



Palliative and end-of-life care in the global response to multidrug-resistant tuberculosis

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Multidrug-resistant (MDR) tuberculosis is costly, difficult to treat, and poses a global threat to tuberculosis control. The high burden of disease and treatment for patients, poor cure rates, and high mortality bring distress to patients, families, and caregivers. Despite guidance to improve treatment outcomes, little attention has been paid to palliative care of patients and families, such as for physical, psychosocial, social, and spiritual difficulties. An international expert symposium was convened to articulate an appropriate palliative care response for people with MDR tuberculosis. Several policies should be updated to ensure that palliative and end-of-life care is in place alongside treatment should cure be achieved, and to the end of life if not. Many services have been developed that exemplify integrated palliative care (ie, provided from within existing tuberculosis care). We recommend that existing expertise within palliative care can be used, which will improve management of problems such as dyspnoea, cachexia, and haemoptysis for patients across care settings, including at home, and enhance performance of control programmes.

Introduction

Multidrug-resistant (MDR) tuberculosis is more difficult and costly to treat than drug-susceptible disease and poses a major threat to progress achieved in global control of tuberculosis.¹ MDR tuberculosis is a form of disease caused by bacteria that are resistant to at least isoniazid and rifampicin, currently the most effective antituberculosis drugs. Extensively drug-resistant (XDR) tuberculosis is a form of MDR disease that is even more difficult to treat, caused by bacteria that are resistant to at least rifampicin and isoniazid, any fluoroquinolone, and one of three second-line antituberculosis injectable drugs (amikacin, kanamycin, and capreomycin). MDR tuberculosis does not respond to standard 6-month treatment with first-line antituberculosis drugs and usually takes at least 20 months or more to treat with drugs that are less effective and more toxic and costly than those used to treat drug-susceptible disease.²

In October 2010, WHO's Stop TB department, the Worldwide Palliative Care Alliance, and the Open Society Foundation convened an international expert symposium. The symposium included representatives from medicine, nursing, palliative care, policy, and affected communities to articulate an appropriate palliative-care response for patients with drug-resistant tuberculosis.

From 115 countries surveyed, the Global Project on Anti-Tuberculosis Drug Resistance Surveillance reported proportions of MDR tuberculosis in previously untreated individuals with tuberculosis of between 0% and nearly 30% of presenting cases.² Rates of MDR tuberculosis greater than 3% of new tuberculosis cases have been reported for at least one country in all six WHO regions.^{2,3} In 2010, an estimated 650 000 cases of MDR tuberculosis were recorded, and in 2008, 150 000 deaths from MDR tuberculosis were estimated annually.^{2,4} The number of people who died from tuberculosis disease fell to 1.4 million in 2010, including 350 000 individuals with HIV infection.⁴ Although drug-susceptible tuberculosis is curable in most patients, global treatment success rates in people with

confirmed MDR tuberculosis are only 53% in countries with a high burden of tuberculosis.⁴ As of January, 2012, 78 countries have reported to WHO at least one case of XDR tuberculosis.² Recent data from South Africa show that in a cohort of patients with XDR tuberculosis, most of whom were coinfecting with HIV, nearly a quarter died before initiation of treatment for their disease, and almost a half subsequently died in the first year of treatment.⁵ Tuberculosis, and particularly MDR and XDR tuberculosis, can thus be deemed a life-threatening disease from diagnosis.

Data from Africa, from populations with advanced HIV disease, show a high prevalence of symptoms, which contribute to a patient's burden of disease.⁶ Individuals in Africa with progressive incurable disease need additional and better information and communication about their disease and its management.⁷ Polypharmacy poses an important long-term challenge to patients and their families with respect to issues of tolerability, adherence, and management of side-effects. At least four different drugs are part of current recommended treatment regimens for MDR tuberculosis, in addition to agents to manage comorbidities such as HIV and diabetes and drugs to treat frequent and severe adverse effects.

The life-threatening nature of MDR and XDR tuberculosis and the burden of disease management in terms of symptoms, adverse treatment effects, adherence, stigma, and subsequent discrimination and social isolation show clearly the need for care that addresses physical, social, and emotional suffering by patients. Here, we argue for an effective and humane response to the drug-resistant tuberculosis epidemic.

Challenges for management of drug-resistant tuberculosis

Improvements in availability of diagnostic services have led to increased detection of people with MDR tuberculosis in low-income and middle-income countries. Therefore, the demand for treatment and need for palliative care has also grown. Responding to

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the epidemic of MDR tuberculosis has been called “one of the most profound challenges facing global health”.⁸ Public health systems face many challenges from drug-resistant tuberculosis, and clinicians deal with complexities with respect to management of uncertainty and the burden of multiple symptoms. WHO’s Stop TB strategy is based on a patient-centred approach to treatment and care, and international guidelines have identified practices resulting in better treatment outcomes. However, alleviation of the patient’s suffering associated with disease and its management has been restricted mostly, and not adequately, to physical aspects.

