The European Union standards for tuberculosis care: do they need an update?

Marieke J. van der Werf[1], Andreas Sandgren[1], Lia D'Ambrosio[2], Francesco Blasi[3] and Giovanni Battista Migliori[2]

Affiliations: [1]European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden. [2]WHO Collaborating Centre for TB and Lung Diseases, Fondazione S. Maugeri, Care and Research Institute, Tradate, and [3]Dipartimento Fisiopatologia Medico-Chirurgica e dei Trapianti, University of Milan, IRCCS Fondazione Cà Granda, Milan, Italy.

Correspondence: G.B. Migliori, WHO Collaborating Centre for TB and Lung Diseases, Fondazione Salvatore Maugeri, Care and Research Institute, via Roncaccio 16, 21049, Tradate, Italy. E-mail: giovannibattista.migliori@fsm.it

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Differences between ESTC and new ISTC discussed to inform clinicians and public health officers on best TB management http://ow.ly/tgbzt

The International Standards for Tuberculosis Care (ISTC), published for the first time in 2006 [1], introduced a new way of looking at clinical and public health guidelines for tuberculosis (TB). The *European Respiratory Journal* published an editorial explaining the ISTC, promoting the rapid uptake of the standards [2].

While guidelines represent a long, comprehensive document containing all the details the physician might need for managing TB, the standards are a simple set of 21 principles that guide day-to-day clinical decisions [3, 4]. In other words, guidelines are usually available in a physician's library while the standards are kept on their desk in the office.

The ISTC prescribe a widely accepted level of TB care which guides all healthcare providers and clinicians, both public and private, in achieving optimal standards in managing patients who have, or are suspected of having, active TB [1–4].

The European Centre for Disease Prevention and Control (ECDC) and the European Respiratory Society (ERS) jointly developed a European Union (EU) adaptation of the ISTC document, known as the European Union Standards for Tuberculosis Care (ESTC) [4]. These standards are tailored to the specific context of the EU/European Economic Area (EEA) as follows [4, 5].

1) Although the majority of EU/EEA member states have a low incidence of TB, it is a heterogeneous setting with some countries having a high or intermediate level of TB, with varying levels of multidrug-resistant (MDR)-TB and TB-HIV co-infection, and some countries bordering non-EU countries with a higher TB and MDR-TB burden.

2) TB services are fully integrated and merged within the health system in the majority of EU/EEA member states. This presents peculiarities in allocating responsibilities for the delivery of TB care.

3) The EU/EEA member states have a long established tradition of TB control that has evolved over the past decades. Implementation of new tools and high standards of diagnosis and care is aimed for in the EU/EEA member states.

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4) Several EU/EEA member states are pursuing TB elimination, sharing a common platform (based on the Wolfheze documents [6] and the Framework Action Plan to Fight TB in the EU [7]) with the ECDC and World Health Organization (WHO)-coordinated TB surveillance network and system [6–9].

The standards are designed as a living document that will be revised as technology, resources and circumstances change. Also, they complement existing national or international guidelines, being consistent with the WHO definitions and recommendations [5]. The ISTC were revised in 2009, while a new third edition has recently been presented to commemorate the 2014 World TB Day [3]. This prompted the ECDC and the ERS to compare the third edition of the ISTC and the ESTC to see what the differences are and to evaluate if a revision of the ESTC is necessary.

The core ECDC and ERS experts who coordinated the effort of the expert group developing the ESTC made a careful comparison of the new ISTC and ESTC standards (table 1), underlining the content that was not shared by both documents and summarising the differences. This will allow clinicians and public health officers to rapidly capture the innovative elements included in the third edition of the ISTC and understand to what extent they can be applied in the EU/EEA setting.

In terms of structure, the ESTC (consistent with the second edition of the ISTC [16]) contained 21 standards organised into four sections: 1) standards for diagnosis; 2) standards for treatment; 3) standards for addressing HIV infection and other comorbid conditions; and 4) standards for public health.

A new standard has been included in the third edition of the ISTC [3], to make clinicians aware that specific risk groups exist and that TB has a higher prevalence in these risk groups than in the general population. This issue is tackled by the ESTC in standards 1 and 4 (table 1).

No relevant differences were found between the ESTC and ISTC in standards 9, 13, 14, 17, 19, 20 and 21.

