Increasing tuberculosis case detection: lessons from the Republic of Moldova
Viorel Soltan,a Asma Khalid Henry,a Valeriu Crudu a & Irina Zatusevski a

Abstract The Republic of Moldova undertook reforms in tuberculosis (TB) control and health care consistent with international recommendations and advanced towards the global target for case detection. The number of TB cases notified increased overall by 50% during 2001–2005. Expansion of the DOTS strategy and full coverage coincided with a greater role for primary health care (PHC) in TB control and the advent of national insurance for TB diagnosis and treatment. These developments and improvements in laboratories, surveillance, medical personnel skills, and public awareness contributed to increased case detection. The Republic of Moldova addressed both demand and supply sides in these efforts. It increased effective demand for TB services by dispersing diagnostic capability, instituting financing mechanisms and saturating the public with information on symptoms, transmission and treatment. It increased the supply of TB services by upgrading the laboratory network, revamping surveillance and training practitioners. The Republic of Moldova’s experience offers lessons for other countries: TB–PHC integration allowed more suspect cases to be diagnosed at nearby PHC clinics, contributing to more cases being notified. Innovative TB communications reached the general public, vulnerable groups, practitioners and the media. TB control projects built on each other and national coordination mechanisms served to identify funding for the most pressing needs. There are challenges remaining for TB control in the Republic of Moldova, not least the stable treatment success rate, but the country can list valuable lessons and achievements.

Introduction
The Republic of Moldova adopted the DOTS strategy in 2001 and committed to reaching the global tuberculosis (TB) targets of 70% case detection and 85% treatment success.1 At the same time, the Republic of Moldova initiated health system reforms, reorienting towards primary health care (PHC) and introducing national health insurance. International donors supported TB control and reforms designed to increase the demand for, and supply of, services. This paper reviews TB case notification in the context of interventions during 2001–2005 to extract early lessons of the Republic of Moldova’s experience. What contributed to detection of new smear-positive cases increasing from 37% in 2001 to 65% in 2005?2 What practical approaches can the Republic of Moldova share with other low-income countries in increasing detection?

Methods
The method used is to juxtapose TB case notifications, sputum smear microscopy (SSM) confirmation, TB diagnostic investigations and PHC patient visits against the timeline of interventions during 2001–2005. These data were selected because they should capture the effects of improved diagnosis, laboratories, surveillance and public awareness. The selected period coincides with the introduction and expansion of DOTS to the entire country; integration of TB and PHC services; and amended payment mechanisms for services. It was a period of intensive effort by the Republic of Moldova to institute internationally recommended policies. Although case detection increases cannot be attributed rigorously to specific interventions, they indicate the relationship between global targets and reforms advocated by international organizations. With additional data and analysis, precise attribution and confirmation of these indications may be possible.

Data presented in this paper were obtained from the National Tuberculosis Program (NTP) and the Ministry of Health (MoH) of the Republic of Moldova. The data cover all of the Republic of Moldova, including Transnistria (a frozen conflict region) and the penitentiary system. Because of data coding and verification revisions related to health insurance and the TB surveillance system, comparable data in some cases are available only for 2004–2005.

Results
Fig. 1 and Fig. 2 show the trends. Fig. 1 depicts the number of all (new and relapse) TB cases notified; the number of new TB cases notified; the per cent of pulmonary TB cases confirmed by SSM; and the timing of principal TB interventions during 2001–2005. Fig. 2 depicts the number of suspected TB patients for whom diagnostic investigations were conducted during 2003–2005 and the number of PHC patient visits for all causes during 2004–2005. Prior to 2004, PHC patient visit data are not comparable because reporting was revised when national health insurance was enacted in January 2004. For TB diagnostic investigations, the data began to be compiled when the network
of microscopy laboratories was established in 2003 and increased when the network was completed in 2004.

**TB control and health-care reforms**

The National Programme for Tuberculosis Control in the Republic of Moldova for 2001–2005 reoriented the Republic of Moldova’s TB system to the WHO-recommended DOTS strategy. In November 2001, the NTP initiated a civilian DOTS pilot programme, preceded by initiation of DOTS in penitentiaries in November 2000. As Fig. 1 shows, DOTS expanded rapidly and 100% coverage was achieved in January 2004. The full coverage of DOTS coincided with the introduction of obligatory national health insurance, which finances a package of health-care services, including tuberculosis diagnosis and treatment. For TB diagnosis, the insurance system contracts with PHC practitioners on a per capita basis and covers laboratory tests and personnel. For TB treatment, the insurance system contracts with hospitals per treated case and covers patient stays, laboratory tests and drugs for treatment of chronic cases and latent infection. Most anti-TB drugs were provided during 2001–2005 through Global Drug Facility (GDF) and Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) grants.

