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Biomedical Informatics and the Digital Component of the Exposome

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Abstract

Biomedical informatics plays a key role in the development of precision medicine and other new technology-enabled health disciplines. In this context, the exposome (defined as the whole set of exposures on an individual) has become a relevant topic. Although most of the research work in the exposome area has been conducted around the physical and chemical world, we sustain that in an increasingly digitised world more attention should be paid to the digital component of the exposome derived from the interactions of individuals with the digital world. We define this "Digital Exposome" as 'the whole set of tools and platforms that an individual use and the activities and processes that an individual engages with as part of his/her digital life. In addition we support that biomedical informatics can and should lead research in this area.

Keywords:

Biomedical Technology; Environmental Exposure; Medical Informatics

Introduction

Advancements in recent years across multiple technological and scientific disciplines (including biomedical informatics), have produced an unprecedented increase in biomedical knowledge. The availability of new analytical tools (e.g. ultrafast DNA sequencing) have facilitated the development of new approaches such as personalized medicine or precision medicine assisting the use and interpretation of individual genetic inforamtion for medical purposes. More recently, the term precision medicine has been popularised, thanks initially to a) the announcement of the Precision Medicine Initiative (PMI) in the US (known now as *All of Us* Research Program) and further b) with the allocation of funding for its development [1].

Precision medicine is often considered as a continuation of the previous personalised/stratified medicine efforts, and it should also be associated with other elements such as participatory medicine, lifestyle, behavior and the individual exposure to environmental factors [2]. This very ambitious initiative explicitly acknowledges that an individual's health status is the result of various complex interactions between their particular genetic make-up (genome) and their environment [3].

A key element in our current understanding of said individual environmental factors, is the concept of the exposome (coined but Wild in 2005). In his original definition, this author referred to the exposome as the whole set of exposures of an individual since conception to death [4]. This definition has been revisited several times since [5,6]. The concept of the exposome has received substantial support both in Europe, the USA and Japan and has been fully embraced nowadays by an an array of scientists and research funding agencies within the context of precision medicine. However, growing interest in environmental factors is neither new, nor uniquely associated with precision medicine. It has a long trajectory in epidemiology. In spite of this, the primary difference between those approaches and current perspectives on the exposome is that in most cases, epidemiology adopts a population perspective [7], whereas the exposome is aimed at studying environmental health at the individual level.

The alternate perspective we wish to consider in this light is that concurrently, our society is immersed within a digital revolution, living in a pervasive landscape of information and communication technologies (ICT), which are penetrating an increasing number of facets of everyday life, including our health. Internet connectivity is becoming so ubiquitous, with individuals increasingly spending more time online, driven by different motivations [8].

Therefore, with this in mind, we ponder the notion that society and individuals alike are living increasingly immersed in a digital world. Hence, it is both prudent and paramount that the concept of the exposome be reinforced to include its digital component. This perspective provides a fuller approach for biomedical research and potential future clinical purposes.

Health outcomes derived from digital environments and digital stimuli

The precision medicine movement builds off the fundamental paradigm shift, suggesting not only that personalised treatment is important, but also that the patient becomes the centre of decision-making, empowered and engaged in health management options [9]. With the rising infiltration of selfquantification devices, social media and other digital tools, it has become a relevant topic for health research along the last few years[10].

Concepts such as 'digital medicine' and 'digital health' have become greatly popular and describe a whole set of tools and approaches to health based on the digital revolution [11-13] These terms cover a broad range of elements. In this context, the concept of exposure to different stimuli and Internet factors is not new and it has been used for different purposes since the early days of Internet [14,15].

In reference to impacts of immersion in digital environments, literature continues to appear in growing prevalence, indicating that health outcomes may be precipitated in relation to use of various digital technologies. For example, social media use and their impacts on health outcomes of people managing chronic illness [16] Whilst health effects are reported both positively and negatively in this context [17], the theory we reiterate in this manuscript is that regardless of outcome, exposure to various digital environments is a key component of the exposome of individuals.

Examples exist all the way through from basic website exposure, through to video games and social media as will be discussed.

Websites:

At a preliminary level, literature has gone so far as to show that browsing content of certain websites can be associated with health effects. This can be seen in the realm of literature commenting on correlation between web-based content and eating disorders (i.e. anorexia nervosa) [18,19].

