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Experiencing syndemic: disentangling the biosocial complexity of tuberculosis through qualitative research

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Abstract

Tuberculosis (TB) remains a major global public health problem that has become a crisis fuelled by HIV and the increasing occurrence of antimicrobial resistance. What has been termed the biosocial nature of TB challenges effective control of the disease. Yet, biosocial interactions involved in the persistence of TB in diverse settings are difficult to systematically account for. The recently developed framework of syndemics provides a way to capture how complex health problems result from the interactions between diseases such as HIV and TB, and harmful social conditions such as unemployment, malnutrition and substance abuse. This article advances the syndemics scholarship by examining health conditions that cluster together with TB in the Russian Federation, by eliciting a set of social processes that precipitate this clustering and exacerbate health outcomes, and by analysing interactions between these health conditions and social processes. To provide an account of this complexity, the article takes a qualitative approach and draws on the perspectives and experiences of people with TB. The results demonstrate emergence of a syndemic of stress, substance abuse, TB and HIV that is sustained by poverty, occupational insecurity, marginalization and isolation. Frictions between the narrow focus of the health care system on TB and the wider syndemic processes in which the lives of many persons with TB are embedded, contribute to poorer health outcomes and increase the risks of developing drug resistance. Finally, the article argues that the large-scale and impersonal forces become embodied as individual pathology through the crucial interface of the ways in which persons experience and make sense of these forces and pathologies. Qualitative research is needed for the adequate analysis of this biosocial complexity in order to provide a solid basis for responses to TB-centred syndemics in various settings.

Keywords: Syndemic; Tuberculosis; Qualitative research

Introduction

Tuberculosis (TB) is one of the top ten causes of death worldwide. It is caused by *Mycobacterium tuberculosis*, which spreads from person to person through inhalation of bacteria and commonly affects the lungs. Despite the existence of effective treatment, TB has remained a global public health problem that now has become a crisis fuelled by the advent of HIV and the increasing occurrence of antimicrobial resistance (Farmer, 1997; Corbett *et al.*, 2003; Chiang *et al.*, 2010). The World Health Organization (WHO) estimates that in 2016 about 40% of deaths among HIV-positive people were from TB and there were 490,000 new cases of multidrug-resistant

tuberculosis (MDR-TB) – that is, TB resistant to at least rifampicin and isoniazid, two of the most important standard anti-TB drugs (WHO, 2017).

On the one hand, the processes that fuel the current TB crisis appear to be biological in nature. Concurrent infection with HIV and TB is associated with more rapidly progressing disease and higher pathogenic load than is a single infection with either agent (Diedrich & Flynn, 2011; Pawlowski *et al.*, 2012). HIV and TB accelerate each other's development: HIV speeds up advancement from latent to active TB, while TB accelerates progression from HIV to AIDS. The notoriously difficult to treat MDR-TB emerges when naturally occurring mutants of *M. tuberculosis* that are less sensitive to anti-TB drugs are selectively favoured in the course of inadequate therapy (Gandhi *et al.*, 2010). That is, if patients receive too few drugs, for too short a period, or receive drugs to which infecting agents are partly resistant, the resistant strains are spared and become predominant in the body. Further, when other individuals are exposed to the mutated bacteria, primary infection with resistant strains of TB may occur (Abubakar *et al.*, 2013).

On the other hand, scientists have long pointed to social processes that contribute to the persistence of TB and more recently, of its deadly convergence with the spread of HIV and antimicrobial resistance (Lönnroth *et al.*, 2009). Poverty, marginalization and stigma, among other circumstances, increase vulnerability to infection, impede access to health care and inhibit ability to adhere to treatment (Keshavjee *et al.*, 2008). Clustering of TB among people who are poor and otherwise disadvantaged has led theorists to offer a biosocial perspective on this disease and associated health problems (Farmer, 1999, 2003). This perspective calls for attention to the large-scale social processes that bind certain individuals and communities to harmful environments with specific negative consequences for their well-being.

Yet, how to actually account for the biosocial complexity involved in the emergence and persistence of concentrated health disadvantage? Because of the considerable difficulties associated with this task, some scholars have focused on identifying social, cultural, historical and political dimensions of tuberculosis, arguing for 'injecting' these dimensions into biomedical research (Simandan, 2017b, p. 563; see also Mason *et al.*, 2017; Simandan, 2017a). Yet, underlying these efforts is a conceptual separation of the 'social' ('how health, illness and medical treatment are understood, interpreted and confronted') and 'biological' ('TB disease') (Mason *et al.*, 2016, p. 206), which makes it hard to analyse how the two interact and mutually shape each other in producing specific health outcomes. Other health research scholars have narrowly focused on the problems of co- and multi-morbidity as co-occurring diseases and other health conditions within a single individual (Weaver *et al.*, 2016). Such studies have resulted in multiple valuable insights on synergistic interactions of disease processes. However, the social conditions that foster and sustain the interactions on the biological level and the ways in which large-scale social forces function to produce specific kinds of health configurations tend to be left out of this scholarship (Manderson & Warren, 2016).

