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### 313. Tuberculosis: epidemiological and public health features

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**P2858****Agreement between Quantiferon-TB-Gold In Tube, T-SPOT.TB and tuberculin skin testing for diagnosing latent tuberculosis infection in a contact tracing study**

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**Aim:** To determine the agreement between Quantiferon-TB Gold In Tube (QFN), T-SPOT.TB and TST in diagnosing LTBI in a contact study.

**Methods:** 753 individuals from contact tracing studies were included in the study. In all cases QFN and TST were performed, and in 141 patients the T-SPOT was also performed. TST was negative when the induration was less than 5 mm.

**Results:** The QFN and TST obtained concordant result in 478 cases from the 753 patients (the overall agreement was 63%), being both tests negative in 145 cases, and positive in 333 cases. From the 275 discordant results, in only one case the TST was negative and the QFN positive (corresponds with a high degree of exposure to the index case), and in 274 cases the TST was positive and the QFN negative, corresponding in 239 cases to BCG-vaccinated patients, and without significant difference between time of exposure to the index case

With regards to the 141 patients tested with T-SPOT both in vitro tests were concordant in 120 cases (85.1%), being in 61 cases both tests negative, and in 59 cases positive. From the 21 discordant results, in 5 cases the QFN was positive and the T-SPOT negative, and in 16 cases the QFN was negative but the T-SPOT was positive, being in 15 of them the time of exposure significantly higher.

**Conclusion:** QFN and T-SPOT.TB have a high concordance in the diagnosis of LTBI. T-SPOT.TB shows a higher number of positive results than QFN. The main discordant results between TST and QFN should be attributed to the BCG-vaccination. Both tests seem useful for the diagnosis of LTBI in the contact studies.

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**P2859****Tuberculosis in health care staff in Romania, 2006-2010**

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**Introduction:** Health care staff represents a well recognized high risk group for TB.

**Objective:** To analyze characteristics of TB cases out of health care staff in Romania during 2006-2010 by demographic, clinical, bacteriological parameters and treatment outcomes.

**Methods:** Retrospective descriptive study of TB cases notified among staff of health care facilities in Romania from 2006 to 2010. Data and information used are from the electronic National TB Register.

**Results:** Total number of TB cases reported in health care workers in Romania from 2006 to 2010 was 843, declining from 224 in 2006 to 139 in 2009 and slightly increasing (to 150) in 2010. Most of them were aged from 25 to 39 years. Conversely to the general population, female gender was predominant (over 70%),

as the residence in urban area (over 70% as well). Even the staff in TB network varied between 2006 and 2008 from 12.9% to 7.7% of all medical staff, TB incidence rate in this group was 114.5‰, versus 51.3‰ in other medical staff, in 2010. Pulmonary cases were from 74.4% in 2007 to 85.9% in 2008. New cases and relapses represented over 96% of all cases (96.8% in 2006 and 99.3% in 2010). In the five years have been reported 18 MDR-TB cases – from 6 in 2008 (6.9% of culture positive pulmonary cases) to 3 in 2010 (respectively 3.8%) and none in 2007. Overall success rate was 98.3% in 2007 and 89.3% in 2006.

**Conclusions:** TB incidence rate in health care staff in TB facilities is 2.2 folds higher than that in the personnel in other health care facilities. New pulmonary cases were predominant, with a few MDR-TB cases and a therapeutic success rate over 89%.

#### P2860

##### Pattern of tuberculosis (TB) among health care Workers (HCW) attending a revised national TB control programme (RNTCP) unit in Kottayam Medical College (Kerala India)

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**Background:** There is paucity of data with regard to pattern of TB in HCW

**Aim:** To study the pattern of TB among HCW

Study setting RNTCP unit of a Medical College in Kerala, India from October 2009-March 2011.

**Methods:** Clinical profile of patients referred to RNTCP unit with a proven diagnosis or with a clinical and radiologic diagnosis made by a specialist medical teacher were gathered by a preset oral questionnaire and clinical examination.

