

Providing Antiretroviral Care in Conflict Settings

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There has been an historic expectation that delivering combination antiretroviral therapy (cART) to populations affected by violent conflict is untenable due to population movement and separation of drug supplies. There is now emerging evidence that cART provision can be successful in these populations. Using examples from Médecins Sans Frontières experience in a variety of African settings and also local nongovernmental organizations' experiences in northern Uganda, we examine novel approaches that have ensured retention in programs and adequate adherence. Emerging guidelines from United Nations bodies now support the expansion of cART in settings of conflict.

Introduction

The rapid expansion of combination antiretroviral therapy (cART) in the developing world has resulted in major health improvements for populations fortunate enough to access it [1]. However, despite the successes, many populations remain excluded from therapy [2]. One population that appears almost systematically excluded are people living in settings of violent conflict. This is in large part because of a long-standing and largely unchallenged view that the provision of medical assistance for chronic illnesses is not feasible in such settings [3].

There has been a tremendous amount of discourse on the epidemiology of HIV/AIDS in populations affected by conflict, and the extent to which war protects or exacerbates the transmission of HIV [4]. The link between violence, HIV, and human rights has also occupied considerable space in the literature; emotions have run high in discussions of violence and sexual violence and its impact on potentially hyperendemic HIV infections in communities [5]. While advocacy groups have called for

specific interventions for populations affected by violence on the basis that these populations have elevated rates of HIV/AIDS, other groups, such as the media, have at times translated these calls for attention into a heightened discrimination by portraying displaced persons and refugees as threats leading to increasing HIV rates in the welcoming communities [6]. Such emotive discourse has reached the highest levels of international decision-making, including the United Nations Security Council [7–9]; meanwhile, discussions on how to actually provide HIV/AIDS care to conflict-affected populations have occupied less space. Only recently has research evidence emerged indicating that HIV/AIDS rates are generally not higher within populations affected by violence.

For the purpose of this article, we primarily focus on HIV/AIDS and conflict in the sub-Saharan region. This setting is disproportionately affected by both HIV/AIDS and ongoing conflicts. Figure 1 displays the overlap of HIV/AIDS and conflict in Africa. Although other major conflict areas, such as Afghanistan, Iraq, or Chechnya, claim a substantial number of lives from violence, destruction of health infrastructure, and diminished access to health services due to insecurity, HIV/AIDS has not yet reached a generalized epidemic status in these countries. As we will briefly discuss, in settings such as Burma (Myanmar) and Nepal, the trade in illegal drugs and human trafficking could reasonably contribute to explaining an increase in population levels of HIV/AIDS [10,11].

There are numerous reasons to expect heightened exposure to HIV among populations affected by conflict and displaced populations. Forced displacement, sexual violence, sexual risk-taking, drug use, and transactional sex, as well as a lack of access to health care facilities and providers, can all contribute to increased incidence of infection [12–14]. Within recent African conflicts, there are well-documented incidents of sexual violence against females and sexual risk-taking among male combatants [15]. In general, however, the real-time collection of data on sexual behaviors, risk-taking, and sexual violence is woefully inadequate [16]. While acknowledging the challenges of undertaking extensive surveys among mobile populations and in situations of high insecurity, the humanitarian community has developed considerable expertise in this area for outbreak monitoring and

