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Review

The challenges of tuberculosis control in protracted conflict: The case of Syria

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ABSTRACT

Objectives: Syria's protracted conflict has resulted in ideal conditions for the transmission of tuberculosis (TB) and the cultivation of drug-resistant strains. This paper compares TB control in Syria before and after the conflict using available data, examines the barriers posed by protracted conflict and those specific to Syria, and discusses what measures can be taken to address the control of TB in Syria.

Results: Forced mass displacement and systematic violations of humanitarian law have resulted in overcrowding and the destruction of key infrastructure, leading to an increased risk of both drug-sensitive and resistant TB, while restricting the ability to diagnose, trace contacts, treat, and follow-up. Pre-conflict, TB in Syria was officially reported at 22 per 100 000 population; the official figure for 2017 of 19 per 100 000 is likely a vast underestimate given the challenges and barriers to case detection. Limited diagnostics also affect the diagnosis of multidrug- and rifampicin-resistant TB, reported as comprising 8.8% of new diagnoses in 2017.

Conclusions: The control of TB in Syria requires a multipronged, tailored, and pragmatic approach to improve timely diagnosis, increase detection, stop transmission, and mitigate the risk of drug resistance. Solutions must also consider vulnerable populations such as imprisoned and besieged communities where the risk of drug resistance is particularly high, and must recognize the limitations of national programming. Strengthening capacity to control TB in Syria with particular attention to these factors will positively impact other parallel conditions; this is key as attention turns to post-conflict reconstruction.
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Introduction

The surveillance, diagnosis, and management of tuberculosis (TB) in protracted armed conflict characterized by widespread violations of humanitarian law, presents particular challenges for global health institutions responsible for TB surveillance and control programs, as well as treating physicians (Liddle et al., 2013; Kimbrough et al., 2012). Since the onset of violence in early 2011 and subsequent escalation into fully fledged armed conflict by mid-2012, forced mass displacement has resulted in millions of civilians living in overcrowded and unhygienic conditions, without safe water or sanitation, with conditions predisposing to the transmission of TB.

During bombardment, families often sheltered underground in overcrowded and poorly ventilated basements, for days, weeks, or months at a time. These besieged populations were denied humanitarian aid, fuel, food, and essential medicines, including anti-tuberculous treatment (ATT) (Abbara et al., 2018a). Detention centers, crowded with prisoners with immune systems weakened by torture and malnutrition, have facilitated not only the transmission of TB, but also the cultivation of drug-resistant TB (Abbara et al., 2018a). The neglect of public health infrastructure and the targeting of hospitals and healthcare workers has led to the widespread destruction of Syria's health system and the attrition of physicians, resulting in limited access to health care. Ongoing insecurity leads to delays in the diagnosis of TB, while multiple displacement and restricted humanitarian access impedes surveillance and compliance with treatment. These factors directly and indirectly affect TB control.

The true extent of TB inside Syria is as yet unknown given the challenges to surveillance, laboratory confirmation, and lack of reliable reporting of notifiable infectious diseases. As seen in the polio outbreaks in 2013 and 2017, official reporting to the World Health Organization (WHO) is inconsistent, with gaps in surveillance and delays in notification (Tajaldin et al., 2015). Concerns over the timeliness and completeness of official surveillance of other communicable disease is well-documented (Ismail et al., 2016; Sparrow et al., 2016). Drug-resistant TB is of particular concern, as interrupted or inadequate treatment promotes the development of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB. This concern is compounded by challenges to diagnosis given the inadequate laboratory facilities and testing currently available.

Although limited research has been published on the control and management of TB among Syrian refugees in neighboring countries (Cookson et al., 2015; Cousins, 2014; Hosten et al., 2018), there are no in-depth research articles examining the problem of TB within Syria's borders. This paper appraises the available data concerning TB epidemiology and control in Syria, before and after the onset of violence in 2011. A scoping review of available academic and grey literature and data provided by the Syrian Ministry of Health (MOH), WHO, World Bank, Global Fund, United Nations Children's Fund (UNICEF), and United Nations Development Programme (UNDP) was performed. This was supplemented with unpublished data from the MOH, WHO, and the Health Directorates of Rural Damascus and Idlib in Syria. The aim was to inform recommendations for the assessment and control of drug-sensitive and resistant TB in Syria and other settings of protracted conflict and political insecurity.