Difficulties faced by patients and families affected by life-threatening disease span physical, psychological, social, and spiritual aspects. The existing WHO definition of palliative care⁹ is appropriate for people with drug-resistant tuberculosis because it aims to optimise quality of life for individuals and their families and advocates for palliative care alongside treatment. Importantly, the definition allows for patients with MDR and XDR tuberculosis to receive comprehensive care from the point of diagnosis to eventual cure or end of life, through an extended disease course with unpredictable prognosis. Early delivery of palliative care recognises that life-threatening illness carries with it a substantial burden of suffering for patients, families, and caregivers, whether or not the disease can be cured.¹⁰ Evidence shows that early delivery of palliative care can alleviate this suffering.¹¹

Important strides have been made in some countries by organisations delivering palliative care to people affected by tuberculosis. The Lighthouse Trust in Malawi, for example, operates a specific programme to support people with MDR tuberculosis and test them for HIV. Its model of care integrates HIV prevention, treatment, care, and support with diagnosis of and treatment for tuberculosis and HIV infections. The Shepherd’s Hospice in Sierra Leone has, since 1995, focused on advocacy for service delivery for patients co-infected with tuberculosis and HIV while providing a service in partnership with community-based DOTS (directly observed treatment short course) volunteers. These volunteers identify and refer potentially affected individuals, provide palliative support (ie, assess and control various difficulties among patients and families) to promote adherence to treatment, and alleviate suffering associated with management of the disease.

Obligations of palliative and end-of-life care

WHO guidance¹² states that we have an ethical obligation to provide palliative care to patients for whom curative treatment options are not feasible. Palliative care must therefore be included in any health-care system and should be provided according to need rather than prognosis. This approach mirrors that for people with HIV infection, for whom palliative care has been identified as an essential component of care from diagnosis and

alongside treatment.^{13,14} All health workers must receive training in palliative care to enable them to undertake routine assessment of patients with tuberculosis and to provide symptom control and support for their problems. Ideally, health facilities should forge links with local palliative care and hospice teams. However, neither trained health workers nor local community-based palliative care resources are usually available in the settings most in need. Assessment of palliative care needs and implementation of country plans to meet these shortfalls is important in view of the MDR tuberculosis part of the Global Plan to Stop TB 2011–15.¹⁵

Although clinical expertise in palliative care for patients who die in respiratory distress has developed considerably, individuals with MDR or XDR tuberculosis are not yet seeing the benefits. Delivery of palliative care from within respiratory clinical services by existing staff with additional training, with clear criteria for referral to palliative care specialists for complex cases, is now established in some countries.¹⁶ Innovative management of problems associated with chronic obstructive pulmonary disease has been described in response to patients’ preferences both for good symptom control and for opting out of futile treatments.^{17,18}

Existing expertise from palliative care, HIV, and respiratory medicine can, therefore, translate directly to tuberculosis. Furthermore, effective control of the various problems faced by patients and their families is possible across many settings (eg, hospital, hospice, primary care, and home-based care).^{19,20} Flexibility in place of delivery is shown by the Hospice Palliative Care Association of South Africa (HPCA). Their programme strongly recognises that tuberculosis is a disease that affects the entire household, and on behalf of the state sector, HPCA has begun to deliver palliative care for tuberculosis in inpatient hospices with isolation rooms available and through home-based care. Importantly, the programme also recognises the threat of infection to staff, especially those who could be immune-compromised. Symptom control is based on local evidence recording a high prevalence (45%) of complications from tuberculosis treatment in people with a coexisting life-limiting illness. The most frequent side-effects identified by patients were pain and lethargy, with further reports of peripheral neuropathy, nausea or vomiting, and skin rash. Since 2008, HPCA has been implementing a programme of early tuberculosis diagnosis, timely referral, and delivery of treatment and care by a palliative-care approach.²¹

The Lesotho model for treatment of MDR tuberculosis in settings with a high prevalence of HIV implements home-based and community-based palliative care, with specific attention to pain and symptom control. The model includes social and nutritional support, twice-daily DOTS, and early empirical use of second-line drugs for tuberculosis.²² Community-based health workers who have been chosen from their peers by the village chief are trained to provide tuberculosis treatment and care and to

deliver various services, including screening for tuberculosis and HIV, psychosocial support, supervision of DOTS therapy, management of adverse side-effects, and education about infection control for patients and their families. Of 150 patients enrolled in 2008, 65% were successfully treated and 35% died. Community-based workers could, therefore, be trained in palliative care to scale up existing health-care delivery to include pain and symptom control.

