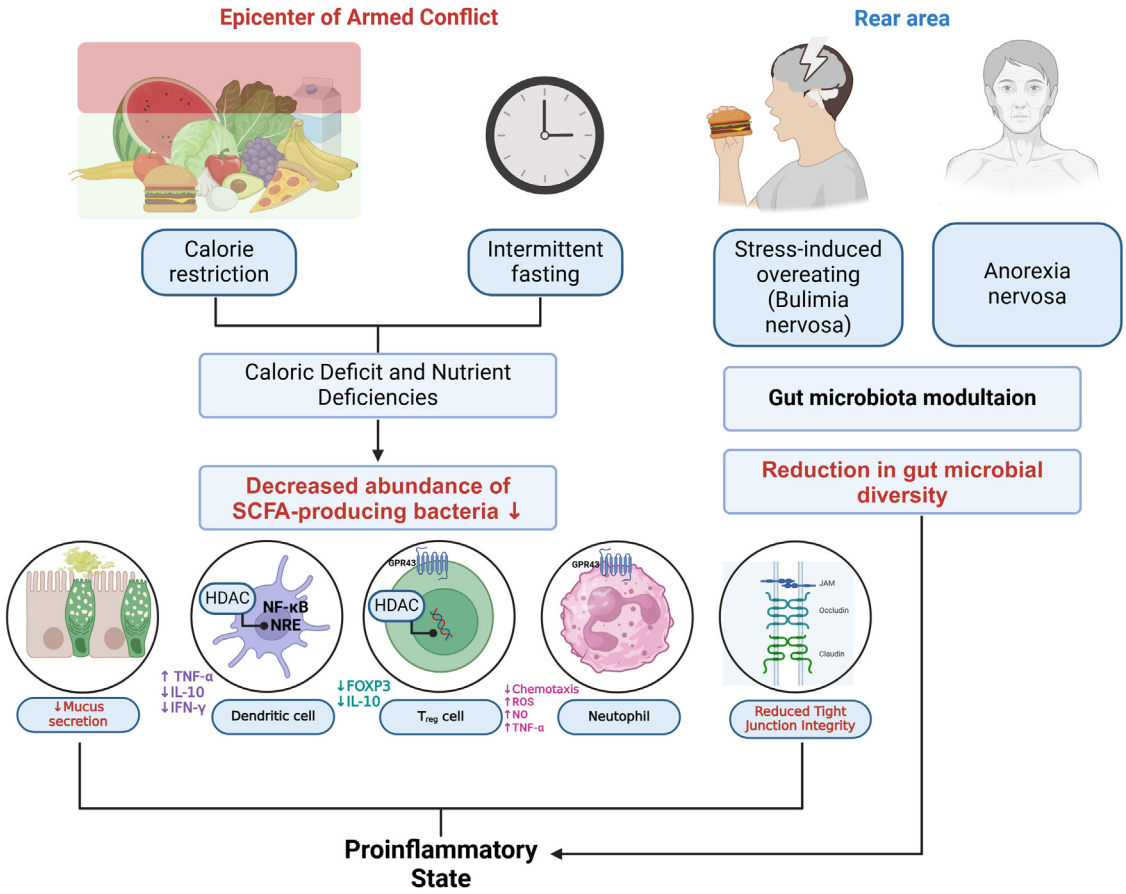

Fig. 3. Effect of diet changes associated with wartime on gut microbiota and metabolites under stress. This diagram highlights how stress-induced dietary changes impact gut microbiota composition and the production of gut-derived metabolites. Altered food intake can disrupt microbial balance, affecting metabolic processes and neurotransmitter production, which in turn influence stress regulation and overall gut health.

related (r=0.49, *P*<.001), 26.1% of people with PTSD did not have high levels of STO, and 36.5% of people with STO did not meet PTSD criteria. This suggests that war affects individuals in different ways, and not all psychological trauma fits into the same diagnostic categories [7].

War does not only affect people living in combat areas. Individuals in neighboring countries and even in distant regions may experience stress, fear, and anxiety due to global instability [8]. The possibility of war spreading, the threat of nuclear conflict, and economic uncertainty contribute to widespread psychological distress [9]. In addition, civilians who take shelter during missile attacks often experience severe stress and panic. The shock of a missile attack while hiding in a shelter can be very traumatic and may lead to long-term mental health issues [10].

Global economic disruptions, such as inflation, supply chain problems, and market instability, also have an impact on mental health [11]. Financial insecurity, lack of essential goods, and healthcare system disruptions can create additional stress. Political uncertainty and migration-related challenges may further worsen the situation [12]. Even in countries not directly involved in war, people may experience PTSD, anxiety, depression, and a lower quality of life due to prolonged exposure to war-related news and global threats [13].

The psychological impact of war varies among different populations. Refugees and displaced persons who have faced direct trauma are at high risk of mental health disorders. However, people who observe war from a distance and feel helpless may also suffer from emotional distress [14,15].

Literature for this narrative review was retrieved using searches in PubMed, Scopus, and Web of Science. Keywords included “war,” “conflict,” “stress,” “nutrition,” “gut microbiota,” and “infectious diseases.” Approximately 503 papers were screened, and studies were selected based on relevance to stress physiology, microbiota research, nutrition, and infectious disease patterns in conflict settings.

3. Effects of global conflicts on nutrition and food choices

Food insecurity is a serious problem caused by many factors, such as changes in population, weak governments, poverty, climate change, natural disasters, and war [16–19]. In recent years, the United Nations has said that war is one of the biggest reasons why people do not have enough food. In 2020, between 720 and 811 million people around the world were hungry [20].

As we mentioned in our introduction, studies in South Sudan show that people in war zones consume cheaper and less preferred food. Many people collect wild green leafy vegetables from open fields to survive [21]. For poor families, these vegetables are sometimes the only food available, especially during times of extreme hunger. These vegetables help people feel full, but they do not provide all the important nutrients. Also, eating only one type of food can lead to a lack of calories, increasing the risk of malnutrition and other health problems [22].