Video Games:

Another area worthy of attention and of great interest for the study of digital health effects is engagement with video games. Gaming has garnered incressing attention in health and biomedical informatics through the inception of concepts such as 'gamification', with several instances of video game use and health outcomes reported [20-22]. This application highlights the power of the digital environment (and digital stimuli) to impact some element of heatth outcomes.

More specific examples of video game immersion have shown that the stimuli associated to recreational use of videogames can in-turn precipitate various effects, some deleterious, [23, 24] including the death of a patient due to cardiac failure associated with the stressed induced from gaming [25].

Social Media:

Social media have become an increasingly important part of everyday life, with literature commenting on social media's impact in health growing exponentially [26] One area where it is clear that digital exposure can play a role in health related outcomes has been in the selection and use of different social media platforms as part of the management of chronic diseases [27]. A 2012 example indicated improved scores on stress, depression and anxiety scales after immersion in a virtual world created for the purposes of delivering mindfulness mediation training [28]

Further Exploring Digital Exposure – A Social Media Case Example

Here we focus on the topical area of social media, examing exposure of patients to different social media platforms based on previous works and experiences of the authors of this manuscript [13,14,24]. Using the case of social media, we present how different digital exposures may be associated with different health outcomes.

Social media or, peer-to-peer networks represent a layer of the digital environment in which participatory citizens are immersing themselves digitally as part of their health management. Empowered individuals are turning to such tools (i.e. social network sites, blogs, microblogs, wikis and virtual worlds) to source information about their conditions, connect with others, chat and share resources about their health, symptoms and treatments [10,16].

The influence of exposure to social media environments on one's health outcomes cannot be overlooked [29]. Previous research has successfully depicted the influence of online social networking on weight loss, smoking cessation, and depression, arguing that decisions to change health behaviours are not only intrinsically motivated but also influenced by the effects of the individuals' online social network [29].

Based on our previous research, the same may be said for patient-reported health outcomes and the influence of social media based environments. Research by the authors of this manuscript [16,27] has qualified how social media use may impact health outcomes through the lens of what social media therapeutically afford the individual. This process has focussed on various health variables such as: cognitive health, social health, psychological health and physical health and the therapeutic affordances of self-presentation in the online world, connection to others, exploration of online information, narration of experiences with illness and through adapting online behaviour based on disease specific needs [16].

Underlying this process is the theoretical proposition that social media exposure impacts the individual. Our research suggests the following social media exposures and their postulated impact:

- Time spent online (engagement): Literature review suggested a positive correlation between the number of times online social networking features are accessed, length of time spent on social networking and participation/engagement in health interventions [16]. Furthermore, statistical correlation also suggested that more frequent use of social media was positively linked to greater reported improvements in both psychological and social health variables in chronic pain management [27].
- Interaction with others (support): People living with chronic diseases (i.e. arthritis, cancer, fibromyalgia, diabetes) have reported a strong sense of support received from social online environments. Exposure to online support through interaction with others has been noted to improve acceptance and validation of one's condition in complex regional pain syndrome and adaptive coping in HIV/AIDS for example [16] [30-32]. Other reports have also indicated exposure to peer support leads to improvements in empowerment, as well as increased participation in positive behaviours and activities [33].
- *Information access*: Information seeking is arguably still the most observed use of social media platforms, despite ability to connect and converse on these platforms [27]. Sourcing and improving disease-specific knowledge is reported as an important factor in self-management [16; 34; 35] and social media use has been shown to correlate to improved cognitive health surrounding one's condition [27].
- Simulated interaction: Virtual and augmented reality environments are becoming more apparent in social media and chronic disease literature. The virtual environment allows users to interact and navigate the virtual world anonymously using an avatar [28,35].

The Digital Exposome

In the recent years, interest in exposome-related research has increased enormously as it provides a framework to access and assess individual exposures relevant for health. In many cases, this access is being mediated by advances in the development, miniaturisation and integration of sensors, enabling the collection of individualised environmental data deemed to be important for individual health management. In this context a "Digital Phenotype" [36] has been previously described considering part of the digital footprint of an individual as a relevant element able to be related with manifestations of disease. Simultaneously, individuals are becoming increasingly engaged with a digitalised environment which undoubtedly has an effect in every individual's health. Therefore there is a growing need to realise the timely relevance and importance of the digital subset of the exposome, the "Digital Exposome", as shown in Figure 1.



