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ADJACENT GOVERNMENT

HEALTH ANALYSIS

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EUROPEAN HEALTH

Addressing Europe's health challenges

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Introduction

The economic crisis forced healthcare budgets to be reduced throughout Europe, putting pressure on officials trying to tackle major health challenges. With an ever growing population, addressing these challenges has become a key priority.

Health and social care is a key policy throughout Europe, and whether it be the UK NHS or European Healthcare, there are still areas that need to be tackled. For example, mental health is a worldwide issue that is of great importance – and falling budgets have caused a lack of support for adults and children with mental health issues.

In this Adjacent Government: Healthcare Analysis document, we highlight mental health and a number of other healthcare challenges that are under scrutiny at present. With expert opinion and debate, this Healthcare Analysis sheds light on how we can create a healthier Europe.

The supplement starts with an introduction to the new European Commissioner for Health and Food Safety – Vytenis Andriukaitis, and his key priorities for the year. It discusses how Andriukaitis has held the belief that health policy has a key role to play in economic growth, with a sentiment that "healthy people are more creative and productive."

Another area that we shine the spotlight on is musculoskeletal disorders, and Vern Putz Anderson from the National Institute for Occupational Safety and Health at the Centers for Disease Control and Prevention (CDC) details the risk factors and prevention of disorders in the workplace.

Elsewhere in the supplement we give consideration to the role of technology in healthcare with an article from Paul Rice, Head of Technology Strategy at NHS England. The article highlights how innovative technologies are helping us to lead healthier and more independent lives.

Adjacent Government: Healthcare Analysis also highlights the benefits of care in the home, with an article from Dominic Carter of the United Kingdom Homecare Associations (UKHCA). He details how homecare can be more flexible, and the benefits it offers both carers and patients.

Other areas highlighted in this special edition include: mental health; liver cancer; chemistry for drug discovery; and healthcare research.

Whether you work in the healthcare sector or not, I hope you find the Adjacent Government; Healthcare Analysis thought provoking and useful. As always I welcome any comments and feedback you may have. ■

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Health in Europe: A matter of good economics

Adjacent Government details the priorities and intentions of the new European Health Commissioner, Vytenis Andriukaitis...

Born in 1951, Vytenis Andriukaitis holds degrees in medicine and history and started his political career just after high school. He is one of the authors of the Lithuanian Constitution of 1992 and a signatory to the 1990 Act of the Re-Establishment of the State of Lithuania. Andriukaitis entered politics in 1976 as an underground Social Democrat, and was among those who re-established the Social Democratic Party of Lithuania in 1989. He was an active member of the Lithuanian Reform Movement Sąjūdis, fighting against the Soviet, before becoming an active politician. He has also served as a cardiovascular surgeon for almost 20 years.

Andriukaitis was also the Minister of Health in the Republic of Lithuania from 2012-2014, and is currently the Vice-President of 67th World Health Assembly.

MEPs approved the new college of 27 Commissioners, including Andriukaitis, as presented by its President-elect Jean-Claude Juncker in October 2014, and is a welcome appointment according to The European Public Health Alliance. Andriukaitis spoke at their annual conference in 2014 where he said, "Health is not a consequence of growth but also a condition for growth. Investments in public health increase productivity and boost job creation. Health should not only be seen as product of growth: health encourages growth."

Emma Woodford, European Public Health Alliance Interim Secretary General reacted to his appointment stating that, "Better attention should be paid to socio-economic determinants of health, health promotion and prevention. Once he is confirmed as Health and Food Safety Commissioner by the European Parliament in October, he should put forward an agenda based on greater investments in health with a focus on social determinants."

Andriukaitis has long held the belief that health policy has a key role to play in economic growth, repeating again the sentiment that "healthy people are more creative and productive. Their well-being sets the foundations that moves societies forward. Health in all policies should be the driving force of our efforts to cut inequalities as it lays the groundwork for social justice and economic sustainability".

In his written answers to questions from MEPs before his official appointment, he provided details of what his top priorities would be in the fields of public health and food safety:

- With regard to past crises such as BSE and SARS, which have shown the economic value of strong health protection, he intends to pursue the highest standards;

- He believes we need 'a new boost for health in Europe' if we are to improve people's health and boost jobs and growth. He therefore intends to "promote investment in health, as an investment in Europe's human capital and an investment in our future";

- The priorities surround promotion, protection and prevention. Andriukaitis intends to deliver real benefits to citizens and support key sectors of the EU economy such as the healthcare sector – as well as the agro-food industry;

- Against a backdrop of population ageing, a growing burden of chronic diseases and increasing demand for healthcare, he will support efforts to make health systems more efficient and innovative; so that they can provide equitable healthcare to all citizens, while remaining financially sustainable;

- To assess the performance of health systems reform within the European Semester;

- To focus on enhancing prevention, as the more health systems invest in this field, the less they will pay for treatment in the future;

- Andriukaitis will seek to make recent EU legislation having an impact on the protection of public health deliver results to citizens. For example, to ensure the timely adoption of secondary legislation foreseen under the Tobacco Products Directive. He intends to work tirelessly with the Member States to ensure the Directive on patients' rights in cross border healthcare translates into citizens' better access to quality care; into in-depth co-operation on e-Health towards better care; and into joint work on Health Technology Assessment to improve patients' access to innovative technologies, business predictability and cost-effectiveness;

- Working with Member States to protect citizens against any cross border health threat;

- Promoting healthy and safe food as a means to prevent unnecessary spending in healthcare and help Member States improve the long term sustainability of their health systems;

- Endeavour to ensure high levels of animal and plant health, providing strict controls on the safety of imported products of both plant and animal origin;

- To work with all stakeholders to maintain and improve food safety systems contributing to President Juncker's plans for a Europe with more jobs and greater prosperity, particularly for SMEs which make up the bulk of the food sector.

Andriukaitis made it clear that all legislative proposals currently under discussion with the European Parliament and the Council are brought to a successful conclusion, including the proposals on animal health, plant health, official controls, novel food, cloning, zootechnics and medicated feed. He also promised that within the first 6 months he would review the legislation applicable to the authorisation of genetically modified organisms.

Health systems performance assessment

In his speech on the 27th January at the launch of the European Health Consumer Index 2014, Andriukaitis reiterated his priority as mentioned above. Namely – promotion, prevention, protection, but also added 'participation' in thanks to his young followers on social media. He also referred to the importance of health systems performance assessment – a useful tool to understand how we work and how we can improve. He believes that the assessment will build up knowledge which can help make evidence-based policies at national and European levels. Member States and the Commission have agreed to pursue a set of common goals, the first of which is a forum where they could:

- Exchange their experiences;
- Present their practices;
- Share success stories; and
- Learn from each other.

The second goal is to support national policy makers by identifying tools and methodologies to improve the assessment of their health systems. Cooperation will also take place with organisations such as the OECD and WHO.

"healthy people are more creative and productive. Their well-being sets the foundations that moves societies forward. Health in all policies should be the driving force of our efforts to cut inequalities as it lays the groundwork for social justice and economic sustainability."

Health information

According to Andriukaitis "health information is at the foundation of good performance assessment", with the European Commission making considerable efforts to "reinforce and ensure the sustainability of actions on health information". Data collection supported by the Health Programmes has led to:

- Improvements of the methodology of statistics collection;
- Development and harmonisation of health indicators; and
- The preparation of health reports.

Andriukaitis recognises that these steps don't go far enough in themselves and wishes to ensure:

- The sustainability of data collection;
- Transparency in the development of indicators; and
- Full participation of Member States in their selection.

For Andriukaitis to realise the intentions and priorities he has laid out, he will need all the enthusiasm and stamina he can muster. An immediate topic at the forefront is the potential for a US free-trade deal agreement which could equate to the world's biggest trade deal to date. However, with no clear majority emerging as yet, and with public opposition within Europe apparent, Andriukaitis will have to work hard to ensure buy-in by all national parliaments. No doubt the negotiations needed to ratify this deal would provide him with an early legacy, but there is still much to do, not just with the free-trade agreement, but on his promises made last year. ■

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Pneumothorax detection with bedside ultrasound

Without prompt treatment, a pneumothorax may progress to cardiac arrest and death. Pneumothorax develops as air becomes trapped in the pleural space from traumatic, iatrogenic, or other causes.[1] A large pneumothorax can cause hemodynamic instability, therefore early recognition is central to management.

Bedside thoracic ultrasound is rapid, portable, and may be performed with the patient upright or supine. Bedside ultrasound is more accurate than supine chest x-ray for detecting pneumothorax, with diagnostic ability approaching that of CT.[2-7]

Air is a poor medium for ultrasound waves due to its low density and slow propagation velocity. Healthy lungs contain air, and are surrounded by the highly reflective bones of the ribs. Rather than visualising lungs directly, pulmonary ultrasound identifies various artifacts or detection of movement.

In a longitudinal view, the acoustic shadowing of the ribs marks the space where the pleural line may be identified. In Figure 1, the acoustic shadow of the ribs (R) is created by the strongly reflective bony cortex, and marks the pleural line (asterix). Since bone reflects ultrasound waves, no signal is detected behind the bony cortex, creating shadowing.

Normal pleural movement demonstrates a "shimmer sign" with B mode imaging. Poor respiratory effort, operator experience or fatigue, and other factors may complicate the identification of a "shimmer sign". M mode imaging uses a high frequency probe to depict lung movement. Using M mode, normal lung that is moving has a homogenous granular appearance under the brightly visualised pleura. Figure 2 depicts this "seashore sign", with the normal lung reminiscent of sand and approaching waves. The loss of granular appearing "sand" on the bottom half of the screen is indicative of pneumothorax.

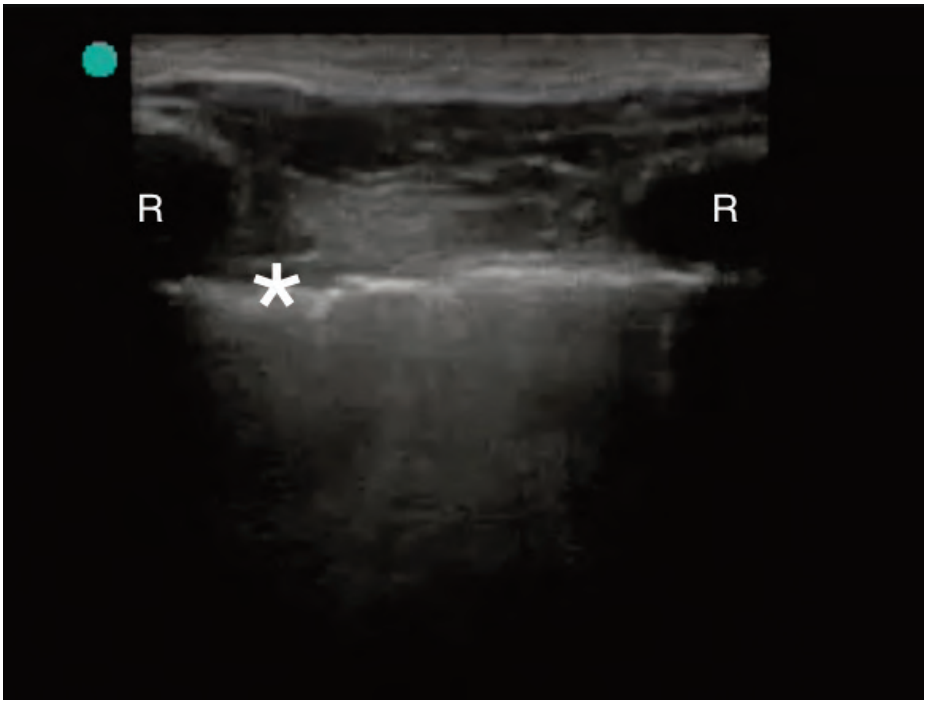

Figure 1: Normal lung between rib spaces

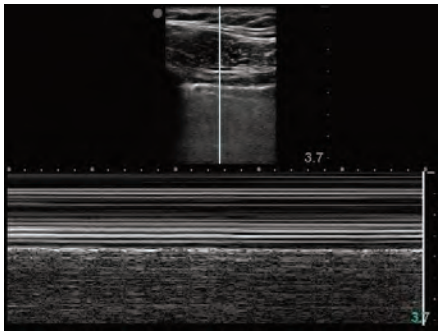

Figure 2: Seashore sign of normal lung

Lung sliding is also detected by Doppler. Power Doppler (Figure 3) utilises an orange scale to detect movement relative to the transducer surface, which is more sensitive for movement as compared to the red blue Color Doppler. A patient with a pneumothorax will not have lung sliding relative to the transducer surface, and no color will be detected in the sample selected (Figure 4).

B lines, also known as comet tail artifacts, represent the common border between the interlobular septa and the alveolar wall.[1] B line artifacts start from the pleural line, and are hyperechoic, or brighter than the surrounding field. B lines move with lung sliding during

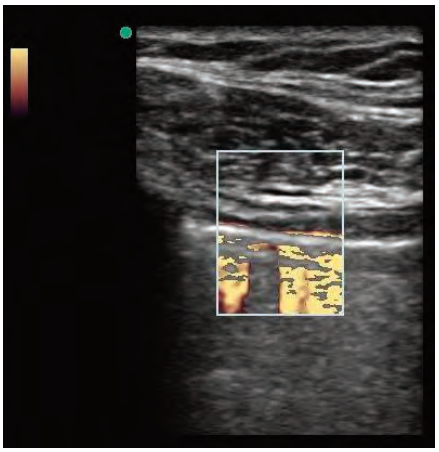

Figure 3: Power Doppler of normal lung

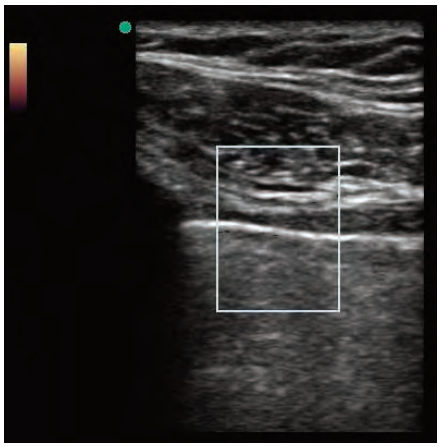

Figure 4: Power Doppler depicting a pneumothorax

respiration. In normal lung the B lines appear to wipe side to side over the stationary appearing A lines, which are the reverberation artifacts of the pleural line. The lack of B line movement also indicates pneumothorax.