In response to this analytical problem, critical medical anthropologists have introduced the framework of syndemics, which has recently been taken up by other fields, including public health, medicine, psychology and nursing (Singer *et al.*, 2017; Willen *et al.*, 2017). This framework provides a way to capture how complex health problems result from the interactions between epidemic diseases such as HIV and TB and harmful endemic social conditions such as unemployment, malnutrition and substance abuse and fully account for interweaving of biological and social processes. That is, the notion of syndemic goes beyond both adding a layer of 'social' to biomedical inquiry and co- and multi-morbidity in that its defining feature is the presence of two or more health conditions (e.g. infections, chronic non-communicable diseases, mental health problems, toxic exposure and malnutrition) that adversely interact with each other, enhancing vulnerability, and are made more deleterious by experienced inequities (Mendenhall, 2016). One of the most cited examples is the consolidation of substance abuse, violence and AIDS as the SAVA syndemic, identified by researchers who were seeking to make sense of an HIV crisis among urban poor in Hartford, Connecticut (USA) (Singer, 1996).

The present article advances the syndemics scholarship by examining health conditions that cluster together with TB in the Russian Federation, by eliciting a set of social processes that precipitate this clustering and exacerbate resulting health outcomes, and by analysing biosocial interactions between these health conditions and social processes. It takes a comprehensive, syndemic approach to disentangling the complexity involved in TB persistence in the country that is one of the most affected by MDR-TB (almost half of the 490,000 new cases of MRD-TB estimated by the WHO in 2016 were located in India, China and Russia) and home to one of the fastest-growing HIV epidemics in the world (Field, 2004). To provide an account of this complexity, the article draws on the experiences of people with TB. In-depth exploration of their experiences allows eliciting how large-scale and impersonal forces become embodied as individual pathology. Thus, the primary emphasis is not on specifying disease–disease interaction about which comparatively more is known due to advances in co- and multi-morbidity scholarship, and not on identifying ‘social dimensions’ of TB, but on mapping socio-biological interactions to inform subsequent research and health interventions.

Importantly, syndemic relationships between TB and other health conditions are context-specific. For example, medical anthropologist Mark Nichter proposed a syndemic set of relationships around which TB might be composed: ‘1) poverty leads to work migration far from home; (2) loneliness, the drudgery of the job and being paid every few weeks lends itself to binge drinking and risky sex in an environment where prostitution flourishes; (3) this leads to sexually transmitted infections such as HIV; (4) rising rates of HIV lead to corresponding rising rates of TB; (5) poor adherence to TB which medications occurs after a few months of home-based treatment (when symptoms abate) among patients who return to migrant labour far from medicine distribution sites; (6) poor management of those seeking treatment for HIV and TB leads to increases in drug-resistant TB; and so on’ (Nichter, 2008, p. 158)

Yet clearly, the role of work migration in a TB-centred syndemic can vary between settings, the weight of the sexual route in overall HIV transmission can be different and the responses of health care systems diverge. Therefore it is crucial to examine the processes whereby syndemics are distinctively configured in diverse settings both to improve the understanding of convergence between disease and social suffering and to guide adequate responses to syndemics.

In what follows, the settings where the study was conducted are presented and the methodology employed is described. Then the results section charts the adverse social processes intertwined with the lives of individuals who have developed TB and health conditions clustered around TB, and the corresponding implications for relations between those individuals and health care. Extracts from interviews with TB patients are used to illustrate how a syndemic of stress, substance abuse, TB and HIV emerges and is sustained by poverty, occupational insecurity, marginalization and isolation. The results section also highlights how frictions between the narrow focus of the health care system on TB and wider syndemic processes in which the life situations of many persons with TB are embedded further contribute to poorer health outcomes and increase the risks of developing drug resistance. Finally, the implications of these results for adequate response to the syndemic and for developing appropriate research programmes for understanding syndemics are discussed.

Methods

Background

Societal transformations accompanying the disintegration of the USSR in the 1990s have profoundly impacted citizens’ health and the health care system in the Russian Federation. A brief outline of these developments is important to understand the contemporary TB situation in the country. Throughout the societal turmoil associated with the end of the communist regime health deterioration swept through Russia. One indicator of this was a dramatic rise in premature mortality, particularly among males of working age, whose life expectancy dropped from 63.8 in

1990 to 57.6 years in 1994 (WHO Regional Office for Europe, 2016). Scholars have identified societal change, including the breakdown of familiar institutions, severe economic crisis and absence of safety nets, in combination with an increase in consumption and binge drinking of alcohol in the context of severe stress, as driving the unprecedented decline in health following the end of the USSR (Cockerham, 1999; Bobak *et al.*, 2000; Cornia & Paniccià, 2000; Nemtsov, 2002).

