Goal
To facilitate the workshop for the Eastern Mediterranean Region on "Revising tuberculosis estimates in the countries of the region"

Objectives
The main objective of the workshop was to help participants to perform record linkage, data analysis and write a preliminary draft report of the findings of the studies that had been carried out in five countries of the EMR.

The main objectives of the studies were:
- To assess the number of cases that are being diagnosed and treated by private providers but not notified, in five countries of the region.
- To use the capture-recapture technique to estimate the proportion of cases detected by the routine notification system based on the extent of reporting/underreporting of private providers.
- To evaluate the case management of TB cases by non-NTP providers, including their notification/referral of cases to NTP practices.

Brief summary
The workshop was attended by NTP programme managers and WHO staff involved in TB surveillance from 5 countries in EMR (2 to 3 persons per country). There were representatives from Pakistan, Yemen, Egypt, Djibouti and Syria. The workshop was facilitated by Amal Bassili, Jane Nicholson and Samiha Baghdadi (WHO-EMRO), and Ana Bierrenbach (WHO-HQ). The workshop was held in English. Workshop materials (presentations, lecture notes, reference papers, practical exercises) were assembled on a CD for each participant.

Background
- Some countries in the EMR have been claiming that their TB case detection rate as estimated by WHO/STOP-TB/TME are low and should be revised.
- There is evidence from previous KAP studies and data collected at review missions done in the region showing that most TB patients have access to health care provided by public or private facilities.
- Patients diagnosed in private and public non-NTP facilities may or may not get referred to NTP clinics and hospitals for treatment.
- Although in some countries of the regions, notification is compulsory by law, there is usually no mechanism to guarantee that the law is implemented.
- Therefore, most TB cases missed from the official NTP notification system are believed to have been missed within the health system.
Given that the number of TB cases seeking care but not being diagnosed and experiencing symptoms but not seeking care is expected to be low, the extent of reporting/underreporting of TB cases diagnosed by non-NTP providers may provide an accurate estimate of the total number of TB cases in the country and the proportion detected by NTP.

Methodology of the studies
A study was carried out during one quarter of year in 5 countries: Pakistan, Yemen, Djibouti, Syria and Egypt. Consented laboratory staff and physicians delivering care to TB patients in the following non-NTP sectors were enrolled in the study:

- **Public**: Public hospitals; Health Insurance facilities; Medical organizations; Ministry of Interior (prisons); Ministry of Defence
- **Private**: Private hospitals; Private clinics; NGOs

In Djibouti and Syria, all non-NTP providers were enrolled in the study. In the other 3 countries, a multistage stratified cluster sample of governorates was selected. Stratification was based on the governorates’ smear positive TB notification rates: very high, high, intermediate or low based on the 75%, 50%, and 25% percentiles for the country. From each stratum, one or more governorate were randomly selected proportionate to the number of governorates in each stratum. All non-NTP laboratories and facilities in that governorate were included in the study.

In Egypt, a second stage sampling was done in 2 out of 4 selected governorates to select some districts within each governorate where it was not possible to cover all non-NTP providers in that the whole governorate. In Pakistan, the primary sampling unit was the district and a second stage sampling was done to select a sample of private providers within each selected district. However, all private laboratories in the selected districts were enrolled. In Syria, for example, the study registers were not introduced in health care facilities, but in all private laboratories performing sputum examinations. Therefore, the study aimed at estimating only the incidence of smear positive TB cases.

A laboratory register was introduced in each of these laboratories including information about the full name of the patient, full contact address (with mobile number), age, sex, source of referral, number of specimens examined, results of direct smear examination, final diagnosis, and treating physician. They were asked to fill information and were subjected to weekly visits by research assistants to record the registered information about diagnosed patients and trace them at governorate TB centres.

Physicians delivering care to TB patients in each selected governorate were also enrolled. These included: GPs, chest physicians, and internists in the public and private institutions as previously described.

These were given a suspect register to record every TB suspect and record their case management without any interference from the research team. They were then subjected to monthly visits to collect information including the total number of suspects out of all clients, diagnostic tests used whether chest X-Ray or sputum smear microscopy, and the extent of referral/notification of cases to NTP.

The list of patients in the study registers were compared with lists of notified cases to find TB cases common to them.

Capture-recapture methods were used to estimate total incident cases (i.e. to estimate not only cases that are missing from notifications, but also to estimate the number of
cases that are missing from all lists i.e. cases that are not in contact with health facilities at all).

Table 1. Comparison between the different countries regarding the study methods.

