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METAFORUM

Metaforum position paper 17

Mobile Health Revolution in Healthcare: Are We Ready?

Position paper working group Metaforum, presented at the symposium of 19 September 2019

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In English:

1. *'A Truly Golden Handbook': The Scholarly Quest for Utopia*, Leuven: Leuven University Press, 2016
2. *A European Social Union after the Crisis*, Cambridge: Cambridge UP, 2017

In Dutch:

1. *Wat met de verkeersknoop?* Leuven: LannooCampus, 2013
2. *Wat met genetica?* Leuven: LannooCampus, 2013
3. *Wat met psyche en pillen?* Leuven: LannooCampus, 2014
4. *Wat met Brussel?* Leuven: LannooCampus, 2014
5. *Wat met kunst en geld?* Leuven: LannooCampus, 2014
6. *Wat met ggo's?* Leuven: LannooCampus, 2014
7. *Wat met de mondige patiënt?* Leuven: LannooCampus, 2016
8. *Wat met ons voedsel?* Leuven: LannooCampus, 2017
9. *Wat met recyclage?* Leuven: LannooCampus, 2017

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10. *Hoe word ik Einstein of Da Vinci? Een inleiding tot wetenschappen vandaag voor de homo universalis van morgen*, Leuven: LannooCampus, 2015
11. *Lutopia, stad van de toekomst*, Antwerpen: Polis, 2016
12. *De cannabiskwestie*, Oud-Turnhout: Gompel&Svacina, 2018
13. *Voor sociale vooruitgang: Professoren op de barricade*, Leuven: LannooCampus, 2019

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CHAPTERS

CO-AUTHORS

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INTRODUCTION

Technology is all around us, so it is hardly surprising that public and academic attention has come to focus more and more on its role in our health and healthcare services. In fact, technology has probably been an important promotor of innovation in healthcare for over 50 years: the evolution of computers and other technical devices have been indispensable components in new discoveries in the area of health (Reiser, 2009). Nowadays, applying technology in healthcare, such as wearable devices, is also viewed as a potential solution for the sustainability of health services (Holeman et al. 2016; Chang et al., 2004). For instance, in a context of growing demand and shortages of professionals, using new technology in current healthcare improves accessibility and can reduce high financial costs. In addition, this technology can effectively provide or exchange information on health in real time, whether for healthcare professionals, users, or the general public.

Modern healthcare strategies, on the intersection between newly developing technologies and health, have generated new terminology, such as e-health, mobile health (m-health), digital health technologies (DHT) and telehealth (Gök et al., 2013). Telehealth and DHT are the broadest terms, defined as the general use of electronic information and communication in health care delivery. E-health implies the use of computers as well as networks to manage and store health information. M-health (or mhealth), a subsegment of e-health, refers to healthcare using mobile devices, computers, smartphones, and tablets.

In particular, we will focus in this paper on the use of m-health, even though a variation of terms is used, such as e-health, telehealth, and wearable sensing. Measuring and monitoring human activity, behaviour, physiology and neurobiology via mobile devices has grown exponentially in recent years, ranging from watches to chest patches, rings, wristbands, vests and even shoe inserts for ambulatory gait monitoring. Dunn et al. (2018) recently published a review of commercially available wearable sensors, but also described the extraordinary potential of many early-stage devices that are potentially applicable in health monitoring in the future. Moreover, usage of mobile devices is already widespread nowadays and mobile technology is accessible almost everywhere in the world. In addition, m-health places the emphasis on receiving information instantaneously and is more personal. These features will have a considerable impact on the way current healthcare is conducted. M-health technology can potentially drag medicine from the clinic to the consumer, where users are able to read, monitor and manage their own health information.

It is obvious that telehealth use is spreading rapidly and exponentially. First of all, there is the proliferation of new technologies, as the public, healthcare professionals and scientists are eager to test and integrate new and preferably effective systems into the medical field. Investors and other third parties certainly have found their way to med tech. Companies are accelerating their efforts by developing or collaborating new e-tools and apps for consumers, patients, doctors and medical researchers. Immediately, this raises a number of societal challenges. For one thing, this is putting considerable pressure on the legislative and institutional framework, not very different from the challenges that digitisation poses in general. It also challenges caregivers and care experts with certain views on the care cycle to take a stance. Advances in personalised care creates new challenges for person-centered care. When looking at healthcare practices worldwide, many health services have already integrated telehealth to ameliorate health problems by prevention, education (e.g. e-learning) and self-help; tracking and record keeping; mediated assessment and diagnosis; and even treatment interventions that are delivered via electronic systems. A 2016 global survey conducted by the World Health Organisation (WHO) (https://www.who.int/goe/en/) showed that 58% of WHO members have a DHT strategy, 55% of countries have legislation to protect electronic patient data and 87% of countries report having one or more national m-health initiatives.

However, DHT may also have negative consequences. There are caveats that still need attention and careful consideration. The public, healthcare workers and researchers are often working with technology they know

little about (Huang, 2017) and DHT is still mostly unregulated territory. This is exactly what the chapters of this position paper, especially in Part I and Part 3, shed light on. There are yet no clear criteria to evaluate the quality, efficacy, and safety of a given application or technology. How, for example, do we assess the quality of a given technology (e.g. accuracy in measuring heart rate and blood pressure can vary considerably between devices), or set of guidelines to deal with unintended side effects (e.g, screen-time can also cause physical problems such as poor sleep, back pain or poor eyesight, and has been associated with mental illness such as addiction). In addition, the use of e-health opens the debate on the importance of face-to-face patient-doctor interaction, as well as ethical and boundary issues related to the use of public technology for personal health issues. For example, issues such as maintaining privacy and confidentiality, maintaining clinical reasoning, establishing realistic expectations regarding digital communications and balancing patient autonomy with clinical boundaries need to be clarified further (Sulmasy et al. 2017; Sabin and Harland, 2017).

An easy-to-read overview, covering the benefits, pitfalls and future prospects of telehealth, from development stage to clinical applicability, is currently unavailable. This present contribution certainly fills the gap by providing up-to-date information on current developments in DHT. Our goal is not to give a complete overview of the field, but rather to offer some insight in its current states, which may support policy and debate. We highlight the potential of DHT, but also address some of the obstacles that still have to be overcome before it can become common use.

A number of different disciplines must be involved of necessity when discussing m-health. Expertise from medical doctors, psychologists, sociologists, bioengineers and engineers is indispensable as we advance field. The authors of this position paper represent different fields. All authors are affiliated with KU Leuven (Belgium) and actively work with digital health technology in their own line of research. They were brought together by Metaforum, the interdisciplinary think-tank of KU Leuven, which brings together educational backgrounds and research specialties around societal themes. This diversity facilitates a unique overview of the current state of the field in e-health, from bench to bedside.

This position paper consists of three parts. Part I explores currently available mobile hardware and mathematical challenges to extract usable information from these devices (e.g. dealing with big data and developing algorithms). Chapter 1 offers a status update on hardware technology or devices, from wearables to beyond, and expected evolutions in their development. We then move to signal processing and remaining challenges. Chapter 2 addresses how raw data, collected by multiple wearable sensors, are transformed into interpretable information for diagnosis and monitoring. Chapter 3 discusses what happens when predictability, a gold standard for any controlled process, confronts living organisms, with some case examples.

Part II discusses current medical applications with regard to specific areas: the medical field, for which a number of clinical examples are given. Other applications pertain to the field of mental care, both from a preventive and disease monitoring perspective. And finally, there are applications in stress reduction and with regard to well-being and preventive healthcare, and behavioural change. They are all examples of potential progress in and challenges to m-health in medical care.

Part III tackles the social implications of digital health technology and potential consequences for patients. Chapter 8 highlights important socioethical issues, such as privacy and data mining, especially by new parties challenging traditional medical professionals, and data ownership. Such issues of course do not apply to DTH alone, but they certainly raise specific questions for the medical field. Chapter 9 looks at DHT from the viewpoint of remote monitoring and discusses what the impact of m-health means for person-centered care and patient empowerment. This position paper concludes with a summary of the most salient points made, and with a number of slightly provocative theses to stimulate further discussion.

Part I: Hardware and algorithms

1. DEVICES: CURRENT STATUS AND EXPECTED EVOLUTIONS

Global demographic evolutions and increasing life expectancy imply that many of us will be suffering from one or more chronic illnesses during a significant part of our lives. It is also recognised that the monitoring and prevention of diseases and follow-up of patients are two key components for improving the *quality of life*. We distinguish between a number of applications, as will be further explored in Part II: medical-grade wearables and other healthcare and wellness applications. Medical-grade wearables exhibit the ambition and untapped potential to become an important technology in the care cycle. It is possible, as we know, to assess a considerable number of vital parameters from outside the body using electrical or optical methods, and chronic patients need tools that can improve risk assessment, follow-up and management, and are able to monitor disease progression and prevent relapse.

Similar technologies can be used as personal trainers, supporting the wellbeing of active people. Smart systems for health and wellbeing are specially designed to measure many physical and physiological parameters simultaneously. Captured data can be analysed in real time to provide the physiological status of the person wearing the device(s). Such body parameters are useful for recording the physiological status of not only people with a chronic disease or frailty, but also those in good health. And in healthy people, the enormous opportunity for wearable sensing has also to do with behaviour change in illness prevention and healthy living.

Unobtrusive, frictionless technology, personalised algorithms/feedback and power autonomy are key requirements for widespread user adoption in this domain. In smart systems dedicated to healthcare and wellness applications, the sensors collect physical, chemical and biochemical data to enable interpretation and monitoring of a person's physiological status, in relation to the actual environmental and social context. To enable complex, multi-parametric, real-time sensing based on several types of sensors in portable smart systems, power consumption per sensor element is clearly a key merit parameter of equal importance to other essential requirements (sensitivity, selectivity, robustness, reliability, integration in advanced silicon platform and/or flexible substrates).

Looking at current sensor devices under development in research labs, a wide range of sensing modalities and approaches is being explored and developed. Such sensors range from measuring electrophysiology at diverse body locations (cardiac output by ECG, brain activity monitoring by EEG, muscle activity and tension by EMG, respiration and body water content by bioimpedance, skin conductance, …), through optical measurements (heartrate at several locations and oxygen saturation by photoplethysmography – PPG) to measuring fluid compositions (sweat analysis, ion concentrations, glucose …), and these are becoming increasingly mature medical grade products. In the following pages, an overview of the current capabilities of such sensor devices is presented and discussed. This is followed by some examples of the ongoing evolution of such devices for more complex measurements and disease monitoring requirements (e.g. smart contact lenses, gastrointestinal non-obtrusive monitoring, ...).

A. TECHNOLOGY AND WEARABLES

PATCHES

A first family of devices is usually referred to as health patches or smart patches. These devices allow mobile continuous cardiac telemetry and contain self-adhesives that stick to the skin and make intimate electrical contact typically by using conductive gels. Examples of such devices are shown in Figure 1.

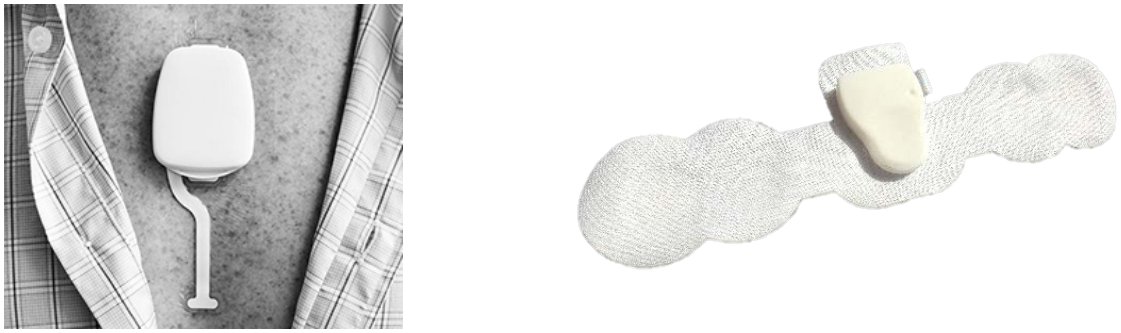

Figure 1, left: ECG recording patch from Bio-Telemetry; right: ECG / bioimpedance patch from imec

These very compact lightweight devices (<30g, Figure 1 Left) enable long time 1-lead ECG recordings for up to several weeks and/or real-time streaming of the data to cloud platforms for continuous monitoring and analysis of e.g. cardiac patients. Such patches can be enriched with other sensors, including accelerometers and bioimpedance measurement capability (Xu et al., 2018) that facilitate additional applications such as measuring respiration rates, lung water content, tidal volume, ..). Signal quality is of the utmost importance in these applications, so the deployment of the said devices implies the development and use of embedded advanced algorithms to identify signal quality and integrity, all challenged by the same low-processing power requirements. Recent developments have tended to construct such patches as very low-cost disposable devices which are environmentally friendly.[1] In addition to their use in traditional longitudinal heart and heart rate monitoring applications, these devices are finding their way into a growing number of extended medical applications. Onera, for example, uses this technology for sleep apnea monitoring, and Bloomlife for pregnancy follow-up. People with CHF (Congestive heart failure) and COPD (Chronic obstructive pulmonary disease) are likewise potential users of this approach.

WRISTBANDS

Wristband devices are rapidly becoming popular consumer sensor devices that allow users to monitor activity and heartrate, mostly in the context of (recreative) sport. Although such devices are becoming increasingly affordable by a broader public, they are limited to the detection of movement and heartrate and combine this limited nonmedical grade health sensing with smartphone functionality and integration. Very few devices are medical grade or measure more and other signals. FDA approved as a research monitoring device, Empatica's Embrace device is one of the exceptions, offering in addition skin conductance (GSR or EDA). The first ECG wrist devices are appearing with FDA classification (e.g. Apple Watch 4) for irregular heart signal detection are appearing only now. The same functionality is also achieved by e.g. Fibricheck, a company that has developed a medical tool to analyse heart signals using a smartphone camera. However, the potential use for wrist worn devices, especially when supplied with a combination of PPG (for heart rate) and GSR can be extended to applications in which stress monitoring is envisaged in ambulatory settings. Furthermore, adding ECG at the wrist is

[1] www.imec-int.com/en/articles/imec-and-tno-launch-comfortable-disposable-health-patch-with-long-battery-life-to-measure-vital-signs

currently driving much research intent on the realisation of cuffless blood pressure measurement with medical quality. The first devices are likely to appear in the course of 2019 (Omron, Asus, Samsung[2]). High signal quality wristbands are definitely one of the most attractive tools for medical applications to monitor people and patients over longer time periods (e.g. in psychological or psychiatric research into anxiety, depression, resilience, …) since no specific additional action is needed from the wearer. All measurements and information can thus be captured in an unobtrusive way.

EEG HEADSETS

In the field of neurology, easy-to-use EEG headsets are drawing considerable attention. Traditional high-density medical EEG systems require time consuming mounting procedures executed by highly specialised professionals. Although many gadget-type devices are appearing in the entertainment arena (Emotiv, Mindwave, …), more solid wearable devices are required to serve true medical problems. Traumatic brain injury or nonconvulsive status epilepticus often go unreported or are misdiagnosed and could benefit greatly from easy to use wearable EEG headsets. Also, intense research into the use of EEG for closing the loop in stroke rehabilitation is ongoing (Monge-Pereira et al., 2017). An example of a system that can be used in this context is a low-resolution wireless headset from Nihon Kohden (Figure 2), specifically designed for quick and easy brain activity assessment in an intensive care unit environment.

Figure 2: wireless headset product from Nihon Kohden (FDMA approved) for use in intensive care units (ICU)

Figure 3: 128 dry electrode prototype wearable system developed by Datwyler

Initial prototypes are appearing for applications in which high resolution is required. These include the research prototype developed by Datwyler and imec using 128 dry electrodes (for easy mounting) integrated in a full system. (Figure 3)

SYSTEM INTEGRATION TECHNOLOGIES

The above-mentioned wearable system examples are all driven by the miniaturisation revolution in nanoelectronics technology: e.g. full high-performance systems, first integrated in small multiboard compact systems (Figure 4) can be redesigned as an extremely compact single chip system (4x4mm^2). This enables the production of ultra compact wearable sensors. In addition, such chip integration also facilitates ultra low power system designs, much needed by limited battery capacity.

[2] www.wareable.com/smartwatches/omron-heartguide-blood-pressure-release-date-price-specs-3943

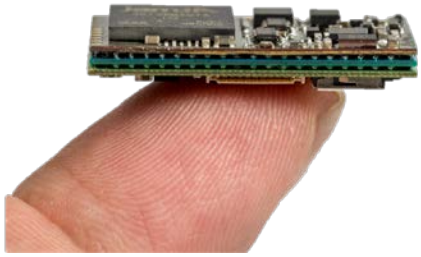

Figure 4: integrated 1 cm^3 vital signal monitor device

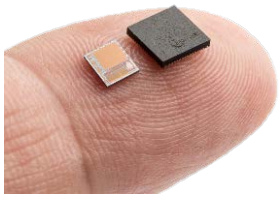

Figure 5: the same vital monitor from Figure 4 in a single 4x4 mm^2 chip (imec)

B. BEYOND WEARABLES

Since the field of wearables for medical applications is so extensive, it is almost impossible to identify general trends. Application domains are emerging in which extreme challenges are being set with respect to system power, system size and body acceptance. We explore two examples: ingestibles and contactless sensing.

INGESTIBLES

Most wearable devices are designed to measure physiological responses in a noninvasive and unobtrusive way on the skin surface. As a result, it is very hard – if not impossible – to monitor e.g. gastrointestinal activity.

Digestive diseases are plentiful and they affect a large portion of the population. Of such diseases, 40% are functional gastrointestinal, and these in particular pose a significant challenge. Since the symptoms involved are very generic, said conditions still tend to be very hard to diagnose.

In the past, smart pills have been proposed and developed to record images during the transit of the pill (Pillcam, Bravo, Smartpill, …) through the body to try to capture more information on gastrointestinal diseases. An interesting and currently emerging variation on these devices is a smart pill that allows us to capture and wirelessly transmit local body fluid information such as pH, specific ion concentrations, temperature, electrical activity, etc., at certain locations on the gastrointestinal path. In particular, the ability to track in-situ measurements over longer time periods is very attractive. Such devices are under development at imec and Johns Hopkins University, enabled by the combination of ULP (ultra low power) nanoelectronics circuitry for signal processing and wireless transmission, integrated electrochemical sensor devices, system packaging, microfluidics technologies for sample uptake and potential local drug delivery. Alongside these hardware developments, advanced data analytics and machine learning techniques need to be used to understand all the information gathered and to extract knowledge on the diseases under investigation.

CONTACTLESS SENSING OF PHYSIOLOGY

Imagine that electrophysiology (ECG, bioimpedance, EMG, …) could be measured by electrodes embedded in furniture (chairs, beds, car seats, …). This presents serious challenges to the required circuitry that must be capable of measuring these faint signals through fabric or clothing. However, current research by several groups (Univ. Rome: Santonico et al., 2017; imec: Chen et al., 2018) shows that first prototypes of capacitive sensing circuitry are delivering promising results in this field. Such systems can, for example, be installed in a car seat.

