National Collaborating Centre for Infectious Diseases

Centre de collaboration nationale des maladies infectieuses

Multi-Drug Resistant Tuberculosis:

Proceedings from a Virtual Discussion with Public Health Decision- makers and Practitioners in Canada

August 2023

Prepared by:

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Acronyms

BPaL – MDR-TB treatment regimen consisting of bedquiline, pretomanid, and linezolid

BPaLM- MDR-TB treatment regimen consisting of bedquiline, pretomanid, linezolid, and moxifloxacin

CTBS- Canadian Tuberculosis Standards 8th Edition

DST- Drug Susceptibility Testing

LTBI- latent tuberculosis infection

MDR-TB – multidrug-resistant tuberculosis

MOH- Medical Officer of Health

NCCID- National Collaborating Centre for Infectious Diseases

PHAC – Public Health Agency of Canada

TB – tuberculosis

WHO- World Health Organization

Definitions

Multidrug-resistant TB (MDR-TB)– tuberculosis disease which is caused by bacteria resistant to isoniazid and rifampin, with or without resistance to other first line anti-TB drugs (1).

Canadian MDR-TB treatment recommendations (issued March 2022) - Individualized long regimen based on results of first- and second-line DST. Regimens should start with 5 drugs for the intensive phase and be reduced, if possible, for the continuation phase and last for a total duration of 18-20 months (1).

World Health Organization (WHO) MDR-TB treatment recommendations (issued December 2022) – Standardized, oral, 6-month regimen composed of bedaquiline, pretomanid, linezolid and moxifloxacin. This regimen is preferred; however, it is not recommended for those with certain kinds of TB disease, those under 14 years of age, and pregnant women. For those who cannot take the 6-month regimen, the WHO recommends a standardized 9-month and 18-month regimen (2).

Drug susceptibility testing (DST)– lab testing on TB bacteria obtained from patient samples to determine which antibiotics which will be effective for treatment. DST can be done in two ways:

> Phenotypic testing involves examining the effectiveness of specific antibiotics on bacteria grown in the lab from the patient specimen. Phenotypic test results are comprehensive and reliable but often take 3-6 weeks from when the sample was submitted (1).
>
> Molecular testing (also known as nucleic acid amplification testing or NAAT) can be run directly on patient samples and analyze the TB bacteria for genetic mutations associated with antibiotic resistance. Molecular DST results can be obtained in hours or days but are not as comprehensive or reliable as phenotypic DST. Molecular DST can only be used as an adjunct to, and not a replacement for, phenotypic DST (1).

Executive Summary

Multidrug-resistant tuberculosis (MDR-TB) in Canada is rare, but nevertheless has devastating effects on individuals, families, and health systems. There are reasons to be concerned regarding increasing Canadian MDR-TB incidence over the coming years. Any increase in incidence is problematic because MDR-TB treatment is extremely barrier-laden and resource intensive for patients and health systems alike. To ensure limited public health dollars are best used to promote health equity, barriers to efficient, patient centred, MDR-TB care must be addressed. Thus, the National Collaborating Centre for Infectious Diseases (NCCID) convened an online dialogue for people affected by MDR-TB and their family members, researchers, and practitioners to discuss existing challenges and potential public health solutions.

Five hours of meetings divided over two consecutive days were planned and people with lived experience of MDR-TB, health professionals, and researchers knowledgeable in MDR-TB care from a diversity of regions in Canada were invited. Thirty-one MDR-TB stakeholders participated in the dialogue which began with presentations from Drs. Sarah Brode and Alice Zwerling. Most of the meeting time was devoted to small group discussion on six key aspects of MDR-TB care (i.e., access to medications, mental wellbeing of patients and family members, health system cost of patient-isolation, financial wellbeing of patients and families, impact of cumulative costs on TB programs, patient and family wellbeing following TB). Through careful review of recordings, three themes were found to be common across the six topics. Firstly, participants consistently commented that the numerous barriers to providing MDR-TB care led to worse patient outcomes and diverted resources from preventative programs. Secondly, participants advocated for more patient and family centred supports to mitigate the mental health burden and the strain of treatment. Thirdly, participants suggested that improved collaboration amongst TB practitioners and policy makers as well as increased resources devoted to MDR-TB were needed. Participants offered specific ways NCCID could support solutions which include disseminating information on new regulatory options for accessing MDR-TB medications and organizing follow-up discussions. Follow up discussions should be focused on increasing national collaboration and include the patient and family member voice.