In standard 1, the ESTC take into account the variability of signs and symptoms TB presents with, while the ISTC make reference to chronic cough as the global ''pivotal'' symptom traditionally allowing investigation of a patient for TB. It seems adequate to describe the reality of the EU setting in the ESTC where chronic cough is more related to smoking and other lung diseases.

In standard 2, while the ISTC recommend Xpert MTB/RIF as the first choice for diagnosis (consistent with the present WHO policy to promote the wide peripheral use of the test [10–12]), the ESTC mention rapid testing for the identification of rifampicin and isoniazid resistance using validated tools. This makes sense in the EU, given the focus is on quality-assured culture-based methods and easy access to drug susceptibility testing (DST). The ESTC does not yet include a negative recommendation on blood-based serological tests since this WHO recommendation was published after the launch of the ESTC [13]. The WHO recommendation is for the use of interferon-γ release assays (IGRAs) in low- and middle-income countries [14]. Specific guidance on the use of IGRAs in the EU is provided by the ECDC [17–19]. In the perspective of TB elimination, IGRAs might gain additional interest in the diagnosis of TB infection.

Similarly, in standard 3 the ESTC advocate the use of culture and DST in extrapulmonary TB, while the ISTC consistently recommend the use of Xpert MTB/RIF.

In standard 5, the ESTC provide guidance on how to diagnose culture-negative TB, while the ISTC focus on smear-negative TB. For diagnosing culture-negative TB, a trial of broad-spectrum antimicrobials may be used according to the ESTC standard, such trial regimens should not include fluoroquinolones. The ESTC specifically recommend expedited investigation of immunocompromised patients, who represent a priority in the EU setting.

Standard 6 of the ISTC indicates that along with sputum smear microscopy and culture, the Xpert MTB/RIF test can also be used for bacterial confirmation of TB in children. The corresponding ESTC standard provides more details on how to diagnose TB in children.

In standard 7, the ESTC underline the need for the treating physician to collaborate with the local public health and/or community health services to perform a contact investigation [20].

Standard 8, apart from the different wording (internationally recommended treatment regimens in ESTC *versus* WHO recommended regimens in ISTC), is consistent in the two documents. The ESTC recommends the use of fixed-dose combinations.

In standard 10, the ISTC is more prescriptive on what test to use for DST when the sputum is still positive at 3 months, *i.e.* Xpert MTB/RIF should be used.

In standard 11, the ISTC is more restrictive in recommending DST. Instead of recommending it for all TB patients, as in the ESTC, the ISTC recommend DST for previously treated patients, patients who remain

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TABLE 1 Differences between the European Union Standards for Tuberculosis care (ESTC) and the third edition of the International Standards for Tuberculosis Care (ISTC)