Since we tend to spend a lot of time in our car, this is a particularly interesting place to perform health check-ups on a very regular basis. The kind of technology, to be embedded in a car seat or other chair, can then be used to assess our health in a completely unobtrusive way.

C. DATA ANALYTICS FOR A WIDE RANGE OF APPLICATIONS

Wearables enable the collection of massive amounts of health- or disease-related data. This is illustrated in Figure 6, which visualises all health and prevention applications to date. Chronic problems and diseases are grouped on the left, while prevention type applications are grouped on the right. All these topics, however, share a significant need for data analytics techniques and approaches in which data from different sources – from wearable data to context information (see above) gathered by smartphones or in large databases such as weather information, traffic information, etc. – have to be combined in practical models. As an example, we believe that stress and depression research can benefit a great deal from such scenarios (see chapter 7.)

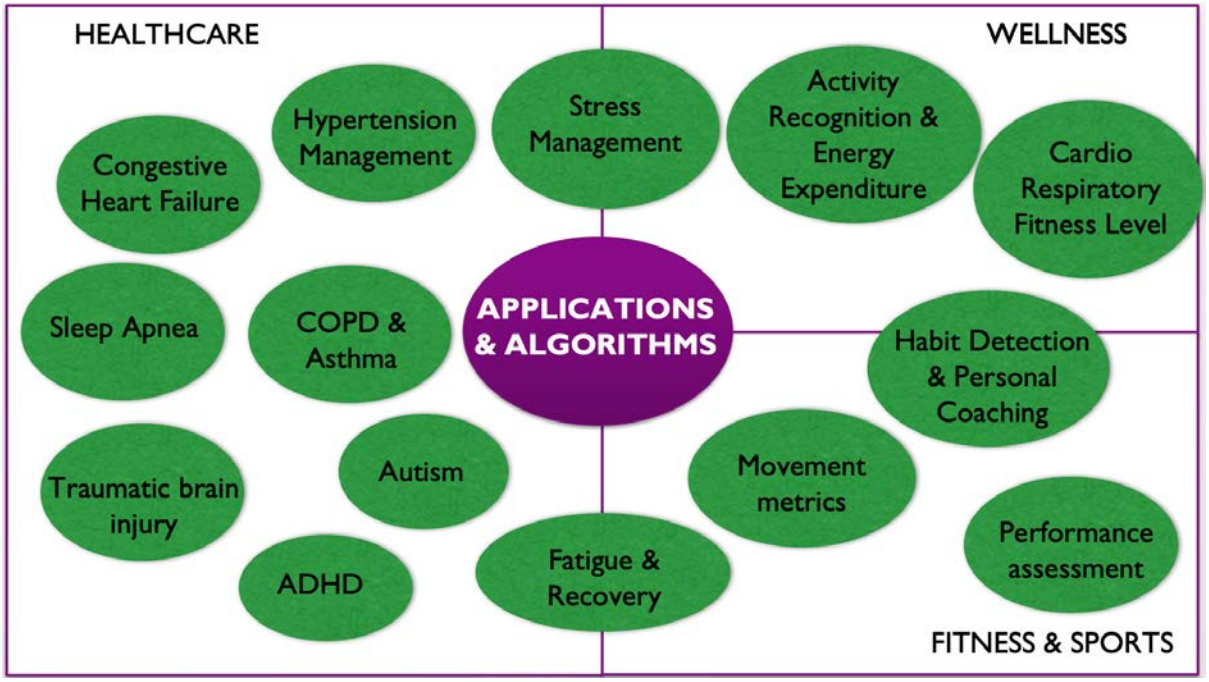

Figure 6: mapping of application domains in which data from wearables can create high amounts of value by detecting faulty body functioning and behaviour

HOW TO UNDERSTAND AND USE ALL THIS DATA?

The true value of all of these wearables comes from understanding the data generated by the systems involved and extracting knowledge from it at various levels. This will be addressed, among others, in the following chapter on signal processing. At the lowest level, knowledge of the quality of the signals (such as ECG, EEG, bioimpedance, …) is key, since this forms the interface between the body parameters and the conclusions drawn therefrom by clinicians. Hardware signal processing and the system software embedded in the sensor belong at this level. At the higher level, information from several sensors is combined (so-called data fusion) in order to create insights/understanding of the behaviour being monitored or the status or evolution of a disease. At this stage, features or characteristics are calculated from the measured data and machine learning techniques are typically used to evaluate and build models that are able to predict an outcome based on all sensor inputs. At the highest level, longitudinal data is gathered and used for analysis of the evolution of diseases or behaviour to facilitate the provision of accurate feedback to patients and/or their caregivers within the framework of a given therapy.

Presently, most of these analyses are still being done ‘manually’ by specialists, but more and more expert systems are appearing, in the field of diabetes and cardiac monitoring for example, and automatic closed-loop systems are appearing on the market. For applications addressing stress-related problems and neurological diseases, for example, tools built around wearable data are offering challenging opportunities (see chapter 3).

2. FROM DATA TO SMART DIAGNOSTICS: THE POWER OF BIOMEDICAL SIGNAL PROCESSING

The previous chapter provided an overview of wearable and ingestible sensor technology that is available or in development. The next step is to translate data collected by wearables in order to start using them for medical purposes. This chapter discusses how the raw data collected by multiple wearable sensors can be transformed into interpretable information for diagnosis and monitoring. The first part will introduce the field of wearable systems for health monitoring. Next, the main challenges in bridging the gap between technological development and diagnosis by means of signal processing will be presented. Finally, some general future challenges will be discussed.

A. TOWARDS WEARABLE HEALTH MONITORING

Currently, the diagnosis and monitoring of almost every disease and condition is performed in a hospital setting, where the use of expensive medical systems is required together with the intervention of trained personnel. Furthermore, most patients can only be identified and diagnosed after they visit the hospital, since the healthcare system relies on cure rather than prevention. Nowadays however, we want healthcare to evolve towards a more personalised system that will facilitate the prevention of diseases, as well as prioritise and tailor both treatment and disease management.

The inclusion of IT solutions into the healthcare system will ultimately lead to the prediction of health transitions, prevention of illnesses, and wellness enhancement (Holzinger et al., 2015). This, however, will only be possible through an increase in patient participation, which will result in a higher demand for such solutions. By way of example, such patient participation has triggered the development of multiple software applications that focus on either the caregiver or the patient. Apps that focus on caregivers aim to assist them with tasks such as patient management, training, education, and in *clinical decision making* (Ventola, 2014), with the purpose of improving long-term outcome for patients. On the other hand, apps focusing on patients, or rather on the general population, aim at promoting health by continuously tracking multiple variables such as mental status, motivation, fitness, diet, and even sleep (Carroll et al., 2014).

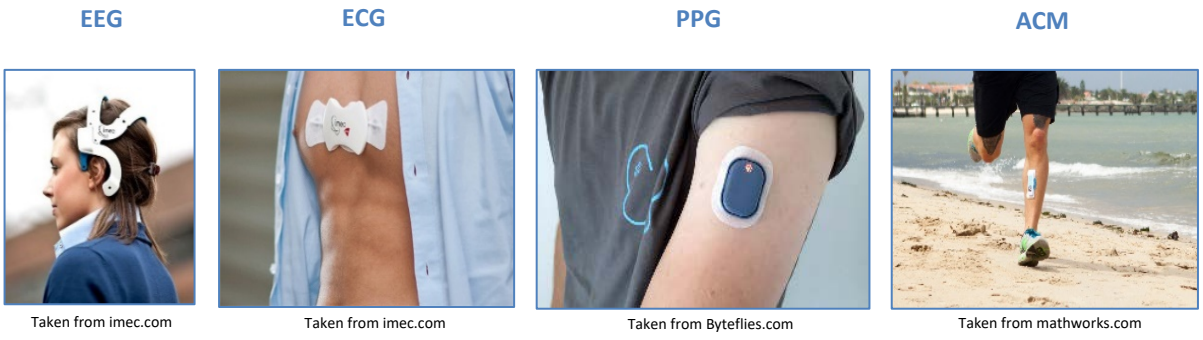

Figure 7: examples of state-of-the-art wearable systems

This can only be done thanks to the miniaturisation and improvement of sensor systems designed to *monitor different physiological signals* on a daily basis. Examples of these signals include the electrical activity of the brain recorded using electroencephalography (EEG); the electrical activity of the heart recorded using either electrocardiography (ECG) or photoplethysmography (PPG); airflow; respiratory effort; blood oxygen saturation (SaO2); movement recorded using accelerometry (ACM), posture, among other things. Figure 7 shows some examples of state-of-the-art wearable sensors. For a more systematic overview, we refer to chapter 1.

So technology has the potential to improve health and wellbeing in the general population. However, challenges still need to be faced in order to fulfil society's many emerging expectations. The market in wearable technology is expected to increase exponentially in the next few years (European Commission, 2016). In addition, the increasingly varied range of (non)invasive sensing devices, registering an increasing scale of signals with improving resolution and accuracy at decreasing size and power consumption, will eventually register a 'tsunami' of medical data. This registration is often done in a long-term fashion, using multiple modalities with different data quality that still demands 24/7 reliability. The widespread availability of these sensing devices and improvements in communication technologies are also driving the booming market in home monitoring. Furthermore, since computational performance is doubling every 18 months (Moore's law), this is having widespread implications for computational intelligence in healthcare (data mining, machine learning, imaging, signal processing, dynamic modelling). Similarly, broadband capacity will enable technologies that cannot be anticipated today – like cloud computing ten years ago –, offering immense possibilities through sharing hardware, software, data and computing resources in the cloud.

The potential tsunami of medical data that will be available in the near future will need to be integrated in some way into our National e-Health platforms. Nevertheless, the validation of medical data is still limited, thereby reducing its benefit for clinical diagnostics. Reasons for this are manifold, but include the reduced interpretability and contextual factors (e.g. environmental factors or activities performed by the subject while being monitored) inherent in the current wearable health monitoring systems (Carroll et al., 2014). Other chapters in this position paper, chapter 6 for instance, broach the contextual factor as well. Much is currently being done to surmount these challenges, so that the usability of wearables is improved, not only for health monitoring, but also for the diagnosis and management of multiple diseases. One way of advancing is by developing powerful signal processing tools that can extract relevant features from the signals recorded using wearables, even in low-quality conditions. These tools allow us to minimize the amount of data to be processed while maximizing the information extracted from the monitoring systems.

B. BIOMEDICAL SIGNAL PROCESSING FOR WEARABLE APPLICATIONS

In order to improve the interpretability and usability of wearable systems, different factors or aims need to be considered:

- Sensors need to be discrete and user-friendly. Moreover, they must be suitable for long-term monitoring.
- The devices need to be cheap in order to guarantee easy access to health monitoring. This immediately limits the computing power available in the wearable systems to process the data.
- Signals recorded with wearable systems are typically characterised by poor *quality* since subjects perform daily activities while moving around in uncontrolled environments.
- *Interpretability* of the data is limited.
- Extensive *clinical validation* is crucial for the inclusion of wearables in the healthcare system.

The first two objectives for wearables dealing with sensor development (user-friendly and easily accessible) are already discussed in chapter 1. Here, we focus on the last three, in which biomedical signal processing can have the largest impact.

The biomedical signal processing field combines signal processing tools and physiology with the purpose of extracting meaningful information from measurements such as ECG, EEG, PPG, etc. These processing tools include filters and denoising techniques that allow the removal of unwanted information from the signals. This unwanted information limits the diagnostic and monitoring capabilities of the wearable systems. For instance, when a subject wears an ECG patch for a long period, the quality of the signal is affected by different factors like the movement and degradation of the electrodes, among other things. As a result, any cardiac information derived from such a system is contaminated by such undesired artefacts. At this point, a way of quantifying the

quality level of the signals is clearly needed to improve the potential role of wearables in long-term cardiac monitoring (European Commission, 2016). Figure 8 shows four examples of ECG segments contaminated by different types of artefact. Different levels of noise could be associated with each example. Signal a), for instance, could be used for further analysis only after filtering out power line interference (or 'noise') at 50 Hz. Signal b), on the other hand, could not be analysed since the signal was completely lost during part of the measurement. Finally, signals c) and d) could be used for certain analyses in which the full morphology of the signal was not needed (e.g. Heart Rate Variability-HRV). Different algorithms that assign a quality level to ECG segments have been proposed in the literature (Varon, 2015; Moeyersons et al., 2018; Clifford et al., 2012). Room for further improvement is possible by the inclusion of additional modalities, for instance ACM or respiration. These modalities are typically recorded by state-of-the-art wearables; hence, a great deal of attention is currently going to the development of a multimodal quality indicator that can be embedded in different wearable devices. Once this is achieved, the reliability of the current monitoring systems can be improved, thereby strengthening their impact in medical-grade healthcare applications.

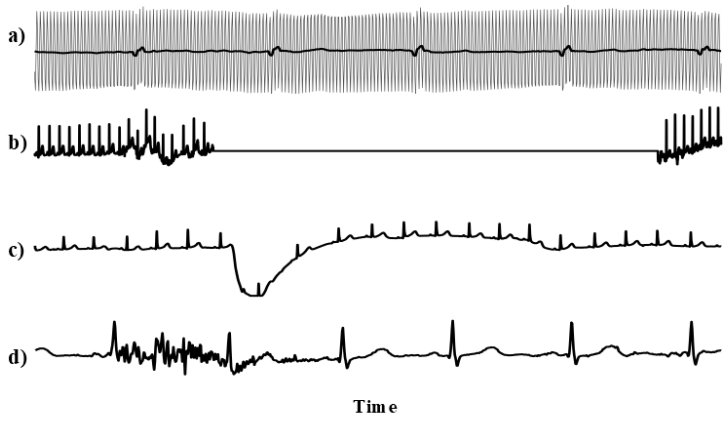

Figure 8: ECG segments contaminated by artefacts. a) In grey the original ECG contaminated by power line interference at 50Hz is indicated, and in black its filtered version. b) Contact noise. c) Electrode motion. d) Muscle artefact.

In addition to signal quality indicators, it is of paramount importance to maximize the amount of health-relevant information extracted from signals recorded with wearable systems. Current studies focus on the extraction of information from each signal separately. However, more information about the physiological systems needs to be explored in the interactions between these modalities. These interactions might reveal novel, unexplored mechanisms that improve our insight into the diagnostics of multiple diseases, and hence the assessment of mental and physical status in the healthy and the health-impaired populations. In this context, biomedical signal processing provides a set of tools to extract meaningful and health-relevant information from different modalities simultaneously in order to infer the status of the physiological system under investigation.

One physiological system that can be easily assessed by means of state-of-the-art wearables is the cardiorespiratory system. This can be done by analysing heart rate and respiration at the same time. These signals yield an enormous amount of information about mental and physical status. The control and modulation of these two signals is done by the autonomic nervous system (ANS), which also plays an essential role in maintaining homeostasis (Garcia et al., 2013). Moreover, the ANS has the remarkable property of quickly modifying not only heart rate and respiration, but also the functioning of several organs within the body. In other words, the ANS regulates the general capacity of individuals to react to different stimuli. With this in mind, many studies have shown that the extraction of information from the interplay between heart rate and respiration allows us to assess the status not only of the cardiorespiratory system but also of the ANS (Redmond et al., 2007; Berntson et al., 1993; Larsen et al., 2010). As a result, the effects that different diseases and conditions have on the physiological control mechanisms of the ANS can be inferred.

The quantification of cardiorespiratory interaction is slowly being integrated into wearable systems. The reason for the slowness is that that algorithms required to do so in an accurate and reliable way are computationally demanding. Moreover, their performance can be strongly degraded by artefacts. The latter can be removed by integrating the signal quality indicator described above. To reduce computational demands, much focus has been on the development of simple and efficient algorithms to quantify these interactions. Nevertheless, this only depends on the requirements of each particular application. In some cases, real-time feedback to the user is needed. The said algorithms must thus be implemented in the device itself so that fast processing can be guaranteed. Instead, when real-time is not needed, this processing can be done on a remote computer or in the cloud, which can improve reliability, but feedback to the user will be delayed. As a result, more complex and demanding algorithms can be allowed. Therefore, the algorithms used to quantify the interactions between different signals need to be designed with computational power, latency, efficiency, accuracy, and interpretability in mind.

For wearable systems to be fully reliable, they need to be extensively validated in a clinical setting. Many studies, combining gold standard medical tests and wearable systems, are currently being carried out. One of the main goals is to correlate findings obtained with wearable systems with the outcome or progression of the disease or the condition observed, using the gold standard. Three examples of such studies are discussed in chapter 4: epilepsy monitoring, sleep monitoring at home, and monitoring functional capacity in rheumatology.

C. FUTURE CHALLENGES

Current societal and technological trends point to an increase in the importance of biomedical signal processing in healthcare. R&D in this domain is booming, but the next stage in development, applications that are widely implemented and adopted by the (complex) healthcare system, is lagging behind.

ICT AS ENABLER OF MORE EFFECTIVE HEALTHCARE

These societal and technological trends are imposing new challenges to decision support systems and the associated biomedical signal processing (He et al., 2013; Linsenmeier, 2013), namely the need to process and integrate all the available information. The 'data tsunami' poses considerable scientific challenges, from generics, such as the storage and manipulation of large data volumes (e.g. through supercomputing), to the specific identification of the information that is hidden in the data. While this can no longer be understood intuitively, it remains highly relevant, for example, for prediction, diagnosis and therapy monitoring. Its importance is underlined by major strategic initiatives being taken worldwide (Kalil & Green, 2013; NIH, 2013). Information technology, mathematical engineering (i.e. the development of new mathematical algorithms that use concepts from statistics, information theory, numerical linear algebra and numerical optimisation) and software design are crucial in facilitating the extraction of appropriate information from these massive data sets. Flanders is likewise focusing on ICT for Health as pointed out by e.g. VRWI (Meditech and I-Healthcare clusters: Vlaamse Raad voor Wetenschapsbeleid, 2008; Health-wellbeing as transition area for Flemish innovation policy prioritisation towards 2025: Vlaamse Raad voor Wetenschap en Innovatie, 2014).

HURDLES IN MEDICAL TECHNOLOGY BUSINESS DEVELOPMENT

As illustrated above, biomedical signal processing will be one of the core needs in the health sector, giving rise to multiple market opportunities. Nevertheless, the hightech sector of medical technology is a complex world with many hurdles: multiplicity of stakeholders, nontrivial business models, hyperregulated environment with separated policy levels in Belgium, interstate variability in health systems, and various ethical and legal issues. Such issues are discussed at length in chapter 8. Moreover, in the niche market of medical diagnostics, societal

valorisation is often more important than purely economic approval. Clinical validation is a long process, which is hindered, moreover, by small patient datasets in every hospital. Therefore, multicenter collaboration is highly recommended to enlarge datasets, enhance innovation and speed up transfer from research to clinical practice and personalised medicine. Combining all these issues with the complexities of CE labelling or FDA approval, clarifies to some extent why business development in this domain is such a challenging task.

3. MONITORING LIVING ORGANISMS: COMPLEX, INDIVIDUAL, TIME-VARYING AND DYNAMIC ALGORITHMS

In chapter 2, we argued that the development of reliable algorithms to translate data collected by wearables is essential to develop tools that can be applied in healthcare. This will require close collaboration between, among others, engineers and bioengineers, as living organisms have a number of specific characteristics that will have to be taken into account. Interestingly, we can learn a number of important lessons from applications that have been developed in cows, pigs and humans.