Introduction

Each year approximately 10 million people around the world are diagnosed with tuberculosis (TB), a potentially fatal and difficult to treat disease with devastating and lasting effects on individual wellbeing, household finances, and national budgets (3). Of these 10 million, approximately half a million will additionally learn that their disease is resistant to standard anti-TB medications and they require treatment for multidrug-resistant TB (MDR-TB) (3). MDR-TB treatment may be three times longer than standard treatment, is less likely to be successful, and requires the use of more toxic medications (2). Thus, it is not surprising that patients diagnosed with MDR-TB often experience anxiety, depression, and other mental health disturbance related to stigma, lost income, and treatment-related side effects (4). Given that MDR-TB is more likely to affect those already living with socioeconomic disadvantage (4), there is considerable potential for difficult MDR-TB treatment regimens to exacerbate disadvantage. To prevent treatment-related exacerbation of health inequality, the World Health Organization (WHO) advises national TB programs to deliver patient-centred supports alongside MDR-TB treatment. Recommended supports include empowering patient education, financial enablers, home visits, and the use of digital adherence tools (5).

Recent pharmacologic advancements in MDR-TB treatment show great promise for reducing patient burden and improving health equity. The WHO recently endorsed two effective six-month MDR-TB treatment regimens with fewer side effect and no painful injections (3). These new treatment regimens are a huge step forward but have been challenging to implement; new drugs are expensive and require advanced testing and close patient monitoring (3).

Thankfully MDR-TB in Canada is rare. Recent reports show that 15- 25 people, or 0.6-1.6% of those diagnosed with TB in Canada each year have multidrug-resistant disease (6,7). Despite these small numbers, each Canadian MDR-TB diagnosis is distressing and poses considerable challenges for local health care systems. The rarity of this event means TB programs often lack policies and procedures to guide practitioners as they struggle with challenging decisions and arranging complex care. Canadian authors have noted problems with MDR-TB care which include extended patient isolation, delayed medication access, the high cost of care, and inability to access required lab test (1, 8,9).

While Canadian MDR-TB incidence has been stable in recent years, rates are known to be affected by global incidence and national immigration trends (S Brode personal communication, April 23, 2023). Looking closely at these factors, there is reason for Canadian public health officials to be concerned about increasing rates. Global MDR-TB incidence increased in 2021, and many migrants arrive in Canada from countries with a high burden of MDR-TB (3, 10-12). A delayed, inefficient, and non-patient centred response to any increase in Canadian MDR-TB diagnoses could result in transmission of a potentially fatal disease, unnecessary health spending, and increased health inequity for affected patients and family members.

In recognition of this situation, the National Collaborating Centre for Infectious Diseases (NCCID) hosted an online dialogue over two successive afternoons to bring together experienced stakeholders in TB care to discuss challenges associated with Canadian MDR-TB care and also potential solutions.

Specific objectives for the dialogue included:

1. To explore public health challenges related to the expense, inequity, and other challenges of MDR-TB diagnosis, treatment, and rehabilitation in Canada.

2. To explore opportunities to reduce the financial, social, and emotional costs related to MDR-TB prevention, diagnosis, treatment, and rehabilitation.

Methods

A draft version of the objectives and agenda for the event was developed by the NCCID team. Two Canadian scholars experienced in MDR-TB care and research were invited to speak at the event and to participate in event planning. After both scholars agreed, they were asked for feedback on the objectives and agenda. To facilitate the focus on collaborative discussion, a plan was made for a small event (i.e., approximately 30 participants), four to five hours in duration, divided over two consecutive days. The list of invitees reflected the desire for representation from multiple health professions and all Canadian regions. Participation from individuals with lived experience of MDR-TB and their family members was also felt to be critical, thus several physicians attending the event were asked to refer interested individuals from their practices. Invitations to the event were shared by email and phone as needed.