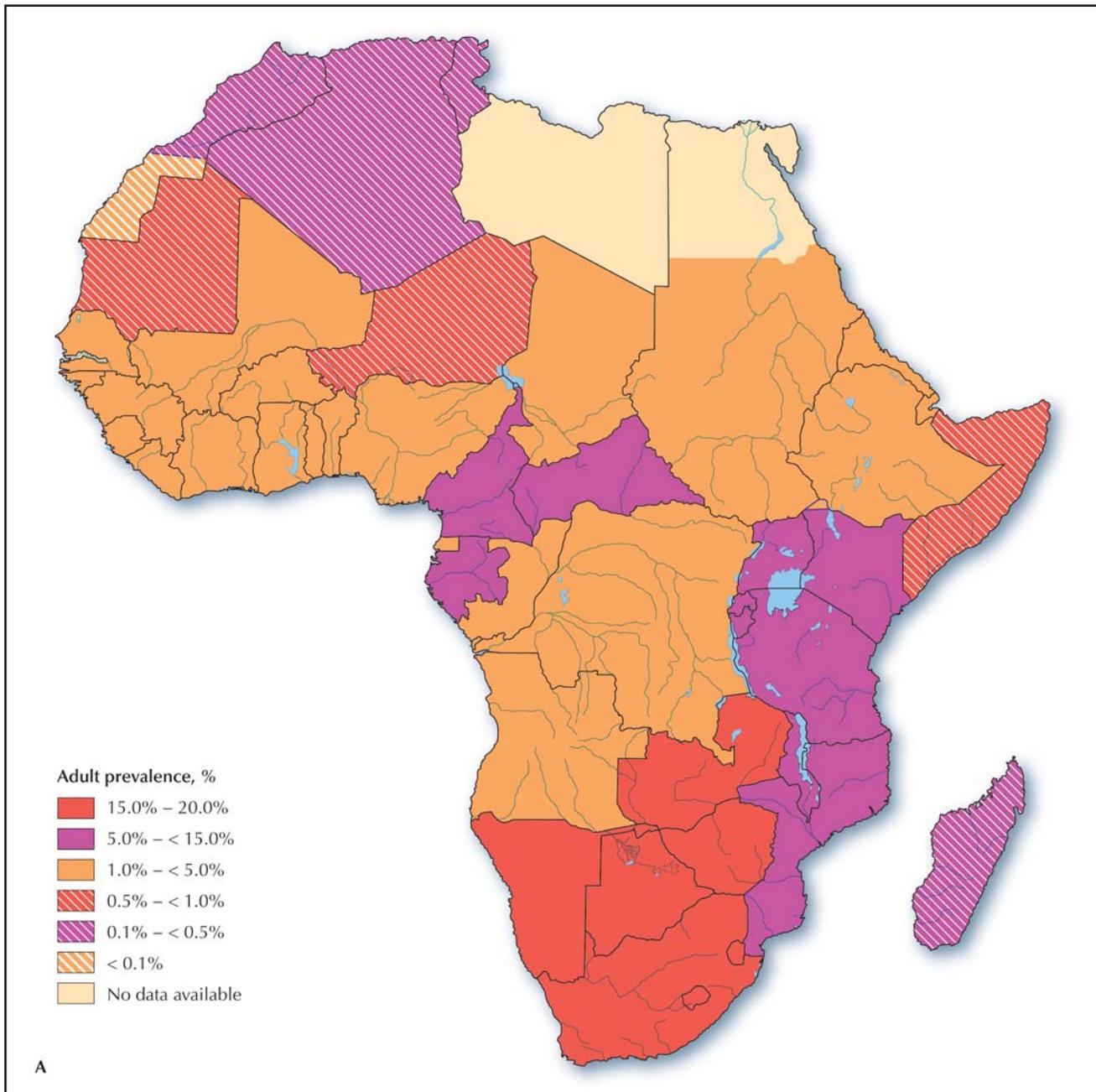


Figure 1. Overlap of HIV prevalence (A) and current conflicts (B) in Africa, 2007.

mortality estimation. Data collection that would increase our understanding of HIV epidemiology in conflict settings can be improved.

Perhaps the single most powerful evidence that contributed to widespread concern about heightened HIV rates came from an unpublished report of 1125 female rape survivors from the Rwandan genocide, of whom about 70% were HIV-positive [17,18]. This unpublished study has never been made publicly available yet received tremendous attention and went unquestioned despite other interpretable evidence that found otherwise. For example, a 1997 study of 4800 surveyed women found only 2.2% had been raped during the conflict in Rwanda, and of rape

survivors, 15.2% were positive for HIV, compared with 11.0% in women not raped ($P = 0.16$) [19]. This difficult topic displays the complex nature of interpreting evidence when emotions, advocacy, and humanitarian action are mixed together. Similar expectations about widespread rape and the use of HIV as a weapon of war have supported these human rights concerns as the dominant theme of discussions at the level of international decision-making [15], potentially at the cost of actually providing treatment to patients.