A. EFFICIENT PROCESS MANAGEMENT IS BASED UPON ACCURATE PREDICTIONS

In whatever process that needs to be controlled, the secret of efficient control is prediction. The reason why people are able to drive a bike or a car in a desired direction is because they learned to predict what the bike or car will do when they change something at the handlebars or the steering wheel. If you want to control a system, you need to know how the process output (e.g. driving direction) will respond to a variation of the control input (e.g. position of steering wheel). This basic scheme has been widely researched and adapted to very advanced technology in many applications, among others like controlling the trajectory of an airplane in which pilots for the most part only intervene on take off and landing. The prediction-based (model-based) systems control has proven to be reliable and is now being tested at new levels, such as autonomous cars. The question is whether this concept is applicable to living organisms, and whether this approach can facilitate more efficient management and help people to stay healthy (Figure 9). Since 1991, this has been the focus of research within the M3-BIORES team at the KU Leuven. The microenvironment includes all possible variables that reach living organisms, including physical environment (light, temperature, humidity, pollutants, etc.), food, medication, and physical training. Social and mental variables, however, are likewise part of the environment reaching humans and animals, among them social ranking, psychological influencing variables, etc.

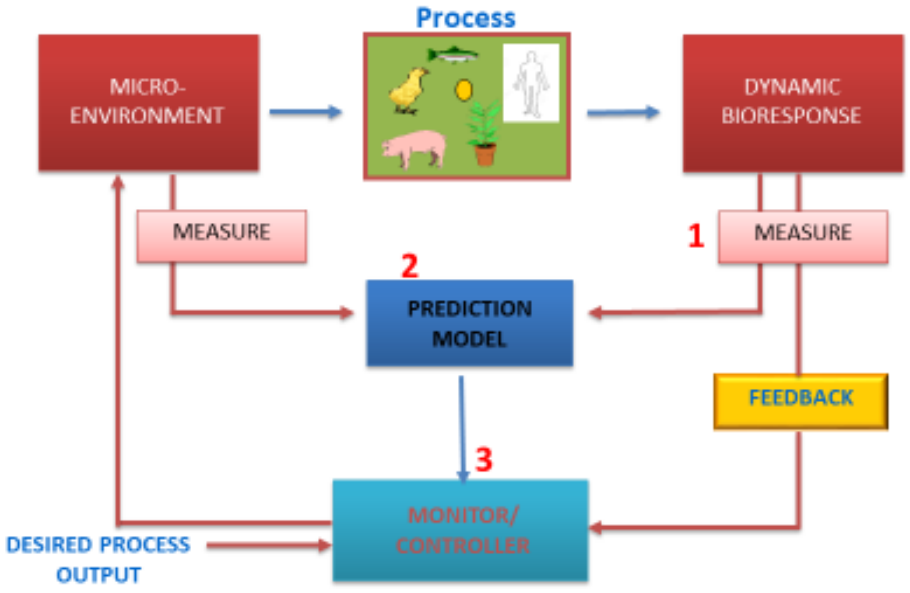

Figure 9: does prediction-based management apply to living organisms?

B. LIVING ORGANISMS ARE CITD SYSTEMS

When exploring whether such an approach can be of value we need to recognize some fundamental differences between electro-mechanical or physical applications and biological processes. In relation to management, living organisms exhibit four important and typical characteristics.

1. Living organisms are far more complex than all other systems on the planet. The complexity of what happens in a human body, for example, is of a totally different order than in any other man-made system or process. Living organisms are more *complex*.
2. Whether we like it or not, living organisms are *individually different*. The way in which one person or animal responds to stress or a specific situation is totally different from the way in which another person will respond. The risk of infection and the response to a threat, for example, are individual processes, since the individual immune system has a different history.
   In the world of technology, and likewise in the world of healthcare, living organisms are often approached as the average of a population. The average of a population is a very useful concept when used to compare groups or treatments applied to groups *versus* a control group. However, no single living organisms will fulfil the values of purely theoretical average of a population when more variables are considered. Every individual living organism is somewhere on the statistical curve with a dynamic behaviour in time (Figure 10). It is important to observe that the standard deviation of this individual is much smaller for most variables than the standard deviation of the theoretical average of the population. One of the main reasons why many of the existing technologies and tools – wearables in particular – are not accurate enough is because they use relations based upon the purely theoretical average of a population and not for the individual being monitored.
3. To make it even more exciting, living organisms are *time-varying* in their responses. This means that a single event (e.g. a challenging physical performance, or a news fact on TV) might induce a totally different response depending on the individual mode or status. For example, a particular stressor (e.g. a particularly urgent request from the boss) will likely induce an entirely different response in the days leading up to our annual vacation than it would on our first day back at work.
4. Finally, living organisms are very *dynamic* and in constant search of the optimal use of the metabolic energy produced by the body.

Living organisms are CITD systems: *Complex, Individually Different, Time-Varying and Dynamic*. This makes it both interesting and challenging to apply the concepts of prediction-based management (see figure 10).

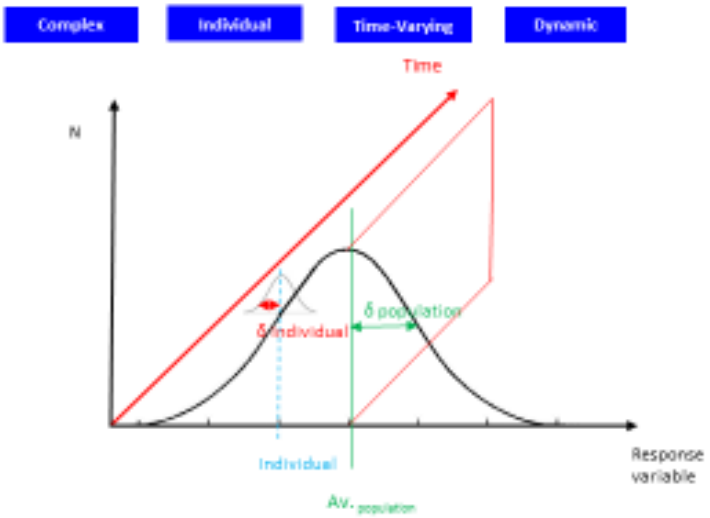

Figure 10: a living organism is individually different and time-varying, and consequently not the average of a population

These specific characteristics of living organisms have consequences for the way we will monitor them if we want to apply the concept of prediction-based management in a more preventive healthcare system. Since living organisms are individually different and time-varying we will need continuous monitoring, where the definition of 'continuous' (every second, hour, day week, etc.?) depends on the variable(s) under consideration. Continuous monitoring of heart rate, for example, needs a different sampling frequency from monitoring weight.

C. REAL-TIME MONITORING AND MANAGEMENT OF LIVING ORGANISMS

Today, modern technology offers a wide range of opportunities to monitor and manage living organisms, even in real-time. Sensors and sensing technologies of different kinds allow us to measure many variables in real-time on the body, such as movement, heart rate, respiration rate, skin conductivity, EEG, etc. In the long run, every imaginable variable will ultimately be measurable, but it will take time to do this in an accurate and affordable way. Cheap calculation power at sensor level facilitates calculating relevant information from the raw data with individualised algorithms. This prevents a data overflow at the higher level, which is completely useless. There is reason to send 10,000 sound samples/second, 25 images/second or 250 accelerometer data/second higher up since transmission demands a great deal of energy. Linking sensors with the Internet of Things allows us to run and copy-protect more sophisticated algorithms in the cloud in order to make predictions for the individual being monitored and to offer advice or (self-)management and send this to professionals in the healthcare system (Figure 11).

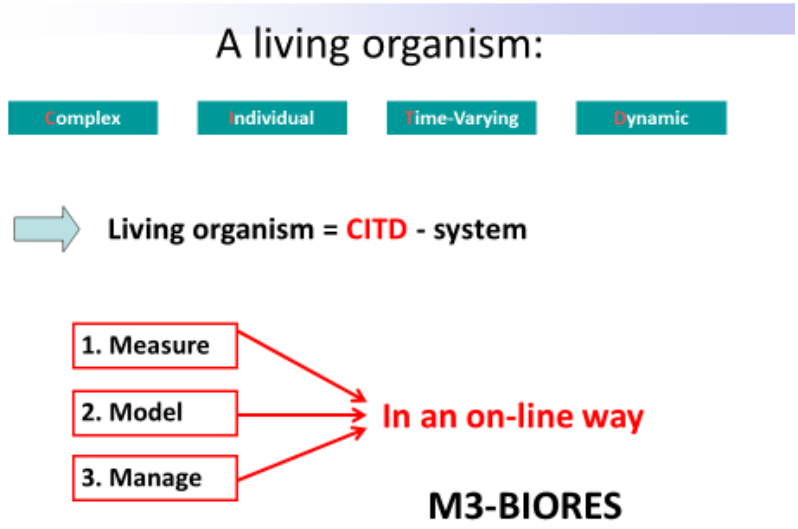

Figure 11: real-time measuring and calculation of prediction by individualised models to finally give management advise for the monitored subject

Mobile health (mHealth) is an interesting way of continuously monitoring individuals and transferring relevant data and information to professionals in the healthcare system and ultimately get individualised advice back to the user. This will be done via bracelets, watches, patches, smartphones etc. wirelessly connected to tablets or the internet. So-called ubiquitous computing and wireless connections have been under development for many years already and will help people monitoring, patient monitoring and managing their individual metabolic energy balance.

D. EXAMPLES OF APPLICATIONS IN COWS, PIGS AND HUMANS

Numerous examples have already been explored by researchers and companies across the globe. Here we present some samples of the latter that are already operational, already deployed in commercial products, or ready to be launched, to demonstrate that this technology is already a reality and there can be little doubt that it will

go much further. The world's population today is around 7.6 billion people and no single country is capable of actively limiting their numbers. In addition, aging populations are presenting governments with an increasingly problematic challenge of keeping their retirement systems afloat.

A more efficient and cheaper healthcare system will be crucial in maintaining the planet's liveability. Most of our diseases are transferred from animals, yet this year over 65 billion animals will be slaughtered for food production. In the Western world many people claim that they intend to reduce their meat consumption, yet they similarly claim that animal welfare is important but they don't want to pay for it. Unfortunately, Europe's efforts to reduce meat consumption will not significantly reduce the increase in worldwide demand for animal products (meat, milk, eggs), which is set to increase by up to 70% by 2050 (FAO)! As a result, a great deal of research has focused for a number of decades on continuous and real-time monitoring of livestock. The following few examples – which can be transferred immediately to human applications – demonstrate the possibilities of applying the new technology.

INDIVIDUAL CONTINUOUS LAMENESS MONITORING BASED ON IMAGE ANALYSIS

Milk is an essential product to feed the world and the production occurs worldwide, but not without issues. One of the primary health and welfare issues in global milk production is lameness in milking cows. Lameness is a deviation in gait resulting from pain or discomfort from hoof or leg problems and diseases. Under normal circumstances, up to 30% of milking cows in a herd develop leg problems and over 200 different causes have been described in literature. In modern farms, milking cows decide for themselves when they eat, go for milking, go out to pasture or sleep since they already wear sensors and are milked automatically when they decide to present themselves. An early-warning solution of the lameness problem was developed by filming each cow when she was walking away from the milking robot. An individual mathematical model was made of the way of walking, calculated on the basis of images, and compared to the previous time the same cow walked away from the milking robot (Figure 12). By comparing the baseline for this cow in a healthy state to variations in the model, an early warning can be given. Experts scored over 3,000 cows on a weekly basis in several different countries to develop this technology, which allows us to detect first sign of a problem in over 80% of cases (Van Hertem et al., 2016). The system sends a warning to the farmer, who can then call the veterinarian to start early treatment before the problem increases. The same concept has also been applied for broilers (Aydin et al., 2015). There is no reason why this technology would not be applicable to humans involved in sports, elderly people or just people in normal activities developing unusual walking patterns for some reason.

Figure 12: automated and continuous lameness monitoring based on real-time image analyses and individualised algorithms

CONTINUOUS INFECTION MONITORING BASED ON REAL-TIME SOUND ANALYSIS

Human and animal health are a primary reason to apply continuous health monitoring and introducing rapid treatment without the unnecessary use of antibiotics. To this end, an infection monitor has been developed based on continuous and real-time sound analysis. The system consists of an intelligent microphone placed in a compartment with between 7 and 250 fattening pigs, which constantly checks whether individual pigs are coughing too much. When the cough index extends above the usual threshold for that group of animals, an early warning is given to the farmer. The farmer can call the veterinarian and treatment can begin with only the animals in direct contact within the same pen, instead of waiting 3 days and treating all the animals with antibiotics. The system has demonstrated in livestock farms all over Europe that infection can be detected on average between 2 and 12 days before the farmer is aware of it (Exadaktylos et al., 2008). The principle has also been applied to cattle (Ferrari et al., 2010).

REAL-TIME MONITORING OF MENTAL COMPONENTS TO REDUCE RISK OF MENTAL STRESS AND OPTIMISE PERFORMANCE

In physiological terms, to live means to produce and use metabolic energy in the body. For homoeothermic living organisms, like humans and many animals, the top priority is to keep the basal functions running including a constant body temperature. This requires energy in addition to other energy consuming components such as physical activities, immune system, cognitive load and emotions (Figure 13). Using the basic principles explained above, individualised real-time algorithms have been developed that calculate these different components of the energy equation for moving subjects by using wearable technology. The fact that this technology works on moving people is important since physical activity and body movement are important in maintaining good health (WHO, 2010a). A smartwatch measures a number of physiological and activity parameters, which are translated into the physical and mental use of energy (continuously, 24/7) and the stress/recovery balance for the monitored individual. The watch connects automatically to the phone where real-time calculation is done and then only the relevant data go to the cloud, where the platform recognises the stressors and relaxing events on the individual level and offers personalised advice for self-management. A clinical psychologist follows the advice and will advise professional help if needed for that person. The system shows the days on which the body has recovered enough (green days) or where the body is lacking sufficient recovery (orange days) based on the measured use of energy and mental recovery during sleep.

Figure 13: the body produces metabolic energy for several purposes

So far, the system has been used on over 100 individuals to monitor their individual stress in the workplace. Measurements taken in several locations demonstrate that people with depression can clearly be detected by the system, which can give a warning when a person's individual energy balance is out of order, thus preventing the user from generating health problems (Figure 14). The mental component in the form of stress is a highly individual component in a human body and mind, where individualised technology will help to collect more objective data. Based on the data collected so far, we propose that the continuous monitoring of individual energy balance and recovery might be a predictor of specific health problems – more specifically burnout – and generate an early warning to prevent them (Kansoun et al., 2019; Selye, 1956). While more large-scale research is needed to scientifically prove and underpin these findings, they still serve to demonstrate the direction in which direction modern technology might help individual users to self-manage their health and provide quantitative and objectively measured information to professional health workers. The technology remains a support tool, however, and will not replace professional health workers. The health of the body and the mind is a far too complex, individual and time-varying process to allow algorithms to take decisions. Technology remains a support when taking appropriate decisions, helping individuals and professionals with real data and facts in a more efficient way.

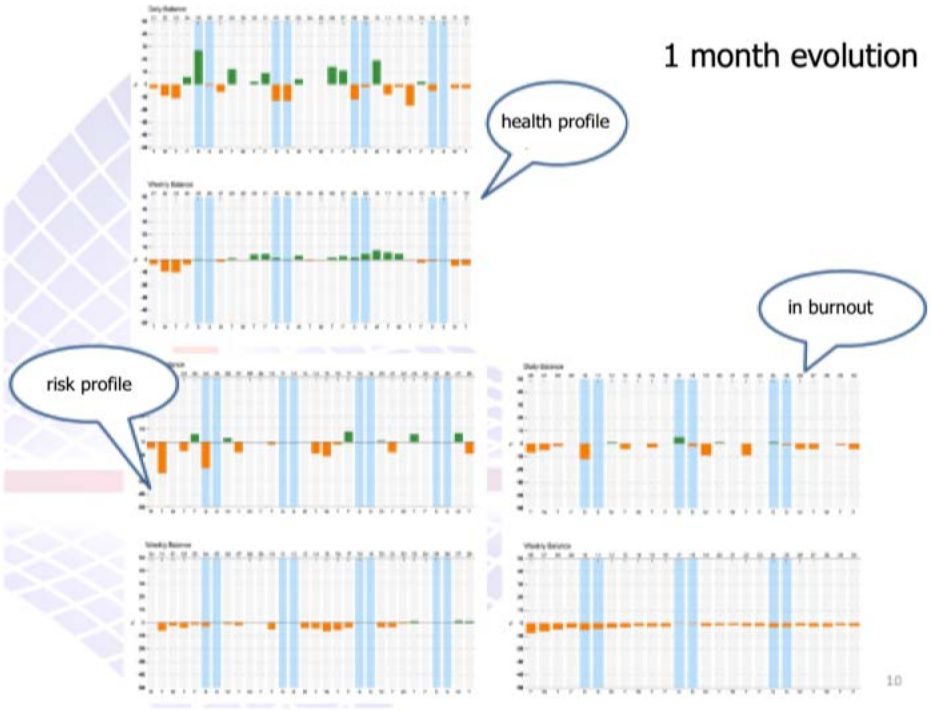

Figure 14: stress/recovery profiles warning for depression or burnout, measured and analysed by an accurate watch combined with an individualised algorithm

A second application of this technology in the world of sports shows how far it has already evolved today. A Formula 1 racing driver can be monitored using technology that calculates the metabolic energy used for mental focus (Figure 15). By relating the real-time measured mental energy component to sector times, the system is able to calculate the kind of mental focus the driver needs to maintain for fast laps. This is the so called 'eustress zone', in which optimal performance takes place (Selye, 1956). The team in the pits can follow when the driver has decided to take over, which always drives him into the 'distress zone' due to the related risk. As soon as the risk is gone (please check the video), the stress is gone. But then the system detects that the driver is pushing himself into the distress zone again because he wants a fast lap and the system gives an early warning for predictive error. The braking error follows. This demonstrates that fully-automated, individualised algorithms can have added value in complex and fast processes such as e.g. Formula 1 driving.

Figure 15: real-time prediction of driving mistake for race driver

E. EVOLUTIONS IN THE HEALTHCARE SYSTEM

It is evident that new technology is able to offer a wide range of possibilities for monitoring humans in a system that aims to keep them healthy, using a preventive approach in preference to using tests when a person is already sick. The possibilities created by wearable technology combined with wireless networks in health applications have been described extensively (Weinstein et al., 2014; Fiordelli et al., 2013; Van de Ven et al., 2015; Vuong et al., 2013). We believe that continuous and individualised monitoring technology will generate objectively measured data and relevant information for (self-)management, and support professionals to be efficient in a preventive healthcare system. Other contributions in this position paper refer to preventive medicine as well. In Part II, Medical Applications, the wearable technology will be approached from a number of medical applications or fields. Moreover, it will be obvious that current systems – e.g. with a standard healthcheck visit to the doctor once a year, during which blood pressure and weight are measured – cannot compete with the systems that will emerge from the use of new technology.