Event proceedings were recorded to allow for detailed reporting. All recordings except for those of the keynote speakers' presentations were destroyed after NCCID staff reviewed and took notes to identify key points, unique perspectives, and common themes.

NCCID staff evaluated the event based on the level of participant engagement during the event, results from the participant evaluation survey, and the number of future activities suggested by participants during and after the event.

Participants

Approximately 31 individuals logged into the on-line platform each day. This included two individuals with lived experience of MDR-TB, one family member, TB physicians, medical officers of health, researchers, TB nurses, TB program managers, microbiologists, pharmacists, epidemiologists, and policy analysts from the Public Health Agency of Canada (PHAC) and Health Canada. Participants represented all the provinces from British Columbia through Quebec, however no participants from the Territories or the Atlantic provinces were able to attend.

Proceedings

After welcoming participants, day 1 began with Dr. Sarah Brode giving a presentation titled "Clinical challenges in MDR-TB care and systems implications". This presentation was followed by Dr. Alice Zwerling who discussed "Equity & social justice: Economics of MDR-TB and international mitigation strategies". These presentations were followed by the first of three breakout sessions (i.e., one breakout session on day one and two sessions on day two). As part of the registration process participants were asked to select between two options (i.e., different topics) for each breakout session. In this way six key challenges in Canadian MDR-TB care were discussed over the two-day event. Table 1 contains a list of topics for each breakout session.

Table 1. Breakout Session Topics

Session #	Topic 1	Topic 2
Breakout session 1 (April 25)	Access to MDR-TB medications	Mental wellbeing of people and families experiencing MDR-TB
Breakout session 2 (April 26)	Health system cost of isolation for MDR-TB	Financial wellbeing of families experiencing MDR-TB
Breakout session 3 (April 26)	Impact of cumulative MDR-TB costs on TB programs	Patient and family wellbeing following MDR-TB

During the first breakout session, Government of Canada policy analysts shared policy options available to public health jurisdictions to improve access to MDR-TB medication. NCCID staff felt this information would be of interest to the larger group and extended an invitation for the Health Canada team to give a plenary presentation the following day. This invitation was accepted and after welcoming remarks, day two commenced with a presentation from Health Canada. The Health Canada presentation was followed by the second and third breakout sessions, and finally a large group discussion regarding next steps. Plenary discussions were energetic, particularly on the topic of medication access, and enriched by those with lived experience of MDR-TB who were able to describe the personal impact of the disease.

Results: Key challenges for responding to MDR-TB in Canada and potential solutions

Power point slides from Drs Brode and Zwerling's presentations are posted to the NCCID website. (13)

Challenge #1: Access to MDR-TB medications

Two small groups discussed this topic.

Summary: Participants expressed frustration that the current process, under the Special Access Program (SAP) for accessing many MDR-TB medications is slow, complicated, and labour intensive. Participants described that (thanks to recent improvements) the delay waiting for SAP approval is usually a few days but is generally followed by a delay of two to three weeks as the respective pharmaceutical company processes the order, arranges for importation, and ships the medication. Participants cited that this delay leads to distressed patients and family members, poor treatment outcomes, and wasted health care resources. Potential solutions offered by participants included developing an accessible national stockpile of medications, setting an acceptable standard for number of days to obtain MDR-TB medications, and formalizing channels for collaboration between TB programs. Additional information on key themes in the discussion of medication access can be found in Table 2.

Table 2. Themes related to MDR-TB medication access.

Key point	Discussion content
Delays and frustration with current process	Participants described that the current process is slow and inefficient, requiring individual practitioners to negotiate a confusing, highly variable process each time an unauthorized medication is needed.
Negative impact of current delays	Both clinicians and people with lived experience acknowledged that delays in accessing medications are "miserable" and scary for patients with a potentially fatal disease as the infection may progress during the waiting period, leading to worse outcomes. Participants spoke about the mental health and resource implications of having patients wait in hospital isolation rooms for weeks whilst waiting to start treatment with effective medications.
Options for faster access	Participants from Health Canada and the Public Health Agency of Canada (PHAC) described several options for reducing delays[1]: • Improving "prepositioning" of MDR-TB medications under the SAP • Using the Urgent Public Health Need (UPHN) program • Using Block Release regulations (new option under SAP)

[1] See Appendix B for more information on prepositioning, UPHN, and Block Release.