Concurrently, previous achievements in TB control that drove the incidence of TB down to 34 reported cases per 100,000 by 1991 were reversed, with TB rates tripling to 90.7 reported cases per 100,000 in 2000 (Perelman, 2000). The health care system was starved of funds, materials and personnel, and its ability to adequately treat persons with TB decreased, while in the context of insecurity and impoverishment, the numbers of those in need of treatment increased. After peaking in 2000, TB incidence has been declining. Although the WHO (2017) estimated 66 cases per 100,000 in 2016, this trend masks a steady rise in co-infections with TB and HIV (an estimated 13 cases per 100,000 in 2016), with the spread of HIV driven initially by injection drug use, as well as a continuous rise in drug-resistant cases (an estimated 44 cases of TB resistant to at least rifampicin, one of the most important TB drugs, in 2016). The foundation of this dynamic was laid by the deterioration of TB care, including shortages of TB drugs, in the 1990s. Russia, then, is a hotspot of the dangerous convergence of TB, HIV and antimicrobial resistance, which makes it vital to understand the interconnected social and health conditions that fuel this convergence (Toungousova *et al.*, 2006; Cohen, 2017).

Setting

This study was conducted in the Russian region of Tomsk Oblast in Western Siberia. Tomsk Oblast has a population of approximately 1.2 million, of whom half live in Tomsk City with the remainder scattered over a 316,900 km² area. Over recent years Tomsk Oblast has served as a pilot area for various TB control initiatives, including an international partnership between Tomsk Oblast TB Services/TOTB and Partners in Health.

Russia's Ministry of Health (MoH) is responsible for developing state policy and regulatory mechanisms for TB control. Further down the line, the regional authorities are responsible for the organization of specialized medical care provided in regional TB clinics (also called dispensaries or pulmonology medical centres). The pulmonology medical centre located in Tomsk City has the following department types: outpatient departments for adults and children, a home care department, a day care department, inpatient departments for adults and children split into sub-departments for drug-susceptible TB and MDR-TB and a diagnostic department that includes a laboratory, X-ray cabinets and functional diagnostics. The Tomsk pulmonology medical centre has a branch with a similar structure located in the north of Tomsk Oblast. Lastly, at the municipality level, there are various city hospitals, including specialized hospitals for infectious diseases such as TB. Facilities providing TB care are financed only from the federal budget. Resources are allocated on the basis of previous budgets, which are based on capacity data such as number of beds (Popovich *et al.*, 2011). Most patients, especially those with the open form of TB, poor health and comorbidities, or who experience severe side-effects from treatment, are hospitalized for at least 2–4 months. Their subsequent treatment is at either the outpatient or day care departments.

Study design, data collection and participants

This exploratory study took a qualitative approach to mapping the syndemic interactions involved in TB persistence in a Russian region, and in doing so, relied on the perspectives of TB patients. This allowed an understanding of how specific social conditions become experienced as adverse by individuals; how this experienced adversity interferes with individuals' health, making them vulnerable to TB, complicating recovery and producing new societal threats such as drug

resistance; and how the health conditions of TB patients exacerbate the social conditions in which they find themselves.

Data collection involved narrative interviews (Riessman, 2008) with 27 persons diagnosed with TB who were using treatment services located in Tomsk Oblast. The informants were nine female patients and eighteen male patients, aged 20–58. The interviews focused on the entire illness trajectory and encouraged informants to tell their stories of becoming sick and coping with TB from their own perspective, with minimal interference from the interviewer. Additionally, three phthisiologists (TB physicians) working in Tomsk Oblast's TB services were interviewed, using semi-structured questionnaires, to obtain additional insights for interpreting patients' stories and more in-depth data on TB care practices and functioning.

All interviews were conducted by WB in English with the help of a translator, audio-recorded with the permission of the participants and transcribed verbatim. Preliminary results of the interviews were regularly discussed with the rest of the research team to inform subsequent interviews and highlight points that required further exploration. All informants provided written informed consent for participation in this study, which was reviewed by Siberian State Medical University Research Ethics Committee.

Data analysis

Interview transcripts and notes generated during the fieldwork were read and discussed by all authors, with the focus on eliciting central themes in the informants' stories about contracting and coping with TB and comparing them across patients and TB physicians. Emerging patterns were used to generate codes that, after initial testing and refining, were applied to the entire dataset for systematic analysis (Boyatzis, 1998). Through coding, a set of themes was developed that emerged from the data and was informed by the existing literature. The codes, themes and analysis process itself were regularly discussed by all authors and differences identified and reconciled.