However, we also exercise caution. Some reservations and careful thinking will be necessary, nevertheless, to implement this technology and thereby create efficient healthcare systems. First, we should exercise caution in using the technology. A recent study that compared 89 wearables demonstrated that most were in fact gadgets and that only 2% had been validated independently against a serious gold standard. In addition, most wearables are not yet accurate and are not based upon scientific evidence.

Second, technology is simply a tool and not a solution. Technology is a support to individuals and professionals, but it will not replace healthcare providers. The process is simply too complex. Technology will provide more quantitative information and help those involved to achieve a faster and more precise diagnosis and treatment schedule. Indeed, it can also assist health workers to improve their personal stress/recovery and work/life balance.

Finally, there is a clear need for collaboration across and between disciplines. It is sad that so many professionals and experts do not really collaborate with those working in other disciplines, especially when so much money is used in research projects and in the healthcare system. The potential of the new technology as a support tool will be developed and exploited by those who collaborate across disciplines, and it remains to be seen whether those who fail to collaborate will remain competitive in the healthcare system of the future. This position paper and the interdisciplinary discussions at Metaforum that preceded these articles can certainly be seen as an example on how to proceed.

PART II: MEDICAL APPLICATIONS

4. FROM DATA TO SMART DIAGNOSTICS: CASE STUDIES

Notwithstanding the challenges that have been described in the previous chapters, the number of available medical applications that offer a clear clinical added value is increasing. This chapter discusses three leading medical applications in which wearable systems together with powerful signal processing algorithms can have a significant impact. These applications relate to epilepsy monitoring, sleep monitoring at home, and monitoring functional capacity in rheumatology. And for each example, DHT is set against the relevant gold standard.

A. EPILEPSY MONITORING

Epilepsy is a brain disorder characterised by the occurrence of unprovoked seizures. Seizures are synchronous or abnormal neuronal discharges that may affect different regions of the brain (Fisher et al., 2005). Their origin can be related to multiple factors, such as brain injuries, brain tumours, strokes, and genetic factors. In most cases, however, the causes are unknown. According to the World Health Organisation, epilepsy accounts for 0.5% of the global burden of disease; nearly 50 million people worldwide suffer from epilepsy; and about 70% of them can be successfully treated with anti-epileptic drugs (WHO, 2018a). Furthermore, epileptic patients suffer from consequences of their condition, including a higher risk of being involved in accidents and of suffering from so-called 'sudden unexplained death'. In fact, when compared to the general population, their risk of premature death is 2 to 3 times higher (WHO, 2018a). The monitoring and follow-up of patients suffering from epilepsy is thus crucial for improving their quality of life and for the prevention of life-threatening events.

Currently, epilepsy management is based either on long-term video-EEG monitoring or on seizure diaries kept by patients and/or their caregivers. However, these two options have multiple limitations that influence the follow-up and adjustment of therapy on the one hand, and the quality of life of the patients on the other. For video EEG monitoring, which is the accepted gold standard for the detection of epileptic seizures, there are a number of drawbacks. It is very impractical outside the hospital (Schulze-Bonhage et al., 2010), it causes discomfort, and it has high costs associated with it. As to the seizure diaries, moreover, it has been demonstrated that seizures are seriously underreported (Van Paesschen, 2018; Elger & Hoppe, 2018).

To solve the problems of underreporting, discomfort, and costs, multiple studies have focused on the development of wearable systems based on less obtrusive modalities, including ECG, ACM, electromyography (EMG), and electro dermal activity (EDA). For instance, many algorithms have been developed to analyse the changes caused by epileptic seizures in both the morphology of the ECG signal (Varon et al., 2015a; Zijlmans et al., 2002) and the heart rate variability (HRV) (Leutmezer et al., 2003; De Cooman et al., 2017a). As a result, about 80% of the epileptic seizures involving motor activity can presently be detected from the ECG, which is better than self-reporting. However, this is still only 80%, and these detections include on average 1.9 false alarms per hour (De Cooman et al., 2017a), mainly due to unwanted artefacts in the recording. It is clear that further improvement in the processing of these signals is still needed, especially in artefact detection. In this context, context-aware algorithms adapting artefact and event detection to the changing daily activity of the patient could be very promising for improving event recognition while removing irrelevant artefacts in every given circumstance.

Another way of improving results is by not only looking at one modality, namely the ECG, but by using a multimodal approach, as demonstrated in De Cooman et al., 2018. After evaluating a combination of ECG, ACM and EMG, the authors demonstrated that the false alarm rate could be reduced by 75% while still detecting about 90% of the seizures. In fact, these results were achieved by means of an algorithm that combines ACM data with the HRV derived from the ECG, which are signals that can be easily recorded in an ambulatory setting. Bearing

this in mind, many of the hardware technologies currently on the market could potentially be used for this purpose.

Despite significant improvements achieved with multimodal systems, many challenges still need to be tackled before they can be used to monitor epilepsy in a reliable way. For instance, these systems often detect sudden changes in either HRV and/or limb activity that can be linked to the occurrence of a seizure. Nevertheless, these changes depend on the seizure type and they can vary from patient to patient. In fact, some seizures (e.g. absence seizures, during which a patient has a epileptic insult causing him/her to physically 'freeze' and dissociate from their surroundings) might not even have an effect on HRV nor on limb activity, which make it impossible to detect them using any modality other than EEG (O'Regan & Brown, 2005). Moreover, seizures with motoric involvement do not always manifest in the same way. During temporal lobe seizures, for example, patients might lose control of both hands or lose consciousness, while during so-called tonic-clonic seizures, patients lose total control of their bodies. Therefore, detection systems must be tailored to each type of epilepsy and each patient in particular. To do so, it is important to learn which sensor is useful for each patient, depending on the seizure manifestation and the type of epilepsy. At this point, the aim is to find a minimal set of sensors needed to detect the seizures accurately without compromising the quality of life of the patient.

Another challenge facing seizure detection systems is that changes produced in the different modalities vary from patient to patient. Temporal lobe seizures often produce changes in HRV, but these changes are conditioned by both the cardiac health and the maximum heart rate of each patient (De Cooman et al., 2017a). With this in mind, De Cooman et al. (2017b) proposed an algorithm based on transfer learning, which adapts the detection system to patient-specific requirements. This method requires a minimal amount of seizures recorded from the patient to retrain the original patient-independent system and make it more patient-specific. This algorithm, based solely on the ECG signal, achieves similar results to those obtained with the multimodal approach. Therefore, it is expected that transfer learning applied to the aforementioned multimodal algorithm could improve performance. This is a topic of ongoing research.

Broadly speaking, context-aware algorithms based on less obtrusive sensors have the potential to bring the management of epilepsy one step closer to a home environment. This will allow the monitoring of epilepsy patients in an ambulatory setting while using low-cost systems. Not only costs will be reduced, but also seizure logging will be improved, which in turn will have a positive impact on the follow-up of patients suffering from epilepsy.

B. SLEEP MONITORING AT HOME

Sleep is a complex process that takes up to one-third of a lifetime and is essential for maintaining wellbeing and overall health (Mancia, 1993). Despite its importance, a significant portion of the population worldwide is not getting the necessary amount of sleep. Reasons for this include the current demands of society and multiple sleep disorders like insomnia, sleep apnea, hypersomnolence (excessive level of sleeping), and parasomnias (Sateia, 2014). Moreover, sleep deprivation has been strongly associated with reductions in cognitive and behavioural performance, depression, memory loss, and cardiovascular diseases. Therefore, it is crucial to identify sleep problems at an early stage, before overall health is compromised in an irreversible way.

Currently, sleep disorders are diagnosed using polysomnography (PSG), which is the gold-standard sleep test usually recorded in a sleep laboratory (Berry et al., 2007). This test, shown in Figure 16, includes the overnight recording of, among other things, EEG, ECG, respiratory effort measured on the chest and abdomen, and blood oxygen saturation (SaO_2). Sleep experts visually inspect these signals in order to annotate the different sleep stages (e.g., rapid eye movement-REM, or nonREM) or events related to sleep disorders. Although PSG is the most powerful tool in sleep medicine, it requires overnight hospitalisation, costly sleep centre facilities and sleep

experts, and the use of instrumentation that might interfere with the normal sleep pattern. For these reasons, many studies have focused on the development of unobtrusive technologies that can be used at home (Figure 16, right) and that can monitor sleep during more than one single night. Here, the aim is to improve clinical practice of sleep medicine and diagnose sleep disorders at an early stage in the home (Redmond et al., 2007).

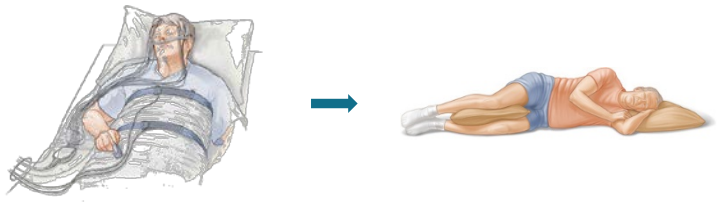

Figure 16: progression of sleep monitoring, from hospital PSG (left) to a home environment (right)

One signal modality that has been considered for monitoring sleep in a home environment is ACM. It is currently recorded in state-of-the-art wrist-worn devices and it has been proven to be useful in the monitoring of sleep in healthy adults (Littner et al., 2003). However, its accuracy in the diagnosis of sleep disorders remains a challenge (Sadeh, 20011). Although it is not ideal for the detection of sleep disorders, ACM is potentially useful for the detection of sleep and wake periods and for the identification of movements that can contaminate other signals like the ECG (Varon & Van Huffel, 2017).

A different modality to monitor sleep is the ECG. It has been shown that thanks to powerful signal processing algorithms, the ECG can be used to extract both cardiac and respiratory information during sleep (Varon et al., 2015b; Widjaja et al., 2012). As a result, only one modality is needed to assess the functional efficacy of the cardiorespiratory system, which changes during sleep and is deeply compromised by sleep disorders. As can be seen, wearable modalities such as ACM and ECG carry valuable diagnostic information for sleep monitoring. Hence, they can be easily implemented in 'off-body' or unobtrusive sleep monitoring systems (Redmond et al., 2007; Willemen et al., 2014; Penzel et al., 2003; Varon & Van Huffel, 2017). In this context, algorithms that can deal with multimodality in a home environment are needed. Moreover, wearables easily enable recording during multiple consecutive nights, which is expected to improve assessment of sleep quality, and better identify any possible sleep disorder.

C. MONITORING FUNCTIONAL CAPACITY IN RHEUMATOLOGY

Chronic musculoskeletal conditions (cMSCs) are important afflictions in the field of Rheumatology. They pose a heavy and ever-increasing burden on society, due to the impact of ageing populations and changing lifestyles. Among cMSCs, low back pain is highly prevalent, affecting up to 33% of the population and influencing their labour activity and wellbeing. Moreover, many cases are never fully resolved and only about 10% have a concrete pathological cause (Woolf & Pfleger; 2003).

Typically characterised by inflammatory back pain, spondyloarthritis is among the better researched cMSCs. Diagnosis and treatment are often based on disease activity, which can only be judged by clinical investigations in the hospital. Indicators include, among others, the presence of the HLA-B27 antigen, MRI imagery, the level of C-reactive protein (CRP) and the erythrocyte sedimentation rate (CRP) (Taurog et al., 2010). Hence, treatment mostly focuses on reducing the impact of the symptoms and the use of the most effective anti-inflammatory drugs. However, physical therapy is also part of the treatment, positively influencing the disease's evolution (Van Tubergen et al., 2001). The latter shifts the point of view to functional capacity, that is, "the ability of a patient to perform a certain task" (WHO, 2002), which is particularly important when deciding whether a patient is still able to work.

This functional capacity can be judged in several ways. Current practice involves the use of (subjective) patient-reported questionnaires, such as the Bath Ankylosing Spondylitis Functional Index (BASFI) (Calin et al., 1994). Alternatively, the capacity can be derived objectively from performance-based tests in which, for example, the duration of specific activities, measured with a hand-held chronometer, is used as a marker (Van Weely et al., 2012).

Wearable sensors offer new perspectives: they allow for objective quantification and remote monitoring. Most often, they combine an accelerometer, gyroscope and magnetometer in one inertial measurement unit. Several such units can be used on various body locations to measure physical activity (Bao & Intille, 2004).

The easiest applications of activity monitoring restrict themselves to measuring energy expenditure (Allet et al., 2010; Altini et al., 2015) or, equivalently, sedentarity (Semanik et al., 2015), to provide an overall impression of the physical activity of a subject or patient over a longer period of time. Similar approaches have been used to estimate the activity level of patients with rheumatoid arthritis, among other things (Fortune et al., 2011). An application in veterinary medicine has been discussed in chapter 3. This activity level can subsequently be coupled with currently-used scoring systems such as the Yale Physical Activity Survey (Semanik et al., 2011). However, applications can also go beyond a general estimation and focus on specific exercises or movements. For example, the abnormal gait of patients with rheumatoid arthritis has already been assessed using the wearable sensors available in common smartphones (Yamada et al., 2012). Also, commercial solutions using two inertial units are already available for assistance in movement therapy targeting the lower spine (Bauer et al., 2011).

Other approaches do not rely on a single activity or a general activity level, but try to combine available approaches in activity recognition and assessment to provide a scoring system, akin to the BASFI questionnaire. With this aim, a series of informative activities, part of the BASFI list, have been selected and incorporated into a protocol that can easily be performed in the home environment. The separate activities can be recognised and activity parameters can be extracted (Billiet et al., 2016). These can be used as intermediate parameters for the follow-up of the disease's progression in between hospital visits.

Finally, it is important that the measures referred to above be incorporated into an overarching system as part of a new digital health paradigm (Kataria & Ravindran, 2018). This involves a distributed ecosphere of personalised and assisted care, mobile health applications, remote monitoring, predictive analytics and lifestyle modifications, all with respect for the patient's privacy.

5. USING WEARABLES AND MOBILE TECHNOLOGIES TO SUPPORT HEALTH BEHAVIOUR CHANGE: OPPORTUNITIES AND CHALLENGES

One area in which the application of wearable technology at once holds a high promise of access but is still fraught with challenges, is health behaviour change. This chapter raises the question whether continuous monitoring can lead to the development of new clinical practices, such as Just-In-Time Adaptive Interventions (JITAIs). Here as in other chapters, issues of personalised medicine and therapy extending beyond the clinical setting (see also chapter 6 on ESM and mental health) are addressed, and new concepts (e.g. JITAIs) are introduced.

A. INTRODUCTION TO HEALTH BEHAVIOUR CHANGE

Noncommunicable diseases (NCDs) are currently the major source of disease burden and premature death worldwide (Suhrcke et al., 2006; Mathers et al., 2003; Nugent et al., 2018). In Belgium, cancer, cardiovascular and respiratory diseases are the three major causes of death and were responsible for about two thirds of the deaths in 2015 (www.statbel.fgov.be/nl/themas/bevolking/sterfte-en-levensverwachting). As noncommunicable diseases are often chronic, they also result in many years of living in ill health, disability and with an impaired quality of life.

Type II diabetes, cancer, cardiovascular and respiratory diseases qualify as 'lifestyle diseases', because a set of changeable behaviours – lack of physical activity, an unhealthy diet pattern, smoking and harmful alcohol use – represent major and shared underlying determinants. Estimates for the US indicate that 40% of premature deaths are due to unhealthy behavioural patterns, thereby greatly exceeding the proportional contributions of other factors, including genetic predisposition, social circumstances and issues related to healthcare (Schroeder, 2007).

These illnesses impose a tremendous economic cost and contribute to steadily growing and untenable health expenses, which now exceed 10% of the gross national product in many Western countries. Last but not least, NCDs are known to enlarge inequity within and between countries, as they are more prevalent in groups with a low economic status and often impose financial difficulties, even for those with insurance coverage (Nugent et al., 2018). It obviously follows – and consensus exists – that a major strategy to improve health in the general population would be to change unhealthy into healthy behaviours (e.g., Lloyd-Jones et al., 2010). As an example, the elimination of physical inactivity would eradicate between 6% and 10% of the major NCDs of coronary heart disease (CHD), type II diabetes, and breast and colon cancers, and increase life expectancy (Lee et al., 2012).

However, behaviour change as a way to prevent lifestyle diseases faces major challenges at various levels. At the societal level, a considerable social gradient exists in many health behaviours. Health promotion interventions often fail to reach or impact on the most vulnerable groups and as such carry the risk of contributing to inequity in a society. This may well be the case for newer types of intervention, implementing wearable or mobile technologies to facilitate healthy behaviours. In addition, although a traditional focus of health promotion in many countries is to structurally organize health education, more recent insights point out that this is far from sufficient to improve health. Ecological models on health promotion have pointed out that it is equally – if not more – important to coordinate the creation of political, economic, social and physical environments that support healthy behaviours and discourage unhealthy, unwanted behaviours (Sallis et al., 2015). A challenge in this respect is that political and economic interests often conflict in the short term with health benefits in the longer term. For example, although taxing unhealthy products is an effective preventive intervention that does not increase inequity (Sassi et al., 2018), politicians can be reluctant to introduce such an unpopular measure because of its unpleasant short-term consequence for the voters.

At the level of the individual, many of us have personally experienced and will therefore easily recognize that turning a habitual, unhealthy behaviour into a healthy one is hard to achieve and even more difficult to maintain. A major reason for this is that knowledge about what is good for you (health education approach) is rarely sufficient to change and maintain new behaviours successfully. No matter how sincere our intentions and plans – e.g. new year's resolutions – they will only influence behaviour if they are remembered, can be implemented, and generate sufficient motivation *at the relevant moment* to overcome competing wants and needs (Marteau et al., 2011). Although we like to think of ourselves as rational and in control of ourselves, many behaviours occur rather habitually and are largely driven by immediate emotional or environmental triggers and the power of immediate pleasures or benefits. Psychologists and health behaviour counsellors can offer help with the endeavour to adopt and maintain more healthy behaviours, but they are not structurally imbedded in our healthcare system. Individual face-to-face and, more recently, online coaching typically applies a range of theory and evidence-based behaviour change techniques, which can be tailored to a specific person to successfully support behaviour change. However, an inherent risk remains that the techniques and strategies learned are not remembered or applied at the relevant moment in the person's natural environment. That is, what is learned sometimes fails to translate in real life situations with an increased risk of engaging in the unwanted, unhealthy behaviour.

