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HEALS

Health and Environment-wide Associations based on Large population Surveys

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D1.1 Can Sensor Technologies Really Define the Exposome?

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Abstract

The advent of the exposome concept (i.e., assessing the totality of exposures through the life course) and the advancement of mobile technology, sensors, and the "internet-of-things" bring exciting opportunities to exposure science. Smartphone apps, wireless devices and the downsizing of monitoring technologies and costs make it possible for various environmental stressors and exposure factors to be measured more easily and frequently, thus providing a more reliable "time–geography of exposure" shifting the current paradigm from a population to an individual level. The Health and Environment-wide Associations based on Large population Surveys (HEALS) project is examining the possibilities of incorporating sensor technologies for measuring environmental stressors from the external exposome in a cohort study. These technologies are evolving quickly, and while they provide great promise for advancing exposure science, many are still in development stages and their use in epidemiology and risk studies must be carefully considered. The possibility of accessing an unprecedented amount of "individualized exposure data," which could greatly improve our understanding of exposure and health associations also comes with various limitations and challenges. These are discussed and the way forward is laid out. The conclusion is that a mix of available sensor technologies and conventional exposure assessment methods is most feasible at this time for characterising the external exposome.

1 Introduction

The exposome represents the totality of human exposures from conception to death, a concept that encompasses not only exposure to multiple environmental stressors such as chemicals but also the interaction of external exposures within the human body and the ways by which broader societal circumstances may influence these exposures (Rappaport and Smith; Wild, 2012, 2005; Wild et al., 2013). Underlying the exposome is the recognition that over time people are exposed to multiple environmental stressors, and as a consequence, their health may be affected by the interaction of those exposures and other personal factors, both physiological and societal. It is now clear that most non-communicable diseases are a result of a complex combination of genetic processes and environmental exposure. Environmental factors have, however, not been comprehensively considered in disease aetiology at the individual level. Indeed, environmental stressors must contribute a large part of the burden of disease, as documented in authoritative reviews on the topic (World Health Organization, 2010); however, in many cases we understand little about their role in disease causation. In this context, a major challenge in the coming decades will be to better define how the combination of the genome and exposome contribute to the risk of disease.

A better understanding of this genome-exposome interaction will allow risk assessment to advance beyond the paradigm of single hazard exposures to mixtures of hazards and personal risk factors. Sarigiannis et al (2009) introduced the concept of modelling biological connectivity across different exposure biology scales. Internal exposure can be estimated by combining information from environmental fate analysis, epidemiological data and toxicokinetic/dynamic models. Biologically-based dose-response estimates can be derived by coupling these data with gene and protein expression profiles as signatures of exposure to classes of toxicants. Using a biological connectivity approach, risk assessment can better account for the variability of exposures and the biological effects of those exposures in individuals. Lioy and Rappaport discuss using both an internal (biomonitoring) and external (measurements of the external environment) approach to quantifying the exposome (Lioy and Rappaport, 2011; Rappaport, 2011; van Tongeren and Cherrie, 2012). The first approach entails analysis of an untargeted suite of biomarkers (of both exposure and effect) to investigate associations with health outcomes. With the second approach, the investigation examines external measures of an individual's exposure to multiple stressors along with related risk factors to relate to health outcomes. The objective of these approaches is to generate new hypotheses concerning causality for further investigation, although exploiting the "external exposome" allows us to more easily design interventions to reduce exposures and potential risks. Ultimately, an effective integration of both internal and external approaches are necessary for better understanding environmental causes of disease (van Tongeren and Cherrie, 2012).

Integration of the internal and external approaches requires a comprehensive interpretation of the data resulting from the environmental, molecular, biochemical, and physiological processes that couple exposure to health outcomes (Sarigiannis et al., 2009, Workman et al., 2006). Exposome studies can help better characterise exposure for examining gene-environment interactions (Thomas, 2010).

Three large exposome studies have been funded by the European Commission through the 7th Framework Research Programme (EXPOsOMICS ("About EXPOsOMICS," n.d.), HEALS ("HEALS," n.d.), and HELIX (Vrijheid et al., 2014)), seeking to integrate external exposure measures, and internal biomarkers (both conventional biomarkers and –omics markers) to investigate the impact of environmental stressors on health at various life stages with the aim of shifting the current risk assessment paradigm from a classical "population-based" one to on that is based on "individual" risk assessment. The HELIX project has demonstrated the use of a set of sensors, including measurements of external exposure, activity, and physiological responses (Nieuwenhuijsen et al., 2014).