PHC began to be developed in the Republic of Moldova in 1998, when the Department of Family Medicine was established at the State Medical and Pharmaceutical University. In 2001, the first PHC clinic opened; with the World Bank’s assistance, the PHC concept was elaborated and physician retraining started. Integration of separate TB and PHC services was shaped by defining diagnostic and referral protocols and training practitioners beginning in 2004. A three-day TB training module was added to an ongoing four-week PHC retraining programme for physicians and nurses.

In devising and implementing the national programme, the NTP received technical and financial assistance from the Global Fund, SIDA (Swedish International Development Cooperation Agency), USAID (United States Agency for International Development)/AIHA (American International Health Alliance) and WHO. Other international organizations, namely KNCV Tuberculosis Foundation and Caritas Luxembourg, were instrumental in TB control in penitentiaries. The Republic of Moldova was the first country to receive a GDF grant and continues to purchase anti-TB drugs under GDF procurement mechanisms. The GDF grant to the Republic of Moldova was from June 2001 to August 2005. Beginning in 2003, the Global Fund Round 1 grant and a USAID-financed
AIHA project enabled the Republic of Moldova to implement the comprehensive measures envisioned in the 2001–2005 national programme. Both projects operated from 2003 to 2007, and activities related to diagnosis, laboratories, surveillance and public awareness are depicted in Fig. 1.

**Interventions and trends**

Interventions to strengthen TB control in the Republic of Moldova include establishing a laboratory network, revamping surveillance, linking PHC and TB, and increasing awareness among practitioners and the public. The microscopy and reference laboratories were reorganized into a logical and geographically dispersed network and quality control was instituted. Facilities were renovated and equipped for laboratory diagnostics in microscopy, culture and drug susceptibility testing. A new surveillance system was developed with more informative forms and reporting sites and electronic data collection and analysis. Communications campaigns targeted and engaged practitioners, journalists and the public across the country. During 2001–2005, related training for these interventions was provided to 1200 PHC practitioners, 250 TB specialists, 200 laboratory personnel and 65 surveillance data-entry operators. Results of the training were monitored through pre- and post-testing of trainees, with retraining provided in some cases. For PHC, an electronic database was created to track trainees. After the conduct of awareness campaigns, the distribution of materials was verified at venues and attendees were asked their opinion of campaigns.

Fig. 1 shows that case notifications increased steadily during DOTS expansion and after nationwide implementation. From 2001 to 2005, the total number of cases increased from 3820 to 5632; and the number of new cases increased from 3418 to 4518. The rate per 100 000 increased at a similar pace because the population remained stable. The total TB case rate per 100 000 increased from 89.4 to 133.4; and the number of new TB cases increased by about 50% from 2001 to 2005. Overall, the number of total cases notified increased by about 50% and the number of new cases notified increased by about 30% during this period.

One of the principles of DOTS is bacteriological confirmation of a TB diagnosis. The percent of pulmonary TB cases confirmed by a positive SSM test is an important indicator in TB control. First, it shows that SSM is recognized as the principal and definitive confirmatory diagnostic test. Second, it reflects SSM quality and diagnostic skills. This rate increased during DOTS expansion, but declined slightly from 2004 to 2005 due to renunciation of reference laboratories in the Republic of Moldova and consequent reduced monitoring of microscopy data. In 2005, 50.0% of pulmonary TB cases were confirmed with a positive SSM test, increasing from 42.2% in 2001.

Fig. 2 shows TB diagnostic investigations and PHC patient visits. Between 2004 and 2005, the number of patients for whom TB diagnostic investigations were conducted increased by 15.3%, from 34 872 to 40 220; and the number of PHC patient visits (for all causes) increased by 13.3%, from 8 937 634 to 10 122 012. Practitioners and patients indicated in interviews that TB awareness campaigns prompted symptomatic patients to seek treatment. Practitioners in Chisinau, Balti, Bender and Tiraspol said that patient visits increased by about 10% in their areas following campaigns. In open-ended interviews at Balti TB hospital, 6 of 62 patients (March 2006) and 5 of 35 patients (March 2007) said that they came in response to TB-related broadcasts or leaflets. Awareness campaigns have been far-reaching, with spots on leading broadcasters Teleradio Moldova, NIT and ProTV, and on 16 smaller television and 12 smaller radio stations. In a country of 337 000 km² and 4 million inhabitants, this saturation of TB information reached most of the population. According to mass media ratings for March–April 2005, AIHA (which conducted the campaigns) was placed fourth among all advertisers, with 7.5% of total advertising space.