**Result:** Out of 1222 TB patients 5.72% (n= 70) were HCW.90% of HCW (n 63) were nurses or nursing students, 10% (n 7) were paramedical staff.No doctors or medical students registered in control programme for treatment. 68.6% (n=48) had extra pulmonary TB & 31.4% (n 22) pulmonary TB (OD 2.725). 63.6% (14/22) of pulmonary TB was smear positive. Occurrence of TB lymphadenitis (n 24) and abdominal TB (n 5) were more common among HCW compared to general category patients (p value of <0.05). 92.8% were newly diagnosed (n 65), 4.2% (n 3) retreatment & 2.8% (n 2) MDR. None had brain or menigeial TB. 92.8% were BCG vaccinated.

**Conclusion:** TB lymphadenitis was more common among HCW compared to general category patients. Majority of HCW coming for treatment in RNTCP were nurses or nursing students. No doctors registered for treatment in control programme.

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#### P2861

##### Tuberculosis (TB) notifications in healthcare workers (HCW) in Liverpool, UK

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**Background:** The number of overseas HCW in Liverpool has grown sharply in recent years. In 2005, an audit demonstrated a rise in the number of TB notifications in HCW (mainly from overseas) in the previous 24 months, and suggested the need for vigilant new entrant screening. We aimed to look at the trend of HCW TB notifications 6 years later to assess the impact of improved TB screening.

**Method:** TB notification data for the calendar year 2011 was collected from the Liverpool TB service. We compared this data with results from the previous audits.

**Results:** See table

|                                 | Years 2001–2002 | Years 2003–2004   | Year 2011     |
|---------------------------------|-----------------|-------------------|---------------|
| Total TB Notifications          | 200             | 125               | 61            |
| TB in HCW                       | 7 (3.5%)        | 20 (16%)          | 5 (8%)        |
| Difference from previous period | –               | +12.5% (p<0.0001) | –8%* (p=0.14) |
| Smear positive HCW              | 2 (29%)         | 7 (35%)           | 1 (20%)       |

\*The difference between 2001-2002 and 2011 was not statistically significant (p=0.15).

All but one were non-UK born and average time spent in the UK was more than five years. No positive contacts were detected and 1 case required an incident report meeting.

**Conclusion:** Our results show that the proportion of HCW TB notifications has halved. There is also a decrease in the number of smear positive cases, and the average time spent in the UK before contracting TB disease was longer than in previous years. Although clinically significant, we were unable to show statistical significance most likely due to type II error.

Nonetheless, this demonstrates that with efficient and organized screening especially among HCW, the high risk cases can be identified earlier and treated for latent disease (when necessary) thus preventing development of pulmonary TB.

#### P2862

##### Tuberculosis among health care workers

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Aim of this study is to assess the occupational risk and characteristic of tuberculosis (TB) among health care workers (HCWs) employed at health institutions in Republic of Macedonia from 2007-2011 year. The diagnosis of TB was based on clinical and radiological findings and confirmed bacteriological or histological. The data were from National TB registry.

**Results:** From total number of 16 HCWs with TB (9 nurses, 3 stomatologists, 1 chemist assistant and 3 other employed), 13(81.3%) were female. The majority of them 5 (31.1%) were on the age of 25-34 years. The pulmonary TB were 9(56.3%), extra pulmonary TB 4(25%) and both pulmonary and extra pulmonary TB 3(18.7%). The SS+ and culture + were 9(56.3%), only culture + were 3(18.7%) and 4 (25%) extra pulmonary TB have histological confirmation. The all 12 (75%) were sensitive on first line drugs. The all registered HCWs with TB were success treated, 6(37.5%) as cured and 10(62.5%) as treatment completed. Between those patients were not employed in institutions for lung diseases and tuberculosis because the infection control is better than in other health institutions.

#### P2863

##### Risk of latent tuberculosis infection among healthcare trainees

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**Objective:** The prevalence of latent tuberculosis infection (LTBI) and the risk of tuberculosis infection in nursing students in Germany are unknown. Therefore nursing trainees were followed over a three-year period for the prevalence and risk of LTBI.

**Method:** In a prospective cohort study, all trainees (n=194) who began training as a nurse or carer at the Vivantes Healthcare Training Institute in Berlin on 1 October 2008, and 1 April 2009, were IGRA-tested at three different times. IGRAs were performed at the start of training and at the end of the first and third years of training. Socio-demographic data and possible risk factors were recorded.