As a general rule of thumb, it is recommended to visualise more than one lung field, and scan areas where there is clinical suspicion for pathology. The BRIPPED protocol is a screening tool for undifferentiated shortness of breath that may be performed with the patient in any position, and utilises high and lower frequency probes using a portable bedside ultrasound machine. The BRIPPED protocol evaluates pneumothorax among other etiologies of shortness of breath.

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To produce healthy pork and poultry

The Kielanowski Institute of Animal Physiology and Nutrition (KIAP&N) in Jablonna focuses on improving feeding recommendations to produce healthy pork and poultry

The Department of Monogastric Nutrition of the KIAP&N in Jablonna (Poland), headed by Professor Jacek Skomial specialises in conducting research on the physiology of nutrition of pigs and poultry (broiler chickens in particular). One line of research focuses on improving feeding recommendations, others investigate the influence of nutritional factors on the development of the gastrointestinal tract, nutrient digestibility and metabolism.

For pigs, particularly for weaned piglets, changes in the composition, form, and quality of feedstuffs may cause health problems and inhibit their growth. Morphological and functional changes in the digestive tract can be modulated by bioactive compounds present in feedstuffs or added to the diet. In addition to changes in morphology, a very important issue is microbial activity, mostly in the large intestine. Species composition, as well as the number of microbes, influences not only fermentation of nutrients reaching the caecum and colon, but also creates the environment for the digesta. Fermentation of carbohydrates leads to increased concentrations of short-chain fatty acids, which are important as a source of energy for the host (i.e., the pig). The decreased pH negatively affects the development of pathogens, thus supporting the health of the animal. Some of the short-chain fatty acids are also important as an indirect source of energy for the intestinal mucosa. The concentrations of ammonia, phenolic compounds, and amines, which are affected by the intensity of protein degradation, can adversely influence health status and indirectly indicate the quality of protein. Protein undigested in the small intestine flows to the large bowel and is degraded by microbial enzymes. This protein is mostly lost for the animal and contributes to environmental pollution.

Recent examinations

Recently, Professor Skomial group have examined the influence of various types of protein, differing in their digestibility in the small intestine, fed with indigestible carbohydrates (resistant starch, pectin, cellulose) on fermentation processes in the large intestine and their role in digestive tract development. They found that the effect of protein type on microbial activity in the large intestine is modified by the type of carbohydrate in the diet and that this should be taken into account during formulation of diets for pigs. In other research connected with digestive tract development and microbial activity, the possibility of using inulin-type fructans from chicory roots or Jerusalem artichoke as feed additives was examined. In piglets and chickens, some beneficial results that depended on the degree of fructan polymerisation were observed. Dietary supplementation with inulin and a probiotic preparation also had a beneficial effect.

Among the studied bioactive compounds, tannic acid was examined as a representative of hydrolysable tannins, which are present in many feeds of plant origin, because they can form indigestible complexes with nutrients, particularly with proteins. Dietary protein bound to tannic acid becomes indigestible in the small intestine and undergoes microbial degradation in the large intestine, leading to increased production of short-chain fatty acids, but also potentially toxic compounds. On the other hand, supplementation of the diet with tannic acid inhibits bacterial β-glucuronidase activity, reducing the risk of carcinogenesis.

Another problem crucial in pig nutrition is establishing the proper level of amino acids and determining their role in pigs. In their previous studies they examined the requirements of growing pigs for methionine, tryptophan, and, recently, threonine, particularly its utilisation when various levels of endogenous amino acids were supplied to diets. One important finding is that threonine-deficient diets decrease the number of acidic goblet cells, which produce mucus, an important component of the intestinal barrier protecting against pathogens.

Broiler chickens

One of the very important topics that Professor Skomial group works on is improvement of the functional properties of broiler chicken meat. Excess saturated fatty acids and a high proportion of n-6 to n-3 unsaturated fatty acids in human diets can promote many diseases of civilisation, such as cardiovascular disease, obesity, cancer, diabetes. Much research has been conducted to increase the deposition of polyunsaturated fatty acids, particularly from the n-3 family, particularly with pigs and poultry. In their experiments, they tried to achieve this improvement by using various sources of unsaturated fatty acids, including fish oil, linseed oil, and rapeseed oil in different combinations and fed them for different times before slaughter. In parallel, they examined supplementation with natural antioxidants. They found that rapeseed and fish oil can be used for the modification of fatty acid composition in broiler meat. The meat and fat of broilers fed diets with rapeseed, linseed, and fish oil can be considered high in n-3 polyunsaturated fatty acids, but the dietary level of fish oil should not exceed 1% to avoid deterioration of the sensory characteristics of animal products. Increased levels of unsaturated fatty acids in the diet, and finally in the meat and fat of broiler products, requires supplementation with vitamin E and selenium to counteract oxidative stress and to increase the stability of these acids during frozen storage.

Since the use of feeds derived from the genetically modified (GM) plants is strongly criticised in Poland, they also investigated the possibility of adverse effects of their use in broiler feed mixtures. The use of GM soybean meal and maize in broiler diets did not affect performance or immunological status, intestinal morphology, epithelial cell turnover rate in the small intestine, intestinal ecosystem composition and activity. However, Clostridia in birds fed GM soybean meal were more resistant to kanamycin compared with conventional soybean meal.

Also the effects of using locally produced plant protein sources as an alternative to GM soybean meal were evaluated. Among others, different varieties of pea and lupine seeds, raw or processed, as well as rapeseed products were used in pig and broiler diets supplemented with enzymes or probiotics. It was found that partial replacement of soybean meal by protein from different legumes or rapeseed products in diets for growing pigs and broiler chickens is possible without adverse effect on feed utilisation and digestive tract physiology. The total elimination of soybean meal from broiler diets is possible only with a complementary dose of potato protein concentrate.

Another important problem is the influence of alkaloids on the physiology of the digestive tract of monogastric animals and the biochemical profile of blood indicating their possible toxic effects. Potato or its by-products like potato protein concentrate can introduce some solanidine glycoalkaloids (solanine and chaconine) into the diet, which can be toxic to animals. In their study, it was shown that chickens are generally less sensitive to this antinutritional factor than piglets.

Publications and future prospects

The KIAP&N publishes its own quarterly international scientific journal, The Journal of Animal and Feed Sciences, in which papers on animal nutrition, breeding and physiology, and feed science, submitted from Poland and abroad, are published. In 2016, The KIAP&N will be a co-organiser of the scientific conference "The 5th EAAP International Symposium on Energy and Protein Metabolism and Nutrition" to be held in Krakow, the former capital of Poland. It is open to co-operation with scientific institutions, feed and food producers, in terms of participating in research and implementation.

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EU funding for health, demographic change and wellbeing projects

Sarah Collen-Godman, Senior Policy Manager – NHS European Office at the NHS Confederation discusses how the Horizon 2020 programme will help to address major societal challenges...

Horizon 2020, Europe's research and innovation programme, was launched at the beginning of 2014 and will run until 2020. It is the EU's overarching, multi-disciplinary research and innovation funding programme that will see more than €70bn dedicated to support the EU's position as a world leader in science, help secure industrial leadership in innovation, and help address major societal challenges.

Research and innovation for health related topics fall predominantly under the highest funded societal challenge on 'health, demographic change, and wellbeing', which has an indicative budget of €7.5bn for the 7 year period. This will fund activities throughout the whole R&D spectrum, from basic research to market, with a new focus on impact and innovation related activities.

The European Commission is increasingly pushing for research and ideas funded to be translated into practice and demonstrate clear advantages to patients and have a real impact on population health and wellbeing.

Taken together, projects supported by the 'health, demographic change and wellbeing' challenge will contribute to:

- Understanding health, ageing and disease;
- Effective health promotion, disease prevention, preparedness and screening;
- Improving diagnosis;
- Innovative treatments and technologies;
- Advancing active and healthy ageing;
- Integrated, sustainable, citizen centred care;
- Improving health information, data exploitation and providing an evidence base for health policy and regulation.

Historically, the UK, particularly its academia, has significant experience of accessing EU research funding and is the largest beneficiary of EU health research funds. The increased focus on impact and uptake of innovation means there is greater scope for involvement of other stakeholders from outside academia, such as healthcare providers, small to medium size businesses, charities and patients groups.

The European Commission has also made a big effort to streamline the rules – and to apply them across the funding stream. The reimbursement rates of project expenses is simpler, with a single reimbursement rate for most projects. That means less paperwork and fewer audits. It has also limited time from application to grant to 8 months, to encourage this to become more accessible to more stakeholders outside of academia. All projects need to have a European added value – going beyond research at national level and should involve participants from at least 3 EU member states.

EU's 3rd Health Programme

The EU's Third Health Programme 2014-2020 has a budget of €449.4m (2014-2020) to support cooperation projects at EU level; actions jointly undertaken by Member State health authorities; the functioning of pan-European non-governmental networks and

cooperation with international organisations.

Through the different funding mechanisms, the EU's Health Programme aims to strengthen public health across Europe through:

- Promoting health, preventing diseases, and fostering supportive environments for healthy lifestyles
- Protecting citizens from serious cross-border health threats;
- Contributing to innovative, efficient and sustainable health systems;
- Facilitating access to better and safer healthcare for Union citizens.

Overarching operational objectives are to identify, disseminate and promote the up-take of evidence-based and good practices, standards, tools and resources through knowledge sharing activities. Where appropriate, this can also include developing coordinated approaches, for example, for use during cross border health emergencies.

How to apply:

Funding is issued through open calls for proposals with strict deadlines for submission of projects. All proposals are submitted electronically. The website dedicated to the electronic administration of the EU Health Programme and Horizon 2020 projects is: http://ec.europa.eu/research/participants/portal/desktop/en/home.html ■

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The potential of the digital revolution and telehealth

Paul Rice, Head of Technology Strategy at NHS England outlines how innovative technologies are helping us to lead healthier and more independent lives...

Information technology is playing an increasingly pervasive and enabling role in many aspects of our lives, in a host of different ways. It keeps us connected to our loved ones as we video call on Skype or Facetime, blog, connect via social media or share the vivid highlights of our day via Facebook and Instagram. Last Christmas expected to see a boom in sales of wearable biometric devices as the new Apple Healthkit suite and Fitbugs, and Fitbits flood into the consumer market, providing detailed data to the user about their general health and fitness and more specific insights into such things as sleeping patterns, body mass index or resting heartbeat. When insight converts to ambition and commitment it is anticipated that more of us will adopt health seeking behaviours and alter our diet and exercise patterns.

For the engaged and connected the internet provides access to a huge amount of expert information from a multitude of professional disciplines. It also enables us, as individuals, to strike up conversations and establish relationships with people we identify with, and whom we share characteristics and experience. "Apps" provide a plethora of information and resource in handy bite-sized chunks extending our ability to personalise our support networks and build self-care competencies.

What is the relationship between these opportunities and capabilities, our health and care system, the NHS, and in particular the experience of the elderly or vulnerable?

The term telehealth has emerged over the last decade to describe a range of interventions and activities where the health and care system has actively engaged with the potential of information technology to eliminate some of the limitations of time and distance. It also encompasses the ability of the individual to capture, track and trend biometric information, about their health status and wellbeing, on the move or at home in a manner that previously wouldn't have been possible outside of the 4 walls of a hospital.

Why has this become so important?
Growing numbers of people with multiple conditions are living longer and resources to support their continued wellbeing are increasingly stretched. Health and social care professionals are expert resources that need to be targeted at those most vulnerable at precisely the right moment. The very experience of travelling for face to face consultation with a health or care professional can be burdensome for patients and their carers, particularly where underlying poor health or a specific feature of their condition (impairment, mobility, cognitive difficulties) makes travel challenging. Through innovative use of technology a consultation can be undertaken between clinician and patient via video link without either of them having to move location. The range of expertise that can be accessed is determined by the skills and experience of the available professional. Increasingly educational and rehabilitation content – for example pulmonary rehabilitation advice and support for patients with Chronic Obstructive Pulmonary Disease (COPD) can be offered remotely. The application of this technology is also not limited to physical ailment or disease. An increasing range of mental health services, covering psychological advice, support and treatment are being delivered by this method too.

In addition to connecting to professional or "expert patient" resources remotely, when an individual uses a biometric or telemonitoring device the clinician has continuous access to an extended range of key data – "vital signs" – and insights – how am I feeling today? Having determined, on the basis of this information, and their knowledge of the patient's history, whether they are stable or deteriorating, the clinician can intervene proactively, advise them to alter their medicines' regime. They can rapidly schedule a face-to-face contact where an immediate and severe need has been identified. The patient too, with appropriate education, can become more aware of the impact of the decisions that they make on their health and wellbeing; this may encourage them to modify their lifestyle decisions accordingly.

The common thread that joins these new models of care is that digital technologies are necessary but not sufficient. On each occasion they deliver the potential to organise services and engage patients and the wider population in a more personal and consistent way, both in managing disease and sustaining independence. For the individual to experience a greater level of control and self- determination the professional patient relationships has to be rooted in collaborating and co-creating health and wellbeing. The current generation of frail vulnerable elderly can benefit from being connected to the community around them, friends and family as well as health and care professionals, enabled as appropriate by technology. They may benefit from specific simple innovations based in the home that directly protect them from environmental risk, the threat of fire or flood, or alert others where they wander unsafely.

These telecare technologies, including simple pendant alarms, may provide much needed reassurance. With appropriate support and as user centred design and consumerism makes the technologies themselves increasingly intuitive and easy to use there is clear potential, as detailed earlier, for their introduction across the generations. As "digital natives" move into their mature middle years there is a building expectation that service models will be sufficiently flexible and designed around the needs of the individual. This is coupled with increased awareness that individuals and communities want and need to take a bigger stake in managing their own health and wellbeing. Information technology can play a huge part in releasing this untapped resource.