The results section elaborates on the set of themes developed to delineate elements of a syndemic in Russia that involves TB as its core component and the relationships between these elements. Because of the exploratory and qualitative nature of the study, the focus in this article is not on exact numbers but on patterns in experiences and meaning- and decision-making. Therefore, the data on the numbers of cases where a certain theme is pertinent are given in general terms, such as 'none', 'a few', 'many' and 'most'. For confidentiality, the informants are represented using codes. For example, the coding I37F#1 follows the format: department (I/O)/age/gender(M/F)/serial number of the interview. The 'I' stands for inpatient department and the 'O' for outpatient department. The physicians interviewed are referred to as 'TB care professional'.

Results

Poverty, occupational insecurity and stress

The stories of TB patients strongly conveyed the stressful nature of their daily life: one that largely had to do with poverty and occupational insecurity. For many TB patients who participated in this study work was a major part of life, as it was the first and sometimes only activity they mentioned when asked about their life before getting sick. They generally had a practical job, such as a cleaner, truck driver or builder. A few explicitly said their job was unofficial, while many others described such job conditions that indicated they did not receive any form of employee protection. This became apparent, for instance, when informants said that they were afraid to be fired when they missed some days of work:

I had work and I couldn't miss two days. Because it was unofficial work. ... I worked at a gas station. It's not an official job, so I can already be fired if I only miss a few days. (I27M#23)

This informant further explained that the fear of being fired prevented him from seeking diagnosis and appropriate care, since when he experienced what he called ‘pneumonia with a bad fever’ several times, he ‘just called an ambulance and the doctor would come ... and give some pills and injections’. The informant narrated that the medication provided was enough for him to recover and continue working. However, when he eventually had a fever of 40 degrees for an entire month, he had to stay at home for a week and was indeed fired. Ultimately, he was diagnosed with MDR-TB. While barriers to seeking medical help are analysed in detail in the last part of the Results section, it is important to highlight here that ‘calling the ambulance’ proved to be a widespread strategy to avoid time-consuming interactions with the health care system and to patch oneself up to continue with daily duties.

A story of another informant demonstrates that the precarious job situation not only delayed seeking medical help, but also often facilitated self-medication, which constituted a health hazard in itself. This informant began his narrative with telling how he became sick in 2011:

Before I had tuberculosis for the first time, I had pneumonia. I was at the hospital, but the head of my job called me and said that I had to go to work and that if I would not come, he would fire me. After that, I went to my work. (I35M#17)

Four months later the informant started coughing again and turned to self-medicating:

I didn’t go to the doctor by myself because I thought that it was pneumonia again. I knew the treatment of pneumonia so I tried to treat it by myself. (I35M#17)

After symptoms worsened, the informant did visit a doctor, MDR-TB was diagnosed and he was treated in the inpatient department for one year. Eventually, his condition improved, and he was discharged and finished his treatment at the day care department. But the disease returned after the informant decided to take another, higher-paid but more physically challenging job:

... some people called me to work at the railroad, there the salary was very high. Therefore I decided to work there, in the north ... because of the good money ... The working conditions were really bad there because I had very long working days and it was in the street. The weather was really bad. At my new job I got tuberculosis again. (I35M#17)

The need to secure an income was not conducive to recovering from MDR-TB for this informant and played a role in the relapse. In several other examples, this need to secure an income interfered with the treatment itself – for example, in the case of a woman (I27F#25) who was initially infected with MDR-TB by her sister-in-law, with whom she shared a room. After receiving her diagnosis, this woman was admitted to the inpatient department and at the time of this research had been treated for 4 months. In this period, she had gone back and forth between the day care department and the inpatient department four times. It was her own decision to go to the day care department each time, because she wanted to work. Each time her condition worsened and she went back to the inpatient department.

Hard and stressful work was not limited to employment; it was present in family lives and especially affected older women, who tended to take upon themselves the burden of numerous care tasks. For example, an informant (I58F#8) narrated that after her husband had died a long time ago because of alcoholism, and she had raised their three children on her own, she was now taking care of her grandchildren, because her daughter and son-in-law were working around the clock to earn money to buy an apartment. The necessity of combining a job with her role as the only caregiver in the context of resource scarcity was stressful:

First I wake up really early, at 5 am. I clean up my apartment. Then I go to work. I don’t have to stay at my job for a specific period time. After I am finished, I can go. After that, I take care of my grandchildren. I am still with them till the late evening. Because of this,

I was paying a lot of attention to my grandchildren, but not to myself. ... I don't have a personal life because of all those things I have to do. (I58F#8)

Many informants emphasized the need to continue working to make ends meet and support their families. Being healthy was considered an instrumental value – a means to work. Poverty and job insecurity were forcing those subjected to them into a survival mode: as long as the disease did not 'stand in the way' of making money and fulfilling their tasks, there was no need to visit a doctor. Tuberculosis symptoms were ignored or treated with self-administered medication, including antibiotics, and medical help was sought in an advanced stage, which allowed the TB to progress and risked spreading the disease to others before treatment was eventually initiated. Furthermore, these social circumstances pushed informants to accept hazardous working conditions and long working days, which detrimentally influenced their health generally. Finally, not being able to work due to the disease had in turn increased poverty, in a vicious circle.