	Participants with knowledge of other mechanisms for accessing for infectious disease medications offered additional options: • Changing federal regulations to allow importation from the Global Drug Facility. The Global Drug Facility is a medication stockpile run by the STOP TB Partnership which cannot currently be accessed under Canadian regulations. • Setting up a regional/provincial stockpile similar to the one currently used in British Columbia for to malaria medication (i.e., artesunate). Participants agreed that a stockpile could be organized at the regional, provincial, or federal levels; however, a federal stockpile would be most efficient given the small quantities of medication required.
Collaboration may create efficiencies	TB physicians identified several instances where they used their informal intra-provincial TB network to share expertise on MDR-TB and expedite medication access. Several participants built upon this idea by suggesting a formal TB network could be organized to concentrate clinical expertise and improve the efficiency and quality of national MDR-TB care. Participants also offered success stories which involved designating a single individual within their TB program to process MDR-TB medication requests. This worked well because that individual was able to develop a level of familiarity and efficiency with the process.
Benefits of setting an acceptable standard	Many participants agreed it would be beneficial to set a national standard for the maximum number of days which should pass between the recognition that MDR-TB medications are needed and the receipt of medications. Participants pointed out that setting a national standard and collecting data is the only way to measure quality of care related to timely access.

Challenge #2: Mental health of people and families experiencing MDR-TB

One small group discussed this topic.

Summary: Participants spoke about numerous mental health challenges experienced by people and family members at various stages of the MDR-TB journey. Participants strongly agreed that action is needed to increase support and bolster patient and family mental health. Participants stated strongly that mental health resilience is key to successfully finishing treatment. Additional information on mental health challenges experienced at different stages of MDR-TB treatment can be found in Table 3.

Table 3. Mental health challenges experienced at key stages of MDR-TB journey.

Key stages	Challenges

Pre-diagnosis	One participant reminded the group that physical TB symptoms exist for months and sometimes years before diagnosis; during this period, patients and family members often experience confusion, uncertainty, and fear.
TB diagnosis	Several participants described that patients and family members may feel relief with TB diagnosis because the disease is treatable and curable.
MDR-TB diagnosis	Participants pointed out that patients and family members may feel a return of fear and confusion upon learning that their TB disease is multidrug-resistant as this version of the disease is less curable. One participant with lived experience described worrying about the cost of treatment, asking themselves if the financial costs would bankrupt the family. A family member shared that they were also afraid of the health implications of the disease for those exposed.
Hospital Isolation period	Participants shared stories of the mental health strain on patients who were isolated for 4 months and separated from young children. Several participants noted that the most challenging aspects of extended hospital isolation are lack of stimulation and the loss of connection to family. One participant said that patients are “literally bored to tears”. Another participant pointed out that the United Nations declared access to the internet to be a human right which should not be denied to people during TB isolation.
Treatment	Participants reiterated that patients and family members require stamina and personal resilience to manage numerous stresses associated with the lengthy treatment. Participants connected good mental health to positive clinical outcomes by explaining that patients who trust their treating team, have good family support, strong personal motivation, and a sense of control are more able to follow the treatment plan. Participants noted that there are currently no systems embedded in TB programs to support mental health. One participant shared her knowledge of how HIV programs incorporate peer and professional support to strengthen patients’ mental health and suggested that similar models could work for MDR-TB patients.

Challenge #3: Health system cost of isolation for MDR-TB

Two small groups discussed this topic.

Summary: Participants itemized the considerable health system costs associated with prolonged hospital isolation of MDR-TB patients. Solutions presented by participants included increasing the uptake of existing de-isolation guidelines, expanding use of new diagnostic technologies, and speeding access to necessary medications. While faster discharge is an important way to reduce costs, several participants reminded the group that transferring complex MDR-TB care from the hospital to the community can have significant negative consequences if community TB programs are under-resourced or unprepared to provide such complex care. Additional information on key themes related to health system costs of isolation for MDR-TB can be found in Table 4.