The war between Russia and Ukraine has also made food shortages worse. Ukraine and Russia are important exporters of grains like wheat, and corn [20]. Together, they provide about six per-

Table 1
Summarizing the effects of calorie restriction (CR) on gut microbiota

Aspect of gut microbiota	Effect of calorie restriction
Bacterial composition [173,175,305]	- Shifts the microbiota towards a profile associated with leaner individuals. - Increases beneficial bacteria such as *Lactobacillus, Bifidobacterium*, and *Akkermansia muciniphila*, which support gut health and metabolism. - Decreases potentially harmful bacteria, including obesity-related or pathogenic taxa. - Reduces Firmicutes and increases Bacteroidetes, linked to a lean phenotype. - Affects less abundant taxa playing niche roles. - Alters transient bacteria due to changes in nutrient availability.
Microbial diversity [306]	- Increases alpha diversity (*e.g.*, Shannon index), reflecting more species and even distribution. - Shows variable changes in beta diversity depending on individuals and CR protocols. - May cause temporal fluctuations in diversity over time. - Influences long-term microbiota stability.
Functional capacity [307]	- Boosts production of short-chain fatty acids (SCFAs) like butyrate, acetate, and propionate. - Enhances carbohydrate fermentation and bile acid transformation. - Alters amino acid metabolism, impacting microbial metabolites. - Changes vitamin synthesis (*e.g.*, B12, K). - Modifies xenobiotic metabolism (*e.g.*, drug/toxin processing). - Improves microbial energy efficiency under nutrient limitation.
Specific bacterial taxa changes and metaproteomic profile [181,308]	- Increases Lactobacillus and Bifidobacterium, known for probiotic benefits. - Elevates Akkermansia muciniphila, linked to better mucin production and insulin sensitivity. - Lowers the Firmicutes-to-Bacteroidetes ratio. - Reduces pro-inflammatory taxa like Desulfovibrio. - Impacts conditionally pathogenic bacteria (*e.g.*, Enterobacteriaceae). - Affects bacteria metabolizing specific substrates.
Metabolic products [182,183]	- Increases SCFA production, especially butyrate, with anti-inflammatory effects. - Shifts bile acid metabolism towards secondary bile acids that regulate lipids. - Reduces pro-inflammatory metabolites like trimethylamine N-oxide (TMAO). - Alters polyamine production (cell growth-related). - Changes neurotransmitter precursors (*e.g.*, serotonin-related). - Modifies gas production (*e.g.*, hydrogen, methane).
Gut barrier function and intestine permeability [309]	- Improves barrier integrity via SCFAs and mucin-degrading bacteria. - Reduces gut permeability, lowering metabolic endotoxemia. - Enhances tight junction protein expression. - Thickens the mucus layer for better protection. - Influences epithelial cell function and differentiation.
Immune system modulation and inflammation reduction [185,310]	- Lowers gut-derived inflammation via reduced cytokines and increased SCFAs. - Influences immune cell activity (*e.g.*, regulatory T-cell expansion). - Alters secretory IgA production for mucosal immunity. - Reduces inflammasome activity (*e.g.*, NLRP3). - Affects gut-associated lymphoid tissue (GALT).
Energy metabolism [190,191]	- Enhances microbial energy harvest efficiency in nutrient scarcity. - Promotes fat oxidation over storage. - Boosts bile acid signaling for energy expenditure. - Alters microbial ATP production. - Impacts host glucose metabolism via microbiota changes.
Host health implications [192,193]	- Improves metabolic health (*e.g.*, less adiposity, better insulin sensitivity). - Reduces systemic and gut inflammation. - May extend lifespan (seen in animal models). - Benefits the gut-brain axis (*e.g.*, mood, cognition). - May lower cardiovascular risks (*e.g.*, cholesterol). - Potentially influences cancer risk (preliminary data). - Affects neurological health.

(*continued on next page*)

Table 1 (*continued*)

Aspect of gut microbiota	Effect of calorie restriction
Pathogen resistance [175,311]	- Increases colonization resistance via diversity and beneficial bacteria. - Reduces opportunistic pathogens. - Strengthens mucosal immunity. - Alters bacteriophage populations that regulate bacteria. - May affect interactions with pathogenic viruses.
pH and gut environment [197]	- Lowers intestinal pH due to SCFAs, favoring beneficial bacteria. - Alters oxygen levels, affecting aerotolerant vs. anaerobic taxa. - Changes osmotic balance due to nutrient shifts.
Host-microbe interactions [199,200]	- Strengthens symbiotic relationships prioritizing host benefits. - Increases microbial signaling (*e.g.*, via bile acids). - Alters quorum sensing (bacterial communication). - Changes microbial adhesion to the epithelium. - Influences host gene expression (*e.g.*, metabolism, immunity).
Regional differences in gut [147]	- Differentially affects small vs. large intestine microbiota (colon more impacted). - Varies between proximal and distal colon. - Influences nutrient gradients along the gut.
Species-specific effects [148,312]	- Shows similarities between rodents and humans, but humans vary more due to diet/genetics. - Impacts microbiota in nonmammalian models (*e.g.*, Drosophila). - May differ by sex.
Antibiotic resistance [313]	- Reduces antibiotic-resistant bacteria via less gene transfer. - Alters the resistome (pool of resistance genes). - Influences biofilm formation, affecting resistance.
Microbial endotoxins [207]	- Lowers LPS-producing bacteria, reducing endotoxemia. - Decreases other toxins (*e.g.*, hydrogen sulfide). - Impacts inflammatory pathways via reduced toxins.
Microbial fermentation patterns [208]	- Shifts fermentation to different substrates (*e.g.*, fibers, mucins). - Changes gas production (*e.g.*, hydrogen, methane). - Alters fermentation efficiency under nutrient limits.
Microbial adhesion to epithelium [209]	- Changes bacterial adhesin expression, affecting colonization. - Alters host epithelial receptors for bacterial attachment. - Impacts immune recognition of adhered bacteria. - Regulation of intestinal mucin glycosylation
Longevity and aging [210,213]	- Potential delay in the onset of age-related diseases; - Extension of lifespan.

cent of the world's food calories. However, because of the war, food storage facilities have been destroyed, and transportation has been interrupted. As a result, food exports have decreased, which has made food more expensive, especially in African countries like Ethiopia, Nigeria, and South Africa, as well as in many other parts of the world [23].