TB in Syria before 2011

Before the conflict, healthcare in Syria comprised a predominantly public-based health system with some private initiatives; the latter became increasingly important in the years leading up to the conflict (Kherallah et al., 2012). Rural areas had fewer health facilities and healthcare workers compared with urban areas, an imbalance that affected healthcare access, particularly for poorer patients with TB (Kherallah et al., 2012; Abbara et al., 2015). The Syrian MOH was responsible for TB surveillance of drug-sensitive and resistant TB and notification to the WHO. In 1990, the prevalence of TB was reported as 86 per 100 000 (WHO, 2011), and Syria's National Tuberculosis Program (NTP) was established in 1991. In 1997, the NTP adopted the WHO Directly Observed Treatment-Short course (DOTS) control strategy, with nationwide implementation by 2000. The case detection rate was reported at 42% in 2005 (UNDP) (UNDP, 2011), but this was revised to 89% for the same year in subsequent WHO reports; the latter figure is closer to the 90% reported for 2010 (WHO, 2011). The rate of MDR and rifampicin-resistant (MDR-RR) TB was estimated to be 8% in a survey performed in 2003 (WHO, 2019).

In 2006, the UN Development Assistance Framework (UNDAF) (awarded in response to Syria's tenth reform agenda) included adoption of the Stop TB Strategy and Millennium Development Goals (MDGs). The UNDAF was supported by a Global Fund grant of US$8 million to the Government of Syria to support the NTP for the period 2007–2012, with the UNDP responsible for implementation (UNDP, 2007). Part of this strategy was to strengthen the health system in general and improve access to healthcare, as well as to increase the number of local centers able to manage TB (UNDP, 2019). It aimed to improve surveillance, address the low case detection rate (including prison populations), and to improve the capacity of diagnostic laboratories for both sensitive and MDR TB. It also laid out plans to improve DOTS coverage to improve completion rates. Stigma towards those with TB was high, due to its association with poverty and incarceration, and a program of advocacy to improve access to vulnerable populations through communication and social mobilization was thought key (UNDP, 2019).

A specialized TB center was set up in each governorate to coordinate TB control activities, in addition to a central reference laboratory in Damascus (UNDP, 2019). Case detection in 2008 was reported to the WHO at 85%, with 86% reported cured (WHO, 2011). By 2010, diagnosis and treatment was reported to be available at no cost in 1796 TB centers across Syria; acid-fast bacillus (AFB) smear testing was available in all 14 governorates and there were 14 laboratories across the country that were able to perform mycobacterial culture. By 2010, incidence was reported to the WHO as 23 per 100 000 population (WHO, 2011).

TB in Syria since the onset of violence in 2011

Since 2016, only eight governorates have had laboratories with the capacity for smear testing, and mycobacteriology culture is only available in the government-controlled cities of Damascus and Homs (Muhjazi et al., 2018). Outside of government-controlled areas (GCAs), microbiology facilities are inadequate and the mainstay of diagnosis is smear microscopy and chest radiographs; this restricts the ability to identify cases of smear-negative, extrapulmonary, or drug-resistant TB, leading to an underestimate of the numbers of cases. Official figures estimate that 46% of TB cases are extrapulmonary; of the pulmonary cases in 2017, 72% were mycobacteriologically confirmed, although the proportion of smear-positive cases was not stated (WHO, 2019). These factors contribute to under-reporting of cases and uncertainty as to the extent of drug resistance. The incidence of MDR-RR TB in 2016 was reported to the WHO as 1.7 per 100 000 population, with an estimated 150 cases of MDR/RR among notified pulmonary TB cases (WHO, 2019). An estimated 8% of new cases and 24% of previously treated TB cases had MDR/RR TB (WHO, 2019).

The incidence of TB in Syria was reported to the WHO at 23 per 100 000 in 2012 and 19 per 100 000 in 2017 (WHO, 2019). This may be compared with a TB incidence of 7.7 per 100 000 in Jordan (relatively stable since 2011) and 12 per 100 000 in Lebanon in 2011, rising to 15 per 100 000 in 2012–2013 and falling back to 12 per 100 000 in 2016 (World Bank Group/WHO, 2018) (see Figure 1). The numbers of cases of TB reported to the WHO annually were 3990 in 2012, 2816 in 2013, 3576 in 2014, 3135 in 2015, 3154 in 2016, and 2845 in 2017 (WHO, 2019). Information by governorate is illustrated in Table 1. The percentage of laboratory-confirmed TB cases was 39% in 2017, with only 5% of total cases notified tested with rapid diagnostics at the time of diagnosis (WHO, 2019). Treatment coverage (notified/estimated incidence) was reported as 80% in 2014, 70% in 2015, 62% in 2016, and 80% in 2017 (WHO, 2019).