Table 4. Themes related health system costs of isolation for MDR-TB

Key point	Discussion content
Contributors to long isolation period	Participants identified that patients' isolation period may begin pre-diagnosis and that difficulties related to diagnosing TB in Canada often contribute to isolation duration. Participants reported that the isolation period is lengthened because the diagnosis of MDR-TB requires culture-based drug susceptibility tests (DST) which take several weeks to produce results. Participants explained that patients can be admitted for weeks to months before they even initiate treatment. Several participants reminded the group of the benefits to hospital admission, explaining that it can be an efficient way to stabilize patients on an effective treatment regimen by completing many medical interventions in a short period of time.
Impact of long isolation period	Participants described three main impacts associated with prolonged isolation of people with MDR-TB which eventually become health systems costs. <u>Occupational staff exposures</u> Hospital staff can be inadvertently exposed to MDR-TB before the diagnosis is made and effective precautions are put into place. Hospital exposures require occupational health and safety assessments which may result in active or preventative treatment for MDR-TB. Participants explained that there is a need for increased staffing levels to accommodate the high

	complexity of care and additional time for donning and doffing personal protective equipment. Purchasing additional personal protective equipment being is also an additional cost. <u>Airborne isolation room</u> Participants reported that MDR-TB patients may occupy an airborne isolation room for weeks or months. In urban settings, airborne isolation rooms are a precious resource in high demand. One participant with rural experience described that rural settings often do not have airborne isolation rooms, and patient transfers must be arranged. Transfers are difficult because the patient is infectious. Participants elaborated that when patients must be isolated far from home there are many barriers to family members' visits which puts increased strain on patient and family members' mental health and may require health care intervention/costs. <u>Un-insured visitors to Canada</u> Several participants discussed the situation visitors to Canada who are diagnosed with MDR-TB and do not have provincial health insurance. Individuals visiting Canada may be asked to pay out of pocket for hospital expenses including expensive isolation. Participants reported hospital bills in excess of $100, 000. There is often a lack of clarity regarding who is ultimately responsible for the bill. Participants reported that TB clinicians often advocate for the health care system to absorb this cost instead of billing patients. Advocacy may take up a lot of the TB clinicians' time which could be better spent on patient care.
Ways to shorten hospital isolation	Participants were optimistic that increased access to molecular DST (e.g., GeneXpert®) would shorten hospitalization period as these tests deliver results within days, as opposed to weeks for culture-based DST. A positive Xpert® result triggers physicians to start the process of acquiring MDR-TB medications in advance of culture DST results. Participants reported barriers to accessing molecular DST in different jurisdictions.

	One participant familiar with the international setting stated that the WHO is currently developing guidelines for rapid DST. One participant from the British Columbia Centre for Disease Control reported that they are also working on technological solutions which deliver rapid results. Participants described using guidelines as a tool to facilitate communication between physicians about the evidence base around decreased infectiousness following treatment initiation. Physician participants reported using de-isolation guidelines in the Canadian TB Standards 8th ed to advocate for shortened hospital isolation for MDR-TB patients. Very few participants had experience with isolating infectious MDR-TB patients in the community. Participants elaborated that housing patients in the community instead of the hospital for isolation may reduce the overall cost to the health care system; however, it involves a large shift in costs, away from hospital budgets to TB program budgets. One participant explained that in the past, their TB program has had to assume the cost of housing, as well as the cost of delivering very complex care to MDR TB patients isolating in the community. Participants stated that such cost-shifts have a significant impact on TB program budgets which are proportionally much smaller than hospital budgets (see Challenge #5 below for more information).

Challenge #4: Financial wellbeing of people and families experiencing MDR-TB

One small group discussed this topic.

Summary: Participants spoke about the financial impacts which cause patients and family members considerable distress. Participants itemized patient-related factors and actions from health care providers which lessen this burden. Additional information on key themes related to the financial wellbeing of patients and families can be found in Table 5.

Table 5. Themes related to financial wellbeing of patients and families.