Many experts warn that the war in Ukraine could cause a global food crisis [24]. There is a growing risk of famine and severe food shortages. Women and children are the most affected by high food prices and lack of food. Children need a lot of nutrition to grow, and pregnant or breastfeeding women also have high nutritional needs.

The war in Ukraine has also affected children's eating behavior [25]. Studies have found that war exposure causes high levels of stress, which can change how children eat. A recent study showed that 63% of Ukrainian children experienced changes in their eating behavior during the war. The most common changes were food cravings, food fussiness, and aversion to certain foods. Many children also developed long-term changes in their attitudes toward food. Food insecurity and displacement were the strongest factors influencing these changes [26]. Since eating habits are learned in childhood and continue into adulthood, these disruptions may have lasting effects on children's physical and mental health.

Besides war, other crises like climate change and the COVID-19 pandemic have made food insecurity worse. Malnutrition may not always be immediately visible, but it increases the risk of disease and can lead to long-term health problems. If people do not get proper nutrition, it can also affect future generations [24].

Another terrible effect of war is starvation [27]. In many conflicts, starvation is not just an accidental result but is sometimes used as a weapon. Some armies block food supplies to weaken their enemies. Starvation has a serious impact on the human body. Studies show that long periods without food can change the gut microbiota, which affects digestion and overall health [28]. People who experience extreme hunger may suffer from long-term health issues, even if they later get enough food.

In addition to the civilian population, problems with access to optimal food rations can also occur in military personnel, for example, during enemy encirclement, which limits the supply of provisions [29]. Military personnel may also consume food from the civilian population or prepare food on their own, which can affect the nutritional balance . Furthermore, stress among military personnel, especially during active offensive or defensive operations, can impact food preferences and eating behavior [30].

4. Mechanisms of stress-induced overeating and eating behavior disorders

Many theories try to explain why people eat more when they feel stressed or have negative emotions. These theories suggest that unhealthy ways of dealing with emotions can lead to overeating. One idea, called the learning theory, was introduced by Kaplan and Kaplan [31]. It suggests that people learn to eat more when they are anxious because it helps them feel better. Another theory, from Heatherton and Baumeister, says that some people have negative thoughts about themselves and feel emotional distress [32]. To escape these bad feelings, they may overeat or binge eat. Other researchers believe that eating is a way to cope with emotions or distract from negative feelings [33,34]. Some studies also show that people with eating disorders, like anorexia nervosa and bulimia nervosa, have stronger anxiety reactions during stressful situations [35,36]. Even though there are different explanations for emotional eating, scientists still do not fully understand the biological reasons behind it or the risks for eating disorders.

One possible biological explanation is related to the hypothalamic-pituitary-adrenal (HPA) axis, which controls the body's response to stress [37,38]. Studies have found a connection between high HPA-axis activity and binge eating disorder, bulimia nervosa, and obesity [39–41]. People with these conditions have higher cortisol levels (a stress hormone) after facing stress compared to healthy individuals. However, some studies found the opposite effect in people with anorexia and bulimia, showing lower cortisol responses to stress [42,43]. These changes in cortisol levels can continue even after recovery [44]. In people with binge eating disorder, higher cortisol levels are linked to a stronger desire to binge eat [45]. However, there is still little research on how the HPA-axis response to stress directly affects eating behavior in people with eating disorders [46].

Studies on healthy individuals also show mixed results. Some research suggests that people who have stronger stress reactions eat more after stress and prefer sweet foods [47,48]. Canadian scientist found that emotional eaters had higher cortisol increases after stress than nonemotional eaters [49]. Another study showed that women with high stress had stronger cortisol reactions than those with lower stress [50]. However, other studies did not find significant differences in cortisol levels between emotional and nonemotional eaters [51]. Even so, emotional eating may influence how cortisol affects food consumption. More research is needed to understand this relationship.

Another possible biological reason for emotional eating is linked to the brain's reward system. The striatum, a part of the brain involved in reward and learning, plays an important role in emotional eating [52]. Some researchers believe that emotional eaters have an overactive food reward system, making them more likely to overeat or binge eat. This idea is supported by studies showing that emotional eaters have higher activity in brain areas related to reward (such as the amygdala and insula) when they see food [53,54]. Australian investigators also found that people who are highly sensitive to rewards are more likely to have symptoms of food addiction, with emotional eating acting as a link between them [55]. However, other studies suggest that emotional eaters have lower activity in reward-related brain areas (such as the putamen, caudate, and thalamus) when they actually eat food [56]. This lower brain activity might cause them to overeat to try and get the same level of reward. Most studies on brain activity in emotional eaters have been done in neutral settings, without stress or negative emotions. One study looked at how emotional eating affects brain activity when listening to sad music and found higher brain activation in emotional eaters under negative emotions [57].

Silvia Papalini added a new idea to this discussion. She explained that people use different ways to cope with stress [58]. Eating can be a healthy way to relax, like enjoying a small treat during a busy day. However, when people eat too much unhealthy food to deal with stress, it can lead to binge eating, obesity, and other health problems. Two popular theories explain stress eating. The Emotional Eating Theory says that people eat to reduce negative emotions. The Incentive Sensitization Theory says that people overeat because their brain's reward system becomes too sensitive to food. Both theories help explain stress eating, but they also have weaknesses. Papalini suggests creating a new model that connects these theories. This model could help scientists understand why stress eating sometimes turns into a serious problem. It could also help doctors find better ways to prevent and treat overeating caused by stress.

5. Infectious diseases during war

Wars have a big impact on healthcare systems and hospitals [59–61]. In war zones, more people get infectious diseases because many risk factors help the diseases spread [62]. Some of these factors are damage to hospitals, lack of clean water, and people moving in large numbers to escape the war. These conditions make it easier for diseases to appear and spread [63].