The NHS has signalled in its Five Year Forward View document that the NHS needs to evolve to meet new challenges and adapt to take advantage of the opportunities that science and technology offer. An engaged relationship with patients, carers and citizens promoting wellbeing and preventing ill health is a prerequisite for this and information technology and telehealth can play a crucial role in realising this ambition. ■

The National Information Board recently launched the Personalised Health and Care 2020 framework – more info can be found here https://www.gov.uk/government/news/introducing-personalised-health-and-care-2020-a-framework-for-action

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High aspirations for Norway in Horizon 2020

Arvid Hallén, Director General of The Research Council of Norway sheds light on how the country will benefit from the Horizon 2020 programme and the opportunities it will present...

Horizon 2020 is an extensive knowledge bank under construction, and it would be unthinkable for Norway as a nation not to participate in this wide-ranging initiative.

It is widely accepted in Norway that taking part in EU-funded research projects gives research communities the opportunity to join important European networks and cooperate with top-notch researchers abroad. Norwegian research policy is based on this premise, and in general the priorities of Horizon 2020 are in line with Norwegian priorities. The Norwegian government has formulated an ambitious strategy to increase the country's participation in Horizon 2020.

Horizon 2020 offers major benefits to Norwegian research and trade and industry

Norway, too, must find ways to resolve societal challenges ranging from an ageing population to renewable energy, and the country cannot do this on its own. Horizon 2020 will play a valuable role in the development of Norwegian research, trade and industry. Increased participation in Horizon 2020 will promote greater internationalisation of Norwegian research, thereby raising the level of quality overall. Further societal impacts are expected in the form of greater innovation, new products and markets for industry and a stronger ability to meet future challenges.

Norway: an attractive partner

Norwegian researchers have achieved good success in the previous framework programmes in fields such as climate, energy, marine and polar research. A number of Norwegian research institutions are world leaders in these fields. As such, they are attractive as partners for their European counterparts and can make an important contribution to dealing with societal challenges at the European level.

Norway possesses unique longitudinal data series, with information about health, education and other socio-economic factors for large segments of the

population over long time periods. The potential of these data series for comparative studies in the health and social sciences should be better exploited by national, as well as international research groups.

Great expectations for Norwegian participation in health-related projects under Horizon 2020

The goal for participation under the Horizon 2020 challenge "Health, demographic change and wellbeing" is to double the number of successful projects compared with the FP7 Health programme, and bring Norway's level up to that of its neighbouring countries, Sweden, Denmark and Finland. The Research Council of Norway is funding 9 national Centres of Excellence (SFF) and 4 national Centres for Research-based Innovation (SFI) within the field of health to build and strengthen research groups of top international standard. Norway also participates in the EU's Joint Programming Initiatives (JPIs) on health and is involved in health-related infrastructures at the European level.

Norway's national biobank is a vital infrastructure for the health sciences. The biobank provides a basis for outstanding research and innovation, enhances Norway's ability to participate in international research projects and makes Norwegian research institutions attractive partners for comparative studies. There is also major potential for the further development of health clusters.

Specially-targeted Norwegian support schemes

The Research Council has initiated several funding schemes to support Norwegian participation in Horizon 2020. This includes funding to cover expenses in connection with the preparation of grant applications and support for institutions taking part in policy discussions at the European level.

Norway has a comparatively large number of independent research institutes outside the university and university college sector. These institutes must be competitive and able to respond to the need for research-based knowledge in both industry and the public sector. The Research Council has introduced a targeted support scheme to encourage these institutes to take part in EU-funded projects.

Arvid Hallén, Director General, Research Council of Norway

The Research Council seeks to align national research programmes and funding schemes with the priorities of various European networks, while facilitating access to the European research front for Norwegian researchers.

We are currently expanding our staff dedicated to mobilising and guiding applicants to more successful participation in Horizon 2020. The Council advises Norwegian researchers to apply for funding under Horizon 2020 before applying for national funding, when possible. Given political willingness and focus, targeted funding instruments and the growing interest in and understanding of researchers of the significance of the EU research arena, we have great expectations and high aspirations for Norwegian participation in the world's largest research programme. ■

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New treatment to prevent long-term complications after deep vein thrombosis

Deep vein thrombosis is a condition caused by the formation of blood clots deep inside a leg. It is an immediate, dangerous and sometimes fatal condition. Despite the current recommended treatment that involves halting the growth of the clot with anticoagulants, a large number of patients develop long-term complications, commonly known as post-thrombotic syndrome. We have recently investigated the use of clot-lysing agents administered through a catheter to rapidly dissolve the clot and restore blood flow, a treatment that significantly reduce the risk of post-thrombotic syndrome.

Responsible radiologist, professor Nils-Einar Kløw (left), former PhD student of CaVenT, now senior consultant Tone Enden (middle), and project leader, professor Per Morten Sandet. Ylva Haig and Ole Grøtta, both PhD students, not present

Acute deep vein thrombosis of the lower limbs occurs in about 1 in 10,000 young people per year, and 1 in 100 advanced age people per year (average 1 in 1,000 per year in the general population). It is associated with high levels of morbidity, being immediately dangerous and sometimes fatal, and causing long-term problems in the legs of a large proportion of the patients. Deep vein thrombosis occurs in the deep veins of the legs that drain blood from the tissues including the musculature back to the heart. Some clots are very large and may stretch from the ankle all the way up to the heart. Smaller or larger fragments of these clots break off and follow the blood stream to the lungs, eventually obstructing the blood flow. Larger clots are immediately life-threatening as they fully block the blood flow through the lungs, a condition known as fatal pulmonary embolism.

Current guidelines recommend use of anticoagulants, such as unfractionated or low molecular weight heparin followed by oral vitamin K antagonists. Recently, novel direct-acting oral anticoagulants have been developed, that have certain advantages, including no need for monitoring. All anticoagulants stop growth of the clot, but do not remove it. Dissolution then relies upon the endogenous fibrinolytic system, but this system is highly variable from one individual to another and cannot provide sufficient dissolution in most patients. Thus, substantial residual clots that obstruct the blood flow, or other damages to the veins, occur in a large proportion of the patients. Around 20-40% of all patients with deep vein thrombosis will develop post-thrombotic syndrome, which is characterised by swelling of the leg, various degrees of pain and sometimes venous ulcers. This often leaves the patients (including the younger ones) immobile, unable to exercise and with reduced quality of life.

Clot-dissolving therapy for the treatment of deep vein thrombosis and pulmonary embolism was introduced in the 1970s. Randomised clinical studies showed that intravenous streptokinase or urokinase, drugs that activate the body's own fibrinolytic system, removed clots and reduced the risk of post-thrombotic syndrome. However, it rapidly became clear that this treatment was associated with a very high risk of bleeding complications. Thus, by the late 1980s, intravenous fibrinolytic treatment with streptokinase or urokinase had been banned by most institutions.

More recently, interventional radiology was introduced for the treatment acute coronary heart disease including acute myocardial infarction, a condition caused in most cases by clot formation. Introduction of a catheter allows topical delivery of a drug at much lower doses than is needed when given as a systemic infusion. This procedure was then developed for the treatment of acute

severe deep vein thrombosis. A catheter is usually introduced into the popliteal vein at the back of the knee joint, using ultrasound to identify the vein, and the catheter is pushed up into the vein between the vessel wall and the clot all the way to the top of the thrombus. The procedure is called catheter directed thrombolysis (CDT). The catheter has multiple side-holes, which may be fitted for the length of the thrombus, and allows local delivery of a thrombolytic agent at much lower doses than necessary with systemic treatment. The time to dissolve the clot may also be reduced and the risk of bleeding complications is reduced. We currently use alteplase (Actilyse), which is identical to the body's own activator of fibrinolysis and is produced by gene technology.

There is good evidence that rapid dissolution of the clot may reduce the occurrence of post-thrombotic syndrome. We and others have shown that opening the vessel is critical to avoid this complication. Known as the "open vein hypothesis", the idea is that if the vessel is opened up and better blood flow is encouraged, blood will pass through the vein and back to the heart without causing problems in the legs.

The CDT technique was rapidly adopted by many centres, particularly in Norway and Denmark and in the US, and a number of case series reports and registry data suggested its efficacy and safety. However, no randomised clinical trials had proven its effectiveness at reducing long-term post-thrombotic syndrome and whether it can actually reduce the risk of bleeding. We therefore decided to perform a randomised clinical trial named the CaVenT study, comparing patients given the conventional treatment of anticoagulants with those treated with CDT. We followed these patients for two years and the main paper was published in The Lancet in 2012. We now have 5 years of follow-up data that will be presented later this year.

The main result of the study was that only 41.1% of patients treated with CDT developed post-thrombotic syndrome as compared to 55.6 per cent among those who received conventional treatment. It was also shown that if veins were open after six months, most patients had no signs of post-thrombotic syndrome, in contrast to those with occluded veins. This supports the "open vein hypothesis", suggesting that it is important to improve flow through the vein.

The CaVenT study has provided the first evidence of the importance of CDT for patients with severe DVT. However, being rather small, more data on the effectiveness and safety of CDT is needed. There are currently two on-going studies, one in the US (the ATTRACT study), and one in the Netherlands (the Dutch CAVA study). These studies have similar protocols to our CaVenT study, but also utilizes additional procedures such as mechanical clot removal through the catheter. The US study recently completed recruitment of patients, but additional two year follow-up is needed. By combining the results of these studies, we will have a stronger basis for clinical recommendations. This is important since the procedure requires early hospital stay and surveillance. However, in the CaVenT study we were able to show that CDT in fact was a cost-effective treatment.

In Norway and Denmark most patients with severe deep vein thrombosis that affects the upper thigh and/or pelvic veins are now considered for CDT. The procedure is also taken up in many other countries. At this time, careful follow-up of the patients in registries will provide further evidence for the utility of CDT in the "real-life" setting. A Norwegian registry was recently funded by the Research Council of Norway.

The CaVenT study has helped to raise global interest in CDT, and once the results of US and Dutch studies are published, there will be enough evidence to make a judgement on whether or not it is a useful and effective treatment. If the studies are successful, they could well signal the beginning of a paradigm shift in the treatment of severe deep vein thrombosis, and help to reduce the number of people who go on to suffer from post-thrombotic syndrome.

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Promoting research in Norway

Adjacent Government highlights how the Norwegian Ministry of Education and Research are ensuring their commitment to research and development over the coming year...

The EU's significant investment in research comes in the form of the Horizon 2020 programme. This programme is the biggest of its kind with nearly €80bn of funding available over 7 years.

In May 2014, Iceland and Norway became the first non-EU countries to associate to the 7 year programme. Norway has been associated to EU research and innovation programmes since 1987, and by associating with the programme, Norway aims to take advantage of the great opportunities it could bring for the country's research and development (R&D).

The Ministry of Education and Research is responsible for research priorities throughout Norway. The Minister Torbjørn Røe Isaksen has set out clear goals in regards to education and research in the country. Over the next 7 years the government has identified 7 measures to help achieve higher quality in research and education across the nation.

The measures detail how "Norway should develop more world leading research. In dialogue with the higher education sector, the government will find and invest in relevant research environments and institutions that can contribute to breakthrough research in the world."

The Horizon 2020 programme offers a number of great opportunities for Norway including:

- Strengthening industrial competitiveness;
- Building up excellence;
- Accessing a wide range of European Infrastructures;
- International Networking;
- Training of staff;
- New level of Benchmarking;
- Expanding to new markets and business;
- Strong focus on support for SMEs.

In an edition of Projects Magazine EU, the Minister explained how there has been "strong growth in both the research and education budgets through the Horizon 2020 programme, compared to the previous FP7 funding period.

"Given that the Norwegian government is spending billions on our participation in Horizon 2020, we believe that this implies an obligation for the research community of Norway," said the Minister.

The government is keen to increase international research cooperation, which it feels is important to help the nation achieve its other research goals.

In 2014, the government presented a strategy for cooperation with the EU on research and innovation which establishes a target to increase Norwegian participation in the EU Framework Programme on Research and Innovation, Horizon 2020 (2014-2020), by about 60%, compared to participation under the previous framework programme.

"An important part of the research will be to solve economic and social challenges Europe is facing, such as climate, environment and population issues," said Isaksen. "This is a massive investment that gives Norwegian minds opportunities to collaborate with some of the best researchers in the world." ■

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The role of chemistry in drug discovery and development

Sriram Radhakrishnan a Healthcare Analyst at Frost & Sullivan details the vital role chemistry plays in drug discovery and development...

Drug discovery and development is one of the most complex and expensive activities within the framework of the pharmaceutical industry. It encompasses a wide array of end-to-end activities with a plethora of supply chain and support services. It is estimated that the average cost to research and develop each successful drug is between $800m to $1bn. Drug discovery and development can be classified into discovery phase, preclinical phase and early stage development, mid stage development and late stage development. Drug discovery has undergone many changes over the years but the goal has remained same: to uncover safer medicines for all diseases. Drug discovery and development is driven by the knowledge of chemistry of the molecules and their association with life process.

The classical or traditional method adopted by medicinal chemists involves modifying bio-active molecules from natural products. These natural products are the source of active ingredients in most of the existing drugs. The current era has witnessed an ever changing role in modern drug discovery. The chemical methods adopted for the discovery of the molecules have also undergone changes leading to the development of technologies such as combinatorial chemistry (combichem), microwave assisted organic synthesis (MAOS) and high-throughput (HTS) biological screening. These new technologies have enabled medicinal scientists to accelerate the discovery process. Drugs are designed, synthesised and purified as the first stage of the development process. The medicinal chemist leverages knowledge of synthetic chemistry, medicinal chemistry and biology to achieve the lead molecule for further clinical development.

The contribution of chemistry is not confined just to the discovery stage. It carries its purpose along the entire spectrum of clinical development. Each and every stage of clinical development involves surplus amounts of formulated drugs for studying potential benefits in human trials. All drugs are manufactured under strict Good Manufacturing Practices (GMP) standards to ensure they meet the compliance requirements drafted by regulatory bodies. Drug developers leverage on the analytical chemical testing and process development for meeting the regulatory compliances. It is estimated that about 50% of the analytical chemistry services are outsourced. The majority of these support services are now being rendered by Contract Research Organisations such as Charles River Laboratory, Covance, Quintiles, PPD, Eurofins, SGS Life Sciences, Wuxi AppTech, etc. Analytical methods and instrumentation are regularly used in the preclinical testing, toxicity testing, ADME analysis, product release testing, formulation and quality control.