ESTC [4]	ISTC [3]	Differences
	1. To ensure early diagnosis, providers must be aware of individual and group risk factors for TB and perform prompt clinical evaluations and appropriate diagnostic testing for persons with symptoms and findings consistent with TB	New standard included in ISTC
Standards for TB diagnosis		
1. All persons presenting with signs, symptoms, history or risk factors compatible with TB should be evaluated for pulmonary and/or extrapulmonary TB	2. All patients (including children) with unexplained cough lasting ⩾2 weeks or with unexplained findings suggestive of TB on chest radiographs should be evaluated for TB	The ISTC standard puts focus on the signs and symptoms of cough and unexplained findings suggestive of TB on chest radiographs, while according to the ESTC persons with any signs or symptoms compatible with TB should be evaluated. The ESTC standard specifically mentions individual risk factors for TB. This is taken into account in the new ISTC standard
2. All patients (adults, adolescents and children who are capable of producing sputum) suspected of having pulmonary TB should have at least two sputum specimens submitted for microscopic examination, culture and DST in a quality-assured laboratory. When possible, at least one early morning specimen should be obtained. In countries, settings or populations in which MDR-TB is suspected in a patient, rapid testing for the identification of rifampicin and isoniazid resistance, using validated tools in a quality-assured laboratory, should be performed	3. All patients (including children) who are suspected of having pulmonary TB and who are capable of producing sputum should have at least two sputum specimens submitted for smear microscopy or a single sputum specimen for Xpert MTB/RIF testing in a quality-assured laboratory. Patients at risk for drug resistance, who have HIV risk or who are seriously ill should have Xpert MTB/RIF performed as the initial diagnostic test. Blood-based serological tests and IGRA should not be used for diagnosis of active TB	WHO recommendations for Xpert MTB/RIF [10–12] are included in the ISTC standard whereas the ESTC standard mentions rapid testing for the identification of rifampicin and isoniazid resistance, using validated tools The ESTC standard recommends DST for all patients The ESTC standard puts more focus on the use of quality assured culture-based methods as these are more broadly available in the EU The 2011 WHO policy statement [13] against the use of blood-based serological tests and the 2011 WHO policy statement against the use of IGRAs [14] in low- and middle-income countries have been included in the ISTC
3. For all patients (adults, adolescents and children) suspected of having extrapulmonary TB, appropriate specimens from the suspected sites of involvement should be obtained for microscopy, culture, DST and histopathological examination in a quality-assured laboratory. In countries, settings or populations in which MDR-TB is suspected in a patient, rapid testing for the identification of rifampicin and isoniazid resistance in a quality-assured laboratory could be performed	4. For all patients (including children) suspected of having extrapulmonary TB, appropriate specimens from the suspected sites of involvement should be obtained for microbiological and histopathological examination. An Xpert MTB/RIF test is recommended as the preferred initial microbiological test for suspected tuberculous meningitis because of the need for a rapid diagnosis	The ISTC standard includes a specific recommendation for using the Xpert MTB/RIF test as the preferred initial microbiological test for suspected TB meningitis because of the need for a rapid diagnosis The ESTC emphasises culture confirmation and rapid testing of MDR-TB for all extrapulmonary TB cases, but does not specify which type of rapid molecular testing to use
4. All persons with chest radiographic findings suggestive of pulmonary TB should have sputum specimens submitted for microscopic examination, culture and DST in a quality-assured laboratory. In countries, settings or populations in which MDR-TB is suspected in a patient, rapid testing for the identification of rifampicin resistance and, when possible, isoniazid resistance in a quality-assured laboratory should be performed	Combined with standard 2	

TABLE 1 Continued

ESTC [4]	ISTC [3]	Differences
5. The diagnosis of culture-negative pulmonary TB should be based on the following criteria: all bacteriological tests are negative (including direct sputum smear examinations, cultures and rapid molecular testing); chest radiographic findings are compatible with TB; there is a lack of response to a trial of broad-spectrum antimicrobial agents (because fluoroquinolones are active against *Mycobacterium tuberculosis* complex and, thus, may cause transient improvement in persons with TB, they should be avoided). In persons who are seriously ill or have known or suspected HIV infection or have any immunocompromising conditions, the diagnostic evaluation should be expedited and, if clinical evidence strongly suggests TB, a course of anti-TB treatment should be initiated	5. In patients suspected of having pulmonary TB whose sputum smears are negative, Xpert MTB/RIF and/or sputum cultures should be performed. Among smear and Xpert MTB/RIF negative persons with clinical evidence strongly suggestive of TB, anti-TB treatment should be initiated after collection of specimens for culture examination	The main difference is that the ESTC standard uses the culture-based case definition and the ISTC standard uses the sputum smear status. The ISTC includes the use of Xpert MTB/RIF as a diagnostic test for patients with pulmonary TB and negative sputum smears. The ESTC does not specify which type of rapid molecular test should be used A trial of broad-spectrum antimicrobial agents is recommended by the ESTC A specific recommendation for expedited investigation of immunocompromised patients is included in the ESTC standard
6. In all children suspected of having intrathoracic TB (*i.e.* pulmonary, pleural and mediastinal or hilar lymph node), bacteriological confirmation should be sought through examination of appropriate biological samples (expectoration or induced sputum, bronchial secretions, pleural fluid or gastric washings) for smear microscopy, culture and DST in a quality-assured laboratory. In the event of negative bacteriological results, a diagnosis of TB should be based on the presence of abnormalities consistent with TB on chest radiography or other imaging, a history of exposure to an infectious case, evidence of TB infection (positive TST and/or IGRA) and clinical findings suggestive of TB. For children suspected of having extrapulmonary TB, appropriate specimens from the suspected sites of involvement should be obtained for microscopy, culture, DST and histopathological examination	6. In all children suspected of having intrathoracic TB (*i.e.* pulmonary, pleural and mediastinal or hilar lymph node), bacteriological confirmation should be sought through examination of respiratory secretions (expectorated sputum, induced sputum or gastric lavage) for smear microscopy, Xpert MTB/RIF test and/or culture	The ISTC standard indicates that as well as smear microscopy and culture, the Xpert MTB/RIF test can be used for bacterial confirmation of TB in children. The ESTC standard provides more details on how to diagnose TB in children
Standards for TB treatment		
7. Any practitioner treating a patient for TB is assuming an important public health responsibility to prevent ongoing transmission of the infection and the development of drug resistance. To fulfil this responsibility the practitioner must not only prescribe an appropriate regimen, but also utilise local public and/or community health services, agencies and resources when necessary, to perform contact investigation, to assess the adherence of the patient and to address poor adherence when it occurs	7. To fulfil their health responsibility, as well as their responsibility to the individual patient, the provider must prescribe an appropriate treatment regimen, monitor adherence to the regimen and, when necessary, address factors leading to interruption or discontinuation of treatment. Fulfilling these responsibilities will probably require coordination with local public health services and/or other local services	The ESTC standard specifically mentions the obligation of the practitioner treating a TB patient to collaborate with the local public and/or community health services to perform contact investigation