Fig. 1 indicates the timing and cohesiveness of TB interventions. The microscopy network was established along with DOTS expansion. This was followed by improved reference laboratories and surveillance, communications campaigns and training on diagnosis and surveillance. With substantially improved physical facilities, equipment and monitoring procedures, reference laboratories expanded the network’s capability in quality assurance and in handling the increased volume. From 2003 to 2005, the number of microscopy laboratories increased from 41 to 57, the average number of smears per laboratory increased from 1072 to 2453 and the total number of diagnostic investigations (patients) increased from 12 625 to 40 220. Reporting and information
flows improved as a result of revised statistical forms, electronic submission of data including laboratory data, and a single system that replaced fragmented and duplicate reporting to the NTP and the MoH. The communications campaigns initially targeted practitioners, who lacked information on DOTS and patient education materials, and then targeted the general public as revised protocols and quality-assured tests were implemented.

Discussion

The Republic of Moldova followed precepts put forward by WHO and other international organizations for reforming health care, health financing and TB control. The concentrated interventions during 2001–2005 built the demand and supply sides, increasing effective demand through insurance, PHC and information; and increasing supply through laboratories, training, drugs and surveillance. The infrastructure for DOTS was put in place and patients were given access to it. The Republic of Moldova’s rapid increase in case detection can be considered to demonstrate the tenets of internationally recommended TB policies carried out in concert. Some explanations of how the interventions may have propelled case detection and practical lessons for other countries are offered. These explanations may be scrutinized further with more extensive data and analysis to link interventions to specific outcomes.

It’s likely that the interventions contributed to increasing case detection in several inter-related ways. Supporting TB–PHC integration through protocols, practitioner training and insurance financing helped make TB services widely accessible. PHC services saw more patients and patients indicated that TB messages alerted them to seek care. Information on TB transmission, symptoms and treatment for professionals and the public was extensive. Improving the laboratory network through updated facilities, revised guidelines on methods and quality control, and training helped make diagnostic confirmation more reliable. More complete and accurate reporting of cases through standardized reporting systems resulted in more of the underlying incidence of TB reflected in case notifications. In 2002, the Republic of Moldova began submitting more complete data, including drug resistance surveillance and treatment outcomes, to WHO and EURO TB (a WHO Collaborating Centre for the surveillance of tuberculosis).

TB–PHC integration: An argument for integrating TB and PHC is to make services more accessible, especially for vulnerable and less mobile populations. A study from the Sudan, for example, found that PHC facilities provided TB care for higher numbers of women and older patients than referral hospitals. A study from Cambodia reported that decentralizing DOTS to PHC centres reduced delays in TB treatment.

In the Republic of Moldova, new case notifications from rural areas (49%) increased more rapidly than from urban areas (33.7%) between 2001 and 2005. This may be related to initial efforts being targeted in cities and the overwhelmingly rural character of the Republic of Moldova. As awareness campaigns reached rural districts, knowledge of symptoms and treatment became available to a larger proportion of the population. The geographical dispersal of PHC clinics eased access for the rural population. Integration increased effective demand by increasing accessibility and increased supply by increasing the number and skills of practitioners. The Moldovan experience indicates that TB diagnosis at the PHC level can help identify more cases and thus increase case detection.

Innovative communications: TB awareness is critical to DOTS because it is premised on passive case finding and self-presentation of symptomatic patients. Increasing case detection means increasing recognition of symptoms and knowledge of treatment. One of the lessons from the Republic of Moldova is that TB communications should take many forms and include practitioners and the media along with the public. A Knowledge, Attitude and Practice (KAP) survey conducted in 2004 revealed that 70% of the Moldovan population recognized familiar TB symptoms and 24% thought TB could not be treated. Because television (79%) and radio (57%) were the principal means of receiving TB information, according to the KAP survey, audio and video broadcasts were produced and transmitted. Direct contact and peer education were used to reach vulnerable groups through shelters and organizations serving youth and prisoners; to reach rural inhabitants through post offices and a Healthy Bus; and to reach urban commuters through minibuses. In Cahul Rayon, the Healthy Bus made 36 field trips to 15 villages selected for low socioeconomic status and gave information directly to 2000 residents. In Balti, 25 trained nongovernmental organization (NGO) workers provided information to 600 drug users and HIV/AIDS patients. Altogether, 160 000 posters, stickers, booklets, brochures and guides were distributed, and 26 hours of free broadcast time was arranged.

