

These include siRNA and microRNA used to degrade mRNA transcripts and suppress protein translation, and antisense oligonucleotides used to manipulate splicing.

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PHARMACOGENETICS AND OTHER FACTORS IN INDIVIDUALIZATION OF ORAL ANTI-VITAMINE K ANTI-COAGULANTS

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Summary: The use of vitamin K antagonists (VKA) is challenging because of their narrow therapeutic index and a large interindividual variability. Pauci data were available regarding the relative contribution of pharmacogenetic and nongenetic factors to VKA response in specific populations (elderly, children, resistant patients). In 2 cohorts of elderly patients receiving warfarin (n = 300) or fluindione (n = 156), genetic factors were the main determinants of the maintenance dose, explaining ~20% of the variability versus ~10% for nongenetic factors. The variables significantly associated with the maintenance dose were VKORC1/CYP2C9/CYP4F2/EPHX1 and age for warfarin, and VKORC1/ABCB/CYP4F2, weight, and amiodarone intake for fluindione by multivariate analysis. During warfarin initiation, VKORC1 genotype had a strong predictive value for warfarin sensitivity. When building prediction models of the warfarin dose, VKORC1/CYP2C9 were the best predictors before initiation, whereas their contribution was negligible once INR value was available after starting warfarin using a standardized regimen.

In the children cohort (n = 120), height and VKORC1/CYP2C9 were the main determinants of warfarin dose requirement, explaining 70% of the variability accounting for 48% and 20%, respectively.

Among the 100 patients resistant referred to us for analysis, only 30 patients were carriers of VKORC1 mutations for which in vitro functional characterization was performed. Our results suggest the involvement of other genetic factors in VKA resistance.

Pharmacogenetics will help the development of personalized medicine to improve safety and efficacy during VKA treatment. Whether genetic testing improves long-term anticoagulation control in patients receiving VKA and prone to instability remains to be determined.

Disclosure of Interest: None declared.

PUBLIC HEALTH GENOMICS AND PERSONALIZED HEALTHCARE

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Summary: Rapid scientific advances and tools in genomics such as in the light of epigenomics, microbiomics, and systems biology supported by new ICT solutions not only contribute to the understanding of disease mechanisms but also provide the option of new promising applications in human health management during the whole life-course. What was a little time ago a vision for a new era of public health, in which advances from the -omic sciences would be integrated into strategies aiming at benefiting population health, is now responding to the very pressing need for the development of effective personalized health care, going even beyond personalized medicine based on a systems medicine approach. Although the utility of most genetic tests and biomarkers is still not evidence based, the real take-home message stops here and is a different one. In the personalized medicine setting, the traditional assessment and evaluation tools just do not work anymore. Thus, we clearly face the need for

a new paradigm moving from population health to personal health. The paradigm shift depends on the willingness to restructure policies, and there is a clear urgency to prepare health care systems and policy makers in time.

So far, all stakeholders, including policy makers and the private sector, are struggling to translate the emerging knowledge into public health. Public Health Genomics (PHG) is the area of public health ensuring that scientific advances in genomics ("from cell...") triggered by innovative technologies are timely, effectively, and responsibly translated into health policies and practice for the benefit of population health ("...to society"). The implementation of PHG requires increased concerted activities. The Institute for Public Health Genomics (IPHG) at Maastricht University aims to fulfill this task in all European Member States by hosting the European Centre for Public Health Genomics (ECPHG) and coordinating the Public Health Genomics European Network (PHGEN). Furthermore, it closely collaborates with the European Science Foundation (ESF Forward Look on Personalised Medicine), the European Alliance for Personalised Medicine (EAPM), and the European Flagship Pilot ITFoM on the future of medicine, being one of the most ambitious worldwide, large-scale, science-driven, research initiatives that aim to achieve the visionary goal of the "virtual human."

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A SYSTEMATIC FOLLOW-UP OF STUDENT-PRESCRIBERS (TRACK): THERAPEUTIC KNOWLEDGE, SKILLS/COMPETENCIES AND ATTITUDE

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Summary: One of the core objectives of medical curricula is to provide graduates with a sufficient level of therapeutic knowledge and skills. Over the last decade, a lot has changed when it comes to teaching medical students how to prescribe rationally. In the Netherlands, most medical curricula shifted from a so-called problem-based learning to a context-learning pharmacotherapy program. However, there is still no systematic approach available for assessing students' therapeutic knowledge and skills during such a context-learning curriculum. Research on this topic consists almost exclusively of descriptive and evaluative studies on different assessment methods. These studies show that the often-used single-shot assessments have their shortcomings and poorly meet the recent developments in medical education (context-learning). What is needed is a systematic approach to assessment.

In this session, David Brinkman proposes a new systematic model (TRACK) for assessing students' therapeutic knowledge, skills/competencies, and attitude during a context-learning curriculum. This longitudinal model is based on a set of assessment principles that are interpreted from empirical evidence. He discusses a number of challenges and opportunities around the proposed model and presents preliminary findings of this new project. One of its prime virtues is that it enables therapeutic assessment toward an assessment design that is underpinned by empirically grounded theory and, moreover, carefully follows students until they are prescribers.