In this paper, we expand on the review for the HELIX study by evaluating the potential advantages and disadvantages of a wide set of technologies for both indoor and personal monitoring. These can be used to quantify the external exposome, although numerous technological, methodological, and ethical issues present barriers to implementation in larger epidemiological studies investigating the exposome.

Ideally, quantification of the external exposome would include all pathways of external exposure (inhalation, ingestion and dermal contact) and relevant stressors, such as air pollutants, contaminants in food and water, soil and dust, radiation, temperature, light, noise, along with quantification of determinants of intake (e.g. inhalation rate, consumption amounts and frequencies, plus macro, meso, and micro level behaviors). Also, physical, social, and individual factors such as diet, physical activity, and stress are important when accounting for the relationship between environment and health. This makes an extensive and challenging task for monitoring. The exposome encompasses a breadth of exposures and risk factors that can vary over many time spatial scales.

The exposome strengthens the exposure component of epidemiology, but also seeks non-targeted (or quasi-targeted) discovery, which could open the door to new mechanisms and areas of study. As this type of analysis can be applied broadly, the type of exposome studies referred to in this paper aim to capture individual interactions on multiple levels that relate exposure to disease. Extrapolation to larger population groups may carried out by advanced probabilistic methods or even agent-based modeling, taking into account the inter-individual differences in exposure and susceptibility characterizing a given population group (Sarigiannis et al, 2009). Under this scope, the need for measuring dynamically in time personal exposure, location and intensity of activity is imperative. Personal sensors support this effort for personalized monitoring.

As personal "smart" technologies become more prevalent there is the promise of portable, lower cost sensor systems that would enable monitoring of either personal exposure or external exposures close to the personal level. These technologies could facilitate wider-scale and longer-term monitoring of multiple exposures at the same time for epidemiological studies or for widespread population surveys of the exposome, due to lower cost and ease of use. Already, commercially available fitness monitors allow individuals to measure their own physical activity, energy expenditure, and sleep (Mammen et al., 2012). Mobile phones and other GPS enabled devices allow for tracking of locations. Respiratory and pulse monitors are available to the general public. The mobile health revolution has allowed for much more widespread dissemination of medical and public health information for both providers and patients. The increasing popularity of small sensors, open-source programs, hardware such as the Arduino microcontroller board, and cloud computing has allowed collection and integration of many types of personal level data. The relatively lower cost and easy access

to some of these technologies have encouraged the development of citizen science projects, crowdsourcing campaigns, and student projects to bring environmental monitoring to the public (e.g. EveryAware and CitiSense projects, Public Lab, Air Quality Egg) (Boulos et al., 2011).

The question for environmental health researchers is whether and how sensor technologies can currently help to define the exposome. This is a fast moving technological field and it is difficult to predict how sensor and associated information technology systems will develop in the future. This paper explores this question within the framework of developing an exposure monitoring protocol for the "external exposome" studies targeting epidemiological cohorts within the HEALS project. The approach is intended to be quasi-targeted, with the aim to measure a wide range of hazards and exposure modifiers integrating personal monitoring systems, indoor and outdoor environmental monitoring, and publicly available data. This approach also incorporates exposure modelling to help fill data gaps in areas where monitoring is less feasible. The goal of this paper is to discuss advantages and disadvantages of available sensor technologies along with their implementation challenges (applicability and feasibility) and in the end assess their place in the current exposure monitoring paradigm.

2 Sensor technologies for external exposure

The key to monitoring the "external exposome" is convenience, weight, validity/reliability of data collected, lightweight, low-noise, and non-interference from the wearer and personal activities. Ideally a sensor system should have the following characteristics:

1. Portable and unobtrusive to the wearer;
2. "Low-cost", i.e. such that widespread deployment of sensors is a practical proposition;
3. Able to collect, store and transmit high-time resolution data;
4. Easy-to-use, i.e. useable by a non-scientifically trained person, and who should have to minimally engage with the sensor system to collect the data;
5. Connected to the internet so that collected data can be remotely accessed by researchers and users;
6. Constructed to predefined quality assurance and quality control specifications, including:
    a. Sufficient sensitivity and specificity to allow useful data to be acquired; and
    b. Reliable so that it can be used repeatedly and with a low failure rate.