Accurate information on diagnosis, transmission, treatment and the DOTS strategy was provided to journalists and medical personnel. This filled a critical gap in the Republic of Moldova, where there had been no TB communications activity for nearly 15 years. Booklets on DOTS and TB, and posters with the scheme of detection and treatment were prepared for physicians. To promote mass media coverage, journalists were engaged through briefings, reviews of articles and broadcasts, and a contest on TB stories. As a result, the number of articles on TB in the Republic of Moldova’s print media increased. Between August 2000 and December 2003, 150 articles had been published. According to the report on the contest, 98 articles were published between October 2004 and March 2005.

Eight volunteer groups comprising medical students and PHC and TB practitioners were organized to convey information directly at places of study, work or domicile. Thus far, they have presented 1000 lectures. Because of interest generated in Balti (the second-largest city) among practitioners, students and patients, an NGO dedicated to TB was formed, the first in the Republic of Moldova.

Local coordination and commitment: The Republic of Moldova’s TB control effort is an example of building on investments and following WHO guidelines. After seeing the promising results of DOTS in penitentiaries, the NTP initiated a civilian programme and used the experience to manage DOTS expansion. The 2001–2005 National Programme laid the groundwork for approval by WHO’s Green Light Committee of DOTS-Plus pilot projects to combat drug-resistant TB in the Republic of Moldova. The pilot was approved in February 2005 and an expansion was
recommended in May 2006. Laboratory and surveillance upgrades made available the laboratory tests, tracking and quality control necessary for DOTS-Plus. A World Bank project helped train PHC personnel about TB and served to effect revised guidelines for PHC and TB.

TB projects depended on local participation and knowledge of how to advance towards international standards. Local project staff and TB officials agreed on approaches through the Country Coordinating Mechanism and filled funding gaps to meet the most pressing needs. This lesson may not be replicated easily, yet it is important in the Republic of Moldova’s drive towards global targets. TB control helped bridge divides. The separate services for TB and PHC, and the separate TB control systems for civilian and penitentiary populations, were integrated. There are even promising developments with respect to Transnistria, where TB control has been effectively integrated with the rest of the Republic of Moldova and improvements in laboratories, surveillance and public awareness extended.

Challenges in TB control: In spite of achievements, many challenges remain for the Republic of Moldova. During a period of increasing case detection, the treatment success rate did not increase. Treatment success rates for new smear-positive cases from 2001 to 2005 were 65.5%, 61.2%, 65.2%, 61.7% and 62.0%.\textsuperscript{11} Stagnant or decreasing treatment success rates have several likely causes. The health system, including the NTP, has gaps in fulfilling management and monitoring functions. More effort, for example, is required in ensuring DOT (Directly Observed Therapy) during the continuation phase of treatment. Current estimates are that 65% of TB cases receive DOT.\textsuperscript{12} The expansion in case notification and adjustments in response to reforms may have stretched treatment capacity. Although drug supplies have been sufficient, staff shortages and turnover have been consistent impediments. Significant outmigration has manifold consequences for TB control in the Republic of Moldova. In addition to trained staff leaving, TB patients leave the country and are lost to follow-up.

Multidrug-resistant tuberculosis (MDR-TB) and TB/HIV are threats to the Republic of Moldova’s efforts to reach global targets. An ongoing study is estimating the extent of drug-resistant TB in the Republic of Moldova. Primary MDR-TB increased from 6.3% to 13.4%, and acquired MDR-TB increased from 36.7% to 49.6%, from 2001 to 2005. This phenomenon is explained by a large number of MDR-TB patients without proper treatment, and contributes to increased numbers of relapse and new resistant cases. It also contributes to the low rate of treatment success, which was 62% for new smear-positive cases and 42.3% for retreatment cases in 2005. DOTS-Plus projects are elucidating the effect of drug-resistance on prevalence and treatment outcomes. In the city of Balti, which has a high HIV prevalence, preliminary data indicate the effect of HIV co-infection. TB/HIV co-infection increased from 7.4% in 2001 to 24.5% in 2005; and TB mortality related to HIV co-infection increased from 10% of total TB mortality in 2001 to 31.6% of total TB mortality in 2005.\textsuperscript{13} Effective action to address TB/HIV, including collaboration between the national HIV/AIDS and the national TB programmes, remains a challenge for the Republic of Moldova.

Competing interests: None declared.