B. OPPORTUNITIES FOR USING WEARABLES AND MOBILE TECHNOLOGIES TO SUPPORT BEHAVIOUR CHANGE

Current models of behaviour change based only on face-to-face visits reduce our ability to acquire an accurate understanding of the antecedents and consequences of behaviour and to intervene at moments when patients most need help (Pagoto & Bennett, 2013). It is exactly here that wearables and mobile technologies may offer an interesting opportunity, as they facilitate the continuous monitoring of internal states and external environments to detect risky situations in real-time (Spruijt-Metz et al., 2015). Such information allows us to develop so-called Just-in-Time Adaptive Interventions (JITAIs), which aim to provide the right type and amount of support in a person's natural environment, at the right and most relevant time and location, by adapting to an individual's changing internal and contextual state (Nahum-Shani et al., 2017). Several continuous information sources (sensors, self-reporting, GPS, ...) and computer algorithms can be used to decide real time which intervention component is most appropriate at a given moment. As a result, appropriate support can be provided when it is most beneficial. This will likely lead to improved adoption and maintenance of the health behaviour in question (Nahum-Shani et al., 2017). As an example, a personalised algorithm might be developed to predict when an individual is about to experience a strong craving to smoke. For person X, this may be the case in the afternoon, when stress levels are on the rise and when the person is approaching a location where he or she has smoked frequently in the past. Based on such predictions, intervention components or prompts can be provided on how to avoid or deal with the upcoming situation, even before the person is aware of the risk of a lapse. A prompt may be given to take another route or to perform a short relaxation exercise; a suggestion can be made to distract oneself from the upcoming craving with another engaging activity; or, feelings of anticipated regret if one were to violate one's intention to abstain from tobacco can be activated. Microrandomised trials offer a methodology to model the causal effects of different intervention components, as well as time-varying moderation of such effects. As such, they allow us to empirically determine which intervention component is most effective in a given state for a specific person at a certain time. The generated knowledge from such trials can be used to create decision rules for when to offer which intervention component and as such facilitates personalised, high-precision, just-in-time interventions (Klasnja et al., 2015; Tewari & Murphy, 2015).

Although some studies have started to design and investigate personalised JITAIs that implement wearable sensors in the context of health behaviour change (e.g., Smith et al., 2017), we are still at the stage of infancy and promise. As an example, a promising JITAI was developed to encourage adults to take regular activity breaks from prolonged sitting (Arrogi et al., 2019). A persuasive smartphone application, called stAPP, was designed by

a multidisciplinary team of behavioural and exercise scientists, health experts, computer scientists, app designers and engineers (Arrogi et al., 2019). The application was designed to stimulate users to regularly interrupt prolonged sitting behaviour. Tailored and adaptive feedback on the sitting behaviour of the user was provided by (a) a timer indicating the length of current sitting time, (b) an alarm that alerted the user after 25 minutes of prolonged sitting behaviour and issued a second warning after 30 minutes and (c) a Sedentary Index score visualizing the user's sitting behaviour. Results of a pilot randomised controlled trial showed that stAPP users significantly decreased their total sitting time, the number of prolonged sitting bouts (>30 minutes of sitting) and average duration of prolonged sitting bouts compared to non-users (Arrogi et al., 2019). After the trial, stAPP users also reported a higher intention to interrupt prolonged sitting behaviour in situations that could be identified as barriers.

C. CHALLENGES FOR USING WEARABLES AND MOBILE TECHNOLOGIES TO SUPPORT BEHAVIOUR CHANGE

Despite the opportunities of wearables and mobile technologies to support health behaviour change and maintenance, a substantial gap exists between the available technologies and their effective implementation. Several challenges need to be overcome to bridge the gap. A first problem is that available devices seem to appeal especially to those who may need them least: young, digital-native and healthy persons with a higher income. Furthermore, once purchased and adopted, a majority of these persons stops using them after a while. In other words, it is still unclear whether sufficient reach and uptake are feasible, especially in less young and less rich 'digital immigrants' who are faced with chronic medical conditions or are at a high risk of developing them (Patel, Asch, & Volpp, 2015).

Second, the majority of mobile applications and wearables are quite generic and only a small proportion of these technologies has been proven effective through rigorous, independent validation (Peake et al., 2018). For instance, The application of wearables for sleep monitoring seems very promising (see chapter 4), but only 3 out of 15 wearable devices designed to monitor and promote better sleep were validated against polysomnography, the gold standard for sleep measurement (Peake et al., 2018). As an example, the Fitbit Charge 2™ showed promise in detecting sleep-wake states and sleep stage composition relative to gold standard (de Zambotti, 2018). Nonetheless, many of the existing mobile applications and wearables are rather limited in their potential to change health behaviour as they merely monitor health-relevant variables. For instance, a question that emerges is how well wearable activity trackers align with the evidence-based behaviour change techniques that have been shown to increase physical activity levels. The majority of wearable activity trackers help users to self-monitor their behaviour, obtain feedback on the user's behaviour, and generally support users in goal setting and comparing their behaviour with their goal (Lyons et al., 2014). However, techniques related to planning and providing instruction are scarce (Mercer et al., 2016). Consequently, wearing such activity trackers may raise awareness, but need not necessarily improve physical activity, as was recently found in a sample of healthy individuals (Thosar et al., 2017).

Third, the design and implementation of many of the available devices and mobile applications often lack a clear basis in psychological theories on behaviour change. It has been argued that typical theories on health behaviour are simply inadequate for capturing the complex dynamics and interactions at play (Smith et al., 2017). So indeed, theoretical development is clearly needed and this is an important challenge. However, new opportunities arise from this at the same time, since wearable technologies that are currently available have the potential to contribute to – and even revolutionise – more dynamic feedback system theories of health behaviour (Patrick et al., 2016: Moller et al., 2017; Riley et al., 2011). For example, a recent study that modelled the coupling between momentary intentions to be physically active and actual subsequent levels of physical activity is particularly promising. Findings showed that intentions were more likely to result in actual behaviour when persons are

in a positive mood (Maher et al., 2017). Such insights may have remained undiscovered without the use of momentary, real-life assessments of actual physical activity and intentions, and can be expected to significantly refine traditional, 'static' social-cognitive theories of health behaviour that have largely failed to solve the intention-behaviour gap.

Fourth, although promising, another open question is whether the use of wearables in digital, mobile interventions is equally or more efficacious than traditional face-to-face health behavioural interventions. Demonstrating this is a challenge itself, since traditional RCT approaches are extremely slow and conflict with the rapid technical developments. In other words, by the time an RCT is completed, a device or the platform used is likely to be outdated. Alternative approaches and rapid research designs to evaluate digital interventions have been recommended, but are far from being fully implemented (Murray et al., 2016; Patrick, et al., 2016; Pham et al., 2016). As an example, McCallum et al. (2018) reviewed 111 studies investigating the impact of smartphone applications and wearables designed to improve physical activity. From the 111 studies included, 55% were RCTs, but only two studies used rapid research designs (e.g., single-case designs). Last but not least, many of the available wearable devices and mobile applications focus on single health behaviours. Apart from the potential of these digital tools to modify health behaviour successfully, previous research also demonstrated that multiple lifestyle behaviour interventions produce greater reductions in the risk of poor health than interventions that target a single behaviour (Prochaska & Prochaska, 2010). For example, having both a poor diet and being physically inactive greatly increases the likelihood of obesity, diabetes, cancer, and cardiovascular disease. Thus, interventions that target both behaviours have the potential to make meaningful contributions to public health (Sweet & Fortier, 2010). As proposed by Pagoto & Bennett (2013), integrative health promotion platforms can be created that integrate data collected via multiple mobile applications. Nonetheless, future research is needed on the optimal number and combination of mobile applications, behaviour change techniques, and the level of user contact needed to maximize user engagement and intervention efficacy.

The points raised above clearly illustrate that in the endeavour to develop JITAIs with wearable sensors and mobile technologies that target health behaviours, a multidisciplinary approach at the intersection of engineering, psychology, behavioural medicine and computational modelling is warranted. Such an approach has the potential to advance each of the respective fields, and may trigger a paradigm shift, especially in the fields of psychology and medicine.

6. MEASURING AND MODULATING MENTAL HEALTH IN DAILY LIFE

Experiences emerge in the realm of everyday life, often in interaction with contextual factors. There is a growing awareness in both psychology and psychiatry that the study of experiences in the context of everyday life may provide a powerful and necessary addition to more conventional research approaches (Mehl & Conner, 2012). Studies are increasingly using techniques such as experience sampling methodology (ESM) (Hektner et al., 2007; Myin-Germeys et al., 2009) or ecological momentary assessment (EMA) (Stone & Shiffman, 1994) to study experiences, including psychopathology, in daily life.

ESM is a structured self-reporting diary technique assessing mood, symptoms, context and appraisals thereof as they occur in daily life (Mehl & Conner, 2012; Myin-Germeys et al., 2009). It typically requires participants to complete a momentary questionnaire several times a day over a number of days. This momentary questionnaire was originally presented for the most part on paper, but today it involves an app that signals participants when to answer a questionnaire, thus representing an active form of remote monitoring. The ESM questionnaires either have to be filled out when specific events occur (i.e. event-sampling) or at specific moments in time (i.e. time-sampling). Most typically, a random sampling design is chosen in which participants fill out the questionnaires at random times over a day and do so for several days. Although more methodological research is needed to identify the ideal design, studies typically sample on 5 to 10 times a day for 5 to 10 days in a row. The ESM thus provides a very rich picture of the individual with often over 40 to 50 reports per individual.

ESM is rooted in ecological psychology, which states that behaviour is radically situated, i.e. it can only be understood in relation to the context in which it occurs (Barker, 1968). In order to fully understand experience and behaviour, they need to be investigated in the real-world context, outside the laboratory. The use of ESM to investigate experiences within, and in interaction with, the real-world context is also consistent with a more recent emphasis on embodiment and embeddedness in the cognitive sciences (Shapiro, 2014). This approach claims that "the way humans perceive, think and act is determined by the kinds of bodies they have and the kind of actions they perform or are capable of" (Myin & Van Eemeren, in press). Therefore, in order to understand or explain experiences, one must examine them in interaction with the context. ESM directly addresses this in that it allows us to study the actual experience as it occurs in everyday environments, rather than assessing people's self-reflections on who they are or how they usually behave.

As experience and behaviour are at the core of mental health research, ESM was quickly adopted by mental health researchers in this field (Myin-Germeys et al., 2009). In addition to its benefits in terms of examining experience and behaviour in interaction with the real-life context, ESM also allows us to study these in the moment, overcoming the problem of retrospective recall bias, and prospectively, allowing us to investigate temporal variability and associations. ESM may therefore fundamentally strengthen the behavioural study of mental health problems and contribute to a contextual approach to personalised medicine in psychiatry.

A. MEASURING MENTAL HEALTH AND MENTAL HEALTH PROBLEMS

How can zooming in on the micro-level of experience and behaviour using ESM help improve our understanding of the phenomenology and aetiology of mental health and mental health problems? First of all, it may shed an alternative light on our insight into the nature of mental health problems, which to date is still fairly limited, partly due to the biases introduced by the retrospective recall of symptoms. ESM addresses this issue by capturing symptoms as they occur. Indeed, studies that compared retrospective and ESM assessment of symptoms reported that the former assessment tends to under- or overestimate depressive symptoms in patients with depression (Ben-Zeev & Young, 2010). Besides providing a more accurate assessment, ESM may be instrumental for obtaining a deeper understanding of how symptoms unfold in daily life over time. A good example is the study of anhedonia, which is a symptom that can occur in several psychiatric disorders such as depression and

psychotic disorder, a mental state in which patients lose touch with reality, often suffering from hallucinations and delusions (Strauss & Cohen, 2017). Anhedonia is generally described as a diminished capacity to experience pleasure. However, what does this mean for our experience and behaviour in daily life? A decreased level of positive emotions in daily life – which has been found in some studies in patients with psychosis (Oorschot et al., 2013; Myin-Germeys et al., 2000) – may reflect a diminished capacity to experience pleasure. Nevertheless, decreased levels of positive emotions may also result from patients' lives being less enjoyable. Indeed, patients with psychosis do report, on average, a lower number of pleasant events in their daily life than healthy controls (Oorschot et al., 2013). In order to disentangle this, positive emotions have been examined at moments when people do report pleasant events. ESM research in individuals with psychosis revealed an intact ability to generate positive emotions upon experiencing pleasant events in daily life (Heininga, 2017), which does not support the widely held assumption that anhedonia reflects a general incapacity to experience pleasure. What then does anhedonia relate to? Gard et al. (2014) distinguished experiencing positive affect in the moment (consummatory pleasure) from pleasure related to future activities (anticipatory pleasure), and found the latter to be particularly reduced in patients with psychosis. Similarly, patients with psychosis and students with social anhedonia (assessed with observer-rated measures) reported higher levels of positive emotions when they were in the company of other people, compared to when they were alone, suggesting consummatory pleasure in social situations. Both groups, however, spent less time with other people compared to healthy controls, potentially because they do not anticipate that being with others will be pleasant (i.e. lack of anticipatory pleasure) (Oorschot et al., 2013; Brown et al., 2007). The use of ESM in clinical populations has thus contributed to a more fine-grained understanding of what elements contribute to the experience of anhedonia.

Third, many mental disorders are characterised by dynamic fluctuations in emotions. The resolution of traditional self-reporting measures for capturing these fluctuations is limited. Multiple measurements within one person in ESM may help to assess affective variability in more detail, as well as to identify the context in which (mal)adaptive emotion regulation strategies are used (Aldao, 2013). A meta-analysis investigating dynamic fluctuations in emotions showed that lower levels of psychological wellbeing were associated with a greater intensity of emotions, larger moment-to-moment fluctuations, and a slower recovery to the average level of emotional intensity, and this was particularly true for negative affect (Houben et al., 2015). The slower recovery to the average level of emotional intensity possibly reflects inadequate emotion regulation strategies.

Fourth, variability does not only pertain to emotions. Most symptoms observed in patients with severe psychiatric disorders reveal meaningful and widespread variation over time. For example, intensity of visual and auditory hallucinations or delusions is highly variable over time (Oorschot et al., 2012a; Thewissen et al., 2008). Identifying what drives this variation, either internally or contextually, may be very helpful in detecting targets for treatment. At the same time, it may help patients to become aware of their own patterns of behaviour. The longitudinal nature of ESM data makes it particularly suited to examine temporal associations between context, experience and behaviour. It has been shown, for example, that increases in paranoia are preceded by increases in anxiety, reductions in self-esteem and engagement in experiential avoidance (Thewissen et al., 2011; Udachina et al., 2014). Similarly, contextual variables can be taken into account as predictors. Collip et al. (2011) found paranoid thinking to be context-dependent in individuals with low or medium levels of trait paranoia. Paranoid thoughts increased when people were in the company of strangers. Yet, for those with high levels of trait paranoia, momentary paranoia became autonomous and independent of social reality. Importantly, these patterns of association may differ substantially within persons. Our group examined the individual data of 64 persons with psychotic disorder and found clear interindividual differences in the temporal order of mood and paranoia, with findings for each case deviating from the overall group findings (Oorschot et al., 2012b). ESM is highly attuned to individual patterns of association, which may lead to person-tailored psychoeducation and identification of individual targets for treatment, thus providing opportunities for personalised medicine.

Fifth, ESM assessments also provide an opportunity for gaining more insight into activities and social interactions of people in daily life. One study found that patients with psychosis spend more time alone and at home, and are more often inactive when compared to a healthy control sample (Schneider et al., 2017). This was also the case for patients meeting criteria for symptomatic recovery (Oorschot et al., 2012c): despite the reduction of symptoms, they were still more isolated and less engaged in goal-directed activities compared to healthy controls. Another study detected that individuals with psychosis set more pleasure-based and fewer effort-based goals, and, similarly, engage in more pleasurable and less effortful activities throughout their daily lives (Gard et al., 2007).

B. MODULATING MENTAL HEALTH

ESM may not only be instrumental for the assessment of experiences and behaviour in daily life, it also may help assess the effect of treatment and may even be used to implement treatment in real life. As ESM provides a fine-grained picture of mental state and functioning, it may be much more sensitive to capturing change and, thereby, significantly improve assessment of outcomes in studies investigating therapeutic effects of biological, psychological and social interventions in psychiatry (Myin-Germeys et al., 2011). In a study evaluating the effect of a mindfulness intervention in depressed individuals, Moore et al. (2016), reported that ESM measures were much more sensitive to changes in the measurements before and after treatment, particularly for depressive symptoms and mindfulness. One study using an ESM approach in patients with major depressive disorder found clear dose-response effects in increases of positive emotions and enhanced responsiveness to pleasant daily-life activities over 18 weeks of antidepressant treatment, which would have probably remained undetected with classical clinical trial methods (Van Os et al., 2014). Another ESM study on psychosis found different dimensions of delusions changing at different rates over time in response to antipsychotic treatment (So et al., 2014). Another advantage is that ESM's sensitivity to change may allow earlier detection of side effects. One study investigating the association between the dosage of antipsychotic medication and emotions in daily life found significant decreases in positive emotions at a much lower medication dose than was needed for the occurrence of more easily observable side effects, such a extrapyramidal motor symptoms (Lataster et al., 2011).

In recent years, ESM has also been used to deliver treatment in real life. Ecological momentary interventions (EMIs) use mobile devices to deliver treatment in the daily life of patients, thus extending the therapy beyond the clinical setting and into daily life (Myin-Germeys et al., 2016). The content of these interventions is highly variable. Some are developed to augment face-to-face contacts with EMI components, such as the recently developed EMI Acceptance and Commitment in Daily Life, where therapeutic sessions are followed by three days of real-life exercises using an ESM app (Batink et al., 2016; Steinhart et al., in press). An example of a fully automated EMI is FOCUS, which has been specifically developed to provide automated real-time and real-world illness management support for psychosis (Ben-Zeev et al., 2014). Although the field of EMI is still in its early stages, recent systematic reviews suggest a high acceptance and feasibility in individuals with severe mental illness (Myin-Germeys et al., 2016; Menon et al., Z017; Naslund et al., 2015). However, whether these treatments really work and whether they outperform classical treatment, remains to be shown. Some early studies do suggest for example that FOCUS does indeed improve psychotic symptoms, depression and general psychopathology after one month of treatment in a sample of 33 participants with a psychotic disorder (Ben-Zeev et al., 2014). In a randomised clinical trial, however, in which patients were randomly assigned to either FOCUS or to a clinical-based intervention (i.e. Wellness Recovery Action Plan), both treatments showed significant effects on recovery (Ben-Zeev et al., 2018).

C. CONSIDERATIONS AND FUTURE OF ESM RESEARCH

Although there has been a rapidly increasing number of studies using ESM in mental health research, it is also important to critically discuss some limitations. An important consideration is consistency and replicability over studies. There is a large heterogeneity in ESM designs and questionnaires. The field should work towards more standardised approaches in order to facilitate replication.

A further consideration is that ESM data collection is time-intensive and may be associated with assessment burden for participants, which questions whether this method can be used in all populations. However, there is strong evidence in support of the feasibility of using ESM in vulnerable populations, including individuals with (severe) mental health problems (Myin-Germeys et al., 2009), which may be due to the nature of ESM as a structured inquiry about current mental states with clear ecological appeal. Furthermore, numerous researchers have raised the question whether being repeatedly asked about particular experiences may, in fact, induce the said experiences (Myin-Germeys et al., 2009; Palmier-Claus et al., 2011). Measurement reactivity is a key challenge for ESM research, yet it remains an under-researched phenomenon (Wray et al., 2014).

There is immense emerging potential for combining ESM with physical remote monitoring technologies. Combining ESM with wearables assessing, for example, physical activity, heart rate variability or sleep, may provide even richer and more detailed insights at various levels of causality (biological, psychological, social) (Kendler, 2008). Another step will be to include data from context-aware systems using sensor data that automatically provide input on relevant context variables (Burns et al., 2011).

In addition, one of the most important – but also most challenging – next steps will be to bridge the gap between research and clinical care that would allow the implementation of ESM in routine monitoring and outcome measurement in mental health services. ESM has enormous potential to contribute to, and improve upon, clinical care. To date, however, it has not been implemented to any significant degree due to issues related to data safety, data ownership, privacy and consent, access to technology, as well as integration of data management systems across mental health services. More implementation initiatives are needed to bridge this gap.