**Results:** The cohort consisted as of the baseline survey (when they began their training) of a total of 194 trainees. 70% were female. The average age was 23. The LTBI prevalence was 2.1% (4/194). 40 trainees quit before completing their training. In the first follow-up test, 2 out of 154 tested IGRA-positive, and 151 had constantly negative results. One IGRA was constantly positive and there was one conversion and one reversion. In the second follow-up test upon completion of the training there was again one conversion, one reversion and one constantly positive test result over the three years (own TB anamnesis). No case of active tuberculosis was diagnosed over the three-year observation period.

**Conclusion:** Prevalence and infection rates are low among trainees. Negative IGRA test results proved very constant. Therefore IGRA testing in this low risk group is feasible. However, screening should focus on trainees with personal risk factors for TB. All others should only be tested after they have been in close contact with a TB index patient.

#### P2864

##### The effect of the introduction of IGRA in screening French healthcare workers for tuberculosis

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**Introduction:** In France pre-employment screening for tuberculosis (TB) is performed for healthcare workers (HCW). Screening is repeated, when exposure to TB patients or infectious material occurs. The results of the TB screenings were analysed in a retrospective analysis.

**Method:** TB screenings were performed with Tuberculin Skin Test (TST) and Interferon-Gamma Release Assays (Quantiferon Gold in tube QFT). If TST was >15mm or TST increased by >10 mm, X-ray and pneumology consultation regarding preventive treatment of latent TB infection (LTBI) was performed. The screening results of 637 HCWs on whom QFT was performed were extracted from the files of the University Hospital of Nantes.

**Results:** In 3 (0.5%) HCWs the QFT was indeterminate. In 22.2% the QFT was positive. A second QFT was performed in 118 HCWs. Reversion rate was 42% (5 out of 17). Conversion rate was 6% (6 out of 98). TST was performed in 466 (73.5%) of the HCWs. TST >10mm results were 77.4%. In those with TST <10mm, QFT was positive in 14% and in those with TST >10mm, QFT was positive in 26.7%. When based on QFT results, X-ray and pneumology consultation could have been reduced to 28.6% of those selected by TST.

**Conclusion:** TST overestimated the prevalence of LTBI in this cohort. The de-

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cision on X-ray and consultation regarding preventive treatment should be based on QFT rather than TST results. The high reversion rate should be taken into consideration when consulting HCWs regarding preventive treatment.

**P2865****Contact screening in tuberculosis. Can we identify those with higher risk?**

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**Introduction:** Contact tracing is part of the tuberculosis (TB) elimination strategy. It is important to know which risk factors are associated with a positive screening. **Objectives:** To identify risk factors associated with a positive screening.

**Material and methods:** During 2011, contacts of patients with pulmonary TB (sputum or broncho-alveolar lavage smear or culture positive), followed for screening in a TB reference centre, were questioned about their exposure to the index case. Positive screening was defined as active TB or latent infection. Contacts with incomplete characterization of exposure, unfinished screening or a past history of TB were excluded. A binary logistic model was used to analyze the variables.

**Results:** We observed 509 contacts of which 359 (153 men, median age: 32 years) were included in the analysis. 76 had a positive screening. Positive screening was associated with a positive sputum analysis of the index case (OR=2.62, 95%CI=1.33-5.14) and with cohabitation (OR=3.42, 95%CI=1.66-7.07). Each additional year in age of the contact implied an increase in the odds for infection of 3% (OR=1.03, 95%CI=1.02-1.05) and each additional day of symptoms by the index case, previous to treatment, implied an increase in the odds for infection among his contacts of 1% (OR=1.01, 95%CI=1.00-1.02). No significant differences were found regarding size and ventilation of the exposure site.

**Conclusions:** This study shows that there is a significant increase in the risk of TB transmission to contacts for every day that the diagnosis of the index case is delayed. Increased risk was also shown for cohabitants, contacts of older age and the presence of positive sputum smear or culture of the index case.

**P2866****Approaching tuberculosis in a vulnerable group**

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**Introduction:** The homeless represents a high risk group for TB, with poor access to health care services. TB prevalence among the around 5,000 homeless estimated to live in Bucharest is not known.