Marginalization, isolation and substance abuse

Closely connected to the nexus of poverty, occupational insecurity and stress was another detrimental nexus of marginalization, isolation and substance abuse. Tuberculosis care professionals who shared their experiences with the study team estimated that more than half of their patients had abused drugs or alcohol to some extent. Many TB patients interviewed admitted experiencing addiction problems at certain points in their lives.

Some informants with a history of drug and/or alcohol abuse described how they turned to these substances after adverse life events, often family-related, and in situations of lack of support from others. Illustrative were the examples of a woman (I56F#13) who began abusing alcohol when her 15-year-old son was incarcerated and conveyed during the interview feeling alone with her worries, and of a man (I30M#7) who, having no social contacts apart from his alcohol-addicted brother, began abusing alcohol after the death of his wife and the removal of his children from the home by the juvenile service.

Other informants with addiction history commonly positioned the origin of these addictions in the company of people who engaged in abusing drugs and alcohol. It was being surrounded by, in the words of a few informants, 'bad company' that they first initiated drug or excessive alcohol use. In extreme cases, being part of bad company involved criminal activities and eventually led to incarceration.

The story of one person with TB provides a vivid illustration of the relationship between substance abuse and TB in the wider adverse social context. He explained that he initially started using injection drugs in the company of a criminal group:

I started using drugs in the 1990s, before I got in prison. It was because of my community, I was part of an organized crime group, they were using drugs. I was part of that. (I30M#12)

He eventually became infected with HIV through sharing injection equipment and in 1996 was incarcerated for 12 years. He described his time in the prison in the following way, explaining how he became sick with TB:

In 1997, because I was beaten by the administration, I cut one of the administrators with a knife. Therefore I was transferred to a special prison with a stricter regime. ... I was staying at a kind of barrack where I only had concrete walls and nothing else, no bed, no anything, only walls. ... In the late nineties, the conditions were really bad. For instance in a room for eight people, there could stay around 30 or 40 people, so it was really crowded. Later, in the 21st century, it became better. ... Because of the prisoners' law [talking about the 1990s], the good [obedient] persons who have tuberculosis could not be isolated from the community, so sometimes the prisoners administration put sick people with tuberculosis in the rooms with people in the prisons that they don't like. And I was one of the prisoners that

had a conflict with the administration ... After I was free, I used a lot of drugs. The drugs were the main reason the tuberculosis progressed. I realized this and stopped using drugs for 3 months and got here [the inpatient department] to get treatment. (I30M#12)

The story of this informant is presented here in detail to illustrate how drug abuse led to HIV and together with violent prison conditions produced a TB infection that upon medical examination was a multiple-drug-resistant kind. The narrative of bad company, often in combination with stress and isolation from broader society, featured also in the stories of those informants who wanted to explain why they proceeded with, or returned to, substance abuse. A man who had also served a sentence in prison and had HIV shared that he originally used injection drugs to 'decrease stress levels' and returned to this practice despite 'being clean' for the 11 years he spent in prison:

I was in a difficult situation. I wanted to decrease pain. There's no prospect for me. I worked in the repairing industry in an apartment with my friends. The problem was that I did my job, but the owner didn't pay for my work. I made money to live, but I didn't receive it. I felt so bad, because it didn't work. ... 'A pig will always find mud.' There were people in my community who were using drugs as well. Most of them were in prison too. ... I was like them. Then, I couldn't stop. (I40M#6)

The bad company in informants' stories appeared to be concentrated among the economically disadvantaged and to offer a way to deal with stress and lack of prospects for the future, at the same time enhancing the isolation of the members from the rest of society. Simultaneously substance abuse facilitates individuals' slide into poverty and marginalization by interfering with study and work and therefore narrows opportunities to secure sufficient income. One TB patient was an example of slowly gravitating towards what can be characterized as a marginalized state:

I studied at school for 11 years and after that I went to college. After college, I went to university. ... The problem with alcohol started in the fourth year when I was a student. Don't know why I started. I started drinking with friends on the weekends, holidays. After that more and more often. And then it was very often. When I took alcohol for a long period, I started having problems with the law, with the university. Some fights. I stopped university after the fifth year. (I39M#20)

After several referrals to a rehabilitation centre, arranged by his parents, he continued drinking, began using injection drugs, partnered with a woman who also had drug and alcohol addiction, and eventually became infected with HIV. Infection with TB soon landed into this combination.

Overall, the processes of isolation and marginalization were not limited to the experiences of those TB patients who had a history of substance abuse. More generally, the majority of TB patients interviewed felt that they came from a 'lower social class' and rarely reported having any contact with those who had more means, thereby conveying a sense of isolation or being locked up in their segment of society.