Figure 1– Both "real" (physical) and "digital" world exposures contribute to different individual health outcomes

In order to identify to what extent the concept of the digital component of the exposome has already been used in the literature, we carried out a Pubmed search using different relevant terms. Table 1.

Table 1– Results of a Pubmed search for different terms
related with the digital exposome

Term	Total number of papers
Exposome Exposome + Internet (MeSH)	222
Exposome + Internet (MeSH) Exposome + Software (MeSH)	1
Exposome + Digital Health Exposome + Informatics	1 24

After conducting this search, it was clear that despite the relevance of the digital component of the exposome for health purposes, it has not as yet been sufficiently considered as a distinct element in the exposome literature.

Whereas in the physical environment the characterisation of an individual's exposome mostly relies in the use of surveys, sensors, geographical information systems, analytical tools and devices [37-40], the digital realm would require a completely different set of approaches reliant on the development of software able to identify those components of the digital exposome deemed relevant for health purposes. In clear contrast with the physical world exposome (where capturing exposure to the different elements quite often requires the development of individual devices), monitoring the digital exposome will require a novel approach. One in which software is developed to trace all digital activities that are relevant to the health of an individual. Some early examples of digital tracing already exist, such as in electronic commerce sites where personalised suggestions are made based on existing electronic

information of previous use of these online platforms (e.g.: Amazon, Netflix). Other attempts showed that although accessing to the individual digital exposome is to some extent technically feasible [41], it presents massive ethical challenges (e.g. data privacy) that require further ellaboration [42]. The quantified-self (QS) movement aims to monitor different aspects of our daily lives and makes extensive use of digital tools [43,44]. Unlike the QS movement, where elements come together to engage with the digital environment to store, analyse and occasionally share this personal information for health and wellbeing purposes, the idea of self-monitoring our Internet use and other digital exposures in an integrated manner has not yet been sufficiently developed.

Biomedical Informatics and the Digital Exposome

The concept of the Exposome plays a critical role in the development of precision medicine. At the same time, the exposome, as a relatively new and strongly interdisciplinary area, poses new challenges for biomedical informatics [45]. The need for formal and systematic approaches to information processing in this context justifies a leading role for Biomedical Informatics within this new research avenue.

Most exposome-related research has been focused around the characterization of the "real-world" exposome, associated with physical, chemical and biological exposures[46,47]. Similarly, in early Precision Medicine studies and applications, "omics" approaches have played the central role, and so too has been the support provided by translational bioinformatics to them.

However, as reported in this manuscript, in modern societies where individuals are spending increasing amounts of time online or digitally connected, our digital exposures are becoming increasingly relevant to our health and therefore should be integrated with and considered as a relevant element of an individual's exposome within a Precision Medicine context. Notably, the role of biomedical informatics goes far beyond these initial approaches. As seen throughout this work, there exist many other areas where exposure information is derived from different online or digital experiences. In these cases biomedical informatics' role expands from the well known aspects of data management and analysis, to becoming an essential player in the generation of individual environmental data, with a particular emphasis on collecting and aggregating individual digital exposome data.

Therefore, further research work will be needed to characterize the digital component of the exposome, which we define as 'the whole set of tools and platforms that an individual use and the activities and processes that an individual engage with as part of his digital life'. In many ways, the digital component of the exposome can be considered alongside the digital footprint of an individual. This concept of the "Digital Exposome" comes to complement the previously described "Digital Phenotype" in an holistic view of how the phenotype of an individual, and her health status, is defined by the complex interactions between the "real" (physical) world its digital component and the genetic component at an individualised level. Figure 2.

It is our aim to raise awareness about the need to monitorise individual exposome data and take into greater consideration the digital exposome as well as to highlight the key leading role that biomedical informatics should play if we are to foster research in this area to improve health outcomes. This could also have consequences in the design and content of biomedical informatics education and training programs.



Figure 2– Phenotypes (including the digital phenotype) are the result of complex interactions between genome and exposome, including the digital exposome.

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