

## Understanding Drug Use and Problems in Europe

by Dr. Bernard Gouget

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As part of an increasingly interconnected world, the European drug market is facing major changes happening at a very fast pace. The old dichotomy between a relatively small number of very problematic drug users—often using intravenous drugs, and a large number of users taking drugs

recreationally or experimentally is disappearing, to be replaced by a more complex and nuanced situation. In its annual report entitled “European Drug Report 2014: Trends and Developments” published late May 2014, the European Monitoring Center for Drugs and Drug Addiction (EMCDDA)

explains that stimulants, synthetic drugs, Cannabis and pharmaceutical products are increasingly becoming more commonly consumed than heroin and cocaine. The reemergence of ecstasy powders and pills is also causing concern. The report confirms the trend toward global stabilization of drug use, but with a more complex drug market, and new challenges continue to appear given the increasing number, variety and availability of new psychoactive substances.

The trend to lower use of heroin concerns use and availability. The number of users entering treatment for the first time has dropped from a maximum of 59,000 in 2007 to 31,000 in 2012. In contrast, stimulants, synthetic drugs, Cannabis, and pharmaceutical products are increasing in importance. The increase in the number, variety and availability of new psychoactive substances is ongoing. In 2013, 81 new drugs, including 29 synthetic cannabinoids, were reported for the first time by means of a European Union early alert system, which brings the number of new substances monitored to 350.

The internet plays a key role in market structure. In 2013, the EMCDDA identified some 650 websites selling these substances aimed at Europeans. It also reported the purchase of new or traditional drugs via “darknets” (clandestine online networks permitting anonymous communication), which is a “new challenge for law enforcement.” New harmful substances such as 25I-NBOMe, AH-7921, MDPV and methoxetamine are sold to replace the drugs that they are designed to imitate, i.e., LSD, morphine, cocaine, and ketamine.

The EMCDDA points out several issues considered to be particularly concerning. In particular, they report disturbing localized and/or national epidemics of synthetic cathinone injection. This practice is a problem in groups of high-risk drug users in countries such as the Czech Republic, Germany, Ireland, Spain, Austria, Poland, Finland, Sweden and the United Kingdom. In Romania, this injection is a more generalized practice. In Hungary, one study showed that in 2012, cathinones were the main drug injected for 36% of users.

An increasingly worrisome behavior has also appeared among homosexuals: the injection of a cocktail of illicit drugs at “chem sex parties.” Thus we see a reversal of the HIV epidemic situation among drug users. The most recent results show HIV outbreaks recently observed among drug users in Greece and Romania and in some Baltic countries, jeopardizing the long-term decline in the number of new HIV cases diagnosed in Europe.

If these drugs are spreading, this is not an accident: for the most part, they are much easier to produce than conventional drugs. They are difficult to detect and classify (overdoses) and [contribute to] the transmission of AIDS in some countries. And from this advantage arises another. Consumed in very small quantities, these stimulants and synthetic drugs have powerful effects. They become difficult to detect and classify, which explains an increase in overdoses, the growth in which is a real public health problem on the continental scale.

Engaging in the fight against drugs and addictive behaviors is the responsibility of any health professional. A broadened conception of prevention should be fostered, educating the public and the scientific community and integrating awareness of all the risks, including behavioral influences related to the internet and social networks, especially in young people.



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## 3rd UK Diagnostics Forum Held at Magdalen Collage, Oxford

by Patrick MM Bossuyt; EFLM WG-Test Evaluation, Professor of  
Clinical Epidemiology, University of Amsterdam, The Netherlands

On March 18-19, 2014, the UK's 3rd Diagnostics Forum was held at the University of Oxford, UK, in the beautiful surroundings of Magdalen College. The meeting was sponsored by the UK Technology Strategy Board, the British In-Vitro Diagnostics Association, the UK National Institute for Health and Care Excellence, and the University of Oxford Nuffield Department of Primary Health Care's Center for Monitoring and Diagnosis. These Diagnostics Fora form a special series of conferences, bringing together over 100 attendees of which 40% are from industry, 40% from academia, and 20% from NICE, from the NHS, and other health care organizations. This mixed audience makes it a special and interesting event and the format of the conference allows both communities to mix and mingle.