Various techniques are adopted by the pharmaceutical industry, commonly known as purification chemistry, to separate the large molecules like monoclonal antibodies, vaccines in order to meet the standards of the regulatory bodies. The current era is witnessing a growth of biologics such as vaccines, growth factors, monoclonal antibodies and biosimilars for the treatment of cancer, diabetes, asthma, rheumatic arthritis, etc. The complexity here is multifold owing to the high degree of purification standards that are required to develop these biologics.

In short, chemistry remains the most invaluable science and plays the most critical role in the drug development process. It serves as the backbone to framework the drug discovery and bolstering the growth of the pharmaceutical industry. ■

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Where will our new medicines come from?

A view from one of the drug discovery teams at the University of Strathclyde, Glasgow, Scotland

I've just completed a three-year term as a 'Public Partner' on the Scottish Medicines Consortium (SMC), which is the body that advises the National Health Service in Scotland on the cost effectiveness of medicines. My job was to make sure that the patient and the public had a voice in the debates. With that in mind, my blunt answer to the title question is that I don't care, provided that the new medicine is effective and safe. However working also in early stage drug discovery (at the University of Strathclyde, Glasgow, Scotland), I must have a starting point from which to begin the search for a new drug. In the history of therapeutics, many things have been used as medicines: plant and animal products, microbiological products, synthetic compounds including both small organic molecules and large proteins, and even a few elements. Almost all of these possibilities remain viable today but different people take different approaches.

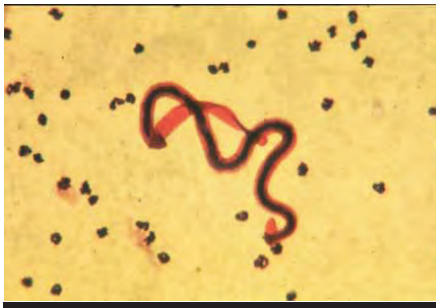
Some pharma companies specialise in proteins, the so-called biologics. This is the most recent source of active compound to reach the market and has had an impact chiefly in the therapy of cancer and inflammatory disease. My experience on the SMC showed that these medicines were high cost, often required out-patient care for administration, and were sometimes challenging with respect to side effects. Other companies maintain an emphasis on small, organic molecules as the active ingredient. Indeed there are pressures for the size of molecule to become smaller in order to get the best value for a drug. Cost and side effects matter with these compounds too. Outwith western industrial pharma an answer from an Indian physician might be "Very little, actually. We've have plenty of good drugs from Mother Nature in our traditional Ayurvedic medicine".

Everybody can't do everything and companies need to make choices but we can't afford to ignore any viable possibilities as a scientific and industrial community interested in improving health and wellbeing. There's no doubt that drug discovery is more difficult than it once was, for many reasons, including: an increasingly challenging regulatory environment, a lack of good druggable targets (all the easy ones having been done), increasingly challenging disease states associated with aging populations, a lack of good quality new chemical entities, and so on. Overall an intrinsically risky business has become riskier.

Now as an academic, one of my principal concerns is to create opportunity from my research, specifically in the field of new small molecule chemical entities for new drugs; most of the work in my labs concerns designed small organic compounds. Our central scientific input is the mature field of heterocyclic chemistry, which, almost uniquely, is able to bridge creatively chemistry and biology and to connect further with medicine. So I make no apology for plugging a science that still makes a difference at the cutting edge. We must continue to teach and train young scientists in chemistry so that they can translate its powerful methodology, and creativity into products containing new chemical entities that will make a difference.

The first purified chemical compound to be used as a drug is believed to be digitalis obtained from foxgloves in the mid 18th Century

No surprise, therefore, that having found something new with potential, I'm very keen for it to be developed in the market and i'm happy to play an appropriate role in that. Gratifyingly I can speak to several new opportunities from my lab in immunomodulation, cardiovascular disease, and most significantly in anti-infective compounds where we have a new antibacterial compound shortly to enter phase I clinical trials, developed by our partner company, MGB Biopharma. We've used three distinct

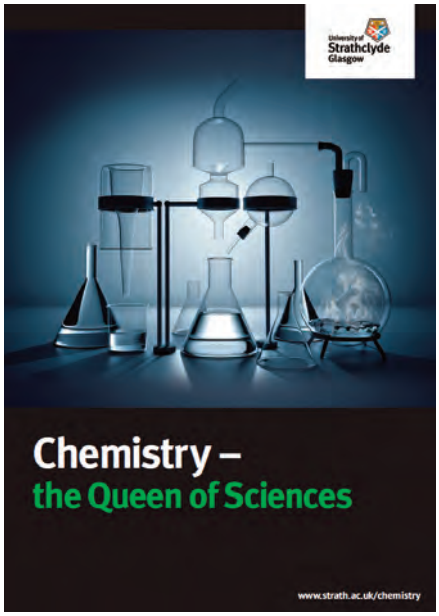


Our immunomodulatory compounds are based upon a protein produced by the parasitic worm, Acanthocheilonema vitae

starting points in our most advanced projects. In the case of immunomodulatory compounds, we've devised very small molecules that mimic the effects of a protein from a parasitic worm that infects animals; our compounds work well in animal models of diseases such as asthma, rheumatoid arthritis, and lupus and are now ready for optimisation and development.

For cardiovascular disease, we've modified one of nature's work-horse compounds to produce a potential drug that responds selectively to an imbalance in the mechanisms responsible for relaxing arteries and easing blood flow. In anti-infective compounds, we have followed the classical approach of taking a microbiological product (from a Streptomyces species) and modifying it to remove toxicity and to provide selectivity. In addition to the antibacterial compound, we have confirmed activity of another compound in an animal model of sleeping sickness in cattle, potentially a very valuable discovery. More details of these projects and our approaches through heterocyclic chemistry have been published in my E-Book, 'Chemistry, the Queen of Sciences' available from the Adjacent Government website.

So what does a heterocyclic chemist do to create opportunities for new drugs? Firstly, there has to be a promising and preferably novel starting



My e-book, describing the approach we take to drug discovery using heterocyclic chemistry. An editorial from the Royal Society of Chemistry provides a supportive context

point, which could be a new compound discovered by screening, usually plant or microbial products or occasionally a compound from animals, or it could be a molecular hypothesis. This is not new at all. In fact it's what has been done ever since chemists got into drug discovery. The new thing, however, is the stringency with which 'promising' and 'novel' can be defined. 'Promising' may relate to an unmet need in medicines currently available. 'Novel' may also reflect unmet need but will also concern the chemical class of compound being investigated. From there, the chemistry-biology interface is so much better developed now that a good deal can be discovered about important things like selectivity and toxicity before a synthetic chemistry programme is begun. Choosing what to make and how to make it with due regard for the probability of a successful development and for chemical novelty is then the key contribution of the heterocyclic chemist. This is the essential link that both mediates between chemistry and biology and also creates the therapeutic opportunities through the new compounds that emerge. What makes today's science so exciting is that the tools and techniques that we have the power to explore the most detailed properties of molecules and the intimate workings of biology. This means that the coupling between chemistry and biology that is essential in drug discovery is stronger than ever before and is why we place such an emphasis on scientific teamwork at Strathclyde, as is also discussed in my e-book.

I'm about to set off on a trip to India for a medicinal chemistry conference and to meet scientists involved in drug discovery. A large number of the papers will contain mediating and creative heterocyclic chemistry, and I expect that many of the starting points will be Indian traditional medicine. This field is one that I don't often have the chance to consider so I shall be looking out for anything that looks 'promising' and 'novel' especially if it concerns heterocyclic compounds that we work with or to an unmet need that we are addressing.

An overview of drug discovery at the University of Strathclyde can be found in the brochure 'New Medicines, Better Medicines, and Better Use of Medicines', which is accessible on the Stakeholder website of Adjacent Government.

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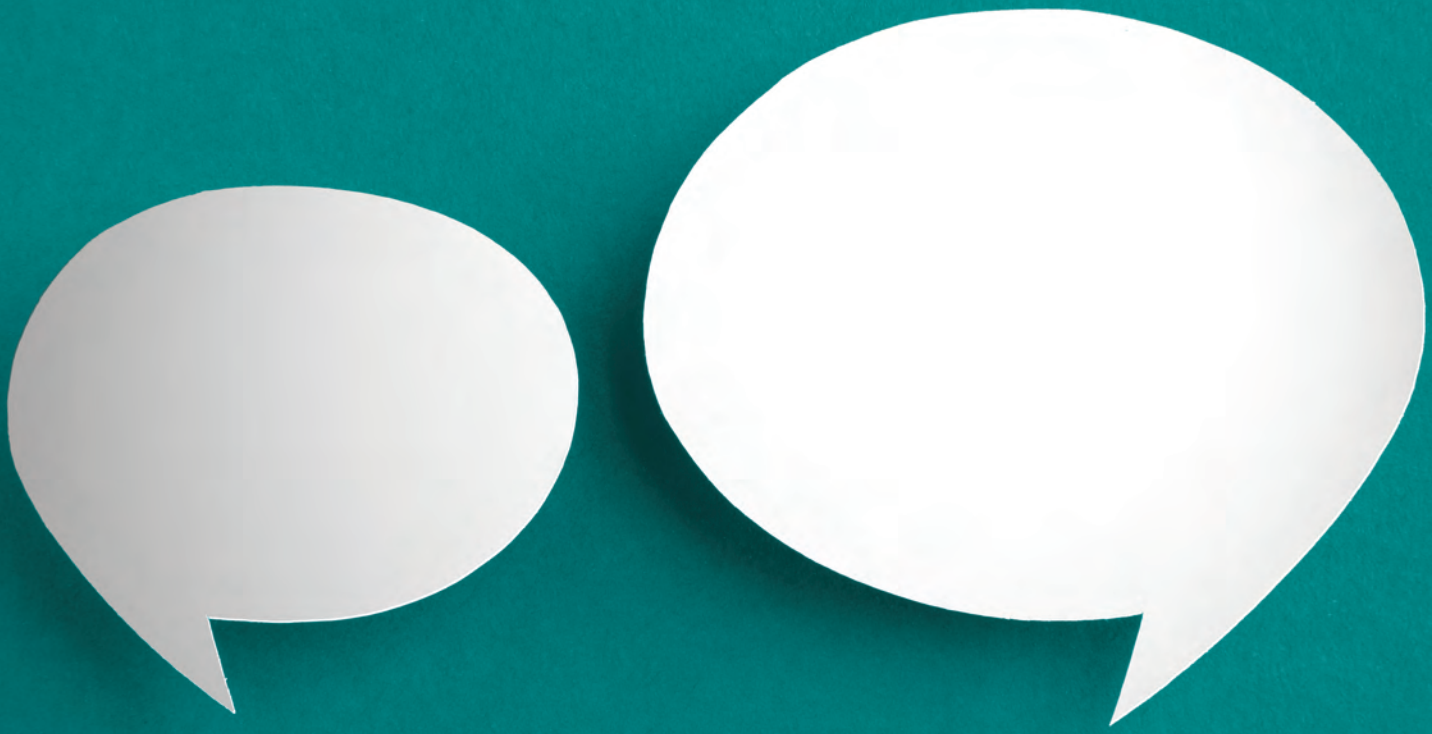

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Improving healthcare through chemistry

Adjacent Government highlights the work of the Royal Society of Chemistry (RSC) and how it supports chemistry's contribution to tackling major health challenges...

Chemical sciences play a major role in everyday life and are crucial to economic development. One area where they are key is the healthcare sector. Chemistry is vital in order to develop new treatments and drugs for major healthcare challenges such as cancer. Chemical sciences are also crucial in improving healthcare and helping doctors to understand an underlying disease and developing better diagnoses and treatments.

Cancer is a leading cause of death worldwide, and according to the World Health Organisation (WHO) accounted for 8.2 million deaths in 2012, with the most common causes being, lung, liver, and stomach cancer.

The Royal Society of Chemistry (RSC) is committed to ensuring that chemical science contributes its full potential to tackling the major global challenges of today and tomorrow. The RSC has been working with doctors, academics, and manufacturers since 1841 to help advance excellence in the chemical sciences.

As the world's leading sources of reliable chemical science knowledge, the RSC's global chemistry community contains the expertise of hundreds of thousands of people, and have over 170 years' worth of top-quality chemical science research publications, data, and reports stored in a cutting-edge online platform.

The goal of the RSC is to connect people with chemical science knowledge by harnessing their information and expertise and making it easily accessible. In order to help support the importance of tackling major healthcare challenges, the RSC understands the importance of drug discovery and new treatment methods for all areas of healthcare.

At the RSC they support the vital contribution that chemistry plays in medical research and drug development in the UK. The RSC believes that over recent years there has been an increasing acknowledgement that the pharmaceutical sector needs to change.[1]

Speaking at a seminar at the RSC in May 2014, Dr Mike Waring from AstraZeneca discussed the relevance of chemistry to the real world and explained how he believed chemistry plays a big role in the treatment of cancer.

"Cancer research is often considered the realm of biology and medicine – but chemistry is an equal player in that arena. History – a lot of people think of cancer as a modern disease but earliest reports go back to Egyptian scientists – Imhotep – to my knowledge that's the earliest written knowledge of cancer – under the therapy section he wrote 'there is none' which remained true for many years and of some cancers even now," he explained.

"One of the big problems is a number of people have said, it's a disease that has been encoded into our own DNA, so inevitable for some people really. I guess as I say in many cases you may say there is no adequate treatment.

"I hope and believe that one day we will beat cancer and certainly see great advances over the next few decades, but I also feel the solution to this lies firmly in the discipline of chemistry. The great advantage of

chemical treatments is you can treat the whole body and target the cancer cells wherever it is. "

As well as treatments for cancer, chemistry also plays a crucial role in developing antibiotics for bacterial infections that not only create healthcare challenges in the UK, but worldwide. The Royal Society of Chemistry also supports the development of antimicrobial resistance through chemistry. It is estimated that around 25,000 people a year die from drug resistant microbial infections in Europe alone.

The UK government have a 5 year antimicrobial strategy in place (2013-2015), which aims to accelerate progress made and build upon previous work done in the UK to tackle antimicrobial resistance.

UK Chief Medical Officer, Dame Sally Davies supports the strategy and has raised the issue in her own annual report.

"There are few public health issues of greater importance than antimicrobial resistance (AMR) in terms of impact on society," she said in the Foreword to the Strategy.