Key point	Discussion content
Significant financial impact for many patients and family members	Participants expressed that financial impact is primarily related to patients' inability of to work which may occur because of lengthy hospital isolation, side effects of medications, consequences of the disease, and numerous appointments (e.g., medication-administration, testing for both treatment effectiveness and medication side effects, and physician appointments). Several participants reminded the group that side effects and disease consequences do not end after treatment is completed, but may permanently impair ability to earn an income. Clinicians reported hearing from many patients that they were very stressed about money and considering extreme options which included leaving hospital against medical advice, declaring personal bankruptcy, and selling large family assets (e.g., homes, land).
Facilitators to reduce financial impact.	Participants itemized three main facilitators. Firstly, patients with provincial health insurance and the ability to work remotely experienced reduced financial impact. Secondly, health systems reduced the financial impact on patients and family members by providing patients with access to the internet while admitted and organizing hospital isolation close to home (to reduce visit-related costs to families). Hospital admission often transfers costs to the health system and away from patients and family members. Other options for transferring patient costs to the health system include the TB UP program in Ontario. Thirdly, health researchers could contribute to reducing the financial impact on patients and families by conducting research on long-term and short-term physical, financial, and mental health impacts of MDR-TB. Such research on patients' and families' wellbeing may demonstrate the need for increased patient support.

Challenge #5: Impact of cumulative MDR costs on TB programs

Two small groups discussed this topic.

Summary: Participants agreed that the cumulative costs for MDR-TB care were difficult to quantify. Nevertheless, participants suspected that cumulative costs were considerable because delivering complex care required significant human resources. Participants had experienced staff being diverted from latent TB care and other prevention and promotion services to care for MDR-TB patients. Several participants argued that TB programs needed additional funding. Solutions to generate additional resources reported by participants included helping decision-makers become more aware of the complexity of MDR-TB care and using new funding models for TB programs. New funding models should reflect patient acuity. Additional information on key themes related to the impact of cumulative costs of MDR-TB on TB programs families can be found in Table 6.

Table 6. Themes related to the impact of cumulative costs of MDR-TB on TB programs.

Key point	Discussion content
Cumulative costs are not known	Participants cited Canadian research which shows the cost of MDR-TB care is 8.1 times higher than for drug susceptible TB (9). Increased costs are mostly due to prolonged hospitalization. However, participants elaborated that the true cumulative costs are not known because they come out of many different budgets (i.e., separate "pots of money" for hospitalization, medications, lab fees, salaries for TB staff). One participant pointed out that pre-diagnostic costs are almost impossible to capture because they aren't attributed to TB. Participants reported large differences in budgeting practices between jurisdictions.
Complex MDR-TB care disrupts public health prevention and promotion	Participants reported that providing complex MDR-TB care is not optional for programs because of the high priority of preventing further MDR-TB. Participants shared experiences where their program had diverted staff and resources away from other preventative services to deliver MDR-TB care when needed. Participants itemized aspects of MDR-TB care which contribute to high cumulative costs: • extra DOT visits • additional physician and nursing appointments • additional case management hours to organize tests and appointments,

	monitor results, conduct contact investigation, organize complex LTBI treatments. Participants also described experiences where the push to discharge MDR-TB patients from hospital as soon as possible resulted in discharging patients to chaotic/stressful situations in the community. Participants discussed the importance of coordinating care between hospitals, TB programs, and public health and the time-consuming nature of this work. Some participants reported that their TB program was well-resourced and could manage complex MDR-TB patients in the community; however, several participants reported working in under-resourced TB programs or with generalist public health programs. Under-resourced programs were forced to divert staff-time from preventative services (e.g., reducing resources devoted to latent TB care, non-TB prevention and promotion) to support MDR-TB patients. Participants suspected that public health decision makers were not aware of the resource-intense nature of MDR-TB care because of the small numbers of cases.
Solutions to reduce impact	Participants anticipated that increased use of short course treatment (i.e., BPaL/BPaLM) will reduce cumulative costs. Participants expressed that TB program budgets could be indexed to patient acuity scores, which may increase funding for programs treating people with MDR-TB. Participants offered that research on the cumulative costs of MDR-TB which took a broad economic perspective would come closer to capturing the true costs. One participant reported she was involved with this type of research in Nunavut for drug sensitive TB. Participants articulated the need for the creation of a national-level network for MDR-TB care and itemized the benefits. Such a network could lead more cost-effective medication purchasing, clinician training, and mentorship which all would reduce cumulative costs.