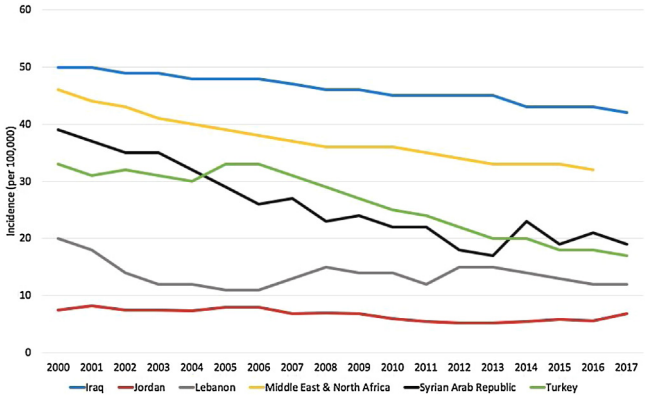


Figure 1. The incidence of TB per 100 000 population (*x*-axis) by year (*y*-axis) for Syria and countries surrounding Syria between 2002 and 2017. Iraq had the highest incidence of TB, followed by Syria and Turkey, with lower rates in Jordan and Lebanon.

Table 1
Number of patients diagnosed with TB in Syria per year, by governorate, from 2014 to 2016, from the Syrian Ministry of Health. The data underestimate the true prevalence of TB given the challenges to comprehensive surveillance, diagnosis, and reporting since the onset of violence, particularly in areas outside of government control.

Governorate	2014	2015	2016
Damascus	1370	1611	1112
Aleppo	605	378	545
Rural Damascus	146	94	447
Latakia	223	188	276
Al-Hasakeh	193	230	204
Hama	171	223	188
Tartus	162	136	142
Homs	138	116	140
As-Sweida	31	27	61
Dara'a	13	12	25
Deir ez-Zour	152	15	9
Idlib	210	20	3
Raqqa	162	84	2
Total	3576	3134	3154

TB, tuberculosis.

TB cases in Syria have been unequally distributed across governorates. Data from the MOH showed Aleppo, Damascus, and rural Damascus to have had the highest numbers of cases, most likely reflecting the governorates in which patients have sought treatment rather than the origin of cases. Although figures reported to the WHO should represent the whole of Syria, due to insufficient diagnostic capacity and different degrees to which the healthcare systems have been affected in areas not under Government of Syria control, it is likely that these figures underestimate the true burden of TB in these areas. Although one update by UNDP claimed that one million internally displaced persons (IDPs) in shelters were screened for TB in 2013 (UNDP, 2019), the official Global Fund progress report did not report any screening of IDPs until 2015, when a total of 5900 were tested (UNDP, 2019).

Syrian refugees in Lebanon and Jordan

Little is published on TB among the 3.7 million Syrian refugees in Turkey. However, reports from Lebanon and Jordan, which host about 924 000 and 660 000 United Nations High Commissioner for Refugees (UNHCR) registered Syrian refugees, respectively (UNHCR, 2018a), suggest an increase in the overall case notification rates of TB, attributed to the arrival of Syrian refugees. Refugees in Lebanon and Jordan face numerous challenges, including overcrowding, poverty, and poor access to healthcare. Figure 1 shows the incidence of TB between 2002 and 2017 in Syria and neighboring countries. Iraq had the highest incidence, followed by Syria and Turkey, with lower rates in Jordan and Lebanon (Ismail et al., 2018).