<table>
<thead>
<tr>
<th>Study duration</th>
<th>Study setting</th>
<th>Study sampling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syria  Q4, 2006</td>
<td>All private laboratories in the country</td>
<td>No sample-comprehensive survey</td>
</tr>
<tr>
<td>Yemen Q1, 2008</td>
<td>Non-NTP laboratories and facilities in 4 out of 17 governorates</td>
<td>Stratified cluster</td>
</tr>
<tr>
<td>Pakistan Q4, 2007</td>
<td>Non-NTP laboratories and facilities in 13 out of 130 districts</td>
<td>Stratified cluster, with second stage sampling of private clinics</td>
</tr>
<tr>
<td>Egypt Q4, 2007</td>
<td>Non-NTP laboratories and facilities in 4 out of 27 governorates</td>
<td>Stratified cluster, with second stage sampling of districts in 2 governorates</td>
</tr>
<tr>
<td>Djibouti Q1, 2008</td>
<td>Non-NTP laboratories and facilities in the country (total=15)</td>
<td>No sample-comprehensive survey</td>
</tr>
</tbody>
</table>

**Methodology of the workshop**
The countries participating in the workshop brought to Cairo electronic lists of patients extracted from the study registries and the TB notification database for the corresponding period. The workshop consisted of theoretical and practical sessions in the following topics:
- WHO recommended methods of estimating TB disease burden
- Development of data analysis plan
- Data cleaning and record linkage
- Descriptive analysis of data
- Estimating the number of TB cases using the inventory method and the capture-recapture technique
- Scientific writing

**Main Outcomes**
Participants understood the principles of data analysis and capture-recapture methodology. Participants understood the main assumptions and pitfalls of the capture-recapture methodology. A preliminary analysis of the data was performed and the main results presented in tabular format.

Preliminary results are presented in Table 2. For Syria and Djibouti, the results intend to be representative of the country as a whole, as the studies comprised comprehensive lists of private health providers from all districts. For the other countries, the results represent the districts sampled in the study, and the effect of the sampling design still has to be verified.
The proportion of cases estimated as being detected in the studies was higher for Syria, Egypt and Yemen when compared to the 2006 WHO estimates for TB case detection rate, and the participants from these countries felt that these results are more likely to represent the true situation. For Pakistan and Djibouti, the proportion of cases detected was lower than the 2006 WHO estimates for CDR. In these countries, problems in data verification and analysis may have contributed to an underestimation of the total number of cases, as explained below.

Table 2. Capture-recapture estimates of TB incidence and proportion of cases notified in five countries of the EMR.

<table>
<thead>
<tr>
<th></th>
<th>Non-NTP cases</th>
<th>NTP cases</th>
<th>Total cases detected</th>
<th>Inventory Method* % detected (95% CI)</th>
<th>Cap-recap Estimates TB incidence</th>
<th>Cap-recap Estimates % detected (95% CI)</th>
<th>WHO 2006 estimates CDR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Status registration at NTP</td>
<td>Status registration at non-NTP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Djibouti</td>
<td>No</td>
<td>Yes</td>
<td>Total</td>
<td>No</td>
<td>Yes</td>
<td>Total</td>
<td>888</td>
</tr>
<tr>
<td>Egypt</td>
<td>124</td>
<td>46</td>
<td>170</td>
<td>373</td>
<td>124</td>
<td>419</td>
<td>543</td>
</tr>
<tr>
<td>Pakistan</td>
<td>1541</td>
<td>336</td>
<td>1,877</td>
<td>6057</td>
<td>336</td>
<td>6393</td>
<td>7934</td>
</tr>
<tr>
<td>Syria</td>
<td>6</td>
<td>41</td>
<td>47</td>
<td>291</td>
<td>41</td>
<td>332</td>
<td>338</td>
</tr>
<tr>
<td>Yemen</td>
<td>37</td>
<td>76</td>
<td>113</td>
<td>358</td>
<td>76</td>
<td>434</td>
<td>471</td>
</tr>
</tbody>
</table>

* The proportion of cases detected by the inventory method is not representative for the whole country for Egypt, Pakistan and Yemen, because of sampling.

** For Syria, the CDR is for smear + TB cases. For the other countries, the CDRs are for all forms.

Discussion points
There was extensive discussion about the validity of capture-recapture estimates, which critically depends upon the model assumptions. If the assumptions were broken, the estimates are questionable. These are the most important assumptions:

1) **No misclassification**: TB diagnosis has to be done following the same criteria for both providers. For all countries, but specially for Djibouti and Pakistan, participants raised doubts about the validity of the diagnosis of TB performed by the private sector. An excess of false-negative diagnosis will lead to the underestimation of the total number of cases; while preponderance of false-positive diagnosis will result in overestimation of the cases. In the EMR studies, TB diagnosis has not been validated, specially from non-NTP sources, which rely on different diagnosis procedures (more on X-ray and less on microscopy).