"Many existing antimicrobials are becoming less effective. Bacteria, viruses and fungi are adapting naturally and becoming increasingly resistant to medicines used to treat the infections they cause. Inappropriate use of these valuable medicines has added to the problem.

"Coupled to this, the development pipeline for new antibiotics is at an all-time low. We must therefore conserve the antibiotics we have left by using them optimally. The process of developing new antimicrobials and new technologies to allow quicker diagnosis and facilitate targeted treatment must be accelerated," Dame Sally Davies added.[2] ■

[1] http://www.rsc.org/campaigning-outreach/global-challenges/health/

[2] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

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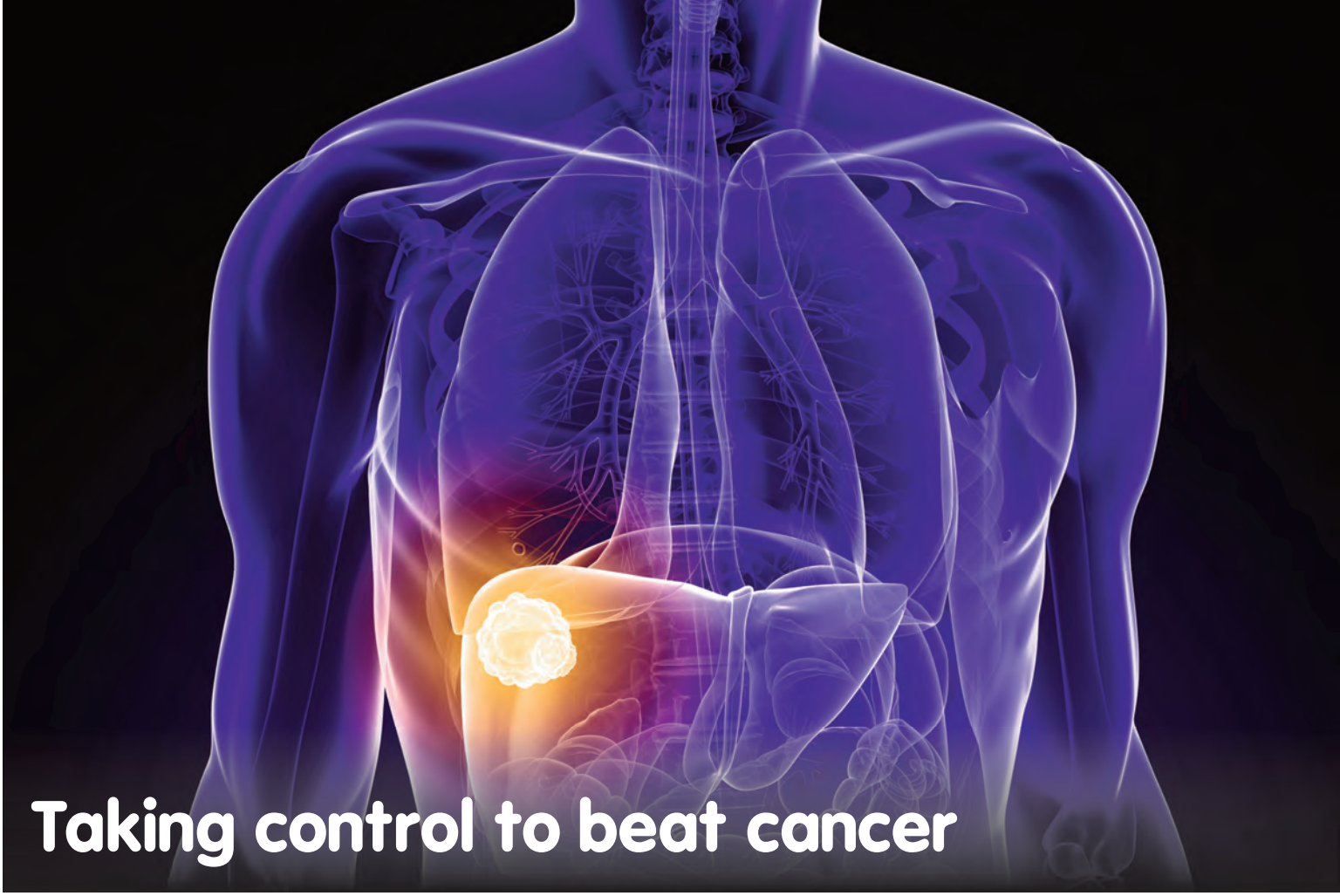

Taking control to beat cancer

Cancer prevention has never been more vital or urgent. Here Rachel Thompson and Sarah West from the World Cancer Research Fund – with a focus on liver cancer, explain why...

In the UK, cancer now affects at least 1 in 3 of us during our lifetime and the risk of being diagnosed is rising.

The good news is that there is a growing body of evidence on the factors that affect our cancer risk, providing us with increasingly robust information about how we can reduce our chance of developing the disease.

Reviewing cancer prevention research

World Cancer Research Fund's Continuous Update Project [1] is an on-going programme that analyses global research on how diet, nutrition, physical activity and weight affect cancer risk and survival. Among experts worldwide it is a trusted, authoritative scientific resource, which underpins current guidelines and policy for cancer prevention.

The findings from the Project are used to update our evidence-based recommendations for cancer prevention [2], ensuring that everyone, from policy makers to members of the public, has access to current information on how to minimise the risk of developing the disease.

As part of the Continuous Update Project, scientific research from around the world is collated and added to a database on an on-going basis and systematically reviewed by a team at Imperial College London. An independent panel of world-renowned experts then evaluate and interpret the evidence to make conclusions based on the body of scientific evidence. Their conclusions form the basis for reviewing, and where necessary revising, our recommendations for cancer prevention.

In the UK today we now know that around a third of cancers could be prevented through a healthy diet, physical activity and maintaining a healthy weight – that's around 89,000 cases of cancer prevented every year.

A focus on liver cancer – the facts

Liver cancer is the sixth most common cancer in the world, with 782,000 new cases diagnosed in 2012[3]. While the majority of cases (about 83%) are found in less developed parts of the world, over 4,700 cases of liver cancer are diagnosed every year in the UK, About two-thirds of these cases are in men.

Survival rates are often poor because symptoms often do not appear until the disease is advanced – just 5% of patients survive their disease for 5 years or more.

The liver is one of the largest organs in the body and has many important functions. It digests proteins and fats, removes toxins like alcohol and helps control blood clotting. Any cause of liver cirrhosis whether viral or chemical is likely to cause cancer of the liver.

Cancer prevention evidence on liver cancer

The global evidence on liver cancer was reviewed in 2007[4]. It showed strong evidence that drinking alcohol increases the risk of liver cancer. We estimate about 1 in 6 cases could be prevented if we all stopped drinking alcohol[5].

Smoking is another significant risk factor[6] – about 1 in 5 cases could be prevented if no one smoked in the UK. Alcohol, when combined with smoking is particularly harmful.

Other established causes include chronic viral hepatitis and liver flukes[2].

To reduce the risk of liver cancer it's best not to smoke and limit alcohol consumption. In our review of the evidence no safe level of alcohol was identified and so for cancer prevention the advice is to avoid drinking alcohol as much as possible.

If alcohol is consumed it should be limited to no more than 2 drinks a day for men and no more than 1 drink a day for woman. Tips for reducing alcohol intake include; opting for the smallest serving size, diluting alcoholic drinks, drinking low calories or low-alcohol alternatives and keeping a few days each week alcohol free.

Alcohol also increases the risk of other cancers, including: breast, bowel, mouth and oesophagus. Scientists are still researching how alcohol can lead to cancer. One theory is that alcohol can directly damage our DNA, increasing our risk of cancer.

While there is still much to learn about preventing cancer, we do have growing evidence available to help us take control and reduce our cancer risk. Cancer treatment alone will not free us from this epidemic. It's time to take control and stop cancer before it starts.

World Cancer Research Fund is the leading UK charity dedicated to the prevention of cancer through diet, weight and physical activity. We fund and support research, develop policy and provide health information so people can make informed lifestyle choices to reduce their cancer risk. ■

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Liver cancer...

...Future scientific and clinical challenges and forthcoming problems in Europe

Hepatocellular carcinoma (HCC) reflects the most common primary liver cancer as well as the 2nd most common cause of cancer related death in humans worldwide.

In most cases HCC is caused by chronic liver damage that is either induced by chronic viral infections (e.g. Hepatitis B or C viruses), by chronic alcohol consumption or by changes in our lifestyle (e.g. high fat, high sugar diet and sedentary life style). So far treatment options and treatment success for patients diagnosed with HCC are small, with surgical interventions being the most successful ones. Consequently, a lot of energy has been invested in the generation of various mouse models for HCC in the last 15 years to mimic human pathology, setting the ground for pre-clinical trials in animals and being the starting point for subsequent clinical trials in human patients.

Due to its unique regenerative capacity, the liver has become an unbelievable playground with several different mechanisms that can cause liver cancer. This has led to a plethora of mouse models that - in part - turned out to be useful to understand the mechanisms involved in liver cancer development.

Still, research with these models indicated that the outcome of liver tumors or HCC is not the only measurement that should be taken into account when identifying the molecular and cellular mechanisms of liver cancer development. It is even more important to identify the character of HCC on transcriptional, genetic, epi-genetic and histological model and to compare it with the human pathology.

As it turns out that "the HCC" does not exist in human patients, but rather a group of subtypes with different etiologies (e.g. viral, dietary), molecular and cellular mechanism, distinct types of inflammation most likely will demand different treatment strategies. A thorough phenotyping of HCC mouse models will be most important for the identification of model with a predictive value for human therapy.

Importantly, aetiologies causing HCC in industrialized countries is slowly changing. Alterations in our lifestyle over the last decades, including high caloric intake combined with a sedentary lifestyle have augmented the worldwide incidence of overweight and metabolic syndrome, characterized by abdominal obesity, insulin resistance and Type-2 diabetes, hypertonia and dyslipidemia.

This trend is not only observed in industrialized countries in the US or Europe but also in developed as well as developing countries. At the moment it is believed that approximately 90 million Americans and 40 million Europeans suffer from a fatty liver (also called Non-alcoholic fatty liver disease (NAFLD). Consequently, the price we will have to pay – from a global point of view – for our consequent aim to achieve progressive industrialisation and enhanced economic development in the 3rd world, as well as developing countries, is the adaptation to the 'Western' unhealthy diet and its concomitant lifestyle.

It should also be mentioned that this development will lead to a huge problem as developing and developed countries will contribute to the number of people suffering from the metabolic syndrome and fatty liver disease. It is estimated that more than 100 million people will suffer from fatty liver disease, the metabolic syndrome and its consequences from China and India alone.

From a European point of view, a further increase of the metabolic syndrome as well as fatty liver disease is to be expected – underlining the need of therapeutic options to efficiently treat these patients in the next 20 years.

We know today that overweight and metabolic syndrome lead to diseases of several kinds. Epidemiological data clearly indicate that overweight and metabolic syndrome are reaching pandemic dimensions in industrialised countries. In the past 10 years, the rate of obesity has doubled in adults and tripled in children in the US. A similar trend has also been observed in Europe, and this trend will accelerate and steepen.

The liver – which is the most important metabolic organ – is strongly affected by a chronic state of overweight and metabolic syndrome. Non-alcoholic fatty liver disease (NAFLD), which is the most frequent liver disease worldwide, is a clinical manifestation of overweight and metabolic syndrome.

NAFLD is a chronic disease that can last several decades, characterised by predominant macrovesicular steatosis of the liver easily getting worse. Although the prevalence of NAFLD is increasing globally, epidemiology and demographic characteristics of NAFLD vary worldwide.

It is becoming increasingly clear that a number of pathways are involved in the pathogenesis of NASH, and its progression to advanced stages of liver disease. These pathways may be diverse in different cohorts of patients with NASH. Understanding of which pathways play a role in the development of NASH will be critical before launching treatment modalities.

A significant number of NAFLD patients develop non-alcoholic steatohepatitis (NASH), fibrosis and consequently hepatocellular carcinoma (HCC). In recent years, obesity has attracted increased attention due to an increased HCC incidence in the US and Europe. Therefore, the most common etiology for HCC in industrialised countries has recently switched from chronic viral infections to obesity, making HCC the most rapidly increasing type of cancer in the US, with a similar trend observed in Europe.

Today, we lack a detailed understanding how chronic steatosis develops into NASH and what factors control its transition from NASH to HCC. At the same time no therapeutics exist to efficiently treat NASH, and treatment options for the therapy of late stage HCC are limited and only prolong the life span of patients between 3 to 6 months.

In laboratory mice, NASH can be induced by several different diets such as methionine/choline-deficient diet (MCD) or choline-deficient diet (CD) but not by a high fat diet (HFD) alone. However, C57BL/6 mice fed with MCD or CD do not develop obesity or metabolic syndrome and the diet has to be discontinued after a few months due to weight loss (up to 40%) or occasional cachexia. Thus, these approaches do not recapitulate NASH and its consequences (e.g. transition to HCC) in humans and appropriate mouse models for genetically and mechanistically dissecting NAFLD induced NASH and NASH triggered HCC development have been thus far lacking.

Deficiency in the essential nutrient choline was described in NAFLD patients to exacerbate NAFLD and NASH. Moreover, humans with inadequate choline uptake were shown to have defects in hepatic lipoprotein secretion, oxidative damage caused by mitochondrial dysfunction and ER stress. Based on the clinical observations of choline deficiency to exacerbate NAFDL and NASH patients, we have recently combined choline deficiency with a high fat diet (CD-HFD) as a chronic diet for laboratory mice, which may lead to metabolic syndrome, steatosis, liver damage and NASH, thus delivering the 'second hit' that promotes dietary-induced liver carcinogenesis – similar to the human situation.

This approach enabled us to establish a chronic mouse model of NASH and metabolic syndrome, triggering subsequent HCC in a wild-type C57BL/6 mouse, in the absence of chemical carcinogens or genetic mutations predisposing to NASH or HCC development (Wolf et al., Cancer Cell, 2014). CD-HFD treated mice display obesity, overweight, insulin resistance, liver damage and fibrosis and hepatic mitochondrial damage, dyslipidemia and NASH as observed in human patients. HCC developed 12 months post CD-HFD start and resembled histologically, genetically and morphologically human HCC.

