We used data from National TB Program and included all cases of TB diagnosed in the Albania from 2010 to 2016. Information on age, sex, year of diagnosis, and anatomic location of the site of disease was retrieved from central database of National TB Program.

In Albania during 2010–2016, 925 cases of extrapulmonary TB were reported, males were 581 (63%) and females 344 (37%). The number of cases diagnosed per year was as follows: 170 (38.2%) in 2010, 129 (30%) in 2011, 108 (25.7%) in 2012, 141 (29.7%) in 2013, 147 (36%) in 2014, 117(28.2%) in 2015 and 113 (27.2%) in 2016.

Sputum smear examination, X-ray and culture examination and tissue biopsy were carried out in 58; 42.3; 18 and 15% of patients respectively for EPTB diagnosis. The most affected age group was < 65 years (23%). Pleural effusion (35%) and lymph node (15.7%) were the most common types of extrapulmonary TB.

Patients live in urban areas (60%) rather than rural (40%). The mean age of EPTB patients is 44.5 and pulmonary TB patients is 41.2. Incidence of EPTB decreased from 5.5/100 000 in 2010 to 5.1/100 000 in 2016.

In Albania, extrapulmonary TB in 2010–2016 showed a slight decrease in incidence, although the rates are still very high. Diagnosis of extrapulmonary TB was made according to national guidelines, however long delay has been reported in most cases before the final diagnosis. Microbiological proof is the key to diagnosis and treatment, and tissue biopsy that should be required regularly.

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DETERMINANTS OF TB RELATED DEATH FROM TUBERCULOSIS PATIENTS IN THE NORTHERN THAILAND

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Tuberculosis is the most common cause of deaths from respiratory infection in Thailand. Understanding the risk of death could provide useful information to provide better clinical care for TB patients. *N-Acetyltransferase 2 (NAT2)* gene is the main determinant of isoniazid (INH) metabolism. *NAT2* rapid acetylator contributes to lower anti-TB drug (INH) serum concentration and increased risk of treatment failure and relapse from INH based TB regimens.

The aim of this study was to determine the effect of *NAT2* acetylator status on TB related death.

TB patients were recruited from the TB registry during 2002–2011 in Chiang Rai province, Thailand. The *NAT2* acetylators (rapid, intermediate and slow) were determined by haplotype specific polymerase chain reactions, HS-PCR. These groups of patients were excluded from further analysis: 1) patients who did not receive the INH based regimens for TB treatment; 2) patients who did not receive the INH based regimens longer than 2 weeks and 3) patients who died within the first 2 weeks of TB treatment. Mortality-associated risk factors within 1 year of treatment were analyzed using Cox-regression model.

Of 1.076 TB patients who met study criteria, 213 (19.8%), 495 (46.0%) and 368 (34.2%) belonged to *NAT2* rapid, intermediate and slow acetylate group respectively. In total, 115 patients died within 1-year follow-up. In the multivariate analysis, rapid *NAT2* acetylator status increased the risk of death when compared against *NAT2* intermediate acetylator (adjusted hazard ratio [aHR]: 1.83, 95%CI: 1.15–2.91). The effect of *NAT2* rapid acetylator on deaths is more significant in HIV positive TB patients (aHR 2.68, 95%CI:1.14–6.26). The risk factors associated with death was different among the *NAT2* acetylators. In *NAT2* rapid acetylator group, elderly people, HIV positive, past TB history and smoking status was increased the risk of death.

The *NAT2* rapid acetylator is related to the mortality during TB treatment. The inadequate treatment with the doses of standard regimens caused by *NAT2* rapid acetylator might increase the risk of death in TB patients, these NAT2 pharmacogenetic risks are interacting with other clinical risk factors, which is depended on the acetylator status.

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CLICHES AND DOGMAS IN MOLECULAR TUBERCULOSIS RESEARCH

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I will present a personal critical view on some hot issues of the molecular epidemiology of tuberculosis, in particular, regarding an uncritical use of some well known online tools and resources. Invaluable for establishing terminology and classification in molecular epidemiological studies of *Mycobacterium tuberculosis*, they are limited by our insufficient knowledge of genome evolution and uncritical perception of their indications. This is exemplified by partly inadequate (sub)clade assignment due to imperfect decision rules, and misleading methodological approach when scientifically unsound phylogenies are built from spoligotyping data.

To begin with, I propose the following definitions. First, "molecular mythology" that relies on minimal array of references that conveniently support long-lasting clichés. Second, "molecular iconography" that relies on dogmatic perception of the current knowledge when online databases are uncritically regarded as ideal icons. Finally, I introduce the term "click science". In contrast to the fascinating and sophisticated click languages, "click science" relies on uncritical and simplified perception of knowledge and a dogmatic, iconographic view of indications provided by increasingly convenient online tools and databases. For example, spolTools is an example of the click phylogenetics when a plethora of statistics is generated in few clicks but their exploration is minimal. In its turn, click systematics is exemplified by SITVIT's (i) reader-unfriendly huge tables with different possible percentages and (ii) easy to read but partly inadequate (sub)clade labels.

Labels are convenient for classification, but should be revisited in the context of modern knowledge. The "we have been taught this way" approach reflects the mentality of a conservative teacher rather than a creative researcher. As Heidegger once said, "knowledge does not think"; indeed why think when it already knows? As far as science is concerned, this quotation from Henry Gee's "The accidental species" is much more appropriate: "Science is about neither Facts nor Truth, but the quantification of doubt".