Despite scant evidence for outcomes in patients with tuberculosis, findings show that existing palliative care expertise effectively manages patients with respiratory disease, cancer, and HIV.^{19,23} We recommend that palliative care for tuberculosis should be integrated with existing services and delivered where the patient is, should allow individuals and families to be supported at home whenever possible, and should include pain and symptom control. Examples of innovation from within sub-Saharan Africa offer important and potentially replicable lessons to guide an appropriate response.

Promotion of palliative and end-of-life care

Existing policy and global targets provide opportunities to mitigate the unnecessary suffering of patients with MDR or XDR tuberculosis. For example, the MDR tuberculosis part of the Global Plan to Stop TB 2011–15 aims to achieve universal access to diagnosis and treatment by 2015.¹⁵ Implementation of palliative care and end-of-life services can augment the epidemiological outcome by addressing adherence to treatment and by undertaking proper infection-control practices in households, especially for patients in whom treatment has failed and who remain a source of infection.

Embracing palliative care will contribute to ensuring that patients are “permitted to live out their life with minimal suffering and loss of dignity”.⁸ WHO’s guidelines for management of drug-resistant tuberculosis were updated in 2008 to include end-of-life supportive measures,²⁴ addressing pain and symptom control (including respiratory insufficiency), nutritional support, need for medical intervention after treatment cessation (including management of psychological morbidity), ensuring appropriate place of care, preventive care, and infection control. The ethical obligation to provide end-of-life care has been articulated in a recent report,²⁵ which states that “WHO member states will establish palliative care for MDR or XDR tuberculosis patients who fail treatment, by the end of 2012”.

We believe good end-of-life care needs to be understood and practised as standard by all attending clinicians in tuberculosis. In international standards²⁶ and the tuberculosis patients’ charter, no reference is made to palliative care. Future inclusion of this topic will have an effect on care practices and enhance outcomes for patients and families; however, the paucity of research on patients’ experiences of disease and their palliative care needs (both medical and non-medical) are major obstacles to such

updates. Tuberculosis research to date has focused largely on development of new methods for epidemiological research, and operational aspects of case finding and holding. The medical, nursing, psychological, social, spiritual, and terminal care needs of patients with tuberculosis, especially those with MDR or XDR disease, and interventions that enhance quality of life in this population are unknown.

Although health services research has been identified as a global research priority in tuberculosis, social science-based research is not yet fully embraced.²⁷ Robust palliative and end-of-life research to identify better ways to care for patients with MDR tuberculosis is needed to support the required advocacy, human resource development, and policy updates to advance care standards.

Improving care for MDR or XDR tuberculosis

We have highlighted several areas for action in palliative and end-of-life care for patients with tuberculosis. First, despite robust surveillance of cases of MDR or XDR tuberculosis, no published evidence could be identified for symptom prevalence, burden, or advanced care needs of this population. As far as we know, no models of care have been assessed to address the suffering associated with management of MDR or XDR tuberculosis. Research is needed to inform clinical guidance and policy on how to deliver better care for individuals throughout the disease course. Second, global policies can facilitate palliative and end-of-life care for patients with MDR or XDR tuberculosis. Strong advocacy to promote transfer of these policies at national level is crucial; civil society and affected communities have an important part to play.

Third, palliative and end-of-life care can be integrated easily into existing services. Palliative care should be available to all people with potentially life-limiting illness, irrespective of whether they need end-of-life care. All attending workers need to be trained in essential skills to assess and control patients’ difficulties, and local palliative care services must be able to provide consultancy for and manage complex cases. These skills should be part of human resource development curricula. Finally, palliative and end-of-life care should be delivered to the patient and their family in the setting where they are receiving care, whether an inpatient, an outpatient, or at home. Some facilities can provide care readily, following the patient from institution to home, with community-based resources and access to the full range of drugs for pain and symptom control.

Clear consensus exists among tuberculosis and palliative-care professionals that palliative care is both appropriate for, and required by, many patients with MDR or XDR tuberculosis around the world. Findings of studies from high-income countries indicate that palliative and end-of-life care provides cost savings^{28,29} and is fairly easy to deliver. Universal access to palliative care, irrespective of diagnosis, disease stage, or place of care, can be claimed

under existing global human rights legislative covenants.³⁰ Skilled palliative care workers can manage side-effects such as breathlessness, fatigue, cachexia, and end-of-life crises such haemoptysis and acute respiratory failure, and anxiety of patients and their families, which typically accompanies these symptoms. However, when discussing integration of palliative care into existing tuberculosis services we note several barriers to uptake among health systems and clinicians. These are principally structural in relation to availability of analgesia, a lack of teaching of clinical skills within existing curricula, and continuing professional development, and scant awareness of and prejudice against palliative-care approaches to patients' management. Our recommendations can help to address these challenges. Stop TB partners and affected communities should take the opportunity to enhance quality of life by embracing palliative care.

Contributors

RH wrote the draft of the report. KMF, SRC, and EJ contributed to, read, and edited the report.

Conflicts of interest

We declare that we have no conflicts of interest.

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