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ORIGINAL RESEARCH

Multidrug-resistant tuberculosis in Moldova and the Former Yugoslav Republic of Macedonia: The importance of health system governance

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Abstract

Aim: Multidrug-resistant tuberculosis (MDR-TB) arises where treatment is interrupted or inadequate, when patients are treated inappropriately, or when an individual has impaired immune function, which can lead to a rapid progression from infection with an MDR-strain to disease. This study examines the role of health systems in amplifying or preventing the development of MDR-TB.
Methods: We present two comparative studies, which were undertaken in The Former Yugoslav Republic of Macedonia (TFYR Macedonia) and Moldova.
Results: The findings reveal several health systems-level factors that contribute to the different rates of MDR-TB observed in these two countries, including: pre-existing burden of disease; organization of the health system, with the existence of parallel systems; power dynamics among policy makers and disease programmes; and the accountability & effectiveness of programme oversight.
Conclusions: The findings do not offer a universal template for health system reform but do identify specific factors that may be contributing to the epidemic and are worthy of further attention in the two countries.

Keywords: drug-resistance, Europe, health systems, MDR-TB, Moldova, The Former Yugoslav Republic of Macedonia, tuberculosis.

Conflicts of interest: None.

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Introduction

Multi-drug resistant tuberculosis (MDR-TB) is now a major problem in parts of Europe (1). Resistance arises when treatment regimens are interrupted or inadequate or when treatment is blind to the sensitivity of infecting organisms, allowing bacilli resistant to a single drug to reproduce. These conditions are most often found where health systems are weak (2) or inappropriately designed (3), providing some treatment, but not in a way that ensures that it is taken appropriately.

In this study we use a comparative case design to gain insights into why two otherwise similar countries, Moldova and TFYR Macedonia, differ significantly in their burdens of TB and patterns of drug-resistance (Table 1).

Table 1. Surveillance data from Macedonia, Moldova, and the European region in 2013 (*source:* European Center for Disease Prevention and Control)

INDICATOR		Macedonia	Moldova	Non-EU/EEA European Region
New TB cases		346	4,203	194,913
	Success n (%)	298 (86.1)	3,205 (76.3)	146,404 (75.1)
	Died n (%)	28 (8.1)	418 (9.9)	14,203 (7.3)
	Failed n (%)	3 (0.9)	125 (3.0)	12,312 (6.3)
	Lost to follow up n (%)	16 (4.6)	331 (7.9)	12,843 (6.6)
	Not evaluated n (%)	1 (0.3)	124 (3.0)	9,151 (4.7)
Laboratory confirmed		188	2,695	117,802
Drug sensitivity testing n (% of those confirmed)		179 (95.2)	2,317 (86.0)	108,746 (92.3)
MDR-TB n (% of those confirmed)		1 (0.5)	912 (33.8)	33,686 (30.9)
XDR-TB n (% of those confirmed)		0	35 (1.2)	393 (0.3)
TB case notification rate / 100,000 population		15.3	144.8	12.7

The notification rate in Moldova per 100,000 population is almost ten times higher than in Macedonia, where it is only slightly higher than the non-EU/EEA countries of Europe. The treatment success rate is about ten percentage points higher in Macedonia than Moldova. A third of laboratory confirmed infections in Moldova (n=912) in 2013 were multi-drug resistant (MDR), with only one case in Macedonia. In the same year Moldova had 35 cases that were extensively drug resistant (XDR), while Macedonia had none.

Methods

We undertook an in-depth comparative case study (4). Data were triangulated from a range of sources including documentary evidence, such as statistical reports, action plans, and activity reports, and interviews with key informants. Key informants were identified using theoretical and snowball sampling to obtain a broad range of insights and perspectives (5). Interviews were semi-structured, including open-ended questions, and were recorded, with contemporaneous notes taken. Interviews continued until data saturation was achieved. Field notes were kept throughout the research.

Letters were sent to key informants outlining the purpose of the research. This sought to ensure "buy-in", both at individual and organizational levels. An initial conceptual framework, based on a literature review, was developed to identify systems-level drivers of MDR-TB but then refined during the interviews.

We interviewed 23 (100% response) informants in Macedonia, and 20 (55.6% response, 11% declined or cancelled, 33% did not respond) in Moldova. Details of those interviewed are presented in Table 2. However, data saturation was achieved in both countries, with no new

themes arising after about 15 interviews, although further clarification and factual information was obtained in subsequent interviews. The participants were equally open, reflective and critical in both countries.