We define "personal sensor technology" as a small-scale device (e.g. one based on a micro-electro-mechanical system - MEMS) with relatively low-cost that can record or wirelessly send data to a computer, smartphone or tablet. We have investigated products that can be commercially purchased and used "off the shelf", rather than devices under development. Literature searches on IEEE Xplore, Google Scholar, and PubMed revealed a range of sensors for air quality, physical activity and mobile health (mHealth). Most of these devices are at the research stage, or not yet "at market." We also investigated the "grey" literature, including internet searches, conference or workshop materials posted online (e.g. the US EPA's Air Sensors Workshop ("Air Sensors 2014," n.d.)) and project reports. We focused on devices that could be used in non-occupational settings, hence at lower environmental

concentrations. In addition to specific devices measuring certain exposures, the smartphone can also be used as a means of gathering data (Donaire-Gonzalez et al., 2013). The prevalence of mobile technologies and internet availability allow for survey data such as dietary logs to be collected with more ease and independence by study participants.
In addition, a variety of applications that may help assess the external exposome by using smartphone features such as GPS (location), accelerometer (activity) and microphone (noise) have been developed. External sensors that can be linked to mobile devices such as smartphones or tablets have also been developed for air quality, radiation, and various other environmental stressors. We will summarize several sensor types in this section and discuss advantages and disadvantages they may have for exposure studies.

Location. Global Positioning System (GPS) devices can be used to track people's location, allowing the matching of pollution data with a person's location. This can be used in tandem with a personal monitor, or, through modelling, can reconstruct a person's exposure (de Nazelle et al., 2013; Gerharz et al., 2009). The information they provide can reduce personal exposure measurement error by providing a more reliable "time–geography of exposure". Either a GPS unit or a GPS-enabled mobile phone can be used, and smartphone apps for the latter are available, where users can enter in location information, providing an aid to data-processing. In terms of tracking location for exposure purposes, there are certain concerns that need to be addressed with GPS data. For example, location accuracy has some degree of error, which can span approximately 20 m and signal strength losses, particularly in certain landscapes such as city street canyons. Additionally, GPS is not very effective at distinguishing whether a user is indoors or outdoors, which is an important factor for exposure, since we spend about 90% of our time indoors (Wu et al., 2010). On this regard Elgethun et al. (2007) demonstrated a serious misclassification of the amount of time spent outdoors at home as reported by individual diaries when compared with actual measurements from GPS leading to a substantial exposure misclassification to pollutants. Various studies have used data mining methods and measurement of additional variables such as temperature to attempt to improve GPS location data and indoor/outdoor presence, although use of temperature needs to be examined across a wide range of climate settings (Adams et al., 2009; Breen et al., 2014; Wu et al., 2011). In addition, the recently developed Indoor/Outdoor Detector (IODetector), uses three types of lightweight smartphone sensors, i.e., light sensor, cellular module, and magnetism sensor and detects whether one is indoors, semi-outdoors, or outdoors. First results of the app, only available on Android operating systems, showed a prompt and accurate detection in various time and environments (Zhou et al., 2012)

Activity. Physical activity is both a risk factor for disease and relates to environmental exposures. Measuring physical activity and respiration is important for estimating exposure variables such as inhalation. A perturbed inhalation rate would also affect the internal exposome by altering blood flow to several tissues and in particular to the liver, which is the dominant site of xenobiotic metabolism. There are numerous types of physical activity sensors available, both designed for research purposes and for public consumption (Bassett, 2012; Yang and Hsu, 2010). Triaxial accelerometers measure acceleration along three orthogonal axes, and can be complemented by gyroscopes, which measure angular motion. Measurement around several axes allows estimation of both movement and posture. Sensors may be worn on a single area of the body (e.g. wrist or waist), or on several areas of the body. The waist is often a default location as it is close to the center of mass of the body, although for long-term constant use the wrist may be more convenient for the user.

The accelerometer output needs to be transformed into a meaningful unit for interpretation, such as steps or metabolic equivalents (METS). The activity counts recorded by the accelerometer can be related to energy expenditure using regression equations or other models (Bassett, 2012). The equations derived from various studies have not necessarily shown good agreement and seem to best fit regular and relatively intense activities, such as treadmill running/walking.