Arguably, the first voice of reason regarding the actual epidemiology of HIV/AIDS in populations affected by conflict has been Dr. Paul Spiegel of the United Nations

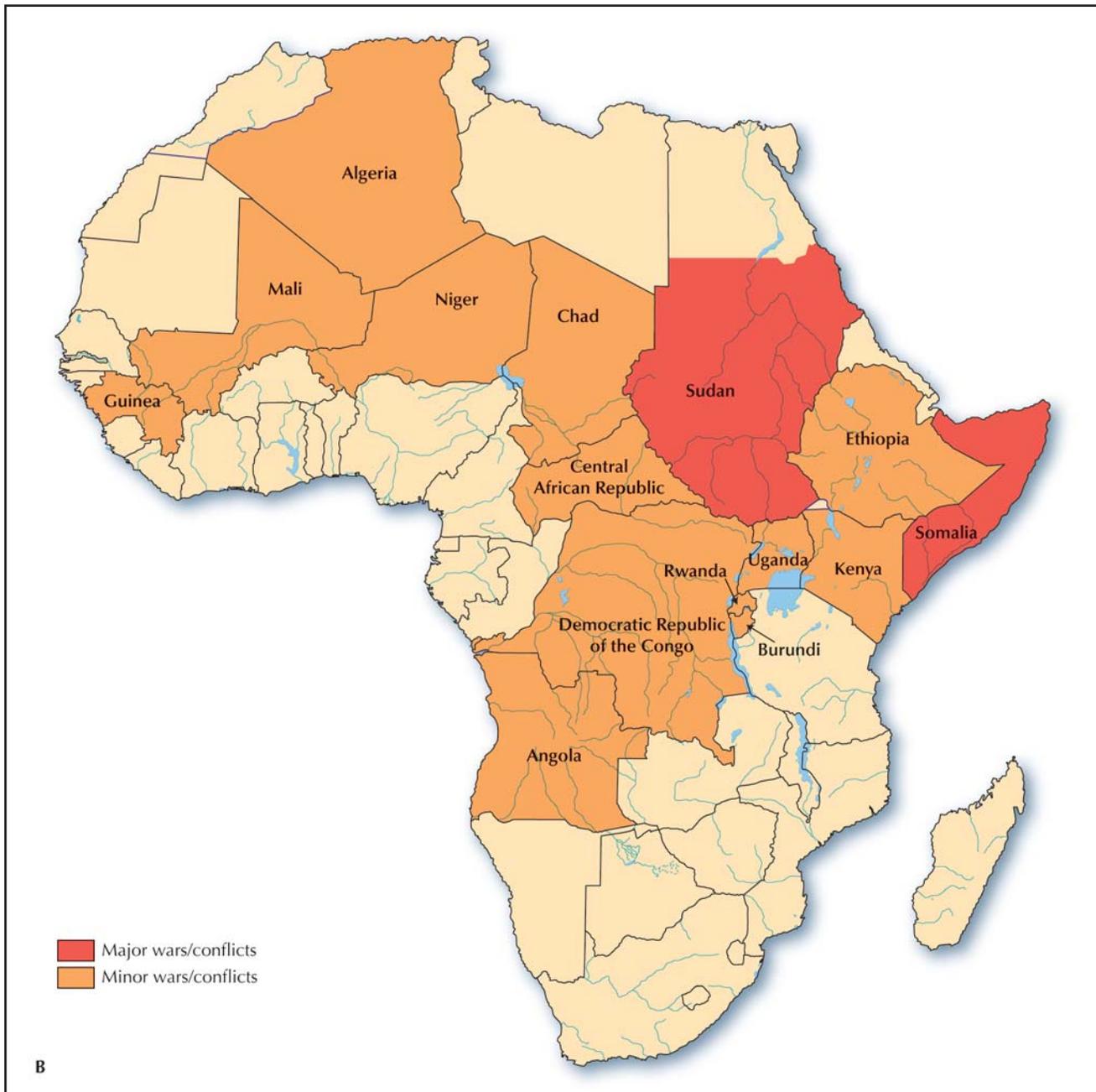


Figure 1. (Continued).