**Aims and objectives:** To detect active TB cases in homeless population in Bucharest.

**Methods:** A screening program was developed based on partnership between the National TB Programme and Samusocial Romania (NGO providing medical, psychological and social support to homeless people). Persons coming to the surgery service of Samusocial have been screened for TB in TB facilities. Any homeless giving a positive informed consent has been included and only exclusion criterion was having another chest X-ray in the previous 6 months.

**Results:** In the 248 cases registered from January to June 2011, 83.9% were males, mean age was 43.9 years (from 18 to 73 years old), 30.2% didn't have any ID document and half were at first medical consultation. TB has been suspected in 44.4% by clinical criteria, but from eligible persons only 48% were screened by chest X-ray, 14.1% refused and 35.5% didn't come back for screening. Active TB has been found in 8 cases (6.7% from the screened persons), 2 of them negative to clinical examination. None was previously examined even though they have free access to TB services. All cases were admitted in long-stay hospitals for treatment and monitoring.

**Conclusions:** In this project the prevalence of active TB was found very high in the homeless population (6,700‰). Providing free access to TB services is not sufficient to detect TB cases in this high risk group and active screening programs are necessary.

**P2867****Tuberculosis and migration: Predictors of epidemiological trends**

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Last years economic migration to the big cities of Russian Federation (RF) from other regions of RF and former Soviet republics has considerably increased. Since 2011 free diagnosis of tuberculosis (TB) and free TB-treatment are not available for foreigners in St. Petersburg, RF.

**Objective:** To determine the impact of health care changes on the incidence of TB.

**Methods:** The study was conducted in the district of St. Petersburg. The population of this district was 178,000. From 01.01.2008 an office for migrants has opened at the TB dispensary. All persons including migrants who addressed the TB dispensary during 2008-2011 were examined. The causes for examination were symptoms of tuberculosis or casual radiological findings. Examinations and treatment were free for all patients. Until 2008, there was no systematic recording of TB in migrants.

**Results:** During 2008-2010 the number of new TB cases in local population decreased, the number of infectious TB has decreased in local population and in migrants. The number of new cases of TB in children (local population and migrants) has decreased. In 2011, the trend reversed.

Number of TB cases

|   | 2008 | 2009 | 2010 | 2011 |
|---|------|------|------|------|
| TB in migrants                          | 35   | 31   | 37   | 22   |
| sputum-positive PTB in migrants         | 17   | 16   | 13   | 10   |
| TB in children (migrants)               | 7    | 5    | 4    | 2    |
| TB in local population                  | 80   | 72   | 54   | 66   |
| sputum-positive PTB in local population | 43   | 33   | 19   | 30   |
| TB in children (local population)       | 6    | 4    | 2    | 6    |

**Conclusions:** To ensure effective control of tuberculosis free access to health care is required for all TB patients, including migrants.

**P2868****New-entrant screening for tuberculosis at port of entry in the U.K.: Is it time to change policy?**

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**Background:** It is shown that 20% of tuberculosis (TB) cases are diagnosed in persons entering UK within 2 years & in 45% within 5 years of arrival. Therefore the first 2-5 years of arrival in UK presents a period of high risk of reactivation of new-entrants with LTBI. This clearly indicates the importance of early screening & reducing the risk of active TB by giving chemoprophylaxis to patients with LTBI.

UK policy at the moment advocates identification of active TB by chest x-ray for all new arrivals intending to stay for > 6 months from countries with a TB incidence 40/100,000; however, screening is very arbitrary & not standardised. The results are forwarded to local NHS TB services where new entrants intend to settle for complete screening.

**Methods:** A retrospective review was conducted of all new-entrants who were referred to our institution during a 2 year period, from January 2010, with supposedly an abnormal chest x-ray at port of entry. All new-entrants were screened for active & latent TB by TST or IGRA

**Results:** 103 patients, 51 females & 52 males were referred, however only 42 patients (40.77%) (26 females & 14 males) attended the TB clinic, of which 31(73.8%) were < 35 years old. Of the 42, 13 patients (31%) were diagnosed to have LTBI, while none were found to have active TB. Six patients with LTBI were from the sub-Saharan Africa, & 7 from the Indian subcontinent. Of 13 patients with LTBI, 10 patients completed 3 month course of chemoprophylaxis.