During and after the two World Wars, outbreaks of diseases such as typhoid fever, cholera, dysentery, malaria, smallpox, typhus fever, and influenza caused many deaths among soldiers and civilians [64,65].

One of the first diseases linked to war was tuberculosis. It became a serious problem in conflict zones [66,67]. Today, most wars happen in countries where tuberculosis is already common. This disease is not only a risk for people in war zones but also for those in safe areas. Many people flee war and move to other countries, bringing the disease with them [68,69]. A good example is the Syrian war, which forced millions of people to move to neighboring countries like Türkiye. The number of tuberculosis cases in Türkiye increased after the war [70]. Tuberculosis patients who did not receive proper treatment during the war were up to three times more likely to die compared to those who got full treatment in peacetime. This was seen in Guinea-Bissau, West Africa [71].

A study on the impact of war on Ebola in the Democratic Republic of the Congo (DRC) showed that conflict made it harder to control the disease. Attacks on healthcare workers and Ebola treatment centers slowed down efforts to isolate sick people, provide treatment, trace contacts, and vaccinate people [72]. War in the DRC also helped spread other diseases like sleeping sickness, river blindness, and pneumonic plague [73,74].

5.1. Oral health in conflict settings

Oral health is often overlooked in discussions of health during armed conflicts, even though the mouth plays a central role in nutrition, immunity, and microbial homeostasis [75]. Stress, limited food options, and disrupted access to healthcare can quickly undermine oral hygiene and contribute to the development of dental caries, periodontal disease, and acute oral infections [76]. Studies from both conflict and peacetime settings show that poor oral

health is closely linked with impaired nutrition, systemic inflammation, and altered microbial communities in the gastrointestinal tract [77,78].

During wartime, the collapse of dental services, shortages of hygiene supplies, and irregular access to clean water create conditions in which oral diseases spread rapidly. Diet also plays an important role. Emergency rations and humanitarian foods often rely on shelf-stable, high-carbohydrate products that are easy to distribute but promote plaque formation and shifts in the oral microbiota. Reduced intake of fresh foods lowers the availability of vitamins and minerals such as vitamin C, calcium, and phosphorus, which are necessary for maintaining the integrity of oral tissues [79]. These changes can impair chewing, decrease food variety, and contribute to malnutrition, creating a cycle in which poor oral health and poor diet reinforce each other.

The oral microbiota is closely linked with systemic immunity. Periodontal inflammation increases circulating inflammatory markers and can facilitate the movement of oral bacteria into the bloodstream, with downstream effects on gut microbial composition [80]. Infections originating in the oral cavity may worsen respiratory diseases and gastrointestinal infections, which are already more common during conflicts due to overcrowding, poor sanitation, and limited medical care [81]. The relationship between oral and gut microbiota appears to be bidirectional: dysbiosis in the oral cavity can promote gut dysbiosis, while nutrient deficiencies and systemic inflammation can encourage the spread of oral pathogens along the digestive tract [82].

Historical and recent case studies illustrate these problems. Reports from refugee camps in Syria, Yemen, and South Sudan describe widespread untreated dental pain, oral abscesses, and advanced periodontal disease, often affecting children and adolescents [83,84]. Such conditions interfere with normal eating and weaken general health, increasing the risk of infection. Similar findings have been documented among soldiers, whose high stress levels, irregular meals, and limited hygiene opportunities contribute to declines in oral health during deployment [85].

5.2. Examples from recent conflicts

Armed conflicts in the 21st century have precipitated humanitarian crises that greatly exacerbate the spread of infectious diseases. Yemen's ongoing civil war (since 2015) has devastated basic services and public health infrastructure. Over 75% of Yemen's population (approximately 21 million people) urgently require humanitarian assistance, with 7.3 million suffering severe food insecurity and 3.3 million internally displaced by the fighting [86]. More than half of Yemen's health facilities have been destroyed or rendered nonfunctional. Simultaneously, the collapse of water and sanitation networks has left entire cities with contaminated water supplies: garbage accumulates in the streets, sewage treatment has halted due to fuel shortages, and sewage has seeped into groundwater. In this setting, a massive cholera epidemic erupted. By early 2018 Yemen had recorded over one million suspected cholera cases – the largest outbreak ever documented – with thousands of associated deaths.

Syria's protracted civil war (since 2011) shows a similar pattern. Conflict has decimated Syria's healthcare capacity: more than half of hospitals and clinics have been damaged or destroyed and many health workers have fled [87]. Over one-third of Syrians no longer have access to safe drinking water, contributing to resurgent waterborne diseases such as diarrheal illnesses and typhoid [88]. Massive population displacement (with millions of internally displaced persons and refugees) has forced people into crowded shelters and camps with unsanitary conditions and inadequate vaccination coverage, creating fertile ground for outbreaks. Indeed, Syria witnessed the re-emergence of polio and large outbreaks of measles and leishmaniasis during the war, after years of disease control gains were reversed. Furthermore, Syria's conflict has driven up rates of malnutrition, especially among children, thereby eroding immune resistance to infection [89]. WHO reports that rising malnutrition in Syria is "decreasing the immunity of children against life-threatening infectious disease."

South Sudan, embroiled in civil conflict since its independence in 2011, has likewise experienced the entwined scourges of hunger and epidemics. Years of fighting devastated agriculture and markets, leading to a famine declaration in 2017 and leaving millions facing acute hunger. Even today, South Sudan endures one of the world's worst childhood malnutrition crises: as of 2025, an estimated 2.1 million children under five are acutely malnourished (including over 670,000 with severe wasting). This malnutrition crisis has greatly weakened immune defenses in the population. At the same time, conflict has crippled water and sanitation infrastructure – half of South Sudan's water points have been destroyed – depriving about 5.1 million people of safe water and basic hygiene. Unsurprisingly, cholera has repeatedly struck South Sudan. Between 2014 and 2017, during the height of the civil war, the country suffered successive cholera epidemics amid mass displacement, flooding, and drought. A major outbreak in 2016 sickened over 5,000 people and caused more than 100 deaths. Even in subsequent years, infectious disease outbreaks have persisted alongside instability; by 2025 South Sudan was battling not only cholera but concurrent outbreaks of measles, vaccine-derived polio, hepatitis E, and other infections in a context of weak health systems and periodic violence.