Table 2. Characteristics of those interviewed

CATEGORY	Macedonia (n=23)	Moldova (n=20)
Stewardship ***(Leadership responsibilities within the health system)***	Senior managers within the TB system	Vice-minister of health
	Senior managers & directors from the Ministry of Health	Hospital directors
	Former Deputy Minister of Health	Senior administrators in the penitentiary health sector
	National Health Insurance Fund	Government administrators / managers
	n= 10	*n=10*
Service delivery ***(Responsibility for service provision within the health system)***	TB physicians	TB physicians
	HIV/AIDS physicians	General physicians
	TB patronage & public health nurses	TB patronage & public health nurses
	Prison health care staff	Pharmacists
	n= 10	*n=6*
Non-government (Representatives from various non-government organisations, with a defined focus, work or interest in TB issues)	Non-governmental organization working with vulnerable populations	Community agencies working with prisoners
	Global Fund country office	WHO country representative
	National physicians association	Academic specialist in public health
	n= 3	*n=4*

This study received approval from the ethics committee of the London School of Hygiene & Tropical Medicine and from corresponding ethics committees in each country. Informed consent was obtained from each participant, prior to the initiation of data collection. All information was made available to participants in their language of choice.

Results

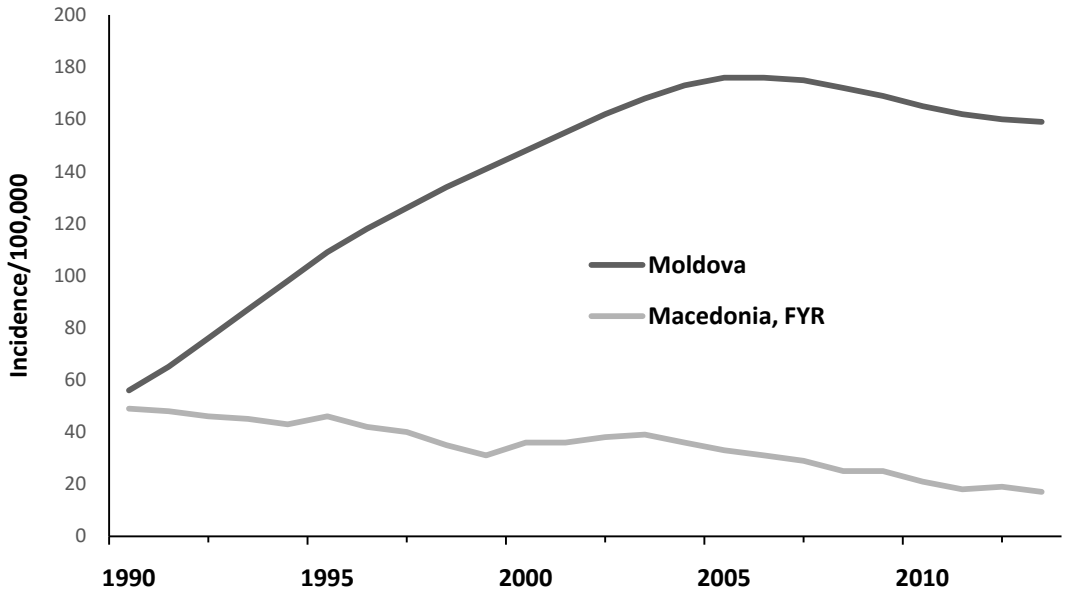
The results from each country were categorised into primary and secondary themes, according to the consistency with which respondents presented topics, the emphasis that they placed on them, and the differences observed between the two countries. The primary (emerging) themes were: (i) pre-existing burden of (TB) disease; (ii) organisation of the health system; (iii) existence of parallel health systems; (iv) degree of accountability and oversight exercised within the system; and (v) power and relationships.

Pre-existing burden of disease

Respondents felt strongly that the pre-existing burden of disease contributed to the current epidemiology. However, in the early 1990s, when each country achieved independence, incidence rates were very similar (6) (Figure 1). Another aspect related to disease burden, raised by some informants in Moldova but not in TFYR Macedonia, was migration. Moldova has experienced large-scale labour migration to Western Europe and the former USSR. Precise data are difficult to obtain because many Moldovans are entitled to, or hold, either Romanian, and hence European Union nationality, or Russian or Ukrainian nationality. However, it is estimated that t he number of Moldovan citizens living abroad is between 11 and 17% of those living in the country (7), but the figure is about a third for those of working

age (8). The challenges of controlling TB where there is large-scale labour migration, are well recognised (9,10).