D. CONCLUSIONS

In summary, we have shown that ESM is an indispensable methodology in psychiatry research. It increases patient empowerment by identifying the individual as the expert of his/her experiences. It adds new insights and additional perspectives to standard approaches, enriches our understanding of psychopathological phenomena and their associated mechanisms, and offers clear opportunities for improving and changing clinical practice.

While a number of challenges remain, using ESM creates the possibility to study and analyse temporal associations in everyday social contexts, as well as tailor treatment to individual needs. It thus offers one of the best opportunities for personalised medicine in the mental health field, both from a research and a clinical perspective.

7. STRESS MONITORING: A WAY TO PREVENT STRESS-RELATED DISORDERS?

For many of the most prevalent and debilitating psychological and psychiatric problems, such as burnout, depression, anxiety disorders, sleeping disorders and substance abuse, stress has been recognised as an important risk factor and long-term, chronic stress in particular has been related to these disadvantageous health outcomes. Also for a number of somatic diseases, such as coronary heart disease and diabetes, chronic stress is assumed to be an important risk factor.

Stress is, of course, a very broad concept. It can refer to external factors that elicit a stress response, such as acute negative life events or chronic exposure to difficult situations. The term can also be used to indicate the stress response itself, i.e. the psychological and/or biological response of a person to stress. The psychological stress-response can be evaluated by asking questions on feelings of anxiety, tension and irritability in response stressors. Widely endorsed scales, such as the Perceived Stress Scale (PSS), have been developed to this purpose (Cohen et al., 1983).

The biological stress response refers to the activation of biological systems that are triggered by stressors. One of these systems is the hypothalamic-pituitary-adrenal (HPA) axis that has been widely studied in relation to vulnerability for psychiatric disorders (for a review, see Claes, 2004). The main hormone resulting from HPA axis activation is cortisol, which can be measured in blood and saliva samples, in order to assess HPA axis activity. Another important part of the biological stress response is the Autonomous Nervous System (ANS). When the ANS is activated in response to stressors, a number of physiological functions will alter. The respiratory rate and heart rate will increase and heart rate variability (HRV), the normal variation in the time interval between heartbeats, will decrease. ANS activation will also lead to increased activity of the sweat glands in the skin, leading to alterations in its electrical properties (electrodermal activity, EDA) and temperature. These changes are induced by the release of hormones such as adrenaline and noradrenaline.

Evidently, the biological stress response developed through evolution and it plays a crucial role in increasing the probability of survival. It prepares the body rapidly for an adequate reaction to stressors by opposing them or seeking shelter (fight or flight response). While adaptive in the short term, a prolonged activation of the biological stress response is thought to be maladaptive, leading to a number of disadvantageous neurobiological and clinical consequences (for a review, see McEwen, 2015).

For these reasons, it seems obvious that careful monitoring of stress, more precisely of the biological stress response, could be a valuable tool for detecting prolonged periods of stress activation, opening the way for timely interventions that decrease stress and reduce the risk of developing stress-related disorders. To this end, the monitoring of ANS activation seems the most feasible way to achieve this goal. The continuous monitoring of psychological aspects of stress is not straightforward, as it requires the individual to fill out questionnaires several times a day for long periods of time. Likewise, the continuous assessment of HPA axis activity is not feasible, as it requires blood or saliva samples and lab analyses. However, measures of ANS activation (such as respiration rate, heart rate, HRV, EDA and skin temperature) can be continuously assessed using smartwear devices, without any burden imposed on the person being monitored. Moreover, the data can be evaluated and fed back in real time, and appropriate interventions can be offered. It is not surprising that many commercial and academic institutions are active in developing such tools. Many devices are already on the market that claim to be able to measure emotional stress and that offer interventions such as short meditation or breathing exercises in real time when stress levels are becoming too high.

While the potential benefits of such an approach in the prevention of stress-related psychiatric and somatic disorders are very substantial, a number of pitfalls need to be considered which the devices that are currently on the market do not address sufficiently. We will not go into the very relevant question of the reliability of ANS

assessment in daily life with wearables, as it is discussed elsewhere in this work (see chapter 1), but assuming that ANS parameters can be measured by wearables with reasonable accuracy, a number of other pitfalls have to be considered.

A. DISCRIMINATING PHYSICAL FROM EMOTIONAL STRESS

ANS activation can be the result of emotional stress, but also of physical effort. Heart rate and breathing rate will increase when people are walking, running or cycling. Evidently, any system that claims to measure emotional (fight or flight) stress through ANS parameters will have to take physical effort into account. Most devices have an accelerometer measuring acceleration in three directions, allowing us to estimate type of movement, number of steps and the expenditure of energy (Henriksen, 2018). This does not completely solve the problem, however. The relationship between physical exercise and changes in heart and breathing rate is highly individual. When a fit person exercises, the pulse and breathing rates rise much less than they do in an unfit person. Furthermore, the recovery time – the time it takes for pulse and breathing rate to return to normal – will be shorter in a fit person. The implication is that wearables aiming at measuring mental stress should be able to correct for physical effort by accounting for the physical condition of the specific individual. Furthermore, ANS activity can be altered by forms of mental stress that are not necessarily unhealthy, such as excitement over your favourite soccer team winning an important match. Again here, the impact of positive versus negative emotional stress on ANS parameters is probably highly personal.

At this stage, more research is needed to determine which ANS parameters are required, and which software algorithms have to be applied to reliably measure negative mental stress (fight or flight stress). Recent studies are encouraging. For example, in one recent study on 201 college students, wearable sensor features, including skin conductance and temperature, reached 78.3% accuracy for classifying students into high or low stress groups and 87% accuracy for classifying high or low mental health groups (Sano et al., 2018). In order to achieve this, a wide set of features was collected, and machine learning techniques were applied.

B. THE DYNAMICS OF UNHEALTHY STRESS

Our stress system is designed to respond acutely to specific stressors and demands, facilitating an adequate behavioural reaction. This means it should be able to do a number of things: react swiftly to stressors that require a behavioural response, modulate the intensity of the response in function of the required action, taper down the stress response rapidly when the stressor has been adequately dealt with, not react to stressors that do not require it, and remain at basal levels whenever this is adequate. This implies that a wearable stress monitoring system that uses cross-sectional data, e.g. a single ANS reaction peak, to warn individuals against excessive stress, will very probably be mistaken. A valid interpretation of ANS data should consider the dynamic nature of ANS activity, accounting for the number of ANS peaks, the tapering down time after individual peaks, the periods spent at basal levels. At this stage our knowledge of which dynamic patterns are to be considered healthy, and which are predictive of stress related psychiatric or somatic disorders, is thin at best. Preliminary evidence seems to suggest that persons with higher levels of anxiety and depression are characterised by a less dynamic response on the part of the stress system. In the SWEET study, Smets et al. (2018) measured psychophysiological scores for a period of five consecutive days in a large cohort of over 1,000 volunteers without obvious psychiatric problems. They found that physiological responses to stress strongly differ among subjects. In general, individuals with a less healthy lifestyle and higher depression, anxiety and stress scores showed a more blunted physiological stress-reactivity (small dynamic range) when compared to persons reporting a healthy lifestyle and low depression and anxiety scores. In a small preliminary study, Schiweck et al. (in preparation) studied the heart rate and HRV response to two consecutive specific stressors, induced in laboratory conditions, in depressed individuals and healthy controls. They reported that heart rate was generally higher, and HRV lower in depressed individuals. Specifically in response to the second stressor, depressed individuals showed less psychophysiological

reactivity. The depressed persons reported the expected *subjective feeling of stress*, but *the physiological signals* did not seem to reflect this. This is compatible with a stress system that might be generally overactive in depression, but less reactive to acute demands. It also indicated some kind of decoupling between subjective stress and physiological arousal in depression. These findings might help to develop a biomarker that can be used to detect a dysregulated stress system in daily life that indicates a developing depression.

C. FROM GENERAL TO INDIVIDUALISED ALGORITHMS

It is clear that the physiological response to stress is highly individual. In order to develop systems that can indicate whether a specific pattern of psychophysiological activation is normal *for a given individual*, or indicative of impending psychopathology, it could be useful to subject individuals first to an individual assessment phase, in which psychophysiological data are validated against psychological measures of stress (anxiety, tension), and where these individuals are tested in basal circumstances, but also after exposure to validated stress tasks. In the large study mentioned above, Smets et al. (2018) applied the Montreal Imaging Stress Task (MIST), a standardised stressor, to assess individual psychophysiological responses, and found a relation between physiological reactions to the MIST and subsequent patterns when measuring during daily-life settings, highlighting the potential of this methodology, in which subject-specific information based on the MIST is transferred for learning ambulant models. This approach is time and labour consuming, and could be restricted to cases for which the validity of the interpretation of wearable data is of high medical relevance, such as individuals with a history of severe stress-related mental disorders.

D. CONCLUSIONS AND OUTLOOK

It should be clear from what we have observed thus far that remote monitoring of psychophysiological features could be an important tool to facilitate the early detection of unhealthy chronic stress, and thereby prevent the occurrence of stress related disorders, such as burnout, depression and anxiety disorders, which are placing such a large burden on our society. On the other hand, it is equally clear that a number of methodological hurdles will still have to be confronted. A number of uncertainties make the use of these approaches for medical purposes (e.g. the prevention of depression) unjustified at this stage. The current application of remote stress monitoring for lifestyle purposes might be ethically less problematic, but it is unclear whether, given the current state of knowledge, it contributes to the actual wellbeing of the users.

Research will have to establish the link between the individual dynamic patterns of stress response and the health status of a person. While this clearly will require more research, there is no good reason to assume that it will be impossible. The technology is increasingly available, and a number of studies have been performed or are underway that will help us to develop better algorithms. To bring the field further, an intense collaboration between engineers and (mental) health professionals will be required.

Once the field is on more solid ground, a series of new questions will arise: will patients accept continuous monitoring? It has been shown that a significant percentage of owners of smart wearables stop using them within six months after purchase (EndeavourPartners, 2017). This might be different when the application of such tools has a clear medical indication, such as the prevention of relapse into depression.

Another intriguing question is whether continuous stress monitoring will not be inclined to make users even more nervous, looking continuously at their smartphones to see how stressed they are, and receiving messages at different points in time to warn them or to offer stress-reducing interventions. This will have to be determined by large studies comparing different ways of immediate versus delayed feedback.

Yet another set of questions about privacy, ownership and liability will need to be answered once the technology evolves into a medical tool. The articles in Part III dwell on the social implications of medical wearables.

Notwithstanding all these domains of uncertainty, it is justified to conclude that remote stress monitoring has the potential to become a major tool to reduce the increasing burden of stress-related mental health problems.

PART III: SOCIAL CONSEQUENCES

In Part II, we looked at the application of digital health technology (DHT) in a number of areas. In Part III, we look at several factors operating on the advancement and introduction of DHT. In chapter 8 such factors are the dream or ideal of patient empowerment on the one hand, and precision medicine on the other, in which DHT would play an important part solving a number of healthcare challenges. There are still hurdles, such as inaccurate data, algorithmic bias, privacy issues, and the consequences of new private actors entering healthcare systems. DHT also challenges patient-centered developments in the care cycle. Chapter 9 explains what patient-centered care is, how it has evolved, who the actors are, and how it would be affected by the introduction of DHT.

8. THE SOCIAL IMPLICATIONS OF DIGITAL HEALTH TECHNOLOGY

"Imagine that in the future, someone seeking medical care meets with a clinician who has a data resource that includes not only her medical history but also her genetic sequence and activity tracker information, as well as data about her housing, water, air quality, and the strength of her social networks. From this data, the clinician would know what diseases she was at risk for before developing any symptoms and would even know which medications would work best if there was disease onset. For some, this scenario is empowering; for others, it's terrifying. Yet, this is the ideal of precision medicine, an emerging approach that aims to capitalize on the growing availability of health data to both deliver better care to individuals and to improve the efficiency of the healthcare system as a whole" (Ferryman & Pitcan, 2018: 5).

In light of our ageing population, spiralling healthcare costs and the rise of chronic diseases, Western policy makers are warmly embracing a new vision of *personalised health* as a way to prevent a healthcare crisis. As part of *precision medicine's* promise to contribute to health outcomes, cost containment and patient empowerment, *digital health technologies* (DHT, e.g., wearables, big data platforms, Electronic Health Records, Artificial Intelligence, and mobile health ['mhealth'] applications) have not only become buzzwords in the tech industry, but have also gained ground in both national and international innovation policy discourses.

With this in mind, the European Union presented the implementation of digital technologies in the healthcare sector as one of its major policy objectives for the future (European Commission, 2018). In 2014, this resulted in the European Commission's launch of a Green Paper on Mobile Health and a staff working document on the existing EU legal framework applicable to lifestyle and wellbeing apps. Work is still underway on European quality frameworks and privacy standards (European Commission, 2014). Although the frontrunner in this area remains the US Food and Drug Administration (FDA) with its Pre-Cert Pilot Program aiming to develop a special regulatory framework for DHT, EU member states like France, Germany, Spain and the UK are trying to keep up by implementing specific guidelines for DHT. In Belgium, the government set aside no less than EUR 3.25 million for the launch of an mhealth pilot project. In view of the promising first results of the project (a decrease in consultations, earlier hospital discharges, improved alignment of medication, and a decrease in emergency visits), the Minister of Public Health recently moved forward by developing an mhealth validation pyramid (De Block, 2018).

Despite DHT being put forward both as a last window of hope for Western healthcare systems as well as a new innovative future for the economy, important social implications of the deluge of health data have been raised, forcing us to dampen down these expectations. By pointing at these emerging social issues, a growing number of social scientific studies are prompting us to consider that this digital health dream might not develop in the ways we expect it to. As such, the full-grown implementation of digital health technologies as an established societal infrastructure or 'new health data eco-system' will depend on the way it enables us to reshape institu-

tions, laws and policies (Lievevrouw & Van Hoyweghen, 2017; Hogle, 2016b). Today, algorithmic biases and numerous legal unclarities are but a few examples of the dissonances that obstruct the full implementation of digital health initiatives in our daily-life healthcare practices.

This chapter aims at providing an overview of the potential social implications that might coincide with recent developments in digital health technologies. How does the discourse on patient empowerment in DHT challenge individual autonomy and the patient/physician relationship? How does the involvement of new private actors in DHT question the public character of our healthcare systems? What are the implications of these technologies for privacy, discrimination, and other mechanisms of classification and social profiling in our contemporary digital societies?

A. DIGITAL HEALTH TECHNOLOGIES, PATIENT EMPOWERMENT AND MEDICAL EXPERTISE

A first cluster of socioethical issues can be situated in the patient empowerment discourse that goes together with big data, precision medicine and mhealth initiatives. It builds on the idea that DHT will enable patients to actively participate in their own healthcare, as opposed to being merely passive actors. As such, the empowerment discourse conceptualises patients as rational consumers, taking responsibility for the management of their own health (Lupton, 2012). In fact, these '*digitally engaged patients'* are already accountable for three billion downloads of health apps worldwide in 2015 (OECD, 2017), ranging from pedometers, diet apps and medication reminders to more advanced mobile-connected glucose pumps, contraction devices and sensor pills. In the case of reminders, for example, receiving a push message from your app to take your medication or to remind you of your doctor's appointment not only has the potential to make your life so much easier, it can also help optimise your care process. Imagine it being possible to swallow a sensor pill that automatically updates your medication diary? With patients tracking their heart rate, sleeping patterns and number of steps on a daily basis, patients themselves acquire a better knowledge than anyone else of their physical condition. Given these promises on empowerment, can we still consider our physician as the only expert on our health? The move towards patient empowerment through DHT clearly challenges the traditional relationship between doctors and patients.

Medical authority is not only challenged by empowered patients, however, it is also challenged by the features of the technology itself (Hogle, 2016a). DHT promises to provide medical practitioners with the necessary tools to help them obtain a more 'holistic' view of their patient. The technology is thus presented as a supporting tool for physicians. However, a recent study comparing the medical diagnoses given by human doctors with the IBM Watson computer resulted in favour of the IBM Watson technology as medical authority (Steadman, 2013). How this will evolve in the future will depend on how the results of these digital health technologies will be interpreted and used in healthcare practices. Will they be considered as merely advisory tools, and as such maintain the medical expertise of the physician? Or will they become instructive and, as such, not only replace the physician's diagnosis but also shape the further understanding of the body, health and illness? What does it mean in terms of medical liability when DHT results that correctly predict health risks are ignored by the doctor?

In line with this, sociologists point to the performative power of DHT algorithms. The latter may well appear neutral at first sight, but the manner in which they are developed is bound up in different power dynamics (Lupton, 2013). For example, who determines '10,000 steps' to be the recommended standard for daily exercise? The increasing sophistication of digital health algorithms poses a risk of making data more opaque. This is especially relevant in the health sector, where accountability is critical in the development of trust. This is all the more pertinent since studies have shown that digital health technologies are often biased and not accurate (Piwek et al., 2016). Since most DHTs target specific patient populations with serious conditions, the lack of accuracy could initiate serious health damage. The recent example of Natural Cycles illustrates the consequences of decisions based on inaccurate health data from a DHT. The app (700,000 users), which uses an algorithm to

determine when women are fertile, became certified in the EU as a form of birth control. In January 2018, it faced with a complaint after being blamed for causing 37 unwanted pregnancies. According to the Södersjukhuset hospital (Stockholm), 37 women visited the hospital for an abortion after becoming pregnant while using the app (Ong, 2018). Even with government approval these validation issues occurred, so what does that say about the quality and safety checks in place today?

Finally, DHT could affect patients' experiences with health and disease. One migh question whether the option to track virtually every aspect of one's life is really worth considering. According to social scientist Lupton (2013), constantly being monitored could also be experienced as a *new set* of obligations. Rather than 'empowering', such digital technologies might also limit our individual autonomy. As such, the practice of metrication through digital health technologies is seen as another tool in the quest to reduce all phenomena, no matter how complex, to numbers, while simultaneously displacing other forms of meaningful expression and lived experience (van Dijck, 2014). Moreover, these digital health initiatives assume 'a rational, emotionally disengaged 'empowered' subject who is motivated and equipped with the economic and cultural capital to engage in self-monitoring and self-care' (Lupton, 2013:262). Given the increasing complexity of data, however, is it fair to place the emphasis on individual responsibility for our health? Also, people with lower levels of income, education and understanding of how to use digital technologies are less likely to engage in them (Lupton, 2017). If policymakers and developers do not account for the impact of socioeconomic differences on its use, DHT could further enforce social inequalities and create new forms of social exclusion.