The focus of this year's conference – for the first time in a two-day format – was on the generation of evidence to support the introduction of novel IVD, and on government support for the diagnostics industry in doing so. Overall, there were a few presentations and posters on the generation of evidence and the methods for doing so (from Jon Deeks and Elisabeth Adams, amongst others), but by and large the main focus of the meeting this year was on funding opportunities, in particular UK initiatives to stimulate innovation and collaboration in developing and evaluating diagnostics.

### Johannes Zander Winner of 2014 Walter Guder Preanalytical Award

The Walter Guder Preanalytical Award 2014, presented by EFLM and sponsored by Becton Dickinson, has been granted to Dr. Johannes Zander for the article:

Effect of biobanking conditions on short-term stability of biomarkers in human serum and plasma. Johannes Zander, Mathias Bruegel, Alisa Kleinhempel, Susen Becker, Sirak Petros, Linda Kortz, Juliane Dorow, Jürgen Kratzsch, Ronny Baber, Uta Ceglarek, Joachim Thiery and Daniel Teupser; Inst. of Lab. Medicine, Clinical Chemistry and Molecular Diagnostics, University Leipzig, Leipzig, Germany; LIFE – Leipzig Research Center for Civilization Diseases, University Leipzig, Leipzig, Germany; Institute of Laboratory Medicine, Ludwig-Maximilians-University Munich, Munich, Germany; Medical ICU, University Leipzig, Leipzig, Germany

The Walter Guder Preanalytical Award is given to the best published paper, as judged by an independent panel of experts, which demonstrates a significant contribution to the improvement of the preanalytical phase. The award is intended to achieve wider recognition of the importance of high quality research in the field of the preanalytical phase among laboratory professionals in Europe. The Award will be presented to Dr. Zander, as submitting author, during the EuroLabFocus Congress in Liverpool (October 7-10, 2014). The award consists of a certificate and a monetary award of EUR 5,000, to be shared with coauthors, in addition to the cost of the participation to attend the Congress in Liverpool.

Please consider that the Walter Guder Preanalytical Award will be awarded biannually, so prepare yourself for the next edition!

Penny Wilson, from the Technology Strategy Board, one of the conference's main sponsors, introduced the Precision Medicine Catapult, announced in August 2013 and targeted at the development of diagnostics for stratified medicine. In stratified medicine, treatment decisions for subgroups are based on specific markers: marker positives would be given one treatment; marker negatives another form of treatment. Catapults are technology and innovation centers where UK businesses, scientists and engineers should work side by side on R&D, transforming ideas into new products and services to generate economic growth.

Several other organizations and programs were invited to introduce themselves these two days. The National Institute for Health Research (NIHR) aims at transforming research in the NHS, to increase the volume of applied health research for the benefits of patients and the public. NIHR has funded several initiatives, such as biomedical research centers & units, the Collaborations for Leadership in Applied Health Research and Care (CLAHRCs), the NHR clinical research network, and Academic Health Science Networks (AHSNs).

The NIHR has also—very recently—provided GBP 4 million funding to four Diagnostic Evidence Cooperatives (DECs), for a four-year period, starting September 1, 2013. These DECs are organizations that are expected to act as catalysts for the generation of evidence for commercially-supplied IVDs. As such, they should foster collaboration between companies involved in the CE marking and marketing of IVDs and other parties.

The four DECs presented themselves at the meeting as well: Dr. John Simpson talked about the Newcastle DEC, Dr. Michael Messenger presented the Leeds DEC, Dr. George Hanna introduced the London DEC at Imperial College, and Mathew Thompson spoke about the plans of the Oxford DEC.

More programs were presented at the meeting. Dr. Mehdi Tavakoli introduced the audience to HealthKTN, which has a Stratified Medicine Inno-



Platform. This platform seeks to build on the UK's strength within the global healthcare industries by working in partnership with 6 other organizations, who together will invest around GBP 200 million over 5 years in the area of stratified medicine. The investment will go into areas such as improved tumor profiling in cancer, novel biomarkers and the uptake of companion diagnostics in the NHS.

Other speakers presented a perspective from industry. David Horne (Alera) described the incredibly complicated healthcare landscape, where a citizen or patient can access the health care system in many different ways (such as the internet phoning 111, High St retailer, pharmacy, walk in clinic, GP, A&E, alternate practitioner, patient associations etc), and where IVD companies face an incredible amount of bodies and acronyms. The UK government, he felt, could simplify things and remove barriers. Government should also support SME and larger enterprises, using competitive tax rates, for example. Industry should change as well, by increasing transparency, generating better and more evidence, learning to partner, and by demonstrating value, rather than being fixated by price.