The foreseeable development of NASH into a pandemic disease in Europe will force health authorities to act. It will need strong political efforts to change the thinking of our idea about living, about nutrition as well as about preventive measures each individual person can take to lead a more healthy life.

Moreover, research has to be strongly supported to find – besides a European wide political strategy of prevention – therapeutic measures to prevent, diagnose, and to treat NASH as well as subsequent diseases of NASH. The monetary effort for such political, educational and research programs is justified and will surely be just a small proportion to what will be needed in 20 years from now. The clock is ticking and unfortunately it appears as if European political decision makers rather want to wait until the problem is evident.

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Improving mental health services throughout Europe

John Bowis, President of Health First Europe details how community care can support better mental health services in Europe...

My first involvement with mental health on the European stage was working with the 1999 Finnish Presidency initiative on mental health promotion. Later, as the rapporteur of the European Parliamentary Report on improving the mental health of the population – towards a strategy on mental health for the EU, l had the opportunity to open the European debate on mental health and mental illness. Since then, several initiatives have been carried out at the European level to promote services for mental health, raise awareness and minimise the stigma of mental disease.

However, despite recent actions at European level, such as the Joint Action Plan on Mental Health and Well-being, many European countries continue to neglect mental health services by under-resourcing the sector. For example, between one-third and one-half of people with disorders do not receive treatment[1]. One of the major reasons behind the gap between the needs of citizens and the availability of mental health services is the lack, or inadequate provision of, community services.

Where we can improve mental health services

In 2006, Members of the European Parliament agreed with my Parliamentary report[2] that while health has continued to be prioritised on European and national agendas, European healthcare systems have not been able to overcome 5 key flaws elevating mental health as part of the public health agenda. Namely:

- the inadequacy of community services;
- the failure to listen to service users and their carers;
- the inability or unwillingness of different agencies to work together;
- serious underfunding; and
- a policy for mental health promotion that is in most countries notable by its almost complete absence.

To tackle these obstacles, there is a clear need for improved community care policies that are aimed at re-organising care around the patient. For mental healthcare, this is especially important because many common conditions such as depression and anxiety are often highly treatable, but too often patients must fit into a system that does not offer adequate funding for mental healthcare services, does not have the appropriate staffing to treat common mental health conditions, and does not provide easy access for patients to specialised services.

Strengthening mental healthcare services

Europe's role in promoting mental health services is often controversial, given the principle of subsidiarity on health related issues. However, the EU can play an important role in supporting the expansion of mental health services by sharing best practices in community care, strengthening anti-discrimination rules where applicable, and by supporting employment policies which incentivise private companies to adopt internal policies to support employees affected by mental-illness[3] and promote the mental wellbeing of all their workforce.

Additionally, the EU should continue to drive the shift of national health systems towards primary care by

incentivising care in the community. To achieve this, Health First Europe developed a model which provides a road map for Member States to the substantive changes required to release the value and power of community care services for all citizens, including those suffering from mental health conditions. As Honorary President of Health First Europe, I believe that this model provides a strong basis for generating EU action on mental health and supporting Member States to find ways to better support primary care professionals to diagnose, treat and manage mental illness.

The Health First Europe Model outlines 6 areas of needed reform, all applicable to the provision of mental health services:

1. **Community Care Policy:** Establishment of a dedicated community care policy and political leadership to implement the policy;

2. **Patient-Centric Care:** A system designed in response to citizen health needs;

3. **Innovation and Value:** Incentivising innovative solutions involving key actors (citizens, carers, technology) across the health system of value to improve health outcomes for the well-being of citizens and society;

4. **Access and Reimbursement:** Flexible funding to increase access to innovative community care solutions including community care products, treatments and services;

5. **Care and Treatment:** Creating a mobile and flexible health and social care workforce bound to the citizen, not the system;

6. **Quality Care and Standards:** Generating quality of care assurance in the community.

The implementation of needed reforms should begin at EU level under the new Commissioner-designate for Health, Vytenis Andriukaitis. By creating

John Bowis
President

a dedicated policy on community care at EU level, the EU can take the lead with Member States to develop best practices on community care services which better support mental health services.

After almost 15 years of closely following EU developments on mental health, I believe it is time to support significant changes to health organisation and help citizens receive the treatment they need and deserve for mental health conditions. ■

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Building a road to resilience

By: Paul Bomke, Nathaniel Kendall-Taylor and David Cawthorpe

The on-going need to improve mental health globally and in Germany places significant pressure on service organisations to design and implement innovative approaches.[1] In an attempt to meet needs with resources that are increasingly limited, the Pfalzklinikum has implemented a novel, international approach to learning and capacity development called the Transnational Leadership Program (TNLP).[2,3,4] TNLP seeks to identify, enable, and support professionals at different mental health services to lead their organisations in the design, implementation and evaluation of innovative ways of addressing social issues. The TNLP seeks to move beyond one-off conferences and meetings (a dominant model of international learning) to a deeper, sustained collaborative way of supporting multi-disciplinary problem solving. Key to this model is sustaining collaboration between disciplines that do not typically come together to achieve a common perspective and plan actions on improving social outcomes.

In the initial phase of work, TNLP was designed and implemented as a single curriculum and a shared understanding of good management and leadership, without a common project. After more than four years of collaborating on this process while working on individual projects, the opportunity for the group to come together around a common issue presented itself. Through established TNLP relationships came the invitation to participate in the Alberta Family Wellness Initiative (AFWI) – The Accelerating Innovation Symposium, 2013 in Edmonton, Alberta,[5] permitting the German members of TNLP to work on a common project based on the AFWI work and aimed at using similar empirical communications research to promote policy change at a regional, provincial and state levels.[6]

During the AFWI symposium, the German members of the TNLP, now called the "German Learning Team", identified prevention as a cornerstone of their innovative mental health strategy.

Upon considering a wide range of potential prevention strategies, the focus on resilience emerged as a uniquely effective way of approaching a prevention agenda. Resilience, both as an inherent and contingent concept, which operates at individual and systemic levels was the key concept.The project, "Building Roads to Resilience" is designed to capitalise on existing assets, whilst leveraging systems and individuals to gain skills and abilities in support of resilience-fostering processes and outcomes.

Based on dialogue with AFWI, the German learning team realised the importance inclusion, joining a wide range of capacities and perspectives in their work. As a result, members from the Ministry of Health and Social Welfare, the state owned Organization for Health Promotion, the Institute for Technology and Labour (ITA) and the American-based FrameWorks Institute[7] joined the German team. This collaborative group is currently building an empirically-based communications platform to shift public and policy-maker concepts underpinning their understanding of mental health and prevention approaches. As the AFWI built the "Building Better Brains" story the German team is adopting the same model to build the Core Story about the importance of prevention and of the potential for a strategy based on building resilience dramatically improves mental health and well-being outcomes in Germany.[8]

What is a core story?

A Core Story is a set of frame elements including values, metaphors and other frame elements that can be combined to create narratives that help people think in new ways about an issue, how it works and how it can best be addressed. The FrameWorks Institute has developed Core Stories with partners in the US[9] and Canada[10] about early child development and with a group of leading foundations on education in the US.[11] A core story is designed and tested to address the fundamental features of public understanding about an issue in a way that increases access to new information and perspectives.

Stanley Park's inukshuk sculpture, Vancouver

Having common narrative elements and a shared narrative structure, but one that has the flexibility to be told in different ways by different groups, has several strategic advantages. First, having a common story provides shared language that brings disparate groups of communicators together around shared issues and priorities. By having a commitment to a common story and a common language to discuss their work, members of a field can come together and forge new partnerships, coalitions and synergies. Second, adopting a common story eliminates message competition, which stalls public mobilisation and short-circuits political will. In short, one concerted story can be a powerful way of moving public opinion than are many dissonant voices in the crowd. When delivered across organisations, sectors and platforms, the dose of an empirically tested narrative is amplified, increasing the chances that it will widen the public discourse and create space for and will behind new ways of using public policy to improve social outcomes.

Social movement and framing scholars have found that having a common but flexible and empirically tested narrative increases the chances of social change by bringing together fields around a message and delivering frames in a way that has the best chance of creating political will and mobilisation around an issue.

How do you build a core story?

FrameWorks' approach to building a core story is a multi-step empirical process. It begins with gathering and distilling a set of "untranslated" messages that represent the content that the core story will be designed and tested to communicate. Establishing this untranslated set of messages involves expert interviews, literature and materials reviews and, importantly, feedback sessions that give experts the opportunity to check and refine emerging messages.

Once the target messages are established, researchers explore the dominant patterns of understanding – or cultural models – that members of the messages' target population bring to bear in understanding the issue. This process consists of long-form, person-centered interviews designed to gather large amounts of discourse in which informants explain, narrate and reason about the target issue. Analysis of these data reveal shared, deeply held assumptions and implicit foundational patterns of reasoning. This culture mapping process might also consist of guided focus groups designed to arrive at an understanding of how social norms and expectations mediate the expression of these cultural models.

The untranslated story and the set of default cultural models are then compared in a process that FrameWorks calls "mapping the gaps". This comparative analysis reveals the primary areas where expert and public thinking on the target issue do not align and where framing work is required to improve the accessibility of expert messages for non-expert audiences.

Armed with a systemic analysis of the locations and features of the gaps in understanding, researchers begin to design framing strategies and test them for their ability to improve understanding of specific components of the untranslated messages. The result is a set of empirically-tested strategies demonstrated to accurately "translate" the target messages distilled at the beginning of the process.

The process of building a core story does not end with research, but continues with training would-be-messengers in framing best practices as well as in how to use specific communications strategies particular to a target issue.

This is the process that the German learning team began in September 2014. During a week in early September, we grappled with developing a set of untranslated messages around prevention and resilience. The cornerstone of the untranslated story that emerged is the idea that focusing on prevention can help systems shift from disease to health frameworks and dramatically improve a wide range of outcomes. Building resilience is an underused, but potentially effective prevention strategy. In this context, we refer to resilience not as an individual trait or exclusively at the individual level. Instead we conceptualise resilience as features of individuals, communities and systems that can be built to improve the ability

The Power of Prevention

What is the story about?

- Preventative approaches have the power to dramatically improve a wide range of outcomes for individuals and society
- Building resilience is a promising prevention concept

What *is* resilience?

- The ability for individuals and systems to cope with change
- The ability for individuals and systems to flexibly respond to challenges to maintain positive functions for individuals and systems
- Enviro factors can increase or decrease resilience
- Two important systems are organisations and communities

How does resilience *work?*

- Resilience develops and changes over time
- Resilience is shaped by interaction between genes and experiences
- Resilient individuals can contribute to resilient systems and resilient systems can increase the resilience of individuals (for example, workplaces and systems are important systems)

What is the *problem?*

- Too few public resources are spent on prevention
- Current approaches are narrowly individually focused
- Current approaches are remedial/reactive
- Building resilience is an underused prevention concept

What are the *solutions?*

- Invest in prevention approaches
- Leverage existing individual resources/skills
- A two-pronged approach – building resilience + improve contexts
- Building a preventative approach requires fostering resilience at the individual and systems levels (family, workplace, community)

of populations to respond positively in the face of adversity.

The graphic above provides a more detailed view of the untranslated set of messages that the arrived at as result of its work.

Ideally, decision-makers and members of the public incorporate the Core Story into how they think about policies and practice in the areas of mental health and beyond, resulting in a shift in understanding and behavior permitting improvement across a wide range of key health and well-being dimensions. The task ahead is to explore the culture into which we will be communicating this idea and to develop and test communication strategies that can effectively help people incorporate this perspective into how they think about their socio-political worlds.

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Care in the home

Dominic Carter, Policy Officer at United Kingdom Homecare Association (UKHCA) details how homecare can be more flexible and beneficial to the patient's needs...

Homecare is a growing and varied service, focused on providing care and support in people's own homes, ranging from shorter visits to remind an older person to take their medication, right through to practical support from a care worker living in someone's home.

In a recent survey, 9 out of 10 people aged 50 years or above said they would prefer their care needs to be met in their own home (Saga/Populus 2014). As, fantastically, more people continue to live longer, healthier lives, homecare workers are increasingly taking on complex health related tasks, in addition to more traditional activities like washing and preparing meals. The flexibility of homecare can enable the individual, their family and the care provider to shape a care plan focused on the aims and desires of the individual as the focus.

Quality standards in homecare are closely regulated. Provider organisations are expected to quality assure their own services, through client and family feedback surveys, monitoring care workers and spot checks. In addition there is a dedicated regulator for every country in the UK, who will carry out inspections, monitor a range of information and publish reports on providers' performance. There is a growing pool of resources to help people choose the care they want, with user ratings included on sites such as www.nhsuk .

Having access to, and remaining a part of, the local community is important for many people using social care. Care workers often help prevent confining people to the home through trips out and signposting of information, events and other services. This can also be a good opportunity to provide respite for

family carers, allowing them to recharge their batteries and in turn remain as a carer for as long as possible. Care workers, ties with the community and refreshed family carers form a strong trio in combatting loneliness and isolation, a significant societal problem and one that has been closely linked with a negative impact on wider health.

Homecare is vital to relieving pressure on hospitals and A&E units. If low-level support is introduced early enough, there is an increased chance that the situation can be managed, helping to reduce the need for stressful, costly hospital visits further down the line. Additionally homecare has a particularly important, if rather undervalued, part to play in people's recovery after leaving hospital, supporting them to manage their condition, readjust and rebuild independence to do what they wish in their favoured environment.

Despite the vast potential for homecare services to help people, there are significant challenges and obstacles. Around 70% of adult homecare in England is funded by local authorities, who have seen their budgets slashed by 37% in the 5 years leading to 2015/16. A direct result of this, is the fees paid to providers have fallen in real terms. Fees are expected to cover staff, training and office costs, and the unrealistic level of investment risks a sector struggling to keep ahead of national minimum wage, creating real issues in terms of recruiting and retaining care workers.

Furthermore, as councils aim to stretch dwindling finances, eligibility criteria have been tightened and fewer people with relatively high needs now receive state funded care. Reduced eligibility means providers are required to work with more complex needs, yet with the same amount of funding. Sometimes, as widely reported recently, councils will purchase homecare visits of 10 or even 5 minutes.