6. Effects of nutrition and infectious diseases on the gut microbiota

Thanks to new genomic methods, scientists now see the gut microbiota as an important link between food, the human body, and infections [90]. The bacteria in the gut help with digestion, produce useful compounds from fiber, affect drug metabolism, support immune system development in early life, regulate immune responses, and protect against infections [91–94]. Changes in the balance of these bacteria have been linked to many diseases, including infections [95–99]. The gut microbiota can either help prevent infections or make a person more vulnerable to them. A study analyzing data from 91 less-developed countries found that drought-induced food insecurity was linked to a higher risk of HIV infection in women [100]. Women often receive less food than men, leading to nutrient deficiencies that weaken the immune system and increase susceptibility to infections. Additionally, food insecurity was connected to social vulnerabilities, such as reduced access to healthcare and, in some cases, forced involvement in risky sexual behaviors. This highlights how nutrition, infections, and social factors are closely connected, affecting overall health and disease risk. A study in Sweden showed that different gut bacteria affect how likely someone is to get a *Campylobacter jejuni* infection [101]. Some bacterial compounds, such as short-chain fatty acids (SCFAs), play a key role in the relationship between gut bacteria and harmful microbes [102].

Diet has a strong influence on the gut microbiota. It changes the types of bacteria and the compounds they produce, affecting health, immunity, and the risk of infections [103,104]. Many factors, such as food choices, antibiotics, probiotics, and prebiotics, can disrupt or improve the gut microbiota [105,106]. Researchers have studied how different nutrients, such as carbohydrates, proteins, fats, and food additives, impact gut bacteria. Diets high in fiber and low in fat, or high in protein, can change the gut microbiota in different ways [107,108]. Nutrients can directly support or

block bacterial growth, affect the immune system, or even introduce microbes from food, such as Candida fungi or lactic acid bacteria [109]. Contaminated food can also cause infections, food poisoning, and other diseases [110,111]. At the same time, infections can disturb the balance of the microbiota, leading to "dysbiosis," which makes it easier for new infections to occur [112,113].

7. Connection between stress and gut microbiota: the gut-brain axis

Chronic stress triggers immune changes both in the brain and throughout the body, leading to inflammation that contributes to neurological disorders such as depression and anxiety [114,115]. These inflammatory responses involve alterations in gut microbiota, which are linked to stress-related behavioral changes and disease progression [116,117]. Several peripheral immune and inflammatory elements, including circulating macrophages, inflammatory cytokines, and hormones, are identified as key factors influencing stress-induced behaviors.

Research has demonstrated a bidirectional relationship between the gut microbiota and the central nervous system, known as the "microbiota–gut–brain axis." This axis plays a crucial role in regulating glial cell functions, making it a potential target for mitigating stress, depression, and other psychiatric or neurodegenerative conditions [118].

The idea that gut microbiota may be associated with mood disorders arose from the observed high co-occurrence of anxiety and depression in individuals with gastrointestinal disorders like inflammatory bowel disease and irritable bowel syndrome [119]. Correlation studies reveal that individuals with anxiety or depression, including those in remission, exhibit distinct fecal microbiota compositions compared to healthy controls [120–122]. For example, women with higher levels of *Prevotella* in their gut microbiota showed stronger negative emotional reactions to distressing images and reduced hippocampal activity compared to those with greater *Bacteroides* abundance [123]..

Animal studies further support this connection. Research on rodents indicates that gut microbiota composition can influence emotional behavior. Mice experiencing gut infections or inflammation demonstrated increased anxiety-like behaviors, such as reduced exploration and heightened behavioral inhibition [124]. Germ-free (GF) mice and rats-those raised without microbiota-exhibited either heightened or reduced anxiety and depressive-like behaviors compared to their specific pathogen-free (SPF) counterparts [125–127]. Additionally, some probiotics have been found to affect mood. Psychobiotics, a subset of probiotics, provide mental health benefits by interacting with gut microbiota, though not all probiotics or prebiotics fall into this category [128].

Studies on gut microbiota changes due to stress show varied results, mostly from rodent research. Stress is often linked to a decreased abundance of *Lactobacillus* and an increase in opportunistic pathogens, such as *Odoribacter, Clostridium*, and *Mucispirillum* [129–132]. *Bifidobacterium* levels also decline under stress, although one study found an increase in stress-resilient mice [133]. These microbiota alterations may differ depending on gut location; for instance, in male CD-1 mice, restraint stress decreased *Lactobacillus* abundance in mucosa-associated microbiota but not in luminal microbiota [132].

Human studies on this topic remain limited. One investigation examined the effects of diet and environmental conditions in astronauts living in confined spaces. It found that interpersonal conflicts led to an increase in Bacteroides fragilis subsp. thetaiotaomicron in fecal samples [134]. Additionally, prenatal stress in pregnant women resulted in persistent microbiota changes in their infants. These changes included higher levels of Proteobacteria and lower levels of lactic acid bacteria, which were associated with increased gastrointestinal issues in the infants [135].

8. Dietary changes due to global conflicts: effects of calorie restriction and intermittent fasting on gut microbiota

It is important to clearly distinguish between structured intermittent fasting (IF) practiced in controlled settings and involuntary, unpredictable fasting that occurs during armed conflicts. While IF follows consistent fasting–feeding cycles and is associated with metabolic benefits, conflict-induced fasting is characterized by irregular meal timing, severe caloric deficits, and nutrient deprivation. These conditions do not replicate the physiological adaptations seen in controlled IF and instead contribute to gut dysbiosis, increased intestinal permeability, weakened immune defenses, and higher susceptibility to infectious diseases. Therefore, findings from IF research cannot be directly extrapolated to populations experiencing food scarcity in war zones [136,137].