Challenge #6: Patient wellbeing following MDR-TB

One small group discussed this topic.

Summary: Participants described a need for MDR-TB-specific supports for patients and family members after treatment is completed. Participants explained that MDR-TB patients concerns have different concerns compared to drug sensitive TB patients (e.g., persistent medication side effects) and require separate supports. However, participants were not aware of any MDR-TB-specific supports available in Canada. Additional information on key themes related to patient wellbeing after TB can be found in Table 7.

Table 7. Themes related patient wellbeing after TB.

Key point	Discussion content
MDR specific concerns post-TB	Participants offered that many patients experience persistent medication-related side effects after treatment such as skin discoloration, joint pain, and neuropathy. These side effects require on-going management. One family member shared ongoing concerns about disease recurrence. Participants discussed the importance of mental health to wellbeing post-MDR-TB but noted that patients also experience high rates of depression.
Lack of supports	One family member regretted that they had no guidance on when the patient should seek medical attention post-treatment. Participants noted that patient support all but stops at the end of treatment. Most patients have no ongoing public health involvement and the (sole) Canadian peer support group for TB is not MDR-TB specific. Participants expressed that good primary care for patients after treatment was critical but noted that many patients are not connected to any primary care when discharged from TB follow-up.

Overarching Themes

Over the course of the two-day dialogue, participants gave voice to many challenging experiences associated with providing high-quality, patient and family centred MDR-TB care in Canada. Many participants believed the central reason for these challenges is the small number of annual cases. Three themes were interwoven through the six small group discussions and plenary sessions. The three themes are as follows:

1. MDR-TB care requires significant health systems resources to overcome numerous barriers. Barriers often delay care which may worsen patient outcomes. TB programs may need to divert resources away from prevention-oriented services (e.g., LTBI care) to manage complex MDR-TB care.

2. MDR-TB has considerable short-term and long-term impacts on patients and their families. There is a need for more MDR-TB specific patient supports to address the potentially devastating mental, physical, and financial needs associated with the disease.

3. Strategies to improve care and decrease health system resource utilization should be focused on:
    - increasing national coordination of MDR-TB care. Increased coordination could improve access to expertise and facilitate better access to drugs and rapid diagnostic testing.
    - increasing funding for TB programs, supports for patients and family members, and research. TB program funding could be acuity based. Topics which require additional research include the long-term sequalae of MDR-TB, MDR-TB health economics, and MDR-TB rapid diagnostics.

Next Steps

Participants suggested NCCID could facilitate positive change in three areas. First, by working with PHAC and Health Canada to disseminate information on legislation to improve access to MDR-TB medications. Second, by organizing follow up discussions which may lead to the creation of a national clinical network to concentrate MDR-TB expertise. Finally, NCCID could conduct a survey on the uptake of new de-isolation guidelines (14), across Canadian jurisdictions.

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Appendix A- Agenda

Tuesday April 25, 2023	
1:30- 140	**Welcome**
1:45 -2:30	Plenary Presentations **Dr. Alice Zwerling** Equity, social justice, and economics of MDR-TB including international mitigation strategies. **Dr. Sarah Brode** Clinical challenges in MDR-TB care and systems implications **Q &A**
2:30 – 3:00	**Concurrent group discussion** Group A – Group A – Mental health of families experiencing MDR-TB Group B - Access to MDR-TB medications
3:15-3:25	Break
3:25-3:45	Plenary Discussion and Wrap up

Wednesday April 26, 2023	
1:30-1:40	**Welcome**
1:40 - 2:10	**Concurrent group discussion** Group A – Financial wellbeing of people affected by MDR-TB and their families Group B - Health system cost of prolonged MDR-TB patient isolation
2:10-2:20	Brief plenary discussion
2:20 – 2:30	Break
2:30-3:00	**Concurrent group discussion** Group A – Patient and family wellbeing following MDR-TB Group B - Impact of cumulative MDR-TB costs on Canadian TB programs
3:10-3:45	Plenary Discussion and Wrap up

Appendix B- Additional Information on Federal Regulatory Options for Improving Accessibility of MDR-TB medications. – April 2023