Thankfully, despite these challenges, the sector is full of dedicated, caring people. As the professional association for homecare, United Kingdom Homecare Association will continue to promote high quality, sustainable care services so that people can continue to live at home and in their local community. ■

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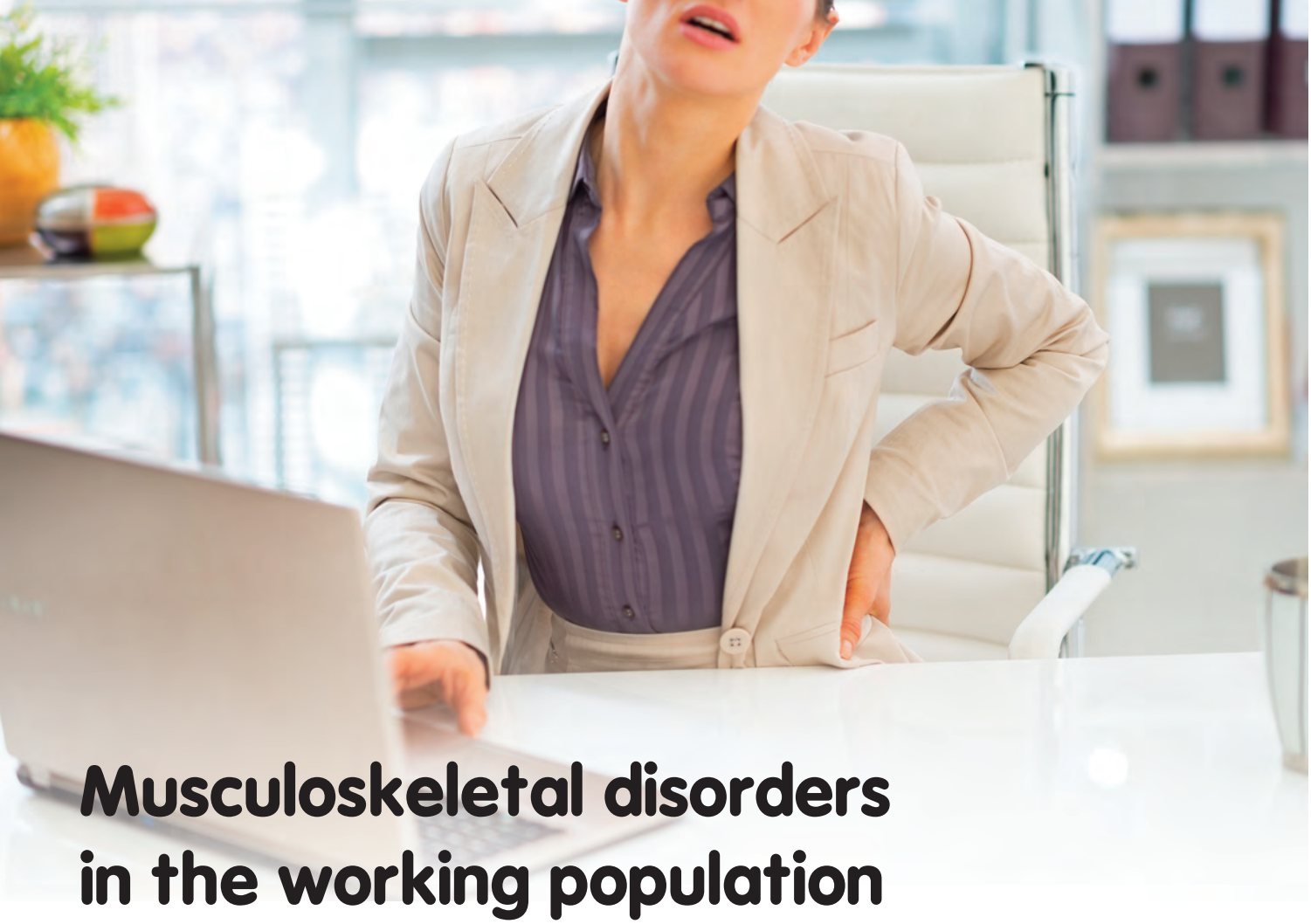

Musculoskeletal disorders in the working population

Vern Putz Anderson from the National Institute for Occupational Safety and Health at the Centers for Disease Control and Prevention (CDC) details the risk factors, symptoms and prevention of musculoskeletal disorders in the workplace...

Aches and pains are a part of life, but musculoskeletal disorders, or MSDs, such as back problems, carpal tunnel syndrome, or tendinitis become a problem when you can no longer recover – and in some cases, no longer work. Workers who perform the same tasks repeatedly, work in awkward positions such as stooping or bending, or exert a lot of effort to complete a task, risk injuring muscles, tendons, nerves, joints, ligaments and other soft tissues. These injuries can cause pain and may ultimately impair your ability to work.

MSDs can take a toll on workers, employers, and society. In the United States for example, MSDs accounted for approximately 30% of occupational injuries that resulted in time away from work in 2013 [1]. These injuries also represent one of the top 3 conditions accounting for the greatest number of "years lived with disability" in the U.S. working population [2].

Overexertion, which occurs when you do more lifting, pulling, pushing, or throwing than your body can handle, is one of the most frequent, costly, and disabling workplace injuries. Overexertion accounts for 25% of annual workplace injuries at an annual cost of $15.1bn [3]. In a work setting, overexertion can happen when employees don't have control over the demands of their job – their work may be paced by machines or customers. Additionally, as workers age, the demands of their job might remain constant, yet their endurance has decreased, and the time they need to recover has increased. In these situations the physical demands of the job exceed the worker's capabilities and can lead to discomfort, chronic pain, or disabling injuries.

Most workers recognise the signs and symptoms of overexertion within a few days – if not immediately. Common symptoms include pain, swelling, and restricted movement. It's important not to ignore the

first signs of work-related discomfort because it can lead to a more severe, chronic condition. At the onset of symptoms, workers should alert their employer to identify and assess problems with their job before it leads to an MSD [4]. This early warning can indicate the worker is not well-matched to the demands of the job. Early recognition and intervention remain key for preventing long-term injuries and costly workers' compensation payments.

When faced with prospective hazards, the ultimate goal is to design the work area to eliminate the hazard by changing the workplace, job task, and/or tools. Although MSDs affect workers across a range of industries and occupations, an example of the positive impact of this practice comes from the healthcare industry. According to the US Bureau of Labor Statistics, more than half of all MSDs that occur in the healthcare industry involved patient handling and accounted for 14% of all MSDs that resulted in at least one lost day from work in 2010 [5]. The single greatest risk factor for overexertion injuries in healthcare workers is the manual lifting, moving, and repositioning of patients – known as manual patient handling.

Evidence-based research has shown that replacing manual patient handling with safer methods guided by the principles of ergonomics, called safe-patient handling, can significantly reduce overexertion injuries to caregivers. The goal of ergonomics is to reduce stress and eliminate injuries and disorders associated with the overuse of muscles, bad posture, and repeated tasks. In the case of patient handling, it involves the use of mechanical equipment and safety procedures to lift and move patients so that healthcare workers can avoid using manual exertions and reduce their risk of injury.

Prior to the introduction of ergonomic principles, employers relied on their workers to meet production and output demands. In short: workers serviced the machines, rather than machines fitting the needs of workers. Today, ergonomic solutions using mechanical equipment that enhances a worker's ability to do a job safely, also called engineering controls, have been developed for a wide variety of occupations and workers including nurses, carpenters, miners, manufacturers, and transportation and retail workers [6-9].

Effective ergonomic solutions in the workplace, like safe patient handling, can lower the incidence and severity of musculoskeletal injuries, which in turn can improve productivity and lower an employer's costs. The National Institute for Occupational Safety and Health (NIOSH), which is part of the US Centers for Disease Control and Prevention, is a leading source on workplace-related musculoskeletal disorders, their causes, as well as prevention and controls. For more information, visit www.cdc.gov/niosh/topics/ergonomics/ .

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of NIOSH. ■

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Strengthening weak muscle

Who has not experienced muscle weakness after a few days in bed due to illness or injury? A report by Professor Martin Flück from the Balgrist University Hospital inquires on the underlying mechanism of inactivity-induced muscle degeneration. Possible remedies that halt the consequent replacement of muscle with fat tissue with prolonged disuse are discussed.

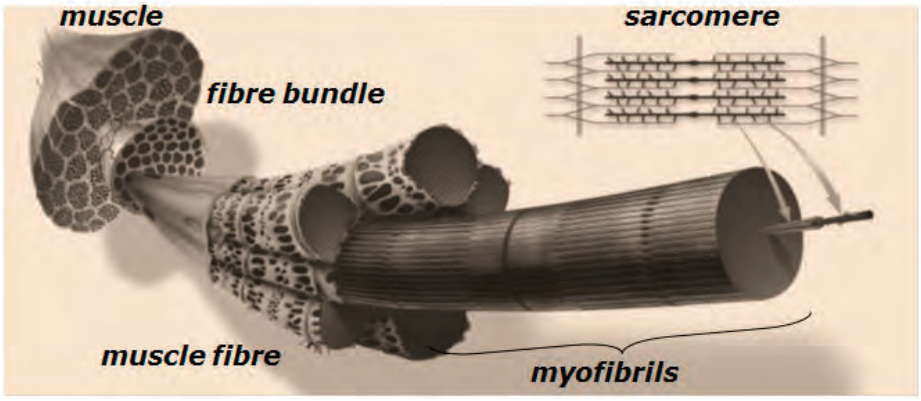

Figure 1: Illustration of the cellular organisation of skeletal muscle.
Adapted from Scientific American.

€500bn are spent per annum in the European Union for days of hospitalisation due to muscle weakness. There is considerable socio-economic potential in the undertaking to empower the musculoskeletal system in affected patients as this reduces costs of care.

The root of physical weakness lies in a critical reduction of skeletal muscle's force producing capacity due to a loss in muscle mass (called atrophy) in conjunction with a deficient neuromuscular activation or a disruption of the functional chain between muscle and bony articulations (or joints) with injury. This develops a pronounced negative impact on mobility and quality of life. Active measures that counter the biological problem are required to allow the affected individuals to exit from their dependence on welfare. In cases of a plain musculoskeletal pathology or injury, orthopaedic surgery readily re-establishes the basic biomechanical aspects of motor function. Subsequent rehabilitation takes care to reset the muscle's functional capacity. However, compared to the maximal effects seen with training of athletes, measures against muscle wasting in patients appear suboptimal. The applied stimulus is often insufficient in magnitude and/or volume and is modulated by individual factors such as constitution and compliance.

In order to tackle muscle loss effectively it is vital to specifically target the mechanisms controlling the build-up (anabolism) and breakdown (catabolism) of muscle matter. In this regard it is important to consider that skeletal muscle is composed of parallel-aligned fibre cells which demonstrate a natural turnover in the order of 0.6% per day (Fig. 1). Mainly this involves the build-up and breakdown of myofibrils that hold the molecular motors, the sarcomeres, which carry out contractile function. Mechanical loading is a major anabolic stimulus for muscle, enhancing myofibrillar protein synthesis to an amount equalling 1% of the total content in myofibrils (Fig. 2). The impact of loading on muscle mass is amply illustrated in situations when muscle loading is reduced due to bedrest, inactivity and spaceflight (Fig. 3). The resulting disuse gives rise to a net decrease in muscle mass, force and power as the latter relies on the cross sectional area, and length, of contracting muscle tissue.

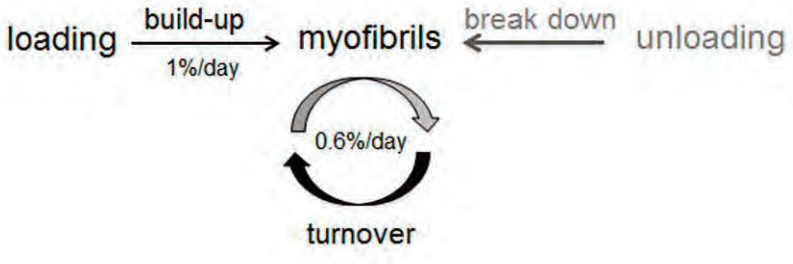

Figure 2: Concept of the load-dependent regulation of myofibrillar protein turnover.

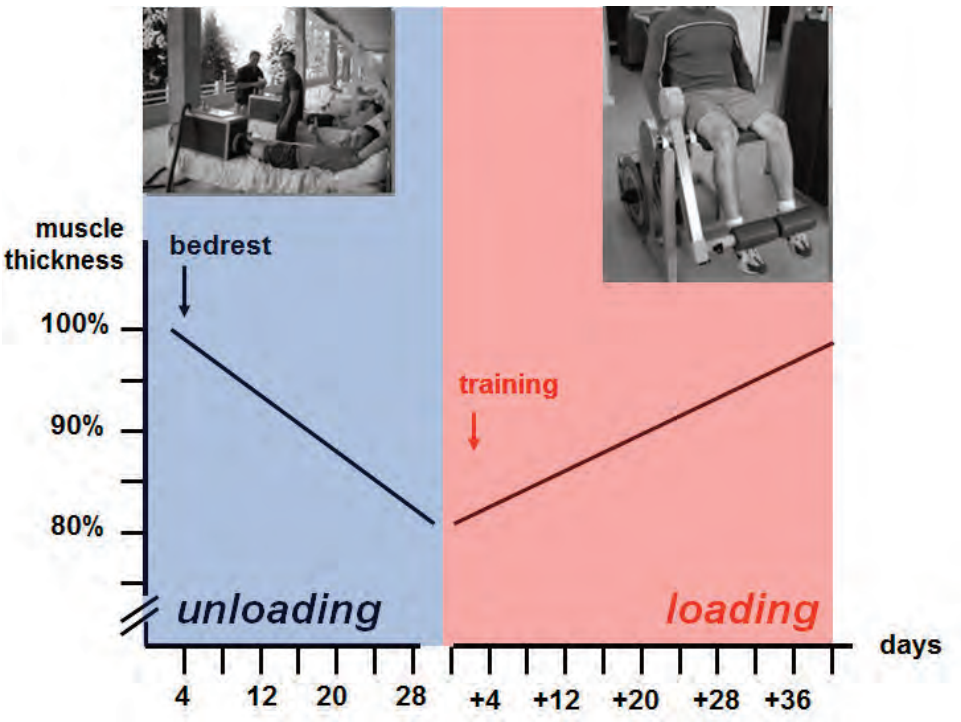

Figure 3: Mechanical loading regulates muscle mass. Illustration of the reduction in muscle thickness through the time course of unloading due to bedrest and reversion with subsequent strength training. *Figure assembled from Narici, Seynnes, Flueck et al. (2011), ECSS conference Liverpool (UK) & Vandenborne et al. (1998), Muscle Nerve 21 (8): 1006-12.*

Correspondingly, resistance type training produces an increase in muscle force and power and this usually involves a gain in mass of the trained muscle groups. Thereby, the observed muscle plasticity is graded to the time muscle is under tension with contraction. Tension builds up internally in muscle fibres with muscle contraction, and externally via the pulling of attached articulations. Today, mechano-regulation of muscle plasticity is well accepted. It is therefore largely insufficient that the conditioning of muscle's functional capabilities by use-dependent stimuli is, with the exception of rehabilitation, rarely actively targeted, or maximised, in the many situations of muscle weakness.