Below are examples of some clichés pertaining in molecular epidemiology of tuberculosis.

Firstly, pathogenic properties of the Beijing genotype are traditionally listed as increased virulence, association

with drug-resistance, high transmissibility and clustering. But they do vary among endemic and sporadic strains, in different settings and hosts, even at within country level.

Secondly, Russian epidemic clone Beijing B0/W148 was commonly regarded as widespread across all Former Soviet Union. In reality, its geographic distribution shows a peculiar clinal gradient with highest frequency in Siberia and sharp decrease in the Asian part of the former Soviet Union.

Thirdly, a global spread of LAM RD-Rio sublineage has been claimed and was attributed to its particular pathogenic properties. A comprehensive analysis of available data shows that RD-Rio strains are rarely present in Russia and East Asia. It appears that there is no global dissemination of RD-Rio due to specific virulence properties of these strains but rather their spread due to human migration (if such migration did take place).

A confusing terminology, misclassification and false clustering are not abstract issues but make a scientific discussion meaningless, and I will propose some courses for improvement of the situation.

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ANALYSIS OF SECONDARY RESISTANCE OF *MYCOBACTERIUM TUBERCULOSIS* TO SECOND-LINE ANTI-TUBERCULOSIS DRUGS IN CASABLANCA

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Tuberculosis (TB) is a major public health problem in Morocco, despite multiple strategies and funds allocated. According to epidemiological data, with about 31.452 TB cases detected in 2016, and a national incidence of about 91 per 100 000 inhabitants per year, TB pose a serious threat to TB management in Morocco, with Casablanca being one of the most affected region.

The objective of this retrospective study was to evaluate secondary resistance of *Mycobacterium tuberculosis* to 2nd line anti-tuberculosis drug in Casablanca.

In this retrospective study, 1300 patient samples from different CDTMRs and hospitals across Casablanca and regions over a 2-year period from January 1st, 2015 to December 31st, 2016 were analysed. Conventional techniques, such as BKD microscopic examination, BKC culture and antibiotic sensitivity were used for the diagnosis of TB.

Our results show that among the 1300 samples analyzed, 600 (46%) were found positive for MTB, of which 58.33% were male and 41.66% were female. Patients aged between 20 and 40 years was the most affected group, representing 78% of patients. Data using the conventional Petroff decontamination and homogenization technique for isolation, identification as well as titration of the "BK" strains were as follows: Negative culture (54%), Positive culture (46%). The antibiogram used for this study gave the following results: 53% were wild strains, 47% were mutants, among which 18% were "MDR" strains and 1% were "XDR" strains.

The results of the present study reflect the importance of a good management of TB cases in order to succeed the treatment regime adopted at the national level and the success of the fight against this scourge in Morocco.

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DEVELOPMENT OF THE EXTERNAL QUALITY ASSESSMENT SCHEME FOR NON-TUBERCULOUS MYCOBACTERIA DRUG SUSCEPTIBILITY TESTING IN EUROPEAN UNION

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Non-tuberculosis mycobacteria (NTM) are increasingly associated with pulmonary and extrapulmonary disease in humans. Although identification and drug susceptibility testing (DST) of NTMs comprises a significant part of the tuberculosis (TB) reference laboratory activities in the European Union (EU), currently no internationally recognised external quality assurance (EQA) schemes exist for NTM DST. It lacks standardization and evidence on how to interpret DST results for specific drugs is limited.

Recognising the need for harmonization of methodologies in EU/EEA, European Reference Laboratory Network for Tuberculosis (ERLTB-Net) in 2017 conducted a pilot study among National Reference Laboratories (NRL) aimed at understanding methods employed for identification and DST and developing an EQA scheme for NTM DST. Pilot study comprised a survey followed by an EQA round using identical panels comprising 10 well characterised rapid (*M. abscessus*) and slow (*M. avium*) isolates.

Completed questionnaires were received from a total of 32 NRLs (97.0% response rate). Thirty NRLs routinely perform identification of NTMs with a majority (77.4%; N = 24) using line probe assays as a primary means of NTM speciation. Reports containing minimum inhibitory concentrations (MICs) and result interpretation for five key drugs (Clarithromycin (CLA) Amikacin (AMK) Moxifloxacin (MOX); Linezolid (LIN), and Doxycycline (DOX) for *M. abscessus* only) were received from 21 NRLs (95.5% response rate).

Interlaboratory agreement rates were higher for *M. abscessus* isolates; all five strains were found to be resistant to DOX by all NRLs (MIC 8.0–16.0 μg/ml). Relatively minor variations were seen in MICs and their interpretations for MOX and AMK while for LIN MIC ranges for individual isolates varied greatly (2.0–32.0 μg/ml) across NRLs resulting in a lower agreement with regards to results interpretation. For slow growers AMK and MOX appeared to be the most problematic drugs both in terms of MIC determination (ranging 4.0–64.0 and 0.5–8 μg/ml in individual strains, respectively) and interpretation.

The results show that inter-laboratory reproducibility is insufficient, highlighting the need for expanding EQA schemes for NTM DST. As EQAs for *M. tuberculosis* complex DST have led to more reliable and reproducible phenotypic DST, we propose to follow a similar approach for clinically relevant NTM.