Figure 1. Trends in TB incidence in Moldova and Macedonia (*source*: World Development Indicators)



Health system organisation

We define organisation as being related to the structure of health systems, from its leadership downwards. Macedonia has a national health insurance system, overseen by the Health Insurance Fund (HIF). In recent years primary health care delivery has been privatized, and general practitioners are paid by a blended model of capitation and incentive payments (i.e. completing specified health examinations). General practitioners act as gate-keepers to the health system, and have become more important, particularly as the number of acute care beds has decreased (11). The National TB Programme (NTP) in TFYR Macedonia is coordinated centrally from the National TB Institute. The NTP is the sole provider of TB services in the country, working through the National Institute in the capital, Skopje, but with affiliated regional hospitals and community dispensaries. The NTP also employs community nurses with responsibilities for directly observed community-based therapy.

Moldova also has a national health insurance programme. While less well established than in Macedonia, Moldova has moved toward a family practitioner model of primary health care. This said, a large stock of hospital beds remains (12), and hospital physicians exercise considerable influence on the health system. Tuberculosis care in Moldova is provided in several systems (e.g. prison, military and general health systems), although points of connection exist throughout. The NTP is coordinated by a manager at the Phthisiopneumology Institute in Chisinau, the capital. Services are delivered through municipal and national hospitals, along with local specialists and family physicians in the more rural parts of the country.

In Macedonia informants spoke positively of the structure, management and clinicians within the NTP, while counterparts in Moldova were critical, specifically of the structure and management of the NTP. Those in Moldova raised particular concerns about the current and future capacity of the NTP, given challenges experienced in recruiting and retaining qualified staff. As TB care is a separate specialty, informants felt that it is not attractive to new clinicians, given the inherent risks to practitioners and the confined scope of practice. This is in contrast to Macedonia, where those providing TB care have transitioned to a broader medical specialization of respiratory medicine.

As both countries have similarly structured NTPs, criticisms raised in Moldova would seem to reflect how the structure translates into service. On closer examination, informants in Macedonia tended to personalise their praise of individuals within the NTP. In Moldova, there was less personification and more reflection on the frequent transitions of individuals. Moldovan informants also reflected on a disconnection between the NTP leadership and local practices and realities, particularly in rural areas. Although informants framed their reflection as an organisational critique, what they were in reality commenting on was the capacity of individuals within the system to deliver the leadership and outcomes desired.

Parallel health systems

There was a consistent narrative in both countries about challenges associated with parallel health systems. In Macedonia these had been addressed by having all TB services provided through a single NTP, including those in the prison system, with prisoners referred to the general health system for treatment. In contrast, Moldova has dedicated prison-based facilities for the treatment of TB, which fall within the prison directorate. While informants highlighted significant advances within the Moldovan prison system, specifically in regard to the treatment of TB, there were concerns about the risk of losing individuals as they transfer into, or out of parallel systems.

Accountability and oversight

In Macedonia, informants felt that service providers were accountable for their actions, supported by training and oversight from the NTP managers. Informants described substantial uniformity in care provided across the country, which they associated with the good outcomes observed. In Moldova there was conflict between the hospital and community service providers. Those in the acute care sector blamed the community service providers for lax practices, whilst their counterparts in the community highlighted a lack of awareness of the realities in communities, particularly in rural settings. Those who are responsible for oversight of the NTP described limited capacity for monitoring and enforcing practice standards, which they believed contribute to variations in practice.

Power and relationships

Power dynamics are an important theme, although this emerged implicitly from the interviews rather than being raised explicitly. Those in Moldova described a persistent tension between acute care institutions and emerging community care service providers. They also spoke about the lack of consistent leadership, which arose from frequent leadership transitions, often due to changing political fortunes. In Macedonia informants also described frequent political transitions, but these spared the management of the NTP, enabling institutional stability. Macedonian informants further described cordial, if not pleasant working relations and communications with many of their colleagues across the country.

Secondary themes

In addition to the primary themes, several secondary ones were identified, which, while not necessarily differentiating the two countries, emerged from the literature as being of potential relevance and, in some cases, offered additional nuanced insights to their performance (Table 3). These will be discussed briefly.