B. DATA AS A RESOURCE: THE ECONOMIC VALUATION OF DIGITAL HEALTH DATA

The massive generation of digital data by individuals requires both data analytics devices and infrastructures to produce, store and analyse them beyond the remit of medical science. Not only is digital health data increasingly being generated by individuals interacting with consumer devices such as mobile phone apps and wearable devices, the technological tools needed to produce, store and analyse this data increasingly lie beyond the remit of traditional medical science. The digital health data ecosystem is expanding, to include new types of data, new methods for analysing it, and new private actors, such as large consumer technology corporations like Google and Apple. Social scientists refer to this phenomenon as the *Googlisation of Health Research (GHR)*, emerging at the intersection of digital health and digital capitalism (Sharon, 2016). Starting a few years ago with initiatives such as Apple's ResearchKit, Samsung's Simband and Google's Verily and Deepmind, all major consumer technology corporations have moved into the domain of digital healthcare and research. As such, they position themselves as platforms, or 'neutral' mediators between governments, developers, scientists and consumers and facilitators for innovation (van Dijck & Poell, 2018). Next to these investments in technology and infrastructure, the corporations in question have broadened their scope by starting to invest themselves in the organisation of healthcare. Apple, for example, plans to open its own two hospitals on the West Coast of the United States (Farr, 2018). Likewise, the announcement of Amazon, J.P Morgan and Berkshire Hathaway to develop their own health insurance companies resulted in an immediate fall in share value associated with traditional health insurers, distributors, and pharmaceutical companies (Scott, 2018). With tech companies gaining ground in the field of healthcare, the digitalisation of health is not merely about creating predictive and diagnostic tools within the highly-regulated hospital setting, it is also evolving toward the deployment of digital health data as a valuable commodity in a broader digital world.

This economisation of digital health data acquired via DHT raises important concerns on privacy and ownership (OECD, 2017). Digital health data is sensitive personal data that needs to be protected from unauthorised access and unintentional disclosure, requiring the use of effective and proportionate privacy safeguards. The European Union recently adopted a General Data Protection Regulation (GDPR, 2016) aiming to protect European consumers from data misuse and privacy infringements. Such reforms attempt to increase the data subject's privacy options and introduce further controls on data use. However, with the multiplicity of private tech companies

gathering data and collaborating with public healthcare facilities and governments, will existing regulatory initiatives around data protection be sufficient to protect the privacy of individuals (Marelli & Testa, 2018)? Critical scholarship in these contexts points to the limitations of protecting privacy by giving individuals more control over their own data, and of relying on 'notice-and-consent' as cornerstones of online privacy (Purtova, 2018). The massive gathering of health data by tech companies also prompts questions about data ownership. Is data really something that can be 'owned'? Can data be 'stripped off' from the individual? According to Neff and Nafus (2016), digital data should be seen as the result obtained by the developer as well as the user, and thus not as a property. Yet, the conceptualisation of ownership in the context of a data society remains an ongoing discussion for policymakers, which places consumers in an insecure position.

Together with the growing role of tech companies in digital health research and care, the economic valuation of digital health data also results in a growing interest in the said data by sectors outside the traditional medical context. This increasingly blurs the delineation between health and other societal domains. Facebook, for example, recently announced that it was using artificial intelligence to scan posts and live video streams on its social network for signs of possible suicidal thoughts (Singer, 2018). Similarly, Mercedes-Benz is investing in cars as a central health hub, aiming to transform vehicles into a key lifestyle component by connecting them with smart devices. As such, these cars could know whether you are stressed, for example, and could nudge you to take a breath before your next scheduled appointment (Heuer, 2017). What are the underlying interests of these companies to 'nudge' their clients to manage their health? Also, private insurers increasingly see the 'disruptive potential' of digital health technologies and data. An increasing number of car insurance companies offer incentives and reduced fees calculated on the data collected by a small device ('car UBI') that insurance holders have to install in their car and that provides the insurance company with a variety of behaviour-based measures (driving habits, speed, duration, timing, etc.) (Meyers & Van Hoyweghen, 2017). Many people seem to be happy to sacrifice their right to privacy for a reduced insurance fee. Will this also hold for health insurance in the future: reduced fees for those patients who allow the private health insurance company to monitor their life(style)?

Both the fact that digital health data are being used in sectors beyond healthcare, and acquired by companies other than traditional healthcare providers, blurs the delineation between the highly-regulated space of healthcare and other industries (Blasimme et al., 2019; Hogle, 2016a). How will governments regulate this new health space, moving beyond the traditional scope of public healthcare systems?

C. THE INTENSIVE GATHERING OF DIGITAL HEALTH DATA: SOCIETAL SPILLOVER EFFECTS OF PREDICTIVE MODELING

The deluge of data through DHT developments can be used for the classification of individuals both in healthcare as well as in other societal domains. Sociologists point toward the performative power of digital health technologies and data in this process, and the possible socioethical risks of so-called *social profiling/sorting* or "the use of information to create profiles that may have consequences for the way individuals are viewed by players, by consumer marketing groups, and others" (Hogle, 2016b: 423). This process of systematic categorisation of people through DHT algorithms is a form of social profiling that may both introduce new categories of people and illnesses and reinforce old beliefs about social differences (Bowker & Star, 1999). As such, the underlying algorithms of big data predictive technologies could raise potential new issues of algorithmic discrimination in diverse domains of social life (O'Neil, 2016).

Within the context of healthcare, the combination of different forms of digital data is used for *predictive modelling*. This implies that the probable associations ascertained through the combination of medical and non-medical data predict the likely behaviours of individuals and, consequently, create new risk categorisations. These predictive risk scorings are used, for example, for hospital administrative purposes (e.g. physician performance and pay) and are included as such in medical diagnostics. As mentioned in the introduction, a medical

diagnosis is not merely based on one's medical history, but also on predictive data about housing, water, air quality, and one's engagement with social networks. What people share through videos and photos on social media, for example, can give spurious insights into their daily activities, interests and habits. The use of these digital traces to create such predictive scores could have profound social ramifications in terms of social stratification. Predictive risk scoring and classifications could loop back to the original data of individuals, for example, when a patient stratified as a 'health denier' may have that designation entered into her medical record. She may then also be required to use a mobile device to remind her to take her medications. Every iteration of the loop provides more data, which is re-entered into an algorithm that 'learns' more about the person in question and refines risk assignment (Hogle, 2016a). Will people who systematically have delayed bank or tax payments be categorised through predictive risk scoring as 'nonhealthy citizens'? This new way of medical classification through the use of both medical and nonmedical predictive data may also worsen health disparities and lack of access to treatment (Ferryman & Pitcan, 2018). What will be the impact of someone's Facebook and Twitter feeds on his/her access to healthcare? Will these algorithms correct for socioeconomic and ethnic biases? What if you do not want to consent to the use of this data? How will this affect your access to healthcare in the future?

Social profiling based on these kinds of digital data becomes even more delicate when the said data is used to categorize for purposes other than health-related research. As such, behaviour profiles detected through predictive algorithms could be used to enact rationing decisions in healthcare (O'Doherty et al., 2016). In insurance, medical data and lifestyle data are already used by health and car insurers to identify noncompliant consumers with a higher risk and cost. As such, these corporations use predictive data to stratify individuals into new types of risk classifications for loans or insurance premiums in order to ensure effective allocation of limited healthcare resources.

Digital profiles raise important new discriminatory issues (O'Neil, 2016). Imagine the genetic condition of your partner affecting your mortgage negotiation with your bank? Since big data analysis is driven by associative rather than causative relations, this could have serious consequences if such decisions were to be based solely on automated assumptions (Hogle, 2016b; Montgomery et al., 2017). Also, who determines the behaviour that should be considered high risk? What underlying power dynamics are at stake here? O'Doherty et al. (2016) envision that with the increasing pressure on the financial sustainability of Western healthcare systems this could evolve towards the adoption of a 'merit-based allocation of health resources', meaning that those considered to be more responsible (according to moral norms) about their health will be rewarded with greater access to health resources.

The intensive gathering of predictive health, social and behavioural data is not only a potential asset for insurance and financial companies, it is also a potential asset for public governance that can be deployed, for example, for the purposes of civil law suits or border security and immigration (O'Doherty et al., 2016). In this way, DHT could become a disciplinary tool for techniques of *dataveillance* (van Dijck & Poell, 2018). The data acquired from 'nonmedical' and conventional medical sources can be combined and repurposed from original contexts and uses, and made available to serve a variety of healthcare, marketing, and governance needs. As a result, traditional flows of information between patients, physicians, providers, payers, and government entities are rerouted, linking the lab to the clinic and to the spaces where people live and work, and vice versa (Hogle, 2016a).

D. CONCLUSION

Along with the promise of DHT to contribute to health outcomes, cost-containment and patient empowerment, social scientists are exploring the important social implications of the deluge of digital health data in our societies. This chapter illustrates some of the socioethical issues of DTH: the changing patient/doctor relationship due to patient empowerment, the implications of the economic valuation of health data, and the effects of social

profiling both in the context of healthcare research as well as for other purposes ('secondary use of data'). Irrespective of the original intentions of the builders and the expressed purposes of digital health platforms, the social implications for which such data collections might be employed are often *unforeseen and unintended*. But it is precisely these unforeseen uses of the increased availability of health data collections that we would like to highlight, as the proliferation of this detailed and highly personal information can have consequences on a broader *societal level* in terms of new forms of social classification and loops.

Both European and national policymakers are developing policy guidelines and regulations to protect European citizens from the possible negative effects of the emerging digital data revolution. The EU GDPR is trying to anticipate the vulnerability of health data by classifying it as 'sensitive' and granting it a higher level of protection. Yet, the impact of these regulations remains to be evaluated. In the context of healthcare, one of the possible pitfalls lies in the interpretation of 'quasi-health data' (e.g. daily diet, sports habits, sleep–wake schedule, alcohol consumption, etc.). Depending on whether the GDPR considers this data as sensitive, the special protection will potentially not be applicable to all DHT (Malgieri & Comandé, 2017).

How can we differentiate between types of data in a world in which health data is used for non-medical purposes and social data could serve as evidence for providing health diagnostics? (Montgomery et al., 2017). As such, the unclear protection of 'health data' has resulted in what we would call 'health data protection grey zones', which will have to be clarified through European case law. The uncertainty for developers, local policymakers and consumers/patients that accompanies this could harm individual privacy. We already experienced the first harms outside the context of healthcare with the recent Facebook/Cambridge Analytica scandal, where personal information was used without proper consent, in addition to the Wannacry cyberattacks, where NHS ICT infrastructures were hacked because of a lack of proper data protection (Powles & Hodson, 2017).

Moreover, while 'privacy' and 'personal data' are mostly associated with the impact of data processing on a single individual, it largely excludes the collective dimension of data-driven harms in terms of *societal harms* requiring a broader framework of data protection (Taylor et al., 2017). Present safeguards in data protection regulation have a strong focus on informed consent and anonymisation, which are aimed at the protection of the individual. They are not intended to address broader societal implications of health data and sample collections (Purtova, 2018; O'Doherty et al., 2016).

The present chapter has highlighted some of the broader implications of DHT on a *societal* level, with newly emerging forms of social profiling and classification. In light of this, we would suggest that policymakers think beyond merely implementing procedural 'check-box' rules around individual privacy and consent and pay attention to the broader societal shifts occurring with the proliferation of digital health technologies in our present digital society.

9. WILL REMOTE MONITORING LEAD TO 'PERSON-CENTERED CARE' AND PATIENT EMPOWERMENT?

A. SOCIETAL EVOLUTIONS AND THEIR IMPACT ON CARE

Important changes in our societies have taken place during the last decades, with an enormous impact on care and care organisation. In our ageing societies, the 'elderly' are increasing in number, while at the same time a shift is taking place from acute to chronic diseases and from single conditions to comorbidities, including a growing demand for healthcare. Today, the elderly are better educated than past cohorts aged 70 and older. Their (health) literacy is higher, supported by access to information about health and care via the internet. As members of the so-called 'babyboom generation', born in the period after the Second World War, they also place greater emphasis on the value of personal autonomy and self-determination. These cultural evolutions involve a shift in the power relations between doctors and patients. Patients are considered active participants in an equal relationship. Even the concept 'patient' is making way for more consumerist terminology such as 'client' or 'service user'.

In the context of chronic, age-related diseases, a cure is often not possible and quality of life is becoming the most important objective. These evolutions have an important impact on care and care relations. A growing number of patients are demanding more involvement in important care decisions and are searching for health information via the internet. In the organisational and policy contexts of care, moreover, the involvement of users has likewise become an important issue. In light of these evolutions, we will discuss the growing importance of person-centered care and patient involvement. Different types of assessment can be distinguished. Remote monitoring will be an important tool in answering the question of patient-centered assessment, potentially contributing to person-centered care and patient empowerment.

B. THE GROWING IMPORTANCE OF PERSON-CENTERED CARE AND PATIENT EMPOWERMENT

The concept of patient centered care is not new. Some authors refer in this regard to Hippocrates and Plato, and more recently to Balint (1957) and Carl Rogers (1961). The definitions of Mead and Bower (2000) and Stewart et al. (1996) are still relevant for the practical definition of the concept. Mead and Bower distinguish five key dimensions in the concept of patient-centeredness: (i) the biopsychosocial perspective of the clinician, (ii) recognising the patient as a person and the personal meaning of the illness for each patient, (iii) equality in the relationship, (iv) the development of a therapeutic alliance, and (v) the doctor as a person. This type of relationship leads to a shift in power from a paternalistic style (the doctor knows what is good for me) towards a style of partnership and shared decision making with empowerment of the patient to make his or her own choices.

The patient-centered clinical method (Stewart, 1996) distinguishes between the illness (the perceptions of the patient) and the disease (based on the analysis by the physician). This distinction is an important point of departure for the medical encounter in which both partners are exploring the disease and the illness together, trying to understand the whole person involved. This means that not only the physical problems is looked at, but also the psychosocial, existential and value context in which the problem arises and hinders the patient. The auxiliary relationship and communication between physician and patient are important aspects of the healing process, which consists of aspects of prevention and health promotion, as well as a realistic timeframe context in which the encounter takes place.

The values in this model differ from a typical disease-focused model in which the physician and patient are in an unequal position. Both partners are considered as equal, but with a different input in the encounter and in the

relationship. Health is considered as a multidimensional concept, defined as "the ability to adapt and self-manage, in light of the physical, emotional and social challenges of life" as in the concept of positive health (Huber, 2011).

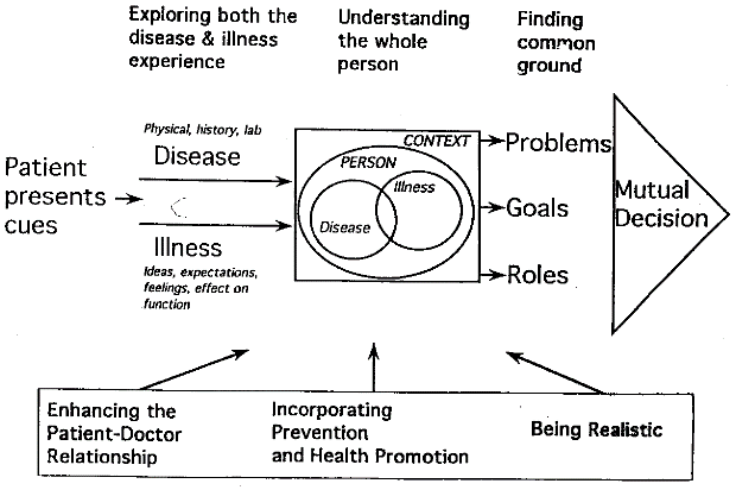

Figure 17: the patient-centered clinical method

A growing number of people with comorbidities, as well as the growing number of frail elderly with cognitive dysfunctions, make care situations more complex. More recently, the Health Foundation (2014) adapted the concept of person-centered care along the lines of the following four characteristics that are better suited to these complexities: (i) affording people dignity, compassion and respect, (ii) offering coordinated care, support or treatment, (iii) offering personalised care, support or treatment, and (iv) supporting people in recognising and developing their own strengths and abilities to enable them to live an independent and fulfilling life.[3]

C. PATIENT-CENTERED CARE AS AN ASPECT OF CO-PRODUCTION

Patient-centered care respects the values, goals and preferences of the individual patient and gives them a central position in the care approach. Respect and dignity are central values in the contact and communication with the frailest patients. The aim, moreover, is to empower the patient and help him or her to self-care wherever possible. The co-ordination and integration of the care provided by different service providers and professionals are also important. This requires good internal communication, information and education of the professionals involved. In addition, the involvement of informal caregivers is possible in cases where family and friends take substantial responsibility for care at home. They also guarantee continuity of care between service providers and timely access to necessary care.

In most European societies, person-centered care is not solely the business of clinicians. The characteristics of care surpass the responsibility of clinicians and require involvement at the organisational and policy level. A multidimensional framework for patient and family engagement in health and healthcare has been developed (Carman et al., 2013). They distinguish three different levels of engagement: (i) direct interaction between clinicians and patients, (ii) the organisational level and, (iii) the policy level. At each level, engagement in diagnostics and decision making can be realised at a lower level of consultation, via an intermediate level of involvement, or as a real partnership in shared leadership.

[3] www.health.org.uk/sites/health/files/PersonCenteredCareMadeSimple.pdf

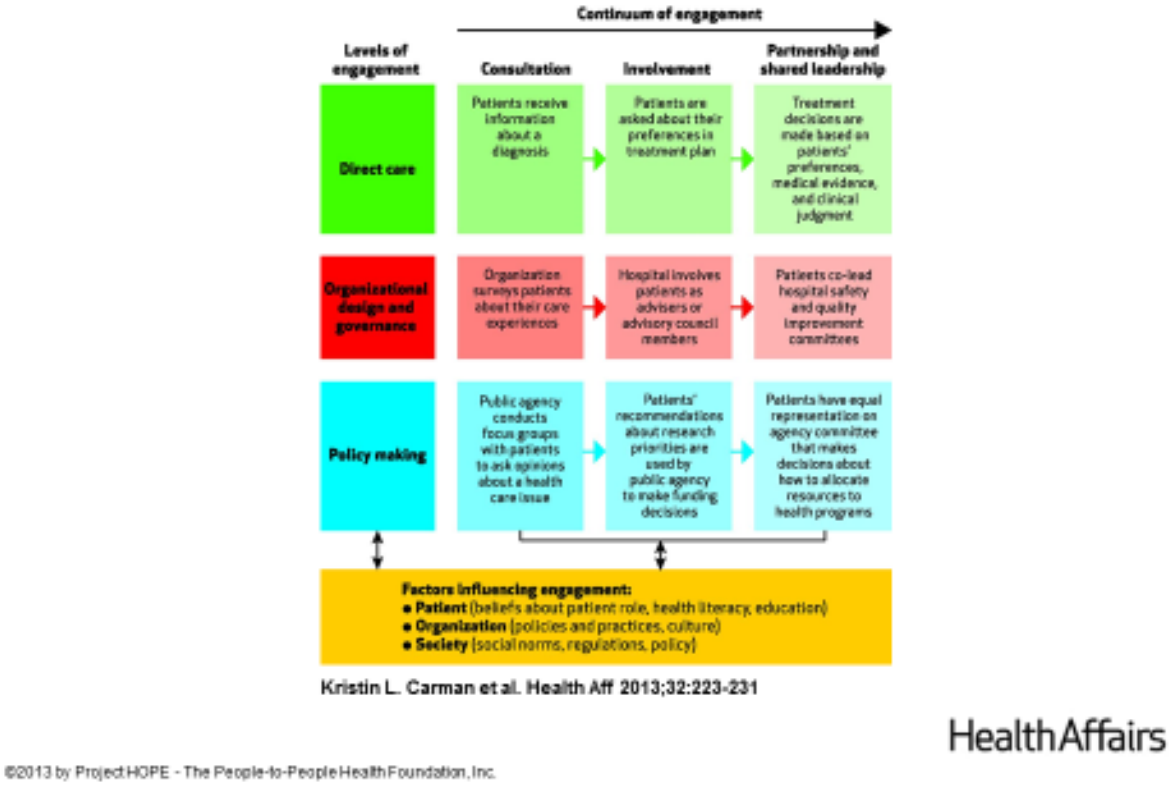

Figure 18: a multidimensional framework for patient and family engagement in health and healthcare

The challenge of growing co-production in equal partnership between professionals and the public is part of innovation movements such as NESTA (Boyle and Harris, 2014) that aim to improve public services: "Co-production means delivering public services in an equal and reciprocal relationship between professionals, people using services and their families and their neighbors. Where activities are co-produced in this way, both services and their neighborhoods become far more effective agents of change." Here co-production is considered as a critical reaction to the way in which professionals and service users have been artificially divided by technology, managerial practices, and exaggerated efficiency. Co-production provides an alternative way to share in the design and delivery of services, and to contribute one's own specific wisdom and experience in order to make services more effective.