**Conclusion:** Screening new-entrants at port of entry is inadequate. New-entrants often do not attend clinic appointments since they have moved elsewhere or do not understand the necessity of being screened for latent or active TB.

**P2869****Impaired pulmonary function and the risk of tuberculosis – A population based cohort study**

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**Background:** Even though COPD is a frequent co-morbid condition in elderly with active tuberculosis relatively little is known to what extent impaired lung

function increases the incidence of active tuberculosis in excess of the direct effect of smoking.

**Methods:** 28,907 participants of the Malmo Preventive Project performed a spirometry at base-line examination and were followed for a mean of 25 years. Pulmonary function was measured as FVC and FEV<sub>1</sub> % of predicted (standardized for age, height and gender) and classified according to the GOLD criteria. Cases of incident tuberculosis, notified in the local tuberculosis register 1989-2008 were identified. Hazard ratios (HR) for subsequent tuberculosis according to FEV<sub>1</sub> and GOLD-stage were estimated using Cox regression.

**Main results:** A total of 26 cases of incident tuberculosis were identified corresponding to an overall incidence of 5.2 (95% confidence interval [95% CI] 3.5-7.6) per 100,000 person-years. The incidence rate was inversely correlated with FEV<sub>1</sub> (% of predicted), HR per 10%-unit increase 0.71 (95% CI 0.59-0.86). The results persisted after adjustment for smoking and age at screening, HR per 10%-unit increase in FEV<sub>1</sub> (% of predicted) 0.75 (95% CI 0.61-0.91).

The incidence of TB increased with GOLD-stage, stage I, crude HR 1.9 (95% CI 0.5-6.7), stage II, HR 5.64 (95% CI 2.2-14.7), stage III+IV, HR 6.9 (95% CI 0.9-52.6),  $p < 0.001$  for linear trend, although only one case of TB occurred in GOLD-stage III+IV.

**Conclusions:** Impaired pulmonary function or COPD is associated with an increased incidence of active tuberculosis.

#### P2870

##### Incidence of tuberculosis: The application of capture-recapture method to compare two sources of information

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**Introduction:** The true incidence of tuberculosis is higher than that in national and international records. Underreporting is estimated to vary between 7% and 27% according to studies.

**Objective:** Estimate the rate of tuberculosis in an area of Leon for the years 2008 and 2009 using the capture-recapture method to compare two sources of information: tuberculostatic drugs prescribed (rifampicin-isoniazid association) and the register of the regional epidemiological surveillance system (SIVE).

**Method:** Retrospective descriptive study in an area of 351,086 inhabitants of the cases of tuberculosis using as source:(i), information on tuberculostatic drugs prescribed, and (ii), the SIVE register. We calculated incidence rates for each source by the capture-recapture method. We analyzed epidemiological and demographic data, symptoms, diagnosis, treatment and monitoring.

**Results:** The incidence obtained in 2008 using the SIVE data was 18,80x100000 and the rate using the pharmacy register was 26,77. In 2009, the SIVE data gave an estimate of 18,23 and the pharmacy register 22,50. When applied the capture-recapture method, the annual incidence for 2008 was 44,14 (95%CI 37,88 - 50,41) and for 2009 of 34,17 (95% CI 30,19-38,17). In each of the years studied the number of cases obtained from the pharmacy register was higher.

**Conclusions:** The SIVE data on the incidence of tuberculosis in the study area underestimates the true incidence rate. The source of information that involves recording cases of tuberculosis in the community is underused. The capture-recapture method is a good alternative to measure the incidence of tuberculosis and to check the surveillance systems.

#### P2872

##### Efficiency of molecular methods for epidemiological investigation in tuberculosis (TB)

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**Introduction:** High prevalence of tuberculosis in Poland may related to active transmission.

**Objectives:** The assessment of the transmission of TB in the city of Krakow with genetic methods and with standardized epidemiological interview and the comparison of these methods.