Global conflicts and periods of socio-economic instability have often led to marked dietary changes, including calorie restriction and intermittent fasting. The beneficial effects are most often associated with daily intermittent fasting, which typically involves approximately 16-hour intervals between meals, aligning with and modulating the body's circadian biological rhythm [138–140]. These dietary changes can profoundly affect the gut microbiota, which plays a key role in host metabolism, immune function, and overall health [141,142]. Emerging research highlights the bidirectional relationship between diet and microbial composition, suggesting that imposed dietary limitations during conflicts may induce shifts in microbial diversity and function with potential long-term health consequences [143–145].

Calorie restriction, characterized by a sustained reduction in energy intake without malnutrition, has been shown to modulate the composition of the gut microbiota [146,147]. Studies indicate that calorie restriction enhances microbial diversity and promotes the proliferation of beneficial taxa, including *Akkermansia muciniphila*, a bacterium associated with improved metabolic health [148–150]. However, prolonged and severe calorie restriction, as often observed in war-torn regions, may lead to dysbiosis [151,152]. This imbalance may disrupt intestinal barrier integrity, facilitating microbial translocation and thereby contributing to systemic inflammation [153,154].

Careful consideration should be given to differentiating between acute, life-threatening food shortages that occur in active war zones and more prolonged, population-level caloric restrictions resulting from economic or supply constraints. These distinct scenarios likely exert differential effects on metabolism, gut microbiota, and overall health, which should be carefully considered when evaluating the consequences of caloric restriction [155,156].

Intermittent fasting, characterized by a regular and controlled eating schedule, produces predictable metabolic adaptations, including improved glucose regulation and lipid metabolism [157,158]. In contrast, conflict-induced involuntary and irregular fasting is unstructured and unpredictable, often leading to severe energy deficiency, gut dysbiosis, and systemic inflammation [159–161].

It is crucial to differentiate the metabolic effects of calorie restriction from those attributable to structured meal timing. For example, religious fasting during Ramadan, which involves time-restricted feeding with documented benefits for glucose homeostasis, lipid metabolism, and circadian rhythm regulation, cannot be directly equated with the unpredictable and disordered food intake patterns that often occur in conflict-affected regions, where severe and prolonged energy deficiency may lead to gut dysbio-

sis, impaired intestinal barrier function, and systemic inflammation [162–164]

Intermittent fasting, which involves alternating periods of eating and fasting, has gained attention due to its metabolic benefits, yet its effects on gut microbiota under conflict-driven dietary changes remain understudied [157,165]. Intermittent fasting has been shown to increase the abundance of *Lactobacillus* and *Bifidobacterium* species, which are known for their probiotic properties [166,167]. Additionally, fasting-induced shifts in microbial metabolites, such as short-chain fatty acids (SCFAs), influence immune function and energy homeostasis [168,169]. However, the unpredictability of food availability during conflicts may disrupt these adaptive microbial responses, potentially exacerbating nutrient deficiencies [170,171].

Many positive effects of calorie restriction and intermittent fasting have been investigated during peacetime [172]. Calorie restriction and intermittent fasting exert significant effects on gut microbiota composition, diversity, and function, influencing various aspects of metabolic and gut health [173–176]. These dietary interventions promote the growth of beneficial bacteria, such as *Lactobacillus, Bifidobacterium,* and *Akkermansia muciniphila*, which are associated with improved metabolic outcomes and gut health [177–179]. These changes in microbiota composition contribute to a leaner phenotype, enhancing both alpha and beta diversity in the gut [180–182]. Additionally, calorie restriction supports the production of short-chain fatty acids like butyrate, acetate, and propionate, which are crucial for maintaining colonocyte health, reducing inflammation, and regulating energy homeostasis [183–185]. Short-chain fatty acids also strengthen the intestinal barrier, mitigating "leaky gut" by maintaining the integrity of the mucin layer and improving gut permeability [186–188]. Furthermore, calorie restriction reduces the abundance of pathogenic bacteria, such as *Escherichia coli* and *Clostridium perfringens*, by altering nutrient availability and enhancing the competitive advantage of commensal microbes [189–191].

Beyond microbiota-related benefits, calorie restriction and intermittent fasting play a vital role in metabolic regulation and immune function [192,193]. These interventions improve insulin sensitivity, glucose metabolism, and lipid homeostasis by modulating gut microbiota composition and lowering levels of inflammatory endotoxins like lipopolysaccharides [194,195]. Systemic and gut inflammation is reduced through the downregulation of pro-inflammatory cytokines, while the production of anti-inflammatory microbial metabolites is promoted [196–198]. Additionally, these interventions support gut-brain axis communication by enhancing the production of neurotransmitters such as serotonin, dopamine, and gamma-aminobutyric acid, which influence mood regulation and stress response [199–201]. Calorie restriction also enhances immune function by modulating gut-associated lymphoid tissue and improving the activity of immune cells, such as regulatory T cells and macrophages [202–205]. Calorie restriction promotes fat oxidation and reduces adiposity by altering bile acid metabolism, increasing energy expenditure, and inducing autophagy-related changes that reduce cellular damage and support longevity-related pathways [206–208].

Furthermore, calorie restriction and intermittent fasting have broader health implications, including metabolic regulation, pathogen resistance, and immune system modulation [209–211]. By promoting fat oxidation and improving insulin sensitivity, calorie restriction enhances metabolic health and reduces adiposity [212–214]. It strengthens mucosal immunity, increasing resistance to opportunistic pathogens, improving colonization resistance, and regulating the gut-associated lymphoid tissue [215–217]. Calorie restriction and intermittent fasting also reduce gut permeability, mitigates metabolic endotoxemia, and lowers the risk of systemic inflammation [218,219]. Moreover, calorie restriction and intermittent fasting influence the gut-brain axis, supporting cognitive function, mood regulation, and stress resilience [159,220]. These effects may also extend lifespan, as calorie restriction has been linked to increased longevity in animal models and could delay the onset of age-related diseases [181,221]. Additionally, calorie restriction and intermittent fasting strengthen the gut microbiota's resilience to external stressors such as chemotherapy, enhancing its adaptability and promoting overall health [191,222].