In Lebanon, where cases consistently declined until 2011, cases increased by 27% in 2012 (Ismail et al., 2018). The proportion of TB patients who were Lebanese nationals declined from 66.7% to 49.4% between 2010 and 2014, while the proportion who were Syrian refugees increased 10-fold, from 1.6% to 16% in the same period. In 2013, the Lebanese NTP noted that 100 cases of TB were notified among Syrian refugees, including three cases of MDR TB (Dabboussi et al., 2015). In Jordan, TB case notification rates among Syrian refugees were almost 40% higher than among local populations; however, the numbers were small with around 74 cases detected in a 12-month period (Cookson et al., 2015; WHO, 2019). A detailed exploration of TB among refugees in Lebanon, Jordan, and Turkey is beyond the scope of this article. Moreover, the closed borders since 2016 and reduction of population flows mean that TB among refugees in these neighboring countries is unlikely to reflect TB patterns inside Syria.

Drivers of TB transmission and drug-resistant TB in Syria

Risk landscape at the population level

More than half of Syria's pre-conflict population has been forcibly displaced, with 5.6 million being refugees and 6 million being internally displaced (Watch, 2018). This mass displacement has led to overcrowded homes, camps, and other collective shelters, inadequate sanitation and waste disposal, insufficient safe water, and interrupted food supplies. The resulting increase in communicable diseases and malnutrition has strained local health systems (Watch, 2018). Overcrowding is a key risk factor for TB transmission, while malnutrition increases the risk of reactivation and progression of TB (Kimbrough et al., 2012). Diabetes and other chronic diseases are increasingly prevalent and poorly managed, further increasing the risk of TB susceptibility and reactivation. This is combined with limited access to healthcare and diagnostics delaying the time to diagnosis and treatment and increasing the risk of transmission within households and communities. Although most IDPs are now in government-controlled territory, most still face inadequate humanitarian or medical aid with poor access to healthcare including specialist TB services, diagnostic facilities, and uninterrupted treatment (UNHCR, 2018b). These factors can all contribute to the development of drug resistance, given the challenges of ensuring compliance with medication and the management of treatment side-effects. Close supervision as per DOTS programs, recommended by the WHO, is extremely challenging under these circumstances.

Bacille Calmette–Guérin (BCG) vaccination, a population-level intervention that can protect infants aged 0–24 months against TB meningitis, was routinely given at birth in Syria prior to 2011 (MSF Syria, 2017). Official figures from the Syrian MOH report 99% coverage of neonatal BCG vaccination between 2006 and 2011. After declining to 68% in 2015, it was reported at 96% in 2016 and 80% in 2017 (WHO and UNICEF, 2017). The WHO and UNICEF estimates are reported as 91% in 2006 and 66% in 2015, 2016, and 2017 (WHO and UNICEF, 2017). As estimates are based on data of variable or unknown quality, the 'grades of confidence' provided by the WHO and UNICEF reflect the degree of empirical support for their estimates. BCG (and all other) vaccination estimates in Syria are graded at the lowest level and it is likely that official percentages are higher than actual vaccination rates (WHO and UNICEF, 2017).

Vulnerable populations

There is increasing concern that TB, particularly MDR and XDR-TB, will rise unchecked within Syria's borders; of particular concern are besieged and imprisoned populations. It is estimated that over 2.5 million Syrians (more than 10% of the population) have lived through besiegement. People forced to live under siege or in hard-to-reach areas are likely to have suffered inadequate access to treatment, and in some cases deliberate denial, with ATT omitted from aid convoys (Watch, 2018). The effects of this may persist even after the siege is lifted. Eastern Ghouta, an area of 110 km^2 on the outskirts of Damascus, was besieged by the Government of Syria between October 2013 and March 2018 (Watch, 2018). During this time, aid convoys were infrequent and even when they were permitted, essential medicines and life-saving equipment were withheld under the inspection of the Syrian Government; this meant that up to 70% of aid in the convoy was removed (UN Security Council, 2019). Populations under siege also face food insecurity (Watch, 2018), with high rates of malnutrition increasing susceptibility to TB; severe acute malnutrition among children in Eastern Ghouta was reported by UNICEF to have reached 12% by the end of 2017 (UN Children's Fund).

In May 2015, Eastern Ghouta had 114 cases registered with TB for a population of roughly 500 000, giving an estimated prevalence of 23 per 100 000. By July 2017, the population had fallen to 390 000, but the number of registered TB cases had increased to 265, giving an estimated prevalence of 66 per 100 000 (Watch, 2018). Despite the Global Fund supporting an uninterrupted supply of ATT, no ATT was permitted in aid convoys to Eastern Ghouta from May 2015 (Al-Kabbani, 2017). Between November 2017 and February 2018, untreated TB caused the deaths of several people, including a 12-year-old girl (Al-Kabbani, 2017).