**Methods:** In years 2007-2011 genomic DNA samples isolated from Mycobacterium tuberculosis complex strains coming from 274 patients were analysed by spoligotyping and IS6110-Mtb1-Mtb2 PCR method. The strains were assessed as identical if their DNA patterns were the same in both methods. In IS6110-Mtb1-Mtb2 PCR method DNA profile obtained in both PCR reactions should be identical.

**Results:** Among 274 strains, 122 genetic patterns (spoligotypes) were identified. Unique spoligotypes occurred in 91 strains; remaining 183 strains belonged to 31 clusters stemming from the same spoligotypes. The application of the IS6110-Mtb1-Mtb2 PCR in next stage of the analysis, allowed reducing the number of clusters to 18 with 91 strains. The clusters included 2-14 patients and covered one third of analysed samples. The clusters were dominated by men below 50 years old, smokers, AFB(+), with strains sensitive to first-choice anti-tuberculosis agents. The standard epidemiological interviews did not reveal neither direct close

nor periodic contacts between the patients included in clusters (only three clusters comprised prisoners from the same penitentiary and three homeless persons with periodic contacts).

**Conclusion:** The assessment of transmission of TB should be based on scrupulous epidemiological interview and on molecular genetic methods. Active transmission in Krakow in years 2007-2011 was responsible for 30% of diagnosed TB cases.

#### P2874

##### Administration of BCG vaccination: Survey of practice in the Mersey region, UK

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**Background:** A UK wide survey in 2005 showed wide variation in BCG practice and that the providers were uncertain in various aspects of the administration. The National Institute of Clinical Excellence (NICE) published guidelines in 2006, which along with Department of Health guidance aimed to standardise practice. We intended to assess regional BCG service 6 years later.

**Method:** 4 TB centres providing BCG vaccination across Mersey region were contacted and data regarding current practice of BCG administration was collected.

**Results:** The adherence to the guidelines was recorded as compliance. See table.

| Questions   | Guidelines Compliance (%) |
|---|---------------------------|
| Administration of BCG at sites other than upper arm   | 50%*                      |
| Re-vaccination in the absence of BCG scar in children | 100%                      |
| Prior assessment of HIV status                        | 100%                      |
| Prior evaluation of anaphylaxis risk                  | 100%                      |
| Availability of resuscitation equipment               | 75%                       |
| Formal training of staff in paediatric resuscitation  | 100%                      |

\* The other sites used were right upper arm or upper thigh. Reasons included patient preference or confusing scar.

There were no recorded episodes of anaphylaxis in the past 12 months. All centres referred patients with severe adverse local reactions appropriately.

**Conclusions:** Our survey demonstrates that NICE recommendations and their implementation were essential in elucidating areas of uncertainty in the administration of BCG vaccination and subsequently the practice is now uniform across the Mersey region. We intend to extend this survey to national level.

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##### Enhancing patient safety: New WHO guidance on pharmacovigilance in tuberculosis care

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Adverse drug reactions (ADRs) can lead to a patient interrupting tuberculosis (TB) treatment before completion, and contribute to avoidable morbidity, treatment failure, loss in quality of life, or death. While many national TB control programmes have a long tradition of monitoring patient care, the surveillance of drug-related problems, or pharmacovigilance, has not been systematic. The increasing worldwide use of more extensive regimens for drug-resistant TB, the concomitant use of antiretroviral therapy in patients with HIV-associated TB, and the imminent release on the market of new classes of medicines to treat TB make the case for pharmacovigilance even stronger.

WHO produced guidance this year on pharmacovigilance for TB through the financial support of the European Commission Seventh Framework Programme. The manual discusses how pharmacovigilance can be effectively implemented in a programme through key stakeholders, and provides a step-by-step approach on how to identify signals, assess relationships between an event and a drug, determine causality, and communicate findings. It presents three methodologies of pharmacovigilance which can be applied for the detection, assessment, understanding and prevention of adverse events or any other drug-related problem under field situations. The first two - spontaneous and targeted spontaneous reporting - can be built into national programmes of routine pharmacovigilance and/or tuberculosis control. The third type, cohort event monitoring (CEM), is an active form of surveillance, similar in design and management to an epidemiological cohort study. CEM would be particularly well suited to the post-marketing surveillance of new drugs.