Although calorie restriction and intermittent fasting have demonstrated various health benefits under normal conditions, their implementation during periods of conflict may lead to negative outcomes [223]. One critical consequence of calorie restriction in conflict settings is the disruption of microbial metabolite production, including SCFAs, which play essential roles in intestinal barrier integrity and immune regulation [224,225]. While moderate calorie restriction can enhance SCFA production, excessive restriction may diminish SCFA levels, impairing colonocyte function and reducing anti-inflammatory effects [226,227]. This can lead to increased gut permeability, facilitating translocation of pathogenic bacteria and heightening susceptibility to infections, which are already prevalent in conflict-affected populations [228,229].

Furthermore, nutrient deficiencies associated with prolonged calorie restriction and intermittent fasting in war zones may exacerbate gut dysbiosis [203]. Deficiencies in dietary fiber, proteins, and essential micronutrients, such as iron and zinc, can lead to a decline in microbial species responsible for fermenting complex carbohydrates [230]. Reduced dietary fiber intake decreases the production of beneficial SCFAs, weakening the mucosal barrier and increasing susceptibility to gastrointestinal disorders [231,232]. The interplay between nutrient availability and microbiota composition underscores the importance of dietary resilience strategies in conflict-affected populations [233,234].

Adaptations in gut microbiota due to calorie restriction and intermittent fasting may have intergenerational effects, as maternal malnutrition during conflicts has been linked to alterations in offspring microbiota and metabolic programming [235,236]. Epigenetic modifications induced by microbial metabolites can influence gene expression related to immune function and energy metabolism [237,238]. Consequently, the long-term health implications of conflict-induced dietary restrictions extend beyond the immediate population, affecting future generations and potentially increasing the prevalence of metabolic disorders [239,240].

Chronic diseases, including metabolic, gastrointestinal, neurological, cardiovascular, and autoimmune disorders, are particularly susceptible to conflict-driven dietary changes due to their reliance on stable metabolic and inflammatory regulation [241,242]. Calorie restriction and intermittent fasting can initially enhance insulin sensitivity and improve glycemic control in early-stage type 2 diabetes; however, prolonged nutrient deprivation may disrupt gut microbiota, increasing gut permeability and systemic inflammation, thereby exacerbating insulin resistance and hyperglycemia [243–246]. Additionally, type 2 diabetes management often involves the use of metformin [247–249], a first-line antidiabetic drug known to influence gut microbiota by promoting the growth of beneficial *Akkermansia muciniphila* and *Bifidobacterium* species [250–252]. However, in conflict-affected populations experiencing chronic malnutrition, metformin's effects may be altered due to microbiota instability, potentially reducing its therapeutic efficacy or increasing gastrointestinal side effects [253–256]. Similarly, gastrointestinal disorders such as irritable bowel syndrome and inflammatory bowel disease are aggravated by microbial dysbiosis and impaired mucosal immunity caused by inadequate nutrient intake [257–259], while osteoarthritis patients, often dependent on nonsteroidal anti-inflammatory drugs (NSAIDs) [260,261], face an

increased risk of gut mucosal damage and dysbiosis due to NSAID-induced alterations in microbiota composition [262]. The gut-brain axis is also highly sensitive to microbial changes, with dysbiosis contributing to neuroinflammation and playing a role in depression, anxiety, and neurodegenerative diseases such as Parkinson's and Alzheimer's, particularly in malnourished populations where serotonin and gamma-aminobutyric acid (GABA) production is compromised [263–265]. Furthermore, cardiovascular diseases (CVDs) may be exacerbated by conflict-induced malnutrition and fasting, as microbiota-derived metabolites such as trimethylamine-N-oxide (TMAO) have been linked to atherosclerosis and hypertension [266–268], while an altered gut microbiota profile may contribute to endothelial dysfunction and systemic inflammation, further increasing cardiovascular risks [269–271]. Autoimmune diseases, including rheumatoid arthritis, thyroiditis, and multiple sclerosis, are similarly influenced by microbial diversity, with gut dysbiosis potentially triggering aberrant immune responses and systemic inflammation [272–275]. The cumulative effect of these disruptions underscores the far-reaching impact of conflict-induced dietary changes on microbiota homeostasis, ultimately influencing disease progression across multiple organ systems and exacerbating health burdens in affected populations [276,277].

Infectious diseases, particularly COVID-19, are also closely linked to gut microbiota, as dysbiosis can weaken the immune response and increase disease severity [278–281]. A reduction in beneficial microbial diversity, caused by malnutrition, stress, and unsanitary conditions often associated with armed conflicts, can contribute to excessive inflammation and impair intestinal barrier function, increasing the risk of secondary bacterial infections [282–284]. Additionally, the use of antibiotics and antiviral drugs [285–287], can further disrupt microbiota balance, leading to dysbiosis, diarrhea, and increased susceptibility to opportunistic pathogens like *Clostridioides difficile* [288–290].

In wartime conditions, where access to medical care is limited and sanitation deteriorates, the risk of severe infectious diseases rises, further complicating the epidemiological situation [291,292]. Caloric deficiency, caused by insufficient nutrition or forced intermittent fasting due to food shortages or irregular access to meals, can further weaken the immune system by reducing antibody production and T-cell activity [293,294]. This not only makes it harder to combat viral infections but also increases the risk of reactivating latent pathogens such as the herpes virus or tuberculosis [295,296]. At the same time, caloric restriction can affect drug metabolism, reducing the effectiveness of antiviral medications or increasing their toxicity due to impaired detoxification in the liver [297,298].

9. Controlled caloric restriction vs. conflict-induced food deprivation

Controlled caloric restriction, as implemented in food-rationing programmes—most notably in the United Kingdom during the Second World War—differs fundamentally from the uncontrolled food deprivation seen in contemporary conflict zones. Rationing policies in the 1940s were designed to preserve an adequate balance of macronutrients and to prevent micronutrient deficiencies. Analyses from that period show improvements in several population-level health indicators, including lower cardiovascular mortality, stable nutrient intake and better overall dietary quality despite reduced caloric availability [299]. These observations accord with current evidence that controlled caloric restriction can elicit favourable metabolic adaptations when introduced under safe and regulated conditions [138,148].