Barriers to health care and alienation from social support

Barriers to health care experienced by those infected with TB were closely related to the conflation of poverty, stress, substance abuse and marginalization. They arose from frictions between the adverse life conditions of TB sufferers and the functioning of the health care system, were distributed throughout the patient trajectory and contributed to poorer health outcomes and increased risks of developing drug resistance.

Many TB patients interviewed highlighted the difficulty of entering TB care. On the one hand, this difficulty was associated with the patients themselves and the circumstances they were in, including precarious employment. As highlighted in the previous sections, many initially responded to TB symptoms with self-treatment because other pressing priorities took precedence

over making the investments necessary to reach a health care professional. On the other hand, some characteristics of the functioning of the health care system appeared to deter those in need of medical help from seeking it. One of the TB care professionals summed up how this could occur:

All care is free of charge. However, it is sometimes very difficult to enter a free hospital or ambulatory care, because of the long queues in the reception. It takes a long time before you can get an appointment with a doctor. Patients are tired of waiting. Some people just go to the private hospital, but you need to have the financial resources for that. Many people in Russia do not like to go to the doctor at all, which is one of the reasons why patients wait so long and enter in a weak condition.

Treatment trajectories shared by TB patients corroborate this account and indicate that apart from waiting lists, patients were often deterred from seeking care by difficulties in navigating the complex referral system and collecting the necessary documents, including the test results. For example, a person who had had TB previously and was familiar with TB treatment routines still experienced difficulties in accessing treatment when he began coughing badly again, despite being highly motivated and persistent:

I wanted to take some analysis there [the outpatient department] to go to this hospital [the inpatient department]. But they said that I couldn't take analysis there, because I should go to my general practitioner and take analysis there. After that, I tried to get the documents to go to the hospital. However, there were many problems. Some doctors sent me to another doctor and at the end I went to the private department of a hospital and made tests with my own money. ... With these tests, I went to the dispensary and on the X-ray they had seen that I had tuberculosis. Then they sent me to this hospital. (I35M#17)

These interactions between the patient and health care system lasted for about 2 months, after which treatment was initiated. Since this informant did have the means to pay, he was able to get an examination at a private clinic and cut through the bureaucratic organization of the public health care system that he did not know how to navigate.

Barriers to health care arose because of the alienation of the bureaucratic organization of health care from the realities of sick people's lives. These barriers disproportionately affected the poor and isolated because they did not have the financial means to enter TB care via private health care and lacked the social capital, such as contacts in the health care system, to avoid the bureaucracy. Many informants 'did not like to visit a doctor' and attempted to treat themselves, only seeking professional medical help at a very late stage when they were not able to function anymore and had to be delivered to the hospital by ambulance. This is illustrated by the story of the woman already mentioned:

I started to use a lot of alcohol when my son went to prison. He had a fight with his neighbour. When he was in prison, he was only 15 years old. ... I was using alcohol a lot and at that time I got a cough and fever for quite a while and lost weight. ... I have chronic bronchitis. Every spring and autumn I have a relapse. I am fine with it and I don't go to the doctor with these relapses. So I treat myself. ... The main reason I eventually called the ambulance wasn't because of the blood in the cough, it was because I couldn't walk for whatever reason. I couldn't go to the hospital because I didn't have the chest X-ray. They made the analysis of the mucus and they transferred me here [to the inpatient department]. (I56F#13)

The emergency condition of this person with TB and others who followed the same course required them to be treated at the inpatient department, whereas in earlier stages, for example when TB was not yet in its open form, they could have had more control over the conditions and

location of their treatment. Furthermore, severely progressed TB and a generally poor health condition negatively affected treatment prospects.

After patients entered TB care, the identified nexus of adverse biological and social conditions continued to affect their health prospects. For example, substance abuse both further weakened the health of the patients and facilitated irregular treatment with TB drugs, which created risks of development of drug resistance. Often substance abuse among the TB patients interviewed appeared to be a reaction to, or way out of, stress, including treatment-related stress, as suggested by a patient with a history of excessive alcohol use who had a relapse of MDR-TB:

It's a psychological challenge when you get a bad test results. When you have bad analyses again and again, I go to my alcohol and drink it because of the bad test results. When I drink alcohol, all my problems go away. (I35M#17)

In some cases, the informants specifically mentioned that they did not have anyone to turn to for support, or, if they did have a community around them, members of that community were also using drugs or drinking alcohol excessively. The existence of a supportive social support network and having resources to survive in times of prolonged illness was paramount for following a long course of treatment, which is especially tedious for MDR-TB and requires strong motivation and the ability to focus on adherence. The narrative of a young woman, who according to TB care professionals had a history of non-compliance with treatment, provides a vivid illustration of this necessity:

I don't have anybody, I only have my mother but I don't have a lot of contact with her. I don't have any place to go when I go out of here. I don't have any home, any apartment. I only receive a pension, but the amount of this pension is really low. It's only the cost of the rent of an apartment. If I would rent, I wouldn't have any money left, because of the small amount. ... My parents are alcohol addicts and they are not interested in my life. When I was 6 years old, my mother went away from the family. I grew up with my grandmother. They used me to pay the apartment. They took my money sometimes. My mother knows about my disease and my surgeries, but she is not interested in my life and I don't have anywhere to go. ... It is tough to me. Nobody will help. At the end of treatment, I will only receive pension from the government. That's all. Nothing else. (I29F#26)

No clear prospect of a better future once this informant recovers, no social network to rely on and lack of social services to resort to in this difficult situation were detrimental to her will to actively work for recovery.

In these ways, the identified forces of poverty, insecurity, marginalization and isolation not only facilitated the clustering of TB with stress, substance abuse and HIV and selectively pre-disposed certain people to ill health, but also worked to decrease TB patients' chances of full recovery and facilitated the development and spread of MDR-TB.

Discussion

The disease histories of persons with TB and the insights of TB physicians interviewed in this study suggest a complex syndemic nexus of interconnections between health conditions that cluster together with TB in the Russian context and a set of social processes that precipitate this clustering and exacerbate health outcomes.

On the one hand, clustering of stress, substance abuse, HIV and TB come to the fore. They adversely interact with each other, enhancing the vulnerability of individuals and aggravating health outcomes. A negative mutual influence of these health conditions has been indicated in the biomedical literature. Associations between psychological stress and disease, including infectious diseases such as HIV, upper respiratory tract infections and herpes viral infections, have been demonstrated (Vedhara & Irwin, 2005). The findings suggest that stressors can

enhance risk for developing infectious disease, prolong disease episodes and, more generally, are linked with morbidity and mortality (Glaser & Kiecolt-Glaser, 2005). Stressful events are thought to influence the pathogenesis of disease by causing negative affective states such as anxiety and depression, which in turn directly impact biological processes and/or behavioural patterns (Cohen *et al.*, 2007). Biological pathways that link stress and disease include stressor-elicited endocrine and immune responses, which increase risk for disease. The 'behavioural changes' pathway linking stress and disease involves coping and adaptation responses such as substance abuse, less exercise and sleep and decreased adherence to treatment regimens. Importantly, exposure to chronic stress (e.g. unemployment) is considered the most toxic form of stress because of the increased likelihood that it will result in prolonged or permanent changes in the emotional, physiological and behavioural responses that influence susceptibility to, and the course of, disease (McEwen, 1998).

Substance abuse is another core component of the health conditions clustered around TB in Russia and, as already mentioned, is linked to stress. Further, causal relationships specifically for alcohol have been suggested by recent studies between alcohol consumption and the incidence of infectious diseases such as TB and HIV/AIDS (Rehm *et al.*, 2009; WHO, 2014). The harmful use of alcohol alters immune function, enabling the development of TB, with this effect becoming more pronounced with heavy drinking (Lönnroth *et al.*, 2008). Alcohol use is also associated with a greater risk of MDR-TB (Miller *et al.*, 2012). The association between alcohol consumption and HIV infection may be facilitated through the increased risk of unsafe sexual behaviour. In addition, a clear deleterious effect of alcohol consumption on the course of HIV has been documented (Azar *et al.*, 2010; Baum *et al.*, 2010). The same can be said for the use of illegal drugs, including injection drugs, which, apart from increasing host susceptibility to infections, make injection drug users highly susceptible to HIV and blood-borne diseases by the shared use of contaminated needles (Friedman *et al.*, 2006). Finally, one of the most well researched connections is that between HIV and TB, where HIV interferes with the immune response to allow the infectious agent to progress from latent to active TB and freely replicate; at the same time, having TB accelerates the progression of HIV disease (Mayer & Duker Hamilton, 2010).

On the other hand, this study highlights that the clustering of stress, substance abuse, HIV and TB in Tomsk Oblast is shaped and driven by a set of social processes that entwine poverty, occupational insecurity, isolation and marginalization. Lack of resources forces people into a survival mode in which personal health becomes subordinate to earning a living and taking care of the family. The strain of surviving is exacerbated by a lack of secure employment options, so that those who need to earn money must grasp at unofficial employment with no protection in case of illness and experience continuous worry about being dismissed at a moment's notice. With bleak prospects, individuals and families become locked in their daily struggle and, in many cases, in communities brought together by harmful practices such as substance abuse. Being isolated in adverse conditions takes an extreme form for those who end up incarcerated in the Russian penitentiary system, where stress, violence and generally poor living conditions have been reported (Bobrik *et al.*, 2005; Drobniewski *et al.*, 2005). Such living can be described as taking place on the margins of society, in almost complete alienation from health care and social support.