The very rich funding alphabet soup served at this conference (with DECs, CLAHRCs, KTNs, AHSNs, and more) figured also in the final words of Matthew Thompson, one of the organizers of the conference. There seem to be many initiatives, many opportunities for funding, but the landscape is quite fragmented, and it may be daunting for the healthcare professional to find the way through the myriad of acronyms, organizations and options.

The Diagnostics Forum has a website, where one can download reports of previous Diagnostic Fora and the presentations and the list of attendees of the 2014 event: [www.oxford.dec.nihr.ac.uk/diagnostic-forum/2014-uk-diagnostic-forum](http://www.oxford.dec.nihr.ac.uk/diagnostic-forum/2014-uk-diagnostic-forum)



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## 21st Romanian National Congress Builds Multidisciplinary Scientific Appeal

by Dr. Camelia Grigore, President of RSML

The 21st Congress of RSML took place on June 4-7, 2014, in Sibiu, Romania. What was the new concept of the event? The Romanian laboratory specialists tried to make of their Congress a multidisciplinary scientific event, inviting as speakers, along with laboratory specialist, clinicians, pharmacists, laboratory technicians, in a word, the whole healthcare team, considering the laboratory as the turnaround point in the medical diagnostic, prognostic and follow up of patients' treatment.

The Congress was divided into several sessions. First day the lecturers were Romanian specialists in laboratory Medicine, hematology, pediatrics, internal medicine, infectious diseases, dermatology, balneo-physiotherapy, rheumatology, gynecology, urology, who spoke about their experience in using lab tests in their diagnostic fields.

The second day the international speakers made a general overview in subjects like: "Bone marrow report"- Dr. Adrian Padurean (Wisconsin, USA); "How we use lab tests in endocrinology"- Prof. Dr. Maria Fleseriu (Oregon, USA); "The importance of Vit. D determination in the medical management of elderly persons"- Dr. Roxana Fournier (Amiens, France); "The stem cells in the treatment of neurologic diseases"- Prof. Cristina

Iftode (New Jersey, USA); "The importance of internal Quality control in laboratory"- Anne Vassault (Paris, France); "The transposition of EU directives into national laws-what are the problems?"- Simone Zerh (Paris, France).

The next two days was the Regional Meeting of The International Association of Therapeutic Drug Monitoring and Clinical Toxicology, International Scientific Society who agreed to join the Romanian National Congress in order to spread their knowledge about personalized medicine, the future of lab diagnostic using new technologies like LC-MS in the follow up of medical treatment and Clinical Toxicology. Romanian laboratory is at the beginning of using these new methods in laboratory, but the idea of the organizers was "If we cannot do everything it is known, at least know everything it is done." In addition, the lecturers covered a large variety of subjects: "Future of Laboratory Medicine,"- Prof. Michael Oellerich (Goettingen, Germany); "How to organize a TDM laboratory"- Prof. Pierre Wallemacq (Brussels, Belgium); "Immunoassays in TDM"- Dr. Eberhard Wieland (Stuttgart, Germany); "Methods of testing drug of use"- Dr. Hans Maurer (Homburg, Germany); "Personalized pharmacotherapy for cancer"- Prof.



Yusuke Tanigawara (Tokyo, Japan); "TDM in epilepsy"- David Berry (London, UK); "Alcohol and drug of use - a deadly combination"- Manuela Neumann (Toronto, Canada); "Medicine in digital era"- Prof. Liviu Iftode (Rutgers, USA).

The audience was very much interested in all the subjects and appreciated the nice mix between specialties, having as central point the improvement of laboratory diagnostics in the benefit of patients. We hope that the motto of the Congress "Good medical science, better practice" has been transposed into practice and will stimulate future collaboration between specialists and scientific associations.

We also have to remark the beauty of Sibiu – a nice town in the center of Romania, known after Forbes classification as "the 8th most idyllic place to live," who was hosting, during this period, the 21st edition of the International Theatre Festival, a big cultural event in this "city of culture, city of cultures," who contributed to the general atmosphere, appreciated by all the participants.