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TABLE 1 Continued

ESTC [4]	ISTC [3]	Differences
8. All patients (including those with HIV infection) who have not been previously treated and without any risk factors for drug resistance should receive an internationally accepted first-line treatment regimen using drugs of known bioavailability. The initial phase should consist of 2 months of isoniazid, rifampicin, pyrazinamide and ethambutol. The continuation phase should consist of isoniazid and rifampicin given for 4 months (2HRZE/4HR). The doses of anti-TB drugs used should conform to international recommendations. Fixed dose combinations of two (isoniazid and rifampicin), three (isoniazid, rifampicin and pyrazinamide) and four (isoniazid, rifampicin, pyrazinamide and ethambutol) drugs are highly recommended	8. All patients who have not been treated previously and do not have other risk factors for drug resistance should receive a WHO-approved first-line treatment regimen using quality-assured drugs. The initial phase should consist of 2 months of isoniazid, rifampicin, pyrazinamide nd ethambutol. The continuation phase should consist of isoniazid and rifampicin given for 4 months. The doses of anti-TB drugs used should conform to WHO recommendations. Ethambutol may be omitted in children who are HIV negative and who have non-cavitary disease	The ISTC standard specifically mentions that patients should be treated with a WHO-approved first-line treatment regimen whereas the ESTC standard mentions an internationally accepted first-line treatment regimen The ESTC standard promotes the use of fixed dose combinations
9. To assess and foster adherence, a patient-centred approach to administration of drug treatment, based on the patient's needs and mutual respect between the patient and the provider, should be developed for all patients Supervision and support should be individualised and should draw on the full range of recommended interventions and available support services, including patient counselling and education. A central element of the patient-centred strategy is the use of measures to assess and promote adherence to the treatment regimen and to address poor adherence when it occurs. These measures should be tailored to the individual patient's circumstances, based on a detailed anamnesis of the patient's clinical and social history, and be mutually acceptable to the patient and the provider. Such measures may include direct observation of medication ingestion (directly observed treatment) and identification and training of a treatment supporter (for TB and, if appropriate, HIV infection) who is acceptable and accountable to the patient and to the health system. Appropriate incentives and enablers, including financial, social and psychosocial supports, may also serve to enhance treatment adherence	9. A patient-centred approach to treatment should be developed for all patients in order to promote adherence, improve quality of life and relieve suffering. This approach should be based on the patient's needs and mutual respect between the patient and the provider	There are no relevant differences between the ESTC and the ISTC standards The ESTC standard provides more details about how and what supervision and support should be provided