Of particular concern is Syria's prison population, with more than 90 000 arrests (many arbitrary and without trial) taking place since 2011, although the actual figure may be higher (Human Rights Watch, 2019). The association between TB, particularly drug-resistant TB, and imprisoned populations is long established and likely amplified in Syria where prisoners face harsh conditions with deliberate overcrowding, torture, deprivation of ventilation, and deliberate starvation causing malnutrition (Abbara et al., 2018a). It is estimated that 25% of 400 fatalities in Aleppo Central Prison between April 2012 and October 2013 were secondary to TB (Abbara et al., 2018a). Even when families supplied ATT for their relatives, it did not reach prisoners, or it reached them intermittently or at suboptimal doses, increasing the risk of drug resistance.

Multiple parallel health systems

Over the course of the conflict, a number of parallel health systems emerged outside of the government-controlled territory, which functioned in parallel with official healthcare provided by the Government of Syria. These health systems included field hospitals and underground facilities in northwestern areas controlled by the armed opposition: northern Hama, Idlib, western Aleppo, Eastern and Western Ghouta in Rural Damascus, the southern governorate of Dara'a, Deir ez-Zour and Raqqa in the northeast (both under ISIS control from January 2014 to October 2017), and the semi-autonomous Kurdish areas in eastern Raqqa and Al-Hasakeh and governorates. The health systems in these areas changed as the conflict progressed (Kherallah et al., 2012; Fouad et al., 2017). Each had their own structure and system of local health system governance (Ho, 2015). Health Directorates in the northwest, for example, worked closely with the Turkish MOH and used EWARN, the non-governmental communicable diseases surveillance system, whose offices are based in Gaziantep, Turkey. Each had their own way of diagnosing and managing TB, with limited interaction between these parallel health systems.

In July 2014, UN Security Council Resolution 2165 authorized cross-border and crossline access to reach people in Syria by the most direct routes. As a result, in September 2014 the UN Office for the Coordination of Humanitarian Affairs (OCHA) established the Whole of Syria (WoS) mechanism to coordinate the delivery of humanitarian aid from three officially recognized hubs in Damascus (Syria), Gaziantep (Turkey), and Amman (Jordan) (Humanitarian Response, 2019). However, this approach prioritized Damascus-based operations and showed preference for pro-government governorates, with less weight and fewer funds given to cross-border operations serving health systems in Aleppo, Idlib, Hama, Rural Damascus, and Dara'a (Humanitarian Response, 2019). The absence of trust between Gaziantep and Damascus meant communications went through Amman. The WoS approach not only failed to redress the particular challenges of the diagnosis and management of TB and contact-tracing in these settings, but humanitarian convoys were unable to provide ATT supplied by the Global Fund to besieged and hard-to-reach areas (Al-Kabbani, 2017; Fouad et al., 2017).

Moreover, the NTP still does not reach crossline to north western Syria. As of June 2019, these non-government controlled areas (NGCAs) include Idlib, northern Hama, western Aleppo, and parts of Latakia — a population of 5.5–6 million (Health Cluster

Turkey Hub, 2018). A WHO evaluation conducted in this area in July 2018 documented 605 cases of TB under treatment (Health Cluster Turkey Hub, 2018). However, based on a prevalence of TB of 21/100 000, this number should be closer to 960 TB patients per year, implying a low case detection rate (Health Cluster Turkey Hub, 2018). In January 2019, Idlib governorate — which only has two TB centers for a population of 3.5 million — documented 307 cases, less than half the expected figure of 733 (Health Cluster Turkey Hub, 2018), underscoring the ongoing barriers to detection. In addition to the insufficiently equipped laboratories and hospitals and the lack trained staff, there are frequent and prolonged shortages of ATT and unreliable local supply chains. Ongoing insecurity, high fuel costs, and poor roads limit not only patient access to healthcare, but also outreach, contract-tracing, and innovative treatment supervision more appropriate to conflict settings, which may include video-DOTS.