D. DIFFERENT TYPES OF ASSESSMENT IN CARE

The use of assessment and monitoring systems can be seen in light of the aforementioned contexts and evolutions in person-centered care and co-production of services. From an experiential psychological perspective, Gendlin (1974) warned against the misuse of assessments and diagnostic concepts that could disturb the person-centered auxiliary relationship between clinicians and patients in psychotherapy, particularly against the risk of substituting concepts or test results for experience, thus skipping the necessary experiential process as well as predisposing a way of hearing instead of an listening actively and openly. He considers it helpful in practice to keep every articulation in constant reference with the immediate and felt experiences of the person.

More recently, the recovery movement in mental healthcare places the responsibility for the process of recovery in the hands of the user (Anthony, 1993). Likewise, in the context of disability, the 'activistic' slogan "nothing about us without us" is well-known.

According to the American Institutes for Research (2017), five principles characterise a patient-centered measurement. First, it is patient-driven, which means that patient goals, preferences and priorities are driving what is measured and how it is assessed. Second, it is holistic and considers the whole person. Third, it is transparent, which means that patients have access to the same data as other stakeholders. Fourth, patients are given timely and easy-to-understand data to inform decision-making and quality improvement. And lastly: patients are equal partners in measuring development and in co-deciding how data is collected, reported and used.

These principles, which are completely in line with the definitions of co-production as to the services provided (see above), are equally essential in the assessment and measurement of important patient characteristics. The authors believe that putting these principles into practice will improve the service providers' ability to stimulate meaningful change toward better health, better care, and lower costs.

E. THE USE OF REMOTE MONITORING IN A PERSON-CENTERED AND EMPOWERING WAY

Whether remote monitoring will contribute to patient-centered measurement and person-centered care and empowerment is not so much a question of the assessments itself, but rather of their use in practice and of the organisational context. Although not all variables and characteristics monitored will be understood by and be useful for the patient without interference or translation by the physician, remote monitoring holds many opportunities to stimulate empowerment and self-control by the patient because the patient is actively involved in the assessment or monitoring. This was more explicitly discussed in chapter 8.

However, as for every tool, remote monitoring can be used in a person-centered or in a physician- or service-centered way. The needs, personal experiences and values of patients, as well as their perceptions of quality of life and quality of care, are particularly appropriate for direct assessment in the person-centered context. Other functional aspects contributing to health or healthcare judgments are less appropriate for person-centered measurement. Here, the role of the clinician as an interpreter and a source of information will be more important, by facilitating a person-centered encounter and a process of shared decision making. A 'paternalistic' or 'expert' position on the part of service providers will be more self-evident in these contexts.

In addition to the patient, other stakeholders are also important in care, including the work environment of clinicians and their organisations. It is of primary importance that the voice of patients and their families be heard and considered of equal importance (at least) with regard to choices in treatments and assessments. This is still not the case, for many reasons. Much resistance remains among clinicians about possibly involving patients in important decisions or in the design and implementation of a diagnostic and therapeutic practice (Légaré & Thomson-Leduc, 2014). Considerable resistance also exists on the part of patients and family members, because they expect clinicians to know what is good for them and often do not expect or even appreciate a more active role in a shared decision-making process in the encounter or in medical assessments or choices (Joseph-Williams et al., 2014).

Clinicians also still need to develop a number of competencies for a real patient-centered approach. While these are often simulated in their academic curriculum, they tend not to sufficiently integrate them in their clinical competencies. For remote monitoring to be empowering and patient-centered, innovations at different levels of services are needed. Person-centeredness should not only be promoted in the clinical encounter, but also in organising services, in the attitudes of patients and family members, communities and neighbourhoods, as well as on a policy level. In short, person-centeredness should be promoted as an important attitude, and interventions should be facilitated to make it happen in practice.

SUMMARY AND CONCLUSIONS

The use of wearables to improve healthcare has all the potential of becoming a major game changer. The number of wearable devices that are available on the market or in advanced stages of development is impressive, ranging from watches to chest patches, rings, wristbands, vests, and shoe inserts for ambulatory gait monitoring. In a recent review, Dunn et al. (2018) list 27 commonly used wearable devices for health monitoring, but many more are on the market. The potential to monitor human physiology, neurobiology, activity and behaviour seems to be almost infinite.

The ambition of this position paper is not to provide a complete overview of the field of wearables and digital health technologies (DHT), but rather to offer an insight from multiple angles into the current state of the field, explore some of its major promises, and highlight some of the major hurdles that still have to be confronted before these promises can become reality. The authors are all active in one way or another in research on DHT, and are confident in its potential value to improve healthcare, both physical and mental, preventive and curative. But we also want to emphasize the many pitfalls and hurdles that still lie ahead.

In the first part, we focus on the actual status of hardware development and on the challenge of developing algorithms for health monitoring purposes. In chapter 1, we describe the current status and expected evolutions in the development of wearables. While many high-quality technologies are already on the market, it is clear that the 'miniaturisation revolution', as the authors call it, will lead to much more compact wearable sensors that will require much less battery capacity. Furthermore, the current 'on-body' devices (wearables connected to the human body), will be joined by in-body sensors (ingestibles) and near-body devices (e.g. sensors integrated into furniture), which will open another set of possibilities.

As also mentioned in chapter 1, the biggest hurdle for the near future lies not so much in questions surrounding how data will be gathered, but in the correct extraction and interpretation of knowledge from the myriad of data that will be generated by wearables. In chapter 2, the authors elaborate further on how raw data collected by multiple wearable sensors can be transformed into interpretable information for diagnosis and monitoring. The validity of collecting useable data via wearables when subjects are physically active is discussed, and the importance of built-in quality indicators is emphasised. Further, the authors stress that much is to be gained from studying the interaction between different physiological signals, instead of studying each parameter separately.

Chapter 3 argues that the application of wearable data for health purposes will have to account for the fact that humans and other living organisms are complex, individually different, time-varying and dynamic. When wearable devices are used to predict upcoming health problems, the data has to be interpreted by algorithms that take these complexities into account. The chapter describes the theoretical background, and offers some examples of applications in veterinary medicine as well as in mental health.

Notwithstanding a number of technological challenges that are still being addressed, medical applications are emerging rapidly. In chapter 4, some case studies are discussed: epilepsy, sleep monitoring, and monitoring functional capacity in rheumatology. They show how significant progress has been made in these domains, but they also stress that some of the challenges mentioned in chapters 2 and 3 still need to be overcome: the need for multimodal approaches, integrating several parameters, and for detection systems that adapt to patient-specific features.

Moving from disease monitoring to preventive medicine and health behaviour, chapter 5 describes how the use of wearables and mobile technologies might contribute to the prevention of a number of very important health problems such as cancer, type II diabetes, cardiovascular and respiratory diseases. The use of wearables might

increase our ability to gain an accurate understanding of the antecedents and consequences of behaviour and to intervene at moments when help is needed most. Likewise in this domain, important challenges remain. A major question is whether digital technologies aimed at altering lifestyle can reach the whole population, or will remain in the playground of young, digital-native and healthy persons with a higher income. The effectivity of many applications also remains to be proven, as some of them exhibit a poor understanding of human psychology regarding behavioural change.

Chapters 6 and 7 move to the field of mental health, both from a preventive and from a disease-monitoring perspective. Chapter 6 demonstrates how the use of Experience Sampling Methodology (ESM) has the ability to improve our in-depth understanding of mental health and mental health problems, as they unfold in continuous interaction with the daily environment, using anhedonia, the inability to enjoy, as an example. As a consequence, ESM offers an increased sensitivity to changes in mental status, opening possibilities for early and targeted interventions. Finally, the authors point at the potential added value of combining ESM with physical remote monitoring technologies, with wearables assessing, for example, physical activity, heart rate variability or sleep. This point is further elaborated in chapter 7. Wearables can be used to monitor stress in a noninvasive way. Such remote monitoring could be an important tool to facilitate the early detection of unhealthy chronic stress, and thereby prevent the occurrence of stress related disorders, such as burnout, depression and anxiety disorders, which are placing such a large burden on our society. On the other hand, it is equally clear that a number of methodological obstacles will still have to be faced. One of these is the valid measurement of stress-related physiological parameters in a subject that is active and moving. Another, and probably more difficult obstacle, is the need for individualised algorithms, which was already mentioned in chapter 3.

In the last two chapters of this position paper, we focus our attention on the societal and psychological aspects of remote monitoring with wearables. In chapter 8, the authors illustrate some of the socioethical issues of DTH: the changing patient/doctor relationship due to patient empowerment, the implications of the economic valuation of health data, and the effects of social profiling both in the context of healthcare research as well as for other purposes ('secondary-use of data'), with all of its potential advantages and dangers. They emphasize that the societal implications of digital health technologies are often unforeseen and unintended by the original developers. Finally, chapter 9 examines whether remote monitoring will lead to person-centered care and patient empowerment. It first describes the evolution of our healthcare to patient-centered care, the importance of patient empowerment, a healthcare that is evolving into a co-production between clinicians and patients. The authors value the possibility that remote monitoring will contribute to person-centered care, but also emphasize that digital health technologies can be used both in a person-centered and in a doctor- or service-centered way.

As a general summary, it is fair to say that the introduction of wearable sensors on the market, which is taking place at great speed, holds considerable promise for modernised medical care, which is patient-based and context-based, rather than hospital-based, and which attributes a shared responsibility to the clinician and the patient for both disease prevention and cure. At this stage however, the staggering number of wearable fitness and wellness tools is disproportionate to the rather slow introduction of wearables as medical devices. The actionability, the actual translation from interesting theoretical concepts to tools that are applied in a medical context, is quite low. We see several causes for this comparatively slow evolution: the need for more scientific data, a complex regulatory framework, and user acceptability.

MORE SCIENTIFIC DATA IS NEEDED

First, clinicians will remain hesitant to introduce wearables as a clinical utility to their patients outside of a research context as long as the underlying evidence for their effectiveness on health outcomes is scarce. We are convinced that clinical evidence is building up, as is discussed in several chapters of this position paper, but this

is necessarily a slow process. At this moment, convincing data on the impact of wearables on health outcomes, tested in real life, is still largely insufficient.

REGULATORY FRAMEWORK

Second, another major possible threat is the regulatory framework coming from the EU, which is quite lenient towards fitness and wellness applications, but strict on medical devices. An important question will therefore be how to draw the line between medical devices, which are subject to strict regulations by the competent authorities and of which the effectiveness needs to be underpinned by high-quality clinical trials, and fitness and wellness tools that need no such regulation and scientific validation. At this moment, there is no strict legal definition of 'wearables' in Europe. The European Commission proposed a definition of smart wearables in its 'Smart Wearables Reflection and Orientation Paper' (European Commission, 2017). The paper defines smart wearables as "body-borne computational and sensory devices that can sense the person who wears them and/or their environment". The paper specifies different applications for wearables, making a distinction between 'healthcare & medical' applications (blood pressure monitors, continuous glucose monitoring, defibrillators, drug delivery products, ECG monitors, hearing aids, …) on the one side, and 'fitness & wellness' applications (activity monitors, emotional measurement, fitness and heart rate monitors, foot pads, sleep sensors, …) on the other. While this distinction seems straightforward, there is certainly a grey zone between both categories. For example, a heart rate monitor could be considered a fitness tool when it helps a person to optimize a personal physical training program, but a medical device when it is supposed to warn someone for dangerous episodes of bradycardia (slow heart rhythm). Likewise, 'emotional measurement' might be considered a wellness aid when used to cope with casual mood fluctuations, but a medical device when it measures sustained mood changes that are indicative of major depression and induce patients and caregivers to start new drug and therapy schemes.

Under the current regulation, as laid out in the Medical Devices Directive (MDD) 93/42, a medical device is defined as "any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, together with any accessories, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means".

Basically, this traces the decision on whether the device is medical or not to the intention of the manufacturer: a device does not fall under the scope of MDD 93/42/EEC when a product was not conceived by the manufacturer to be used for medical purposes. This was confirmed by the European Court of Justice, for example in a case against a company named Biosemi and Others, which marketed a system called 'ActiveTwo' which enables human brain activity to be recorded. According to another company, Brain Products, ActiveTwo is a medical device and since BioSemi and Others did not have CE certification for such devices, the marketing of the said product should be prohibited. BioSemi and Others submitted that since ActiveTwo is not intended for medical use it cannot be classified as a 'medical device' within the meaning of Directive 93/42. Moreover, the fact that the said system can be transformed into a diagnostic device does not lead to it being classified as a medical device. The case against Biosemi and Others was rejected by the court, who concluded that "in situations in

which a product is not conceived by its manufacturer to be used for medical purposes, its certification as a medical device cannot be required."[4]

The MDD 93/42 will be replaced by the Medical Devices Regulation 2017/745 (MDR) from 26 May 2020 onward. Although no dramatic changes are anticipated in comparison with current legislation, the scope of wearables that will fall under the medical devices regulation may become somewhat wider. More specifically, applications that are intended to predict the probability of people to develop a given disease will be considered medical devices. Also, within the medical devices group, many wearables are qualified as 'class I devices' under the existing MDD regulation, which implies that they do not have to be certified by a notified body. Under the new MDR, however, more wearables, such as those measuring physiological processes, might fall under class IIa or even IIb, which will imply a more complex process involving notified body certification. A wise equilibrium will have to be established: locating wellness and fitness devices too readily in the medical category will unnecessarily hamper the development of the whole field. On the other hand, presenting medical devices as wellness tools in order to facilitate marketing is a clear threat to patient safety.

USER ACCEPTABILITY

Even when sufficient data and certified tools will be available, the question remains whether users will accept the use of these devices. The experience in ongoing research projects indicates that the way patients judge the utility of remote monitoring tools is often very divergent from the clinician's view. Any successful implementation of wearables in a clinical context will therefore critically depend on careful integration of the user's opinion and experience. Acceptability of DHT will also depend on the ownership of the data collected by wearables. The exclusive ownership of such data should belong to the user, which is crucial to protect privacy. The patient will have the right to decide whether or not to share the data with specific care providers for specific purposes and for a specific period of time. Sharing such data with health insurance providers will clearly increase the risk of discrimination, and should probably be avoided. On the other hand, sharing the data with public health authorities on an anonymous basis in order to improve healthcare policies might be in the general interest. Further clarification of these issues will be needed in order to enhance user acceptability.

Finally, many chapters in this position paper make clear that the successful introduction of wearables as medical devices will require intensive collaboration between several scientific disciplines, including engineers, bioengineers, medical doctors, psychologists, behavioural scientists, lawyers, sociologists, and ethicists. It will also require continuous communication between companies, medical organisations, health insurance agencies and regulatory instances. This text, the fruit of an academic interdisciplinary group, is meant to be a contribution to stimulate this discussion.

[4] http://curia.europa.eu/juris/document/document.jsf?text=&docid=130247&pageIndex=0&doclang=EN&mode=lst&dir=&occ=first&part=1&cid=112018

THESES FOR DISCUSSION

The aim of this position paper is not only to inform the interested reader on a status of the field, but also to encourage and feed a multidisciplinary discussion on this highly relevant topic. In order to facilitate such a discussion, the authors have formulated a number of theses about the use of wearable devices for medical purposes. These theses represent the actual opinion of one or more of the authors, but are also slightly provocative.

ON THE FUTURE ROLE OF WEARABLES IN MEDICINE

- In order to focus on prevention, it is expected that in the near future most of the general population will wear health-monitoring systems on a daily basis.
- Remote monitoring will soon become an integral part of preventive medicine. Individuals who refuse to be monitored for reasons of privacy, or who neglect the signals provided by monitoring, will face higher health insurance fees.
- Within 15 years, innovations in telemedicine, wearable sensing and patient-centered AI will have moved healthcare away from the hospital to the home environment.

ON WEARABLES AND THE INTERACTION BETWEEN PATIENTS AND CAREGIVERS

- Wearables as such will never lead to healthier behaviour. An individualised and thorough functional analysis of someone's health-related behaviour will always be needed in order to induce effective and lasting changes in behaviour.
- Remote monitoring will not decrease, but rather increase the role of medical experts, because they will be needed to correctly interpret the signals collected by wearables.
- With empowered patients tracking their heart rate, sleeping patterns and number of steps on a daily basis, can we still envision physicians as the only experts on our health?

ON WEARABLES, BEHAVIOUR AND MENTAL HEALTH

- Companies developing wearables tend to underestimate the complexity of behaviour, and underuse existing knowledge on determinants of behaviour. Multidisciplinary collaboration is therefore a must.
- Real-life self-assessment of mental state and life circumstances should be an integral and necessary part of the assessment and diagnostic process in psychiatry.
- No one should prescribe a treatment in psychiatry, either psychological or pharmacological, without properly evaluating the real-life effects on mental state and life circumstances for that specific individual.

ON WEARABLES AND PRIVACY

- In order to improve the monitoring of different diseases, patients must be willing to share the different activities they perform on a daily basis.
- GDPR reduces the notion of privacy to a procedural 'checking the box' element for digital health developers. Policymakers should think beyond merely implementing procedural 'check-box' rules around individual privacy and consent and pay attention to the broader societal shifts occurring with the proliferation of digital health technologies in our present digital society.
- Many people seem happy to sacrifice their right to privacy for the sake of a reduced insurance fee. This will also hold for health insurance in the future: reduced fees for those patients who allow a private health insurance company to monitor their life(style).

ON SOCIETAL CONSEQUENCES OF WEARABLES

- Increased pressure on the financial sustainability of Western healthcare systems could lead to the adoption of a 'merit-based allocation of health resources', meaning that those who are more responsible with their health will be rewarded with greater access to health resources.
- The process of systematic categorisation of people through DHT algorithms is a form of social profiling that may introduce new categories of people and illnesses and reinforce old beliefs about social differences. As such, the underlying algorithms of big data predictive technologies could raise potential new issues of algorithmic discrimination in diverse domains of social life.
- To use remote monitoring correctly in the framework of prevention, an individual will need to be able to buy costly devices and deal adequately with the stream of information. For the most part, only highly educated people will benefit from these new tools. Remote monitoring will therefore increase the social gap in healthcare.

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