Table 3. Case study themes

THEME	Macedonia	Moldova
Major themes		
Organisation	✓	X
Pre-existing burden of disease	✓	X
Parallel health systems	✓	X
Power	✓	X
Accountability & oversight	✓	X
Secondary themes		
Political Commitment	✓	✓
Infrastructure	X	☑
Historical trajectory	X	X
Institutional memory	☑	X
✓ Positive factor ☑ Mixed x Challenges		

Political commitment: in both countries informants described a high degree of political commitment to tackling TB but, perhaps surprisingly, none believed that this had any influence on the TB programme. It could be that this was taken for granted and it would have attracted more comment if it had been lacking. However, there was also a degree of cynicism as many felt that the commitment was because of the external funding attached to it, as both countries were recipients of Global Fund grants at the time of the study.

Infrastructure: Moldovan informants highlighted particular challenges in instituting uniform practices and standards in rural settings where there are difficulties recruiting and retaining health workers and where clinicians are overworked and largely disconnected from the broader health system, with its focus on larger policlinics and hospitals (13). From our observations, it was apparent that Moldova was well-equipped in respect to the diagnostic capacity available, particularly in the reference laboratories. This is the direct result of capacity building funds offered by the Global Fund to Fight AIDS, Tuberculosis and Malaria; United States Agency for International Development (USAID); World Bank, and other donors. In contrast, Macedonia did not have in-house access to high-technology equipment (e.g. Polymerase Chain Reaction or PCR), but this seemed to have little impact on the overall system of care. This observation strengthens our initial hypothesis, in that the systems of care have a greater impact on outcomes than does technology.

Historical trajectory: One phenomenon that characterised Moldova's early post-independence years was the growth of social inequality and breakdown of health services (14,15). This was exacerbated by a lack of management capacity in all post-Soviet republics outside Russia, in part consequent on the previously centralised system in the USSR (16). It

is plausible that some differences between former Soviet and former Yugoslav republics can be accounted for by the long history of decentralization in the latter (17,18).

Institutional memory: A loss of institutional memory may have played a role in Moldova, with frequent leadership changes in the political realm impacting substantially on the NTP. This has ripple effects on the continuity of policy, programmes and funding, as staff operate within an environment facing continual change (19,20).

Discussion

This study points to the importance of tackling not just the immediate causes of infection and resistance, but also the upstream factors, related to the way in which the health system is governed and organised. Key factors emerging from this research are congruent with those reported from other countries, including the challenges when patients cross boundaries between parallel health systems, or from a well-developed acute care sector to the community (21-23); a lack of accountability and oversight for TB treatment (14,23); the challenges arising from a strong centralized hospital sector, with consequent power imbalances (14,24-26); and the challenges of recruiting and retaining health staff in rural areas (16).

Consistent with the now extensive body of research on how some countries achieve good outcomes at low cost (27), we see that there is no single reason why Macedonia gets better outcomes than Moldova. These other studies have failed to find a single 'magic bullet', but have identified several factors that increase the likelihood of success, such as effective governance systems and institutional continuity, both present in Macedonia, but weak in Moldova. Informants praised leaders in Macedonia, but those in Moldova were seen as weak, and afflicted by frequent changes. Fragmentation was a key issue, with Moldova unable to integrate prison care, contrary to what was done in Macedonia. This creates inevitable problems as there are well known challenges in enforcing uniform standards across multiple systems of care (28). The risk of losing patients to follow-up in such circumstances, particularly for people who are vulnerable or marginalized, is ever present (29). Prison health systems are a neglected political priority globally, and often provide substandard care compared with mainstream health systems (30). This being said, the Moldovan prison system is not entirely separate, maintaining some connections, as is usual in countries with parallel systems (31). Weak governance can also be inferred from the problematic relationships between different providers in Moldova.

This study has a number of limitations. The most obvious is attribution. While it is possible to infer certain relationships between observed characteristics of the two health systems and health outcomes, it is not possible, in a non-experimental study, to determine cause and effect. However, the associations observed, with weak governance, lack of institutional stability, and the existence of parallel health systems being seen in the country with the higher burden, and not in the one with less MDR-TB, is both plausible and consistent with the evidence on health systems performance more generally. The second is that, although the two countries have many similarities, they are not identical and have different historical legacies, and policies take place in different political, social, and economic contexts. These are likely, at least to some extent, to explain the differences in governance systems.

Notwithstanding these limitations, this study does add to the sparse literature on the association between health systems and the development of MDR-TB and points to the need to address the overall governance of the health system, as well as more downstream measures such as the promotion of rational prescribing.

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