Attacks on healthcare

Since the protests started in March 2011, at least 912 healthcare workers have been killed (as of August 2019) (Physicians for Human Rights, 2019), and more than 70% of health facilities in areas under opposition control have been directly targeted (Haar et al., 2018). The widespread destruction of healthcare facilities has limited the number of functioning TB treatment centers and mycobacteriology laboratories. Attrition of medical staff through death, migration, or flight has similarly limited skilled technicians, microbiologists, and TB physicians and nurses (Health Cluster Turkey Hub, 2018; Sahloul et al., 2016). The exodus of an estimated 15 000 doctors including TB clinicians, specialists, and microbiologists has left gaps in the diagnosis, investigation, and management of TB patients (Fouad et al., 2017; Abbara et al., 2018b). This compounds the pre-existing lack of expertise in TB in Syria before 2011, when it had mostly been managed by pulmonologists. In Aleppo between 2012 and 2017, there were no pulmonary or infectious diseases specialists. As of July 2019, there are less than half a dozen microbiologists remaining in the whole of Syria (Abbara et al., 2018b).

Lack of diagnostic capacity

The control of TB depends on the diagnosis of possible cases, availability of uninterrupted treatment, and successful contact-tracing. As protracted conflict makes active case finding challenging, most diagnosis relies on self-presentation. However, TB's non-specific symptoms of cough, weight loss, and fever may result in late presentations or low suspicion for TB. This is compounded by a lack of molecular diagnostic methods such Cepheid GeneXpert, which has a higher sensitivity than smear testing and is recommended by the WHO (WHO, 2015). TB is even more challenging to diagnose in young children who are unable to provide sputum.

Cepheid GeneXpert can provide a result within 2 hours, including the presence of rifampicin resistance (WHO, 2015). The laboratory diagnosis of suspected MDR or XDR TB is particularly important in Syria, given the potential for emergence of drug resistance in besieged areas and detention centres (Abbara et al., 2018a; Cousins, 2014); however, GeneXpert is only available in Damascus. An update on Syria's NTP reports that only the two central laboratories in Homs and Damascus have the ability to culture *Mycobacterium tuberculosis* (Muhjazi et al., 2018), with none in NGCAs, notably Idlib and Aleppo. The mainstay of diagnosis in NGCAs relies on symptoms, chest radiographs, and sputum smear, meaning that those with extrapulmonary TB (EPTB) or with smear-negative pulmonary TB (PTB) and cases of drug resistance may not be diagnosed or are diagnosed late. Despite plans to introduce GeneXpert machines into the two TB centers in Idlib governorate, as of October 2019, these plans are unrealized (Hub. HCT, 2019).

Table 2
Recommendations to address TB, including drug-resistant TB in Syria as the conflict continues.

	Recommendation
(A) Prevention	
TB screening program	Re-establish a screening program in collaboration with the public health authorities to identify contacts of active TB and at-risk populations with LTBI. These would include healthcare workers, those living in IDP camps or collective shelters, and those with particular risk factors, e.g., immunocompromised, diabetics, children.
Latent TB infection treatment	LTBI treatment (either rifampicin/isoniazid for 3 months, isoniazid monotherapy for 6 months) as recommended by the WHO will significantly reduce the risk of reactivation and onward transmission among vulnerable populations.
Active case finding	Screening high-risk populations for active TB for early diagnosis and treatment will help reduce spread. These include IDP, those in detention, and contacts of active TB patients.
Improve nutrition and sanitation	Ensure populations, particularly vulnerable ones (IDP, those under siege, those imprisoned, children) have access to adequate nutrition. Address overcrowding and improve infrastructure.
BCG vaccination	Reinstate BCG vaccination at birth and consider catch-up vaccinations for those who have missed this during the conflict.
(B) Improving diagnosis	
Laboratory capacity	Building microbiology services in general and mycobacterial capacity in particular are key. There are two laboratories in Syria that are able to perform mycobacteriology (Damascus, Homs); however there are none in areas not under government control. As of July 2019, there are plans to open two mycobacteriology laboratories in the north west of Syria (in Idlib and Aleppo governorates).
Novel diagnostics	TB molecular diagnostics, e.g. Cepheid GeneXpert, have been made available by the WHO to lower and middle-income countries to provide rapid diagnostics as an adjunct to sputum smear and can detect cases of drug-resistant TB.
Human resources for health	Invest in the education and training of current laboratory technicians and microbiologists in TB diagnostics.
(C) Improving management	
Access to anti-tuberculous therapy	Ensuring ATT access for patients in prison, under siege, and in NGCAs should be a key function of the Syrian national TB program.
Remote directly observed therapy	Barriers to population movements including roadblocks make patient and health professional movement challenging. Different monitoring strategies including video observed therapy (VOT) could be useful strategies to ensure monitoring.
(D) Population level	
Attacks on healthcare	Attacks on health facilities and healthcare workers impede the ability of the health system to function with consequences for TB.
Prison population	There are over 90 000 prisoners in Syria suffering from conditions ripe for developing TB and drug resistance. Ensure screening for TB and sustained supplies of ATT.
Besieged populations	Around 2.5 million Syrians have been besieged: those now living in IDP camps or displaced to NGCAs must be screened and have access to ATT.