It must be highlighted that the connections between the health conditions and social processes described are not one-directional; rather, the elements that together form a TB-centred syndemic in Russia mutually influence each other. For example, where earnings are low, heavy drinking may further impoverish the drinker, the drinker's family or a whole community (Schmidt *et al.*, 2010; De Silva *et al.*, 2011). Or, contracting HIV may contribute to further marginalization of an individual if the disease status becomes known (Kiriazova *et al.*, 2017), with the increased marginalization then feeding back into the person's health condition because, as research has reported, the care given is likely to be inferior, or the access to health care worsened, if the patient is seen as someone with a degraded status (Santana, 2002; Mitchell *et al.*, 2009).

The outline of the syndemic presented in this article must be interpreted with caution. It is useful for grasping the mutually reinforcing nature of the health and social crises that face those with the least means to deal with them. This entails that TB in Russia is a problem that is not entirely separable from stress, substance abuse and HIV and from the context of a perpetuating configuration of poverty, occupational insecurity, isolation and marginalization. Yet, individuals who become sick with TB may differ from each other in their position in relation to this syndemic nexus. Moreover, although much of the problem of TB is confined to the poor and otherwise marginalized, *M. tuberculosis* does reach those who appear to be far removed from the core of the syndemic. For example, one participant of this study was markedly different from others. With a well-paid job and high educational background, he actively sought medical help as soon as he experienced the first symptoms of TB and was able to successfully navigate the intricacies of the health care system. When MDR-TB was diagnosed, a separate apartment was arranged by his family for him, family and friends delivered food and comfort and he was on paid sick leave and able to focus on recovering. Nonetheless, the general persistence of TB in the Russian setting is fuelled by the syndemic interactions mapped in this article and requires a response that is attuned to these interactions.

Currently the response is insufficient because the health care system focuses narrowly on treating TB, while clustered health conditions and, especially, the larger social processes involved in the syndemic remain generally unaddressed despite multiple attempts, especially in Tomsk Oblast, to find more comprehensive models of care. Moreover, this article shows that lack of attention to the social conditions in which persons with TB find themselves results in frictions between the world of health care and that of patients, with patients having difficulties in navigating the complexities of the health care system and in following long and tedious treatment in the context of their daily struggles. These frictions are directly related to the antimicrobial resistance that is increasingly complicating the situation around TB in Russia because they encourage individuals to resort to self-treatment, including self-treatment with antibiotics, and refrain from attempts to seek medical help until the moment they have to be delivered to the hospital by ambulance. These frictions also limit individuals' ability to adhere to treatment. The rise of drug-resistant TB has been facilitated by the lack of recognition of, and appropriate response to, the stress – the substance abuse–HIV–TB syndemic. Drug resistance has now become an element of this syndemic on its own.

Most importantly, this study demonstrates how syndemic-forming health and social conditions are experienced and made sense of by those who end up affected by their adverse interconnections. It attests to large-scale and impersonal forces becoming embodied as individual pathology through the crucial interface of the ways in which persons experience and make sense of these forces and pathologies. That is, the connection between health conditions that cluster together and a set of social processes that precipitate this clustering and exacerbate health inequalities necessarily involves people who experience anxiety, feel hopeless or disoriented or are determined to provide for their family and crushed by their inability to do so.

In conclusion, the framework of syndemics enables accounting for the biosocial complexity involved in the persistence of TB and for the emergence of novel related health problems such as MDR-TB. Drawing on the syndemics framework, this study demonstrates how in Russia a syndemic of stress, substance abuse, HIV and TB arises and is sustained by poverty, occupational insecurity, marginalization and isolation. The adverse interactions taking place between the health conditions identified are fuelled and aggravated by social disadvantages. The narrow focus of the health care system on treating TB comes into conflict with the wider syndemic processes fuelling TB, while this tension itself further contributes to poorer health outcomes and facilitates the development of drug resistance.

Further research on TB-centred syndemics, including the syndemic in Russia, will need to involve both qualitative and quantitative methodologies. Quantitative studies are crucial for unravelling how epidemics and large-scale social forces interact at both the population and

individual levels to worsen the burden of disease. Analysts have recently argued for developing new quantitative multilevel models that can account for both how individual-level risk factors interact to affect disease outcomes and how large-scale social forces condition the distribution of individual-level risk factors or expedite their interaction and translation into disease states (Tsai *et al.*, 2017). Yet qualitative social science studies have an equally central role to play in the efforts to understand and respond to syndemics, because they are uniquely suited to exploring how those who are affected by the syndemics experience and make sense of syndemic-forming health and social conditions. In-depth engagement with the lives and environments of those who are affected by TB makes visible the range of context-specific biosocial interactions involved in TB-centred syndemics. Inclusive interdisciplinary inquiry that builds on such a variety of insights is necessary to provide a solid basis for adequate responses to the TB-centred syndemics in different settings.

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