2) **Perfect linkage**: there has to be no matching error. False negative matches will lead to overestimation of the case counts, while false positive matches will lead to underestimation.

For all studies, linkage depended exclusively on the variable name of patient and age, and not on other variables such as date of birth or name of mother. Therefore the
matches are based on the assumption that there are no or very few homonyms in these populations. For Pakistan, there were important difficulties while linking the records from the 2 electronic sources of data. This was due to the fact that many names in the study register were incomplete (just the first name) and to the translation of the names from Urdu to English in both sources (which induced all types of misspells - this did not occur in the other countries, as names were written in Arabic). Therefore, the initial analysis, as presented in the table, was based exclusively on the linkage performed in the field by the field supervisors. This may have been one of the causes contributing to an underestimation of the total number of cases detected, and consequently to an overestimation of the CDR. More matches may be found, if the contents of the variables name and address in the study register electronic list are revised, cross-checking with the hard copies of the data collection forms.

3) **Homogeneous catchability**: all the members in the population should have the same chance to be listed in the source. The comparisons are done in between NTP and private providers.

4) **No dependency between sources.** This is a critical assumptions of 2-sample capture-recapture method. In countries that have implemented PPM, there is dependency as private providers know that they have to report to NTP. PPM has not been implemented in these EMR countries.

   In the 2-sample method, it is impossible to check this assumption mathematically, and therefore, the researchers have to make their own judgement, intuitively, to see the sources meet the independence requirement. If there is positive dependency, the 2-sample estimate should serve as the lower bound of the true number of cases, if only 2 negatively dependent sources are available, it is not recommended to employ capture-recapture method as the over estimation can be extreme under some condition and the results will not mean anything.

   For Egypt, given the high number of cases, it may be possible to separate the non-private cases into two sources, namely the private providers and the health insurance organizations. Therefore, with 3 sources being available, it will be possible to check mathematically for source dependency.

5) **Closed population**: no births, no migration, no deaths. Among the 5 countries, this assumption seems to be most endangered in Djibouti, given its high interchange of people across the borders with Somalia and Ethiopia, for various reasons including migration to seek health care.

6) **Small numbers**: This is not really one assumption, but of course there small number of cases from one or more sources may lead to random errors in the estimations, which should be calculated. The non-NTP sector can be further categorized into: health insurance, NGO, public or private hospitals and public or private clinics. One question to be further discussed is: what is the minimum number of cases recorded by one category to consider it as a separate source of data?
Apart from the effect of the possible breakdown of assumptions on the results, the inference of the results for the population of the country as a whole will also have to consider the sampling designs.

Conclusions
The method used to collect TB data by implementing study registers in various non-NTP providers proved to be easily implemented at low costs. However, a more comprehensive sampling strategy would have greatly modified the costs and the time spent in data collection.

As there is no formal way of checking the assumptions using the 2-source method, the decision to accept the capture-recapture estimates will have to be based on the intuitive judgement of the researchers, and on other supporting evidence from each of the countries.

Recommendations
For WHO (HQ & EMRO):
1. Further discuss the protocol and findings of the various studies with experts on capture-recapture methodology. The first opportunity to do that will be during the Task Force on TB Impact Measurement meeting next week, with Dr Ibrahim Abubakar from the UK.
2. Use the software R to calculate the capture-recapture estimates for Egypt using the 3 available sources.
3. Establish a mechanism with EMRO to be able to follow-up on the country's needs for technical assistance while writing the final versions of their study manuscripts.
4. Refine a template protocol to be used in similar studies to be done in other countries.
5. Discuss criteria to recommend that similar capture-recapture studies be performed in other countries during the Task Force meeting.

For countries:
1. Pakistan and Djibouti:
   • To verify the diagnosis of the cases treated in the private sector;
   • To cross-check the names in the data entry file with the data collection form;
   • To cross-check the registration status of cases detected by private sector;
   • Clean the data accordingly and send to EMRO by the end of November.

2. All countries:
   • Send files with population numbers per governorate and district to EMRO, so that sampling weights can be calculated and considered in the analysis.
   • Further develop manuscripts. Egypt has to wait for new analysis.