TB, tuberculosis; LTBI, latent TB infection; IDP, internally displaced persons; WHO, World Health Organization; BCG, bacille Calmette–Guérin; ATT, anti-tuberculous treatment; NGCA, non-government controlled areas.

The prolonged duration of TB treatment (at least 6 months for drug-sensitive TB and a minimum of 9 months for drug-resistant TB) and the requirement for a high degree of fidelity to prevent the development of drug resistance mean that DOTS is a key requirement of TB treatment in Syria. Although Syria's NTP has continued to operate out of Damascus, DOTS has been effectively dismantled due to insufficient numbers of trained staff to deliver such programs and the lack of humanitarian access in NGCAs (Muhjazi et al., 2018). Innovations such as video-DOTS are limited by the lack of a consistent supply of ATT in NGCAs.

What can be done to address TB in Syria?

The conflict has created ideal conditions for the transmission of TB and for the cultivation of drug-resistant TB. The challenges of running an NTP during the Syrian conflict have been described (Muhjazi et al., 2018), but among the other health priorities in Syria now, investing in rapid molecular diagnostics and ensuring the immediate and sustained availability of ATT following case confirmation is key. Screening and active case finding must focus on IDPs, prisoners, and the estimated two million Syrians who have lived through siege (Abbara et al., 2018a). The diagnosis and management of drug-resistant TB present particular challenges due to the expertise required, the need for a sustained supply of second- or third-line ATT, the associated drug side-effects, the need for robust diagnostic laboratory support, and the prolonged duration of treatment. Providing support in NGCAs, supporting the training of staff, improving access to healthcare and diagnostics, and open supply chains of ATT are key steps in identifying the scale of drug-resistant TB and managing it.

Table 2 summarizes the recommendations to address TB in Syria. These recommendations were formed through discussion with stakeholders and experts on TB in Syria who work with the WHO, Syria's NTP, and the heads of health directorates and non-governmental organizations (NGOs). These recommendations can be divided into (A) prevention, (B) improving diagnosis, (C) improving management, and (D) population level interventions. Addressing the prevention, early diagnosis (including active case finding and contact-tracing for latent TB infection (LTBI) and active cases), and management of TB are important for TB control. Addressing LTBI is a key aspect of TB control programs in Syria to successfully reduce rates of active TB. Additionally, there are few estimates of LTBI prevalence in Syria, although there are some limited data from refugee screening programs that suggest high rates of LTBI among Syrian refugees (Cookson et al., 2015). Data on LTBI from within Syria are limited; however one study of an internally displaced population in Aleppo reported a figure of 29% (Almekhlef et al., 2016).

Conclusions

TB in Syria, particularly drug-resistant TB, is likely to have been adversely affected by the conflict, consequent large-scale population movements, and attacks on healthcare, which have continued and in some areas have escalated. Official reporting through the NTP likely underestimates the actual rates of TB in Syria, particularly in areas not under government control. As the conflict winds down, TB could appear less of a priority, due to its chronic course, potentially delayed presentation and diagnosis, and relative complexity of management. However, failure to address the drivers of TB and drug resistance during the Syrian conflict will affect the current and future control of TB in Syria, with potential consequences beyond its borders. Strengthening capacity to control TB in Syria will affect other parallel conditions; this is key as attention turns to the post-conflict reconstruction of Syria's decimated health system.

Author contributions

AA, LR, and AS conceptualized the paper. AA, MA, IA, HA, WE-A, and NK contributed to the first draft and subsequent reviews. AA, NK, WE-A, LR, IR, MA, ZS, AT, and AS contributed to further reviews and revisions.

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Conflict of interest

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