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## Registration Underway for 14th EFLM Postgraduate Course in Dubrovnik

by Elizabeta Topic, EFLM Education and Training Committee Faculty  
of Pharmacy and Biochemistry University of Zagreb, Croatia

We are glad to inform you that the 14th EFLM Postgraduate Continuous Course in Clinical Chemistry and Laboratory Medicine "New Trends in Diagnosis and Management of Diabetes Mellitus: Diabetes Mellitus Revisited 14 Years After the First Dubrovnik Course" is now open for registration ([www.dubrovnik-course.org/registration](http://www.dubrovnik-course.org/registration)).

The Course will be held at the Inter-University Center Dubrovnik on October 25-26, 2014, with the goal to bring a lot of new information documenting the progress in diagnosis and management of Diabetes Mellitus in the last 14 years. Most importantly, this event brings together Europe's specialist trained in Laboratory Medicine and physicians focused on Diabetes Mellitus and its complications, one of the most frequent diseases worldwide. It will be an opportunity not only, to listen to the renowned expert in the field, but also for active participation of attendees with poster presentation. These results presented as posters, will reflect attendees contribution in the care of Diabetes Mellitus across Europe.

We would like to draw your attention to the date of the registration fees: EUR 150 before, and EUR 250 after August 1, 2014. More information can be found on the web ([www.dubrovnik-course.org](http://www.dubrovnik-course.org)).

For the poster session, the participants are invited to submit their posters before August 1, 2014. Several interesting posters will be chosen for short oral presentation. The best poster chosen by Scientific and Organizing Committee will be awarded.

EFLM will announce bursaries for young participants (<35 year). Applications should be submitted by July 1, 2014, electronically. All applicants will be notified about the results by e-mail, latest by the end of July 2014. Further detailed information will follow in May. The course will be accredited by National Society rules.

We look forward to welcoming you in Dubrovnik where you will have the opportunity for an interactive discussion during the course as well as during social events

### Preliminary Program

#### Saturday, October 25, morning

- Introduction
- Part I : Epidemiology, prevalence, the major complications of DM
  - The diabetes epidemic – prevalence and classification
  - Complication of diabetes – strategies for reducing the risk of long term complications
  - The role of diabetes registries to monitor the treatment and complications of diabetes
  - Poster presentation
- Part II: The role of testing in the diagnosing and management of DM
  - Guidelines and recommendations for testing in diagnosis of DM: The role of HbA1c
  - HbA1c analyzing – challenges for the laboratory – internal and external QC
  - Post-analytical factors – how should HbA1c results be communicated to clinicians
  - Poster presentations

#### Saturday, October 25, afternoon

- Part III: Do we have markers for early diagnosis of diabetes?
  - Early recognition of gestational diabetes (Introduction of new guidelines and practice) – how



- should the routines be?
  - How to diagnose the pre-diabetes
  - Diabetes in children – Impact of obesity on development of diabetes
  - Poster presentations
- Sunday, October 26, morning
- Part IV: Can good management prevent the diabetic complication
    - POC testing instruments for diagnosing and monitoring diabetes in clinical settings
    - The impact of preanalytic factors of glucose measurement
  - Self measurement of glucose – how useful is it and how can it be done
  - Poster presentations
  - Break, poster walk, exhibition
  - Part V: Can good management prevent the diabetic complication
    - Obesity and Diabetes. The role of Laboratory Medicine
    - Pros and Cons of Incretin therapy in Type 2 diabetes
    - The practical issues in patient management – pharmacogenetics

# EuroLabFocus

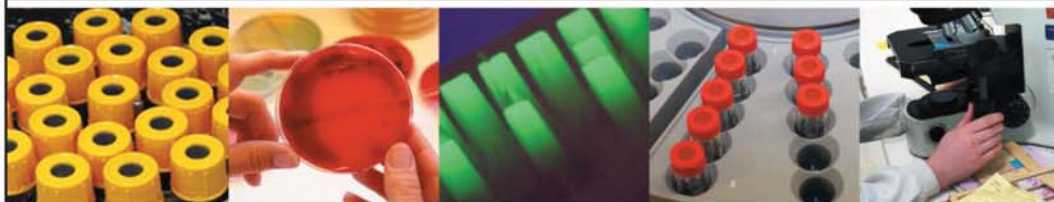


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## Impact of Analytical Method Performance on Clinical Decision Making and Health Outcomes

by Christopher P Price, Visiting Professor in Clinical Biochemistry,  
Department of Primary Care Health Sciences, University of Oxford, UK

One of the foremost features in the evolution of laboratory medicine has been the pursuit of quality in the performance of analytical methods. Highlights include the creation of international reference materials and reference methods<sup>1,2</sup> alongside the underlying concepts of how these can be translated into the creation of calibration materials that can be employed in the methods routinely used in the laboratory, and at the point of care<sup>3</sup>. These achievements have been complemented by developments in quality control and external quality assurance<sup>4</sup>. More recently we have seen the call for harmonization of analytical methods<sup>5</sup>, as it has become obvious in recent years that the underlying principles of the analytical methods can also impact on day to day performance. All of this activity has been primarily driven by the pursuit of analytical and scientific excellence, which is traceable to a robust point of reference<sup>6</sup>.