By contrast, modern conflict settings are marked by erratic access to food, widespread damage to agricultural systems, disrupted supply chains and pronounced micronutrient deficiencies [20,24]. Individuals may endure prolonged periods without food, depend on nutritionally inadequate emergency rations or subsist on monotonous, carbohydrate-heavy diets lacking essential amino acids, fats and micronutrients [300]. Such circumstances give rise to physiological and metabolic effects that bear little resemblance to the adaptive responses associated with structured dietary restriction. Uncontrolled food deprivation promotes gut dysbiosis, impairs intestinal barrier integrity and weakens immune function, thereby increasing susceptibility to infectious disease.

10. Role of AI technologies in simulating comorbidities: big data analysis in nutrition, microbiota, and infectious disease research

Comorbidity is defined as the simultaneous presence of two or more diseases in an individual, encompassing both physical and mental health conditions [301]. Patients with comorbidities often have a higher risk of mortality and a lower quality of life compared to those without multiple health conditions [302]. With increasing life expectancy, healthcare systems worldwide must address the growing burden of comorbid diseases. One possible solution is the use of artificial intelligence (AI), particularly machine learning (ML). ML models can analyze large datasets, such as electronic health records (EHRs), to predict the likelihood of a patient developing a comorbid condition based on their medical history, demographics, and other important factors [303]. By identifying patterns in patient data, AI can help detect risk factors for specific conditions, enabling targeted prevention and treatment strategies (Fig. 4).

AI also plays a crucial role in studying the interactions among bacteria within the gut microbiota and in identifying potential microbial biomarkers for disease prevention and treatment [304]. Traditional approaches for detecting microbial biomarkers are often limited due to the complexity of large datasets with multiple influencing factors. AI-powered algorithms, particularly machine learning and deep learning, are highly effective in analyzing vast amounts of microbiome data to uncover meaningful patterns and relationships. AI models can process multiomics data, including metagenomic, metatranscriptomic, and metabolomic information, to identify specific microbial taxa or functional genes associated with health outcomes. Since gut bacteria play a crucial role in various diseases and health conditions, understanding individual differences in microbiota composition is essential. These differences arise from genetic, dietary, lifestyle, and environmental factors.

A new field known as personalised microbiota analysis, driven by AI, helps researchers explore why people have unique microbiomes. AI-based personalised microbiota profiling analyses complex microbiome data to create dietary and lifestyle recommendations that support gut health and overall well-being. AI applications in custom microbiota profiling have the potential to revolutionise personalised health strategies by offering tailored interventions based on an individual's unique microbial composition.

Traditional microbiota research methods require extensive time and effort, making large-scale studies difficult. AI-powered tools, particularly machine learning and deep learning, enable rapid analysis of large and diverse microbiome datasets. These advanced methods can identify specific microbial taxa and functional genes associated with health outcomes, providing a comprehensive understanding of an individual's gut microbiota. By using AI, researchers and healthcare providers can develop personalised treat-

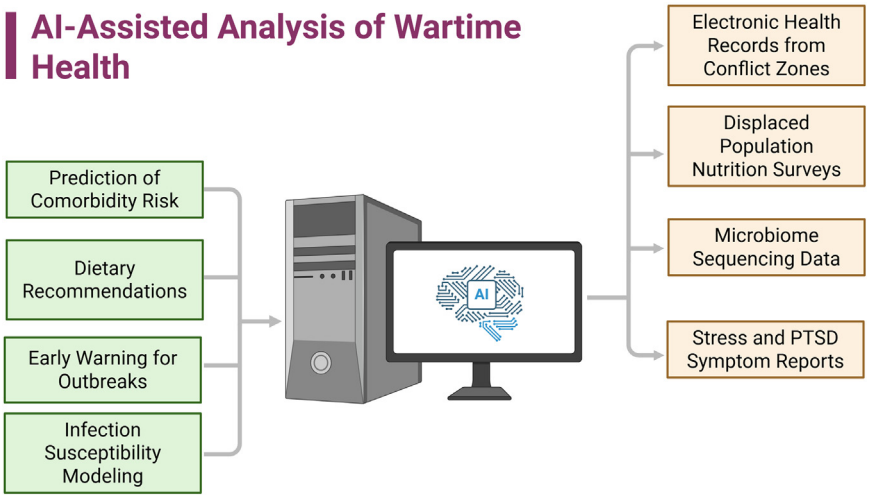

Fig. 4. AI-assisted analysis of wartime health. Overview of how artificial intelligence processes data from conflict-affected populations, such as electronic health records, nutrition surveys, microbiome sequencing, and PTSD reports, to generate predictive insights on comorbidities, dietary needs, infection risk, and early outbreak warnings.

ment plans to improve health, manage stress-related conditions, optimise nutrition, and support the treatment of infectious diseases.

11. Intervention strategies for supporting nutrition and gut microbiota in conflict-affected populations

Improving nutrition and supporting the health of the gut microbiota during wartime requires coordinated measures for both civilians and military personnel. Key steps include:

(1) ensuring access to balanced rations that provide enough fibre, essential fatty acids and important micronutrients;
(2) offering probiotic and prebiotic supplements where feasible, together with additional vitamins and minerals (such as iron, vitamin D and zinc) to prevent major deficiencies;
(3) securing clean water and safe food storage to reduce the risk of gastrointestinal infections;
(4) providing mental health support;
(5) designing ration systems that maintain an appropriate balance of macronutrients even when overall calorie intake is reduced.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Declaration of competing interests

The authors declare that there are no conflicts of interest.

CRediT authorship contribution statement

Pavlo Petakh: Writing – original draft, Visualization. **Iryna Halabitska:** Writing – original draft. **Halyna Petrecka:** Writing – original draft. **Wolfgang Huber:** Writing – review & editing. **Oleksandr Kamyshnyi:** Writing – review & editing, Writing – original draft, Supervision.

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