Résumé
Renforcement de la détection des cas de tuberculose: enseignements provenant de la République de Moldova
La République de Moldova a entrepris des réformes dans les domaines de la lutte contre la tuberculose (TB) et des soins aux tuberculeux pour se conformer aux recommandations internationales et progresser vers les objectifs mondiaux de détection des cas. Globalement, le nombre de cas de TB notifiés a augmenté de 50 % sur la période 2001-2005. L’élargissement de la stratégie DOTS et l’obtention d’une couverture totale ont coïncidé avec l’affectation aux soins de santé primaire d’un rôle plus important dans la lutte antituberculeuse et avec la mise en place d’une assurance maladie nationale financant le diagnostic de cette maladie et son traitement. Ces évolutions, accompagnées d’une amélioration des compétences du personnel de laboratoire, de surveillance et médical et d’une sensibilisation du public, ont participé à l’augmentation du taux de détection des cas. Dans le cadre de ces efforts, la République de Moldova a pris en compte à la fois l’offre et la demande de services. Elle a accru la demande effective de services liés à la TB en dispersant géographiquement les capacités de diagnostic, en mettant en place des mécanismes financiers et en diffusant amplement à la population des informations sur les symptômes, la transmission et les traitements. Elle a augmenté l’offre de services dans ce même domaine en modernisant le réseau de laboratoires et la surveillance et en formant des praticiens. L’expérience de la République de Moldova peut apporter des enseignements à d’autres pays : l’intégration de la lutte antituberculeuse et des soins de santé primaire a permis de diagnostiquer davantage de cas suspects dans les dispensaires de soins de santé primaire voisins, d’où une augmentation du nombre de cas notifiés. Des communications innovantes sur la TB ont atteint la population générale, les groupes vulnérables, les praticiens et les médias. Les projets de lutte antituberculeuse se sont renforcés entre eux et des mécanismes de coordination nationaux ont permis d’identifier et de satisfaire les besoins financiers les plus pressants. Il reste à la lutte antituberculeuse des défis à relever en République de Moldova, dont le moindre n’est pas la stabilisation du taux de succès du traitement, mais ce pays a déjà à son compte des enseignements et des réalisations utiles.
Aumentar la detección de casos de tuberculosis: enseñanzas de la República de Moldova

La República de Moldova ha emprendido reformas en materia de control y atención de la tuberculosis en la línea de las recomendaciones internacionales y ha hecho progresos en pos de la meta mundial establecida para la detección de casos. El número de casos de tuberculosis notificado aumentó en total en un 50% durante el periodo 2001-2005. Paralelamente a la expansión de la estrategia DOTS y la plena cobertura, se otorgó más importancia a la atención primaria en la lucha contra la tuberculosis y se implantó el seguro nacional para el diagnóstico y tratamiento de la enfermedad. Estos cambios y mejoras introducidos en los laboratorios, la vigilancia, las aptitudes del personal médico y la concientización de la población permitieron detectar un mayor número de casos. La República de Moldova centró sus esfuerzos tanto en la parte de la oferta como en la demanda. Así, estimuló la demanda efectiva de servicios contra la tuberculosis dispersando la capacidad de diagnóstico, estableciendo mecanismos de financiación y saturando al público de información sobre los síntomas, la transmisión y el tratamiento. Y por otro lado amplió el suministro de servicios antituberculosos mejorando la red de laboratorios, modernizando la vigilancia y formando a los profesionales. La experiencia de la República de Moldova brinda lecciones para otros países: la integración de la tuberculosis y la atención primaria permitió diagnosticar más casos sospechosos en los dispensarios de atención primaria cercanos, lo que contribuyó a que se notificara un mayor número de casos. Se hicieron llegar mensajes innovadores sobre la enfermedad a la población general, los grupos vulnerables, los profesionales y los medios de comunicación. Los proyectos de lucha antituberculosa se reforzaron mutuamente y los mecanismos de coordinación nacionales permitieron obtener financiación para las necesidades más urgentes. El control de la tuberculosis sigue trepando con algunas resistencias en la República de Moldova, una de las cuales, y no la menos importante, es la estabilidad de la tasa de tratamientos satisfactorios, pero el país logró logros y lecciones muy valiosas.

References

5. Interviews with practitioners Ludmila Balteanu and Rodica Ignat, lecturers in the Department of Family Medicine, State Medical and Pharmaceutical University, Chisinau (March 2005); Raisa Barbata, Head of TB Dispensary, Balti (September-December 2005); and Petru Dermenji, Chief Physician, TB Hospital, Bender, and Nina Loseva, Principal Phtisisiopneumologist, Tiraspol (June 2006); and with patients were conducted by the staff of USAID/AAH’s Strengthening Tuberculosis Control in Moldova project.