TABLE 1 Continued

ESTC [4]	ISTC [3]	Differences
10. Response to therapy in patients with pulmonary TB should be monitored by follow-up smear microscopy and culture at the time of completion of the initial phase of treatment (2 months for drug-susceptible TB). If the sputum smear and culture are positive at completion of the initial phase, sputum smears should be examined again at 3 months and, if positive, DST should be performed. In patients with extrapulmonary TB and in children unable to produce sputum, the response to treatment is assessed clinically	10. Response to treatment in patients with pulmonary TB (including those with TB diagnosed by a rapid molecular test) hould be monitored by follow-up sputum microscopy at the time of completion of the initial phase of treatment (2 months). If the sputum smear is positive at completion of the initial phase, sputum microscopy should be performed again at 3 months and, if positive, rapid molecular drug sensitivity testing (Line-probe assays or Xpert MTB/RIF) or culture with DST should be performed. In patients with extrapulmonary TB and in children, the response to treatment is best assessed clinically	The ISTC standard specifically mentions that patients diagnosed by a rapid molecular test should be monitored The ISTC standard mentions that if sputum is still positive at 3 months a rapid molecular DST (Line-probe assays or Xpert MTB/RIF) or culture with DST should be performed. The ESTC standard does not specify the test to be used for DST
11. An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms and the community prevalence of drug resistance, should be obtained for all patients. Rapid testing, including rapid rifampicin and isoniazid resistance testing should be performed for all patients suspected of resistance as defined in standards 2 and 8. Furthermore, patient counselling and education should begin immediately for all TB patients, in order to minimise the potential for transmission. Infection control measures appropriate to the setting should be applied as recommended in ESTC public health standard 20	11. An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms, and the ommunity prevalence of drug resistance (if known), should be obtained for all patients. DST should be performed at the start of therapy for all previously treated patients. Patients who remain sputum smear positive at completion of 3 months of treatment and patients in whom treatment has failed, have been lost to follow-up, or relapsed following one or more courses of treatment should always be assessed for drug resistance. For patients in whom drug resistance is considered to be likely, an Xpert MTB/RIF test should be the initial diagnostic test. Line-probe assay or culture and testing for susceptibility to at least isoniazid and rifampicin should be performed promptly if rifamycin resistance is detected. Patient counselling and education, as well as an empiric second-line treatment regimen, should begin immediately to minimise the potential for transmission. Infection control measures appropriate to the setting should be applied	The ISTC standard is more restrictive in recommending DST. Instead of recommending it for all TB patients (ESTC) it recommends DST for previously treated patients, patients who remain sputum smear positive at completion of 3 months of treatment and patients in whom treatment has failed, who have been lost to follow-up, or who relapsed following one or more courses of treatment The ESTC standard recommends rapid testing, whereas the ISTC standard recommends using the Xpert MTB/RIF test for patients in whom drug resistance is considered to be likely, followed by a Line-probe assay if rifamycin resistance is detected. A note to the ESTC standard stresses that rapid molecular testing does not rule out the requirement to perform culture DST to confirm results
12. Patients with, or highly likely to have, TB caused by drug-resistant (especially MDR-/XDR-TB) organisms should be treated with specialised regimens containing second-line anti-TB drugs. The regimen chosen may be standardised or based on suspected or confirmed drug susceptibility patterns. At least four drugs to which the organisms are known or presumed to be susceptible to, including an injectable agent and pyrazinamide, should be used. Treatment should be given for at least 20 months, the recommended intensive phase of treatment being 8 months (instead of 6 months as in previous recommendations)	12. Patients with, or highly likely to have, TB caused by drug-resistant (especially MDR-/XDR-TB) organisms should be treated with specialised regimens containing quality-assured second-line anti-TB drugs. The doses of anti-TB drugs should conform to WHO recommendations. The regimen chosen may be standardised or based on suspected or confirmed drug susceptibility patterns. At least pyrazinamide and four drugs to which the organisms are known or presumed to be susceptible, including an injectable agent, should be used in an 8 month intensive phase and at least three drugs to which the organisms are known or presumed to be susceptible should be used in the continuation phase. Treatment should be given for at least 18–24 months beyond ulture conversion. Patient-centred measures, including observation of treatment, are required to ensure adherence. Consultation with a specialist experienced in treatment of patients with MDR-/XDR-TB should be obtained	The ISTC standard recommends that the doses of the anti-TB drugs should conform to WHO recommendations The ISTC standard specifies that the continuation phase needs to contain at least three drugs to which the organisms are known or presumed to be susceptible