In more recent times there has been a parallel evolution in evidence-based laboratory medicine, which has a different point of reference, namely the impact of a test result on clinical decision making and health outcomes<sup>7</sup>. In this evolution it soon became clear that the evidence base was poor, and furthermore the gener-

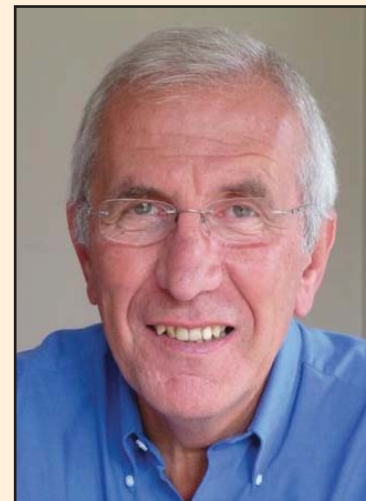
ation of the required evidence was challenging<sup>8</sup>. A test result, of itself, will not have an impact on a health outcome; it requires appropriate clinical decision making and action<sup>9</sup>. It was inevitable that, at some point, the impact of analytical performance on the delivery of health outcomes would be questioned. This has been addressed in terms of desirable analytical performance, by reference to the biological variation of the analyte and its impact on the quality of decision making<sup>10</sup>. An alternative approach has been to employ modelling of the clinical decision pathway. An early example was the modelling work of Bruns and Boyd on the impact of blood glucose measurement imprecision of insulin dosing<sup>11</sup>.

A recent paper by Langlois and colleagues reporting a collaborative project, sponsored by the European Federation of Clinical Chemistry and Laboratory Medicine and the European Atherosclerosis Society, investigating the impact of the method bias in routine HDL and LDL cholesterol methods on cardiovascular risk stratification, in hypertriglyceridemia<sup>12</sup>. The authors used the results from the Dutch National External Quality Assurance program to study the risk of misclassification due to method variability. Data from three normotriglyc-

eridemic pools and two hypertriglyceridemic pools were selected on the basis that their mean concentrations were close to the high risk cut-points for HDL and LDL cholesterol. The target values were assigned by a Lipid Reference Laboratory. They simulated the risk classification using HDL – and sex-specific SCORE multipliers applied to two fictitious moderate risk patients with an initial SCORE of 4% (male) and 3% (female). In addition they examined the concordance of classification into treatment groups using the relative numbers of LDL cholesterol concentrations above the high risk cut-point for each of the methods contributing to the quality assurance scheme. The authors observed biases in hypertriglyceridemic sera beyond the recommended limits which impacted on the proportion of high risk classifications, and which varied between methods. The errors in the HDL cholesterol measurements also impacted on the calculated LDL cholesterol values and the assignment of treatment goals. Clearly method performance was shown to have the potential to impact on clinical decision making and subsequent treatment actions.

There are important messages in this paper, as well as indicating the way that laboratory professionals and manufacturers of diagnostic technologies should be appraising the output of the services they provide. There are three important conclusions from this study (i) the choice of method employed to generate the evidence on the use of the analyte for clinical decision making should be clearly stated; it should be a method with traceable calibration, and with minimal risk of bias (ii) the impact of variation in method imprecision and bias and their impact on clinical decision making and outcomes should be modelled wherever possible, for the routine methods used in the laboratory practice, and (iii) clinicians should be made aware of the risks of poor method performance on clinical decision making and health outcomes. A similar approach should also be considered when using semiquantitative methods for rule in or rule out decisions.

This study is to be welcomed as it highlights an important tool for the laboratory medicine professional to employ in both quality improvement and innovation. Furthermore it provides a means of demonstrating how the laboratory professional plays a crucial role in the work of the clinical team.



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