Several types of activity sensors have been developed for use in research studies (Appendix 1, Table 1). The Actigraph has been used in various studies, including in the U.S. National Human And Nutrition Examination Survey (NHANES) (Loprinzi et al., 2012). IDEEA and SensePro also have been used in population studies (Yang and Hsu, 2010). CalFit, a software application for Android systems, was used in Barcelona to estimate inhalation doses (de Nazelle et al., 2013, Donaire-Gonzalez et al., 2013). Orient (Bates et al., 2010; Mann et al., 2011) was developed at the University of Edinburgh and tested in the laboratory for its ability to measure respiratory rate, although it has not yet been tested in population studies. The company Zephyr has developed the Bioharness which comprises a small disk-shaped module that can be attached to a chest strap or compression shirt to measure heart rate, R-R interval, breathing rate, posture, activity level, acceleration, speed, distance and location (Hailstone and Kilding, 2011).

Commercially available activity monitors are becoming more common for people interested in tracking their activity, sleep, and diet, and for motivation to live a healthier lifestyle (Appendix 1, Table 2). These monitors consist of a sensor unit that can be clipped onto a belt or trouser pocket or worn on the wrist. The sensor unit syncs its data with a computer and/or a smartphone or tablet, with newer models using Bluetooth for wireless connection. Additionally, smartphone apps are available that can track a person's location using the phone's GPS system along with movement via the phone's accelerometer. Phone apps alone, however, require the user to carry the phone with them at all times, the app be switched on at all times, often with GPS and Bluetooth active, all of which increases battery drain. User behavior may result in loss of data, as found during a study using an app to reconstruct exposures (de Nazelle et al., 2013). Figure 1 shows a comparison between daily step counts from a mobile phone application (Moves) and a commercial electronic activity monitor (Fitbit One) carried every day by one of the authors over a year. Here the phone app on average recorded 31% lower step count, but on occasions when there was data loss or the phone was not consistently carried the counts were even lower.

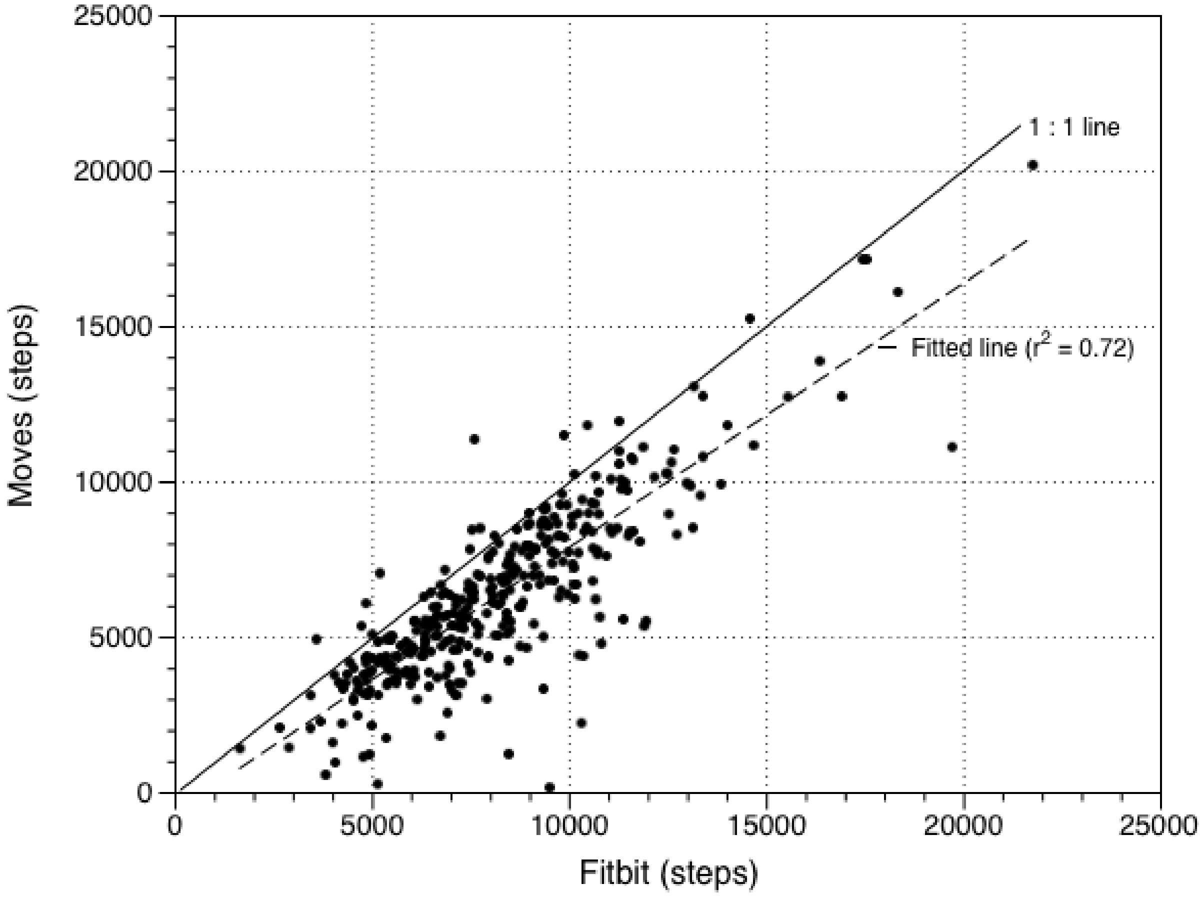

Figure 1: Comparison of Fitbit One and Moves daily step data for one person over one year

Wrist mounted sensors, in particular, can be worn at all times, even in the shower, if the device is waterproof. This likely improves compliance and reduces the chance of data loss due to user behavior. Few of these activity systems have been validated with a "gold standard" or more accepted research methods. Of the studies that have compared sensors, there appears to be good inter-device reliability (>95% agreement or intra-class correlation >0.95) between Fitbits (Montgomery-Downs et al., 2011; Takacs et al., n.d.). A comparison of the Fitbit and Actical found that data from the two instruments had high correlation with each other, and both gave significantly higher estimating energy expenditure compared with the K4b^2 indirect calorimetry device (Adam Noah et al., 2013). The Fitbit Ultra, however, was better correlated with the K4b^2. The Fitbit and Actiwatch-64 were both found to overestimate sleep duration and efficiency, compared to polysomnography (Montgomery-Downs et al., 2011). The Fitbit was also found to be more accurate in counting steps than the Yamax pedometer, which is often considered a gold standard for pedometry (Mammen et al., 2012) as well as compared to other step and activity devices (Guo et al., 2013). Although there are several other devices similar to the Fitbit on the market, thus far there have only been published studies using the Fitbit, which shows that it has comparability with Actigraph meters.

Personal sensors specifically developed for infants and toddlers are *Mimo Baby*[1] and *Sensible Baby*[2]. Both can track movement and other parameters such as infant's respiration, skin temperature, body position, and activity level. The user can see the data in real time or download them on a computer through ad hoc apps available for the most common smartphone operating systems. A different approach to gather information on human location and movement makes use of direction detectors and image-video capture through stereovision camera. This method is particularly suited for detection of children's location indoors and outdoors as it avoids exposure to electromagnetic waves or light rays which are generated by many detection devices (Shinno et al., 2008). With this method it was possible to detect human location with high accuracy without identify individuals and so not infringing on privacy issues.

Air quality. Air pollution sensors can be separated into two main categories, those that measure the concentration of gas phase species and those that measure either particulate matter mass concentrations or various properties of particles (e.g., through scattering or absorption methods). Lower-cost air pollution sensors are available for several gases and particles (Snyder et al., 2013). These sensors are less expensive than the air sampling equipment that is normally used for regulatory purposes or in other similar circumstances. Along with this decrease in cost, however, is a difference in performance and reliability compared to certified reference methods. This section summarizes a few commonly found sensor types for air pollutants.

Lower cost and smaller air pollution sensors can provide possibilities for expanding stationary sampling networks, allowing for greater information on the spatial distribution of air pollutants, or for unobtrusive personal monitors (Appendix 1, Table 3). A larger area sampling network may be of interest for improving air pollution exposure estimates for epidemiological studies, or for supplementing information from conventional air quality networks. Indoor and personal monitors can be of use for examining pollutant concentrations at specific locations and specific activities, and this type of data can be useful for parameterizing exposure models. Placement of sensors indoors can also provide information about air quality in homes or workplaces, where people tend to spend much of their time. Knowledge of exposure at an individual level resolution can also help inform the development and evaluation of interventions.

Gas sensor technologies include metal oxide semiconductors (