Pharmaceutical companies must seek market authorization from Health Canada for a drug to be accessed using traditional pathways (15). Pharmaceutical companies are not compelled to seek market authorization for their products in Canada. Clinicians who require access to unauthorized medications for a specific patient can request access through Health Canada's Special Access Program (SAP) which is a 2-step process involving Health Canada and the appropriate pharmaceutical company (15). First clinicians request approval from Health Canada for use. Once approved, clinicians then request the medication from the pharmaceutical company who arranges for importation and shipment. Pharmaceutical companies may or may not fulfil product orders and do so following their own timelines and procedures.

During the 2-day NCCID dialogue on MDR-TB, representatives from Health Canada and PHAC expressed awareness of current delays associated with the use of MDR-TB medications. They also shared information on their work to reduce delays. PHAC and Health Canada representatives also explained that they had spoken to several of the relevant pharmaceutical companies. Federal representatives felt it was unlikely these companies would seek market approval for MDR-TB drugs in Canada, given the small size of the market. On April 26, a Health Canada representative provided additional information to the group on three options available under current regulations for Canadian TB clinicians to obtain faster access to MDR-TB medications in their jurisdiction:

Improved function of pre-positioning of MDR-TB medications under the Special Access Program – Health Canada grants pharmaceutical companies' approval to "pre-position" certain non-approved drugs inside Canada to facilitate faster access once federal approval is granted (15). One participant from Health Canada explained that Janssen has already pre-positioned bedaquiline; therefore, shipping times should be faster than the 2-3 weeks reported by participants. Participants from Health Canada stated they would contact Janssen to understand and reduce current delays.

Declaration of an Urgent Public Health Need (UPHN)- Under the UPHN, Medical Officers of Health may access larger quantities (i.e., for a population) of non-approved medications to address an urgent public health need (16). The UPHN amendment to the Food and Drug Act is currently being used to access rifapentine for LTBI treatment (17). To access medication under the UPHN, Medical Officers of Health (MOH) must first declare a public health emergency and are responsible for managing the distribution of the medication after it has been received (16). The UPHN amendment to the Food and Drug Act does not allow for stockpiling as there must be a plan for immediate use. Only medications authorized for sale in the United States, European Union, or Switzerland can be accessed under the UPHN and off-label use of medications are not permitted (16).

Block Release Regulations- Under the Block release regulation, a Medical Officer of Health (MOH) may request a pharmaceutical company sell them a quantity of non-approved medications in anticipation of an urgent need (18). Several conditions must be met before Health Canada will approve such a sale, including that the requesting MOH must have declared a public health emergency and accept responsibility for distributing and completing post-distribution safety reports. Block release regulations

facilitate the development of a stockpile as purchases are not limited to small quantities (i.e., an amount needed to treat an individual patient), nor require a plan for immediate use (18). The Health Canada representative explained that if a stockpile of MDR-TB medications was created, it could be accessed quickly when needed as only approval from the respective MOH would be required.

Appendix C- Evaluation Results

Seventeen participants (of 31 who are not employees of NCCID) responded to a request to complete the online evaluation. Nine respondents were health care providers, three were health care managers, three were patients or family members, and two were researchers.

Most respondents agreed that the dialogue met the stated objectives which were 1) learning about challenges and solutions related to MDR-TB care, 2) increasing understanding of MDR-TB challenges and solutions, and 3) providing opportunities to discuss challenges and solutions. The average rating for questions related to the objectives was 4.25/5. A score of 5 indicated that the objective had been fully achieved.

For open text questions, respondents shared that the most valuable aspect of the dialogue was the opportunity to hear from a broad array of stakeholders in MDR-TB care and get a sense of the national picture on MDR-TB, particularly regarding medication access. Respondents were asked to provide suggestions for ways the dialogue could have been improved. Suggestions included sharing a list of attendees, more time in large group discussion, and increasing the quantity and quality of discussion around population level factors and MDR-TB determinants. When asked how they would use what they learned, many respondents offered that they would bring information and motivation to improve care back to their colleagues. Several respondents expressed hope that follow up discussions would be organized but did not specify who should organize such discussion groups.