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STRATEGIES FOR THE DEVELOPMENT OF TDM FOR TARGETED ANTICANCER AGENTS

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Summary: Most of the novel targeted anticancer agents share classical characteristics that define drugs as candidates for blood concentration monitoring: long-term therapy; high interindividual but restricted intraindividual variability; significant drug–drug and drug–food interactions; correlations between concentration and efficacy/toxicity with rather narrow therapeutic index; reversibility of effects; and absence of early markers of response. Surprisingly though, therapeutic concentration monitoring has received little attention for these drugs despite reiterated suggestions from clinical pharmacologists. Several issues explain the lack of clinical research and development in this field: global tradition of empiricism regarding treatment monitoring, lack of formal conceptual framework, ethical difficulties in the elaboration of controlled clinical trials, disregard from both drug manufacturers and public funders, limited encouragement from regulatory authorities, and practical hurdles making dosage adjustment based on concentration monitoring a difficult task for prescribers. However, new technologies are soon to help us overcome these obstacles, with the advent of miniaturized measurement devices able to quantify circulating drug concentrations at the point-of-care, to evaluate their plausibility given actual dosage and sampling time, to determine their appropriateness with reference to therapeutic targets, and to advise on suitable dosage adjustment. Such evolutions could bring conceptual changes into the clinical development of drugs such as anticancer agents, while increasing the therapeutic impact of population PK-PD studies and systematic reviews. Research efforts in that direction from the clinical pharmacology community will be essential for patients to receive the greatest benefits and the least harm from new anticancer treatments. The example of imatinib, the first commercialized tyrosine kinase inhibitor, will be outlined to illustrate a potential research agenda for the rational development of therapeutic concentration monitoring.

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ADVANCES IN GENOMICS OF BLOOD PRESSURE—TIME FOR TRANSLATION

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Summary: In 2025, there will be 1.56 billion people worldwide with hypertension. Although evidence-based interventions have transformed blood pressure control, public health data show there is still poor blood pressure control, and new therapies are still needed. Paradoxically, more sophisticated understanding of pathogenesis coincides with a decline in licensing of new medicines for hypertension. Using discoveries from genomics of blood pressure could be used to select and validate drug targets, combining expertise in this area with model organism phenotyping, experimental medicine, and pharmacology alongside medicinal chemistry may assist. To reduce the cost, we could utilize the untapped potential of the electronic health record for clinical trial delivery, and “real-world” evaluation of clinical effectiveness could reduce some of the risks and costs of clinical development, allowing a new generation of molecules to be generated in an affordable manner.

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ELECTRONIC SOLUTIONS TO SAFER HOSPITAL PRESCRIBING

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Summary: Routine clinical care in hospitals has become more reliant on digital technologies over the last decade. There are now a wide

variety of electronic solutions aimed at improving patient safety and optimizing the use of medicines. This focused session will describe technologies available at key stages in the prescribing process: the decision to prescribe, the prescription generation, and the ongoing monitoring of therapy.

To support the decision-making process, prescribing information is available in many different point-of-care digital solutions across various platforms such as online computerized guidelines and smartphone applications. However, there is often overwhelming information available to prescribers. Clinical decision support (CDS) tools can help because they allow more relevant information, often specific for the patient, to be embedded in the clinical workflow. Better still is the use of electronic prescribing medication administration (EPMA) systems either as standalone systems or as part of a wider electronic patient record. Such systems may influence prescribing decisions; for example, by promoting efficacious and cost-effective therapy. Other steps in the medicines use process can also be targeted by novel technologies such as automated dispensing systems and positive patient identification through barcode medication administration systems. Electronic medication administration records enable the precise monitoring of medication use on an individual patient surveillance level through to providing data for hospital-wide medication management strategies.

Individually, all of these have been shown to effect safe prescribing. The advantage of combining these technological advances—which are already available in a limited number of integrated systems—cannot be underestimated and will become increasingly important to support tomorrow’s prescribers in providing optimal patient care.

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HOW TO GOVERN A SELF-POWERED PATIENT: PRIVACY AND BIOWEAPON

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Summary: A range of new technologies is about to enable patients to produce a steady flow of information about their bodies: for example, heartbeat, blood pressure, sugar level, calories spent, temperature, sleep pattern. They are seen as useful to improve the quality of life and the accuracy of treatment for many patients, especially those with chronic diseases. This is probably the case when data are collected and analyzed by professionals. But since patients (or persons not suffering from any disease) will also be to monitor their own data without immediate supervision, there is a risk of misuse and getting lost, that can lead to false or dangerous “homemade” medicine. Also, privacy of patients may be in danger. This is not only about preventing unauthorized persons from accessing these sets of very sensitive data, but probably to protect patients against themselves. Indeed, as some of them already post their genetic pattern on social networks, disclosing one’s own body’s parameter can potentially become a common practice. That would be extremely profitable for drug companies to sell their products, for example, or for insurance companies looking to filter good risks from bad ones. The lesson to be learned is that one should not consider that the data are available for any purpose just because the person decided to make his or her own data public, something that nobody will be ever able to forbid. Unfortunately, current data protection policies still consider data made public as... public. In fact, even a perfect protection of privacy could not address the problems of a complex relationship between information and power. To shed light on this subtle relationship, I will use the Michel Foucault’s concept of “biopower.” It will reveal that the project of developing techniques to build self-powered patients