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TABLE 1 Continued

ESTC [4]	ISTC [3]	Differences
13. A written record of all medications given, bacteriological response and adverse reactions should be maintained for all patients	13. An accessible, systematically maintained record of all medications given, bacteriologic response, outcomes and adverse reactions should be maintained for all patients	There are no relevant differences between the ESTC and the ISTC standards
Standards for addressing HIV infection and comorbidity conditions		
14. HIV testing and counselling should be recommended to all patients with, or suspected of having, TB. Testing is of special importance as part of the routine management of all patients in areas with a high prevalence of HIV infection in the general population and in patients with symptoms and/or signs of HIV-related conditions. Because of the close relationship between TB and HIV infection, integrated approaches to prevention and treatment of both infections are recommended	14. HIV testing and counselling should be conducted for all patients with, or suspected of having, TB unless there is a confirmed negative test within the previous 2 months. Because of the close relationship of TB and HIV infection, integrated approaches to prevention, diagnosis and treatment of both TB and HIV infection are recommended in areas with high HIV prevalence. HIV testing is of special importance as part of routine management of all patients in areas with a high prevalence of HIV infection in the general population, in patients with symptoms and/or signs of HIV-related conditions, and in patients having a history suggestive of high risk of HIV exposure	There are no relevant differences between the ESTC and the ISTC standards
15. All patients with TB and HIV infection should be evaluated to determine if ART is indicated during the course of treatment for TB, according to the severity of their immunodeficiency. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. However, initiation of treatment for TB should not be delayed and the antiretroviral treatment prescribed as soon as possible based on evidence	15. In persons with HIV infection and TB who have profound immunosuppression (CD4 counts <50 cells·mm^{-3}), ART should be initiated within 2 weeks of beginning treatment for TB unless tuberculous meningitis is present. For all other patients with HIV and TB, regardless of CD4 counts, ART should be initiated within 8 weeks of beginning treatment for TB. Patients with TB and HIV infection should also receive cotrimoxazole as prophylaxis for other infections	The ISTC standard includes the 2013WHO recommendation that ART should be initiated within 2 weeks of beginning treatment for TB in persons with profound immunosuppression unless tuberculous meningitis is present [15]. For all other patients with HIV and TB, regardless of CD4 counts, ART should be initiated within 8 weeks of beginning treatment for TB The ESTC standard does not provide recommendations for patients with HIV infection, while the ISTC standard does, *i.e.* co-infected patients should receive cotrimoxazole as prophylaxis for other infections
16. Persons with HIV infection who, after careful evaluation, have a positive test for presumed LTBI with *M. tuberculosis* (TST and/or IGRAs) but do not have active TB should be treated with isoniazid for 6–9 months or any new regimen for which evidence becomes available	16. Persons with HIV infection who, after careful evaluation, do not have active TB should be treated for presumed LTBI with isoniazid for at least 6 months	The ISTC standard recommends that all persons with HIV infection and without active TB, independent of having a positive test for LTBI, are treated for presumed LTBI whereas the ESTC standard only recommends preventive treatment for those with a positive LTBI test or who are highly probable to have LTBI
17. All providers should conduct a thorough assessment of conditions that could affect TB treatment response or outcome. At the time the case management plan is developed, the provider should identify additional services that would support an optimal outcome for each patient and incorporate these services into an individualised plan of care. This plan should include assessment of and referrals for treatment of other illnesses with particular attention to those known to affect treatment outcome, for instance care for diabetes mellitus, drug and alcohol treatment programmes, tobacco smoking cessation programmes and other psychosocial support services, or to such services as antenatal or well-baby care	17. All providers should conduct a thorough assessment for comorbid conditions and other factors that could affect TB treatment response or outcome and identify additional services that would support an optimal outcome for each patient. These services should be incorporated into an individualised plan of care that includes assessment of and referrals for treatment of other illnesses. Particular attention should be paid to diseases or conditions known to affect treatment outcome, *e.g.* diabetes mellitus, drug and alcohol abuse, under nutrition and tobacco smoking. Referrals to other psychosocial support services or to such services as antenatal or well-baby care should also be provided	There are no relevant differences between the ESTC and the ISTC standards