Refugee Agency (UNHCR), who has tracked the best available local evidence demonstrating that HIV/AIDS is counter-intuitively lower within populations affected by violence [20,21•]. Possible explanations for this include the breakdown in sexual networks, a decrease in travel from rural to urban settings, and a general decrease in sexual activity among the general population. Mathematical modelling postulates that sexual violence may only contribute to a small number of new HIV infections, the majority of infections occurring due to multiple sexual exposures with a partner or concurrent partners, rather than single, even violent, exposure [22], even acknowledging that rape may involve more than

one perpetrator. Even in the most extreme situations postulated, in which 15% of the female population was raped and HIV prevalence among assailants was eight times the country population prevalence, and the HIV transmission rate was highest at four times the average high rate, widespread rape increased the absolute HIV prevalence of these countries by only 0.023%. It is only now that the international community is beginning to consider the epidemiology of HIV/AIDS within these populations using evidence rather than anecdote and emotion, but this remains a major problem in improving dialogue and funding for the provision of care to these populations.

Guidelines

Early guidelines addressing the provision of care for populations affected by conflict recommended caution in providing cART to these populations. Of particular note, the SPHERE Guidelines—a set of guidelines that aim to provide minimum standards in disaster responses and have been adopted by over 400 nongovernmental organizations [23]—indicated that the provision of cART in populations affected by conflict was not feasible [24,25] due to associated population movements and poor access to basic health services [20]. Recognizing that the SPHERE Guidelines were published in 2004, when the scientific community appeared to be overly concerned with drug resistance and the expectation that adherence would be poor, the Guidelines do not seem out of line with the scientific and political thinking of the day. More recently, the World Health Organization (WHO) and UNHCR issued a position statement indicating that provision of cART to HIV-infected individuals in emergency settings represents a public health and human rights imperative [26]. The UNHCR has since developed clinical and operational guidelines for the management of cART in conflict-affected and displaced populations [27].

Although guidelines now exist for the provision of basic clinical care and cART, the realities of providing care may be much more challenging than any guideline committee may anticipate. The lack of or poor access to health services remains a core challenge to providing any clinical care in these populations, and the small number of medical attendants or nurses may be overwhelmed by the heightened burden of other medical priorities, such as diarrhea, respiratory illness, trauma and obstetric surgery, malnutrition, and the need for mass vaccination [28]. In the face of so many acute needs, chronic conditions such as AIDS may be considered nonessential during periods of emergency and requiring a certain level of stability before drugs can be acquired and delivered and staff trained to provide care. One clinical challenge that remains very poorly understood is the potential interaction between HIV and other health conditions that are exacerbated during conflict, such as cholera, malnutrition, and malaria.

A major political challenge is determining whose responsibility the population may be in the absence of a functioning host government. In the Great Lakes region of east Africa, for example, populations affected by conflict will frequently traverse borders to escape violence or access humanitarian aid. It is important to note the distinction between refugees (those who have crossed a state border into a country that is not their own) and internally displaced persons (IDPs; those who have relocated within their own country). Refugees may be able to attain a degree of protection in a refugee camp established and monitored by an international organization such as UNHCR and are guaranteed rights under international law. IDPs and unregistered refugees, on the other hand, are likely to be worse provided for than refugees residing in camps. IDPs are frequently excluded from

national AIDS plans and may be discriminated against by their own government because they do not have agencies to advocate on their behalf [29,30]. Finally, in many instances, refugees are denied their rights by being denied refugee status—the term *externally displaced person* is often used by host governments to avoid their obligations under international law.