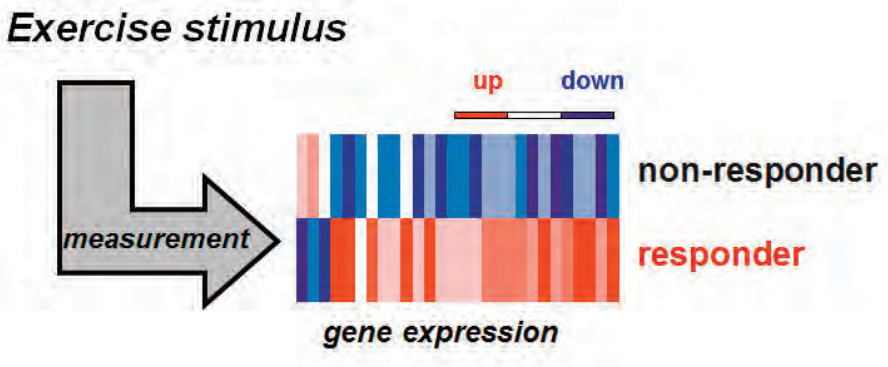

Figure 4: Genome encoded program fortells muscle response. Composite figure illustrating the response pattern of gene expression for a set of markers to an exercise stimulus for two groups of subjects. The two groups differ regarding their responders due to the presence or absence of a gene polymorphism in the gene for angiotensin converting enzyme. *Assembled from Vaughan et al. (2013) Eur J Appl Physiol 113 (7): 1719-1729.*

Forward to this point, our research explores the molecular events underlying muscle atrophy and tests the effectiveness of pharmacological and mechanical measures to counteract muscle wasting. Using this approach we demonstrated that mechanical factors and gene-pharmacological interventions importantly interact regarding the regulation of muscle mass. We also pointed out that an important down-regulation of mechano-sensory processes becomes manifest in anti-gravity muscles after 3 days after unloading. This has important implications for the therapeutic window when a treatment can, and should be applied. This important interdependence of regulation indicates that a pharmacological approach alone, is probably not efficient to halt and reverse muscle atrophy. However, a multidisciplinary approach does not yet appear to be part of the portfolio of major stakeholders, such as the biomedical research industry, despite their recent strategic investments in research aimed at tackling muscle atrophy.

Towards this end we test the effectiveness of exercise treatments and exposing factors that dictate the individual training response of muscle mass and function in subjects. Our molecular-biological studies highlight that muscle adaptations with reduced or increased loading, are reflected by the activation of a genetic program, which involves the copying (expression) of genes. Measurement of this expression response allows conclusions on the efficiency and specificity of a muscle stimulus (Fig. 4). Specific gene polymorphisms of major structural and metabolic regulators are recognised to explain inter-individual responsiveness to mechanical and metabolic stimuli. Currently we work

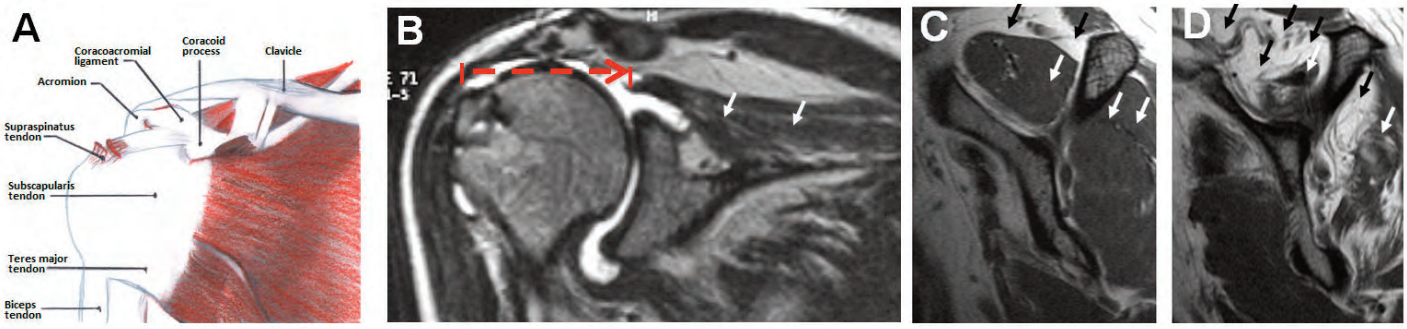

Figure 5: Fatty degeneration with tears of rotator cuff muscle. A) Drawing of the human rotator cuff with the indication of a rupture of supraspinatus tendon. B) Coronary and C,D) Sagittal images of a MRI scan of the shoulder of a patient at two time points after a full tear of the supraspinatus muscle tendon. The rate of retraction respective to the site of supraspinatus tendon attachment is indicated with a stippled, red arrow in panel A. Fat tissue (indicated by black arrows) appears in white above the darker contrast of muscle and bony tissue (white arrows).

towards testing the influence of specific gene polymorphisms on the effectiveness of exercise treatments. The goal is to develop personalised approaches that circumvent, or reverse muscle loss by maximising plasticity of the musculoskeletal system. Our model offers a platform for interactions with commercial partners aimed at tackling this major health problem of our post-industrial society.

An important aspect of our research concerns the clinical observation that the loss of myofibrillar material in fully unloaded muscle goes in parallel with an increase in muscle fat content. This is for instance indicated after tears of a tendon or ligaments (Fig. 5). This is a relatively frequent situation, affecting as many as 100 per 100,000 persons each year for joints of the locomotor system such as in the anterior cruciate ligament. The highest incidence is seen for rotator cuff muscles of the shoulder, affecting two out of five individuals above sixty years of age. The observations highlight that mechanical factors govern the conversion of muscle into fat tissue. This implies that the muscle unloading produces defects in energy supply, which may culminate into a fatty degeneration of muscle cells. At the same time, high-load type training of weak muscles based on eccentric contractions appears to reduce the lipid content of muscle tissue. The relationship between muscle atrophy and the accumulation of metabolic stores is poorly understood; yet this has large implications for control of body homeostasis. Nutritional factors aside, the usage and load-dependent preservation of muscle mass may importantly contribute to the variability in the relationship between contractile and fat tissue in healthy human populations (Fig. 6). This observation suggests that mechano-regulation of muscle mass is related to obesity, which is one of the largest co-factors for morbidity in the western civilisation.

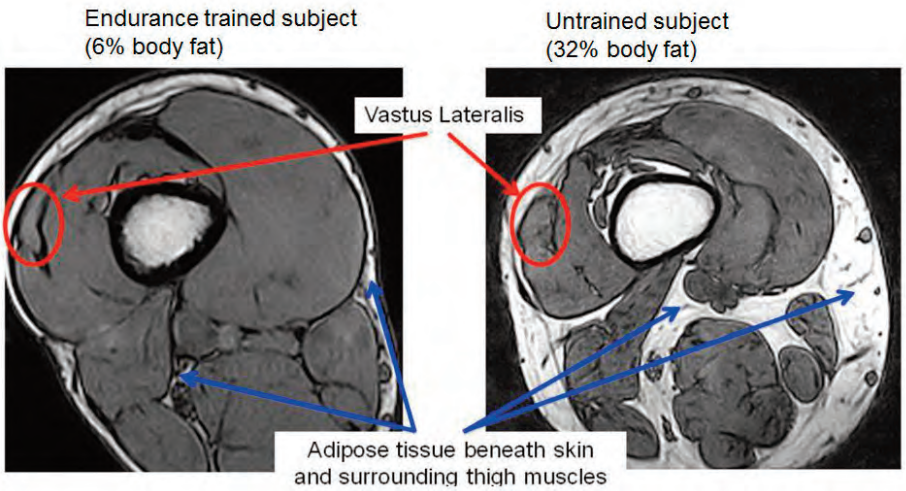

Figure 6: Increased extramyocellular fat with relative inactivity. Magnet resonance images showing the cross-sectional area of the thigh at a standardised, anatomical position in a trained and untrained subject of the same age. The increase in adipose tissue at the expense of the quadriceps and hamstring muscle area can be readily identified from the indications. The area corresponding to the *vastus lateralis* muscle is indicated by red circles. *Picture courtesy of D Vaughan (2012).*

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Halting the rise in obesity

Obesity is a worldwide problem that can lead to other healthcare challenges. João Breda and Margarida Moreira dos Santos from the World Health Organization (WHO) detail how they are helping to tackle the problem...

The core mission of the World Health Organization (WHO) is to address public health on a global scale. This is tackled by monitoring health trends, providing leadership on matters critical to health, articulating policy options for health and shaping the health research agenda. In September 2011, the United Nations held a Summit Meeting on non-communicable diseases (NCDs), the second high-level meeting of its kind ever held to focus on a global disease issue. Two years later, in the 66th World Health Assembly, the WHO Member States have agreed on 9 voluntary global NCD targets, one of which is to "halt the rise on diabetes and obesity" by 2025 [1].

Over 50% of the adult population in Europe is over-weight, and at least half of those adults are obese. Obesity prevalence has tripled in many countries since the 1980s. It is already responsible for 2–8% of health costs and 10–13% of deaths in different parts of the region, and the numbers of those affected continue to rise at an alarming rate, particularly among children. Excess weight drastically increases a person's risk of developing a number of NCDs, including cardiovascular disease, cancer and diabetes. Together with chronic respiratory diseases and mental disorders, these 5 health conditions are responsible for a large part of the disease burden in Europe, accounting for an estimated 86% of the deaths and 77% of the diseases burden in the 53 countries covered by the WHO European Region. The risk of developing more than one of these diseases (co-morbidity) also increases with increasing body weight.

Obesity became a primary focus of current worldwide efforts to tackle the increasing epidemic of NCDs, which are worldwide severe public health problems. Obesity can be attributed by large to social changes, since obesity has been related to diet and physical inactivity. Both societies and governments need to act to curb the epidemic. National policies should encourage and provide opportunities for greater physical activity, and improve the affordability, availability and accessibility of healthy foods. They should also encourage the involvement of different government sectors, civil society, the private sector and other stakeholders.

To assist on these matters, the Nutrition, Physical Activity and Obesity Program at the WHO Regional Office for Europe in Copenhagen develops norms and standards, provides technical support and building capacity, guidance and public health tools to help countries implement effective programs and address risk factors, amongst other actions. Highlights on the ongoing work at the region level include establishing the world–leading Childhood Obesity Surveillance Initiative (for primary school children) and providing innovative technical advice to Member States in the full range of policy areas (including recent work on nutrient profile models that countries can use as a tool to implement the recommendations on restrictions on marketing of unhealthy food to children) and producing guiding documents on governance.

In September of the current year, the Food and Nutrition Action Plan was endorsed by the WHO Regional Committee for Europe [2]. This was a major breakthrough towards the promotion of healthy food environments for everybody and throughout life. It should be used by Member States to adopt specific measures related to the coordination of trade, food and agricultural policies with the protection and promotion of public health, encourage consumers to

demand for healthy foods and meals and promote healthy nutrition of infants and young children.

Tailored to each country, measures on both increasing public awareness and facilitating healthy choices needs to be adopted. Policy makers may consider: creating healthy food and drink environments and encouraging physical activity for all population groups, promoting healthy diets throughout life, especially for the most vulnerable (e.g. promoting, protecting and supporting exclusive breastfeeding in the first months and introducing healthy school meals and school fruit schemes as standard), reinforcing health systems to promote healthy diets (nutritional counselling and obesity management should be available) and engage everyone in making change (e.g. engaging governmental departments outside the health sector and identifying joint goals and actions, in a health-in-all-policies approach). National recommendations should support a diet that is healthy, affordable, accessible to all, culturally acceptable and environmentally sustainable.

The WHO recommends adults to walk, cycle or make sports 150 minutes per week, since this can significantly reduce the risk of hypertension, coronary heart disease, stroke, diabetes, breast and colon cancer and depression, keeps bones strong and helps weight control. However, 6 in 10 adults never or seldom exercise or play sport, and 3 in 10 never engage in any kind of physical activity at all (average for the European Union). Increasing physical activity is a societal, not just an individual responsibility. Promoting physical activity demands a population-based, multi-sectoral, multi-disciplinary and culturally relevant approach. A Physical Activity Strategy is under development, to be adopted next year.

Individuals should be supported in following the recommendations, through sustained political commitment and the collaboration of many public and private stakeholders; regular physical activity should be promoted and healthier dietary choices available, affordable and easily accessible to all – especially those of poor and disadvantage groups, who appear to be more exposed to at least some unhealthy food. Overweight and obesity are more common in low socioeconomic groups and, in some countries, the gap is widening, thereby contributing to growing inequalities in health [3]. The WHO considers health a fundamental human right, and directs all its efforts to assure that everyone has the highest possible level of health. ■

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FATTY LIVER DISEASE

AND THE CONSEQUENCES FOR EUROPE

Alterations in our lifestyle over the last decades, including high caloric intake (e.g. through a high fructose and high fat diet) combined with a sedentary lifestyle have augmented the worldwide incidence of overweight and metabolic syndrome, characterised by abdominal obesity, insulin resistance and Type-2 diabetes, hypertonia and dyslipidemia. At the moment it is believed that approximately 90 million Americans and 40 million Europeans suffer from a fatty liver (also called Non-alcoholic fatty liver disease (NAFLD)).

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