TABLE 1 Continued

ESTC [4]	ISTC [3]	Differences
Standards for public health and TB prevention		
18. All providers of care for patients with TB should ensure that persons who are in close contact with patients who have infectious TB (*e.g.* in families, congregate settings like migrants shelters, schools and prisons), are evaluated and managed in line with international recommendations. The risk of TB transmission depends on the concentration of the mycobacteria in the air, the duration of the contact and the susceptibility of the contact to infection and disease. The determination of priorities for contact investigation is based on the likelihood that a contact has undiagnosed TB, is at high risk of having been infected by the index case, is at high risk of developing TB if infected, and is at risk of having severe TB if the disease develops	18. All providers should ensure that persons who are in close contact with patients who have infectious TB are evaluated and managed in line with international recommendations. The highest priority contacts for evaluation are persons with symptoms suggestive of TB, children aged <5 years, contacts with known or suspected immunocompromised states (particularly HIV infection), and contacts of patients with MDR-/XDR-TB	The ESTC standard does not provide a list of priority contacts for evaluation, instead it provides the determinants of TB transmission and susceptibility of a contact that should be assessed
19. Children <5 years of age and persons of any age with HIV infection who are close contacts of an infectious index patient and who, after careful evaluation, do not have active TB should be treated for presumed LTBI with isoniazid	19. Children <5 years of age and persons of any age with HIV infection who are close contacts of patient person with infectious TB and who, after careful evaluation, do not have active TB should be treated for presumed LTBI with isoniazid for at least 6 months	There are no relevant differences between the ESTC and the ISTC standards
20. Each healthcare facility caring for patients who have, or are suspected of having, infectious TB should develop and implement an appropriate TB infection control plan	20. Each healthcare facility caring for patients who have, or are suspected of having, infectious TB should develop and implement an appropriate TB infection control plan to minimise possible transmission of *M. tuberculosis* to patients and healthcare workers	There are no relevant differences between the ESTC and the ISTC standards
21. All providers must report both new and retreatment TB cases and their treatment outcomes to local public health authorities, in conformance with applicable legal requirements and policies	21. All providers must report both new and re-treatment TB cases and their treatment outcomes to local public health authorities, in conformance with applicable legal requirements and policies	There are no relevant differences between the ESTC and the ISTC standards

TB: tuberculosis; DST: drug susceptibility testing; MDR: multidrug resistant; IGRA: interferon-γ release assay; WHO: World Health Organization; H: isoniazid; R: rifampicin; Z: pyrazinamide; E: ethambuthol; EU: European Union; TST: tuberculin skin test; XDR: extensively-drug resistant; ART: antiretroviral therapy; LTBI: latent TB infection. Xpert MTB/RIF test is manufactured by Cepheid (Sunnyvale, CA, USA).

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sputum smear positive at completion of 3 months of treatment, and patients in whom treatment has failed, patients lost to follow-up, or patients who relapsed following one or more treatment courses.

In standard 12 the recommendations are quite similar. The ESTC contain an EU-adapted supplement focusing on the need to treat MDR-TB cases in specialised settings with individualised and DST-based regimens, and under the guidance of a panel of experts [21–24].

The ISTC standard 15 includes the recent WHO recommendations to initiate antiretroviral treatment within 2 weeks of beginning TB treatment in HIV-infected individuals with profound immunosuppression or within 8 weeks for all others [15]. The ESTC specifies that patients with TB and HIV should be evaluated to determine if antiretroviral therapy is indicated.

The main difference between the ISTC and the ESTC in standard 16 is that the ISTC recommend treatment of latent TB infection for all HIV-infected persons who do not have active TB whereas the ESTC only recommend it for those either infected or likely to be infected by *Mycobacterium tuberculosis*.

In standard 18 the ISTC provides a specific list of priority contacts for contact evaluation, whereas the ESTC states which determinants of TB transmission and susceptibility of a contact should be evaluated.

The analysis of the differences between the two documents (table 1) shows the consistency of their recommendations given the different setting (EU *versus* global) in which they are applied.

As new evidence is rapidly growing, a revision of the ESTC will be appropriate in about 2 years. The critical elements that will require modification will be represented, in our opinion, by the following factors: 1) the WHO post-2015 strategy, which will emphasise elimination and will pose new targets and milestones; 2) the progressive implementation of the ECDC elimination framework *vis-à-vis* the evidence on how the interventions necessary to reach elimination are applied in the EU [6, 25, 26]; and 3) the introduction of new drugs and new regimens (potentially involving delamanid, bedaquiline and PA-824) to treat MDR-TB, but also potentially drug-susceptible TB and latent TB infection [27–30].

We hope that the comparative analysis of the two documents will further contribute to help clinicians in making the correct diagnosis and in the undertaking the correct treatment and public health actions, to ensure the best management of TB and MDR-TB cases.

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