The Médecins Sans Frontières Experience

The provision of antiretroviral therapy in resource-limited settings has been a controversial issue for humanitarian agencies that are traditionally unwilling to engage in the provision of care for chronic diseases that require lifelong assistance. Médecins Sans Frontières (MSF) has been a strong advocate for treatment in the developing world. As of mid-2009, MSF programs were directly supporting the provision of antiretroviral therapy to about 140,000 people.

In 2003, MSF began a pilot program to provide cART in conflict settings in the Democratic Republic of Congo (DRC) and has since established programs in a number of conflict-affected countries [3]. The organization's willingness to develop approaches to treating HIV in a conflict setting built on past efforts to address tuberculosis (TB). As with HIV, aid agencies have traditionally been reluctant to address TB in emergency settings out of fear for creating drug resistance. However, in many conflicts, TB, which flourishes in conditions of overcrowding (as can be found in refugee settings), was responsible for considerable mortality. In the face of considerable policy resistance, MSF established a TB treatment program in the Lankien, south Sudan in 2001 [31]. The program admitted around 250 patients each year, and the defaulter rate was very low (< 1%), due largely to the very high level of community demand for the program, the firm commitment of patients, and possibly reduced mobility of patients [32].

This successful experience led MSF to challenge the assumption that cART should not be provided in conflict settings. In late 2003, a program began to provide cART to conflict-affected populations in Bukavu, a city of 600,000 inhabitants in eastern DRC, bordering Rwanda [33•]. Despite a 2001 peace agreement the region still saw sporadic fighting. Bukavu was initially chosen as a site for HIV care because it had a high HIV prevalence (estimated to be as high as 9%) and was an area of relative calm in a region of conflict. By January 2006, 494 patients had started ART. Most were started at an advanced stage of disease, presenting with WHO stage III (49%) and IV (34%) illness. Early outcomes were excellent, with a median CD4 gain at 6 months of 163 (interquartile range [IQR] = 82–232). The 12-month mortality rate of 7.9% (IQR = 3.6–12.1) and loss to follow-up of 5.4% (IQR = 3.2–7.4) compare favorably to peaceful settings [33•].

In mid-2004, rebel forces invaded Bukavu, resulting in the death of hundreds of civilians and thousands of displaced persons and refugees crossing over into neigh-

boring Rwanda. Movement of staff and patients was curtailed, and all expatriate MSF staff were evacuated from the city. Basic HIV clinic and hospital functions were maintained during most of the conflict period by a Congolese nurse who lived nearby, although the clinic remained inaccessible to many due to distance and insecurity. Communication during this time was difficult but continued via a radio broadcast and “word of mouth.” The MSF pharmacy was not looted. Of the 66 patients who had been initiated on ART during this period, only five experienced a significant treatment interruption [33•]. Fourteen other patients reported having sufficient supplies of medication that they did not need to attend the clinic. Three were hospitalized and had ready access to cART, 41 attended the clinic for their cART, and three were able to collect cART over the border in Rwanda in collaboration with another MSF mission.

The AIDS Support Organization’s HIV/AIDS Program in Northern Uganda

In 2004, at the same time that international guidelines stated cART provision was untenable in conflict settings, The AIDS Support Organization (TASO) began providing cART in the regions of northern Uganda. Northern Uganda had been in a state of humanitarian emergency for over 20 years, in what has been called one of Africa’s longest standing armed conflicts and neglected humanitarian emergencies. Of the estimated 1.6 million people displaced in northern Uganda between 2002 and 2004, most continue to reside in protected camps [34]. Gulu is the largest inhabited district of the area—Gulu district and municipality have a population of approximately 566,000 inhabitants. The crude mortality rate in the area has been high, reaching 1.22 per 10,000 per day (95% CI = 1.00–1.44) among camp residents and 1.29 per 10,000 per day (95% CI = 1.04–1.53) in the surrounding community. These mortality rates far exceed the emergency threshold of 1.0 per 10,000 per day [35]. Violence is a leading cause of death in Gulu district, accounting for approximately 11% of all deaths. The overall violence-specific mortality rate in Gulu district is approximately 0.17 persons per 10,000 per day (95% CI = 0.12–0.21), corresponding to about 2400 violent deaths per year [10,36]. The regional referral hospital, St. Mary’s Lacor Hospital, reports that HIV/AIDS is the most common reason for death in the region [36]. A recent sero-surveillance study in Gulu district found that HIV prevalence among antenatal clinic attendees was 10.3%. Women living in the communities surrounding IDP camps had more elevated HIV prevalence compared with those living in IDP camps (11.6% vs 6.3%), suggesting that IDP camps may have a protective impact on HIV transmission in Gulu [37]. Rural districts outside Gulu have varying prevalence rates. Gulu district has 14 HIV voluntary counseling and testing sites, five clinics

(PMTCT), and six sites providing cART to eligible individuals. Most of these health services are located in the (urban) municipality [38].

Since 2004, TASO has initiated cART in 1625 adults and 53 children in this setting, but only 227 were registered IDPs [39,40•]. Most patients had received therapy for about 1 year (11.6 months; IQR = 7.3–16 months), and 69 (4.2%) patients died during the period of follow-up, almost all within the first 3 months of therapy, giving a mortality incidence rate of 3.48 per 100 person-years (95% CI = 2.66–4.31). Of the 1519 patients with complete data for adherence, 1401 (92.2%) had adherence 95% or greater, with adherence appearing to wane over time. Loss to follow-up was 5.1%. As with most African settings, men presented at a later disease stage and with more advanced CD4 depletion.

In the past year, Lord’s Resistance Army–related violence has decreased in northern Uganda, and individuals are beginning to return to their ancestral villages. However, most are returning for several days and then returning to the camps for stability. As more individuals return home, the challenges will include home-based care and retention of patients in the program.

Evidence to Support cART in Other Conflict-Affected Settings

While violent conflicts in Africa have predominantly addressed ethnic violence, other regions of the world that have conflicts may have diverse political or economic reasons for violence and a resultant breakdown in health care infrastructure. Nepal, for example, has experienced an insurgency led by Maoist rebels that has depleted the region of health infrastructure and allowed security breaches to override good public health and security.

The affected vulnerable groups are primarily comprised of returning migrants from India in both western and eastern hilly areas, IDPs as a result of the conflict, injecting drug users from the inner cities and the border areas, female sex workers and their clients along the highways and in the inner cities, and men who have sex with men (MSM). Along with poverty, stigma and lack of awareness, conflict-related displacement, economic migration, and closure of HIV programs have exacerbated the HIV situation in Nepal.

There are more than 120,000 people living with HIV and AIDS in Nepal. Among them, it is estimated that more than 9000 people have a more advanced stage of AIDS and are in dire need of highly active ART. There is lack of data on sexual behavior of MSM and data on HIV rates among transgendered persons. There is no information on orphans of persons living with HIV and AIDS. Most of the HIV-infected people live in the remote villages; they are often geographically hard to reach with proper information packages, let alone lifesaving ART. The rugged mountainous terrain with limited infrastructure support, much of which has been destroyed by the conflict, makes

the delivery of highly active ART in remote areas challenging. The government's strategy has typically excluded IDPs. Very few organizations, such as the Blue Diamond Society, which works primarily with MSM, are working to provide both humanitarian assistance as well as ART to HIV-affected persons in the Kathmandu valley.

Similarly, Burma (Myanmar) has suffered from an ongoing ethnic and political conflict involving the ruling military junta and ethnic tribes including the Karan and Kareni peoples. Current estimates place the generalized epidemic above 1.3% of the population and higher within at-risk subgroups [41]. Burma has traditionally invested only a small amount of resources in health, and although HIV monitoring began in 1992, current estimates are unreliable. Among the populations targeted by the conflict, the provision of cART is limited to the Thai–Burma border camps and administered by medical aid organizations, such as MSF, although even their presence has been challenged by the ruling junta.

Important work by Beyrer et al. [42] in 2000 showed that hyperendemic infection areas appeared to be linked to the illegal drug trade in heroin and other narcotics. Given the difficulties in conducting research within Burma, the extent of HIV infection will remain unknown for some time and the impact of Global Fund–supported cART will remain a mystery [43].

Postexposure Prophylaxis

It would be inappropriate to address cART provision in settings of violence without calling for the use of cART for postexposure prophylaxis (PEP). The UNHCR Guidelines recommend PEP availability in settings of conflict due to the likelihood of sexual violence [44]. In reality, many victims of rape are unable to access appropriate clinical care because they may be unaware of PEP options, may be physically unfit to attend a clinic, or may feel stigmatized about the sexual exploitation. Although PEP may be available in UNHCR-coordinated camps for refugees (and occasionally IDPs), there tends to be a low knowledge about PEP availability in less organized camp settings.

PMTCT

Another important aspect of antiretroviral provision in conflict-affected regions is PMTCT. PMTCT can be overlooked in aid programs in conflict settings [45]. However, as with PEP, PMTCT is a short and highly effective preventive intervention; unless it is given greater priority, children who manage to survive through conflict may then die of HIV because health services fail to provide a relatively simple intervention. PMTCT services require infrastructure that includes antenatal care and HIV testing services. These usually exist even during periods of violence and impending violence, because birth attendants and nurses frequently have access to test kits.

Lessons Learned

Important lessons have been learned since the first guidelines were written and since agencies such as MSF and TASO began providing cART in these settings.

Communications

Communications plans are essential to maintaining cART in periods of instability and conflict. Several recent examples provide lessons for the future regarding what works well and what could be improved.

Communications during periods of violence are key to any successful delivery of care, and integrated networks of care across regions and between states may be necessary to ensure that patients remain on therapy. During the ethnic and political violence in Kenya in 2007/2008, official estimates report that over 1200 people were killed and over 300,000 people were displaced from their homes. cART providers in western Kenya quickly communicated with cART providers in Uganda, including TASO, reporting on where clinics would be able and willing to dispense cART to Kenyan refugees. Again, during this crisis, several hotlines were made available to patients to identify clinics and to answer AIDS-related questions. MSF's hotline in the Kibera slums of Nairobi reported mixed successes, with staff unprepared to answer non-HIV-related questions from patients and many patients unable to access the telephone number because they subscribed to another mobile provider. MSF concluded that an established hotline, prior to the violence, may have had greater success [46]. One research study team at the University of Nairobi/Manitoba was conducting a randomized trial of cell phone–based messaging to promote cART adherence at the time of the violence. Using the phone numbers of all enrolled patients, the study team was able to maintain contact with 211 of 267 patients and provide guidance and counseling even to those directly affected by violence. The system is not perfect: at least three patients reported losing mobile phones while fleeing violence. Others were denied access to air-time “top ups” by poor security or economic fallout or were forced to remain in remote areas without network coverage. This may represent an example in which an established network could preempt the loss of patients, and as a result, did not lose any participants from the clinical trial.

During periods of violence and subsequent lock-downs in the northern Uganda region, TASO used innovative strategies to communicate with patients. A telephone hotline was established that detailed where clinics would be available to camp-dwellers and those outside of the town. TASO worked with the Ugandan military to provide secure transportation of patients from rural areas to the main TASO site, when necessary. Although many programs in Africa are affected by considerable loss to follow-up [47], TASO compensates for this by employing a special counseling and home-based care team on motorcycles to consistently track patients. Motorcycles represent an important step forward in delivering care in rural regions because they can quickly

traverse over difficult conditions, require only one rider (thus saving on driver costs), and can be relatively easily maintained. The motorcycle-based teams can reach distant patients and regions and frequently bring drugs, nutrients, and other related care packages to rural patients.

Runaway cART packages

One of the major concerns with the emergence of immediate violence is that patients already on cART will be separated from their medications. As mentioned earlier, communications between cART providers in the Kenyan crisis assisted in minimizing this impact. Similarly, agencies such as MSF have been providing patients with several months' supply of cART that they are instructed to take with them during any planned move. There are obvious costs associated with giving a long supply of medicines when anticipating an emergency and the possible disruption to patients' regular supply; they may determine that they do not need to return to pick up their regular drugs because they have a long supply anyway. Nevertheless, such approaches are proving valuable in ensuring continuity of medication when routine services are disrupted.

Links with neighboring areas and providers

The Kenyan crisis and subsequent involvement of agencies such as TASO displays the need to involve partner agencies in the delivery of care during times of crisis. Similarly, the MSF program in Bukavu established links with programs in neighboring Rwanda. However, these successes should not overshadow the very real challenges experienced by cross-state agencies, and the unwillingness of governments to provide health services to migrants. In the case of Burmese refugees to Thailand, for example, Thai cART providers have in the past been unwilling to assist Burmese migrants in starting or continuing to receive cART. Similarly, Zimbabwean migrants in South Africa have struggled to access HIV/AIDS care. This may be due to local (clinic level) discrimination against foreigners who are seen as an additional burden to overstretched services, or part of a broader government policy of exclusion.

Patient-held cards

In the case that patients do successfully interact with a provider in a different setting or cross-state setting, it is important that providers are able to quickly assess health status, including laboratory and clinical presentations, and regimen history. One solution that has been proposed is patient-held health cards that patients can take with them and present to new providers with details of their drug regimens and medical history, including last CD4 count. Such opportunities would decrease the costs to the new provider in terms of laboratory tests and clinician time, but raise issues of confidentiality.

Awareness campaigns

In many developing settings, the radio and local newspapers are the most common forms of news media. This

represents a powerful communications tool for providers with patients and their families about risks in transportation, availability of clinic staff and drugs, and availability of related items, such as food. In Uganda, for example, radio stations have been successfully used by the Joint Clinical Research Centre to announce clinic openings, availability of staff, and also to report on signs and symptoms of illness and where HIV testing may be available. Similarly, in Bukavu, radio was used to inform displaced patients about the status of clinic services and alternative opportunities to access care.

Patient-reported concerns

Although few studies have reported on patient-level problems and concerns regarding accessing therapy, adherence, and retention in programs during conflict, the issues raised by patients appear to be similar to those in non-conflict settings, with the exception of security issues. To our knowledge, only two studies, one from northern Uganda [48•] and one from Kenya [49], have specifically addressed adherence and retention issues, using interviews with patients and health workers. Issues affecting rural populations, such as lack of health workers, distance from clinics, stigma and disclosure, and food insecurity, predominate patient concerns. However, specific to security, patients report that they may be unable to attend health centers to pick up their drugs or may be unable to keep appointments when there is concern (either real or perceived) that the roads are insecure. In keeping with transportation difficulties, patients in northern Uganda may face stock-outs of drugs when they eventually reach the clinic setting. Although stock-outs are becoming much rarer, thanks in large part to the US President's Emergency Plan for AIDS Relief (PEPFAR) preparations, they remain a reality in non-PEPFAR-funded programs.

Conclusions

The drive to provide cART in Africa began in 2001. However, it is only now, in 2009, that the international community is beginning to give serious attention to providing cART to populations affected by violence. A paucity of epidemiologic data, lack of program experience, and political unwillingness to prioritize the needs of displaced populations have all contributed to this neglect.

Recognizing that not all conflicts are equal, security and epidemiology will condition the relative degree of priority that should be given to cART as part of the overall humanitarian response. At the same time, governments and agencies involved in health care provision can no longer argue that such programs are not feasible. It is no longer possible to claim that nothing can be done.

Disclosure

No potential conflicts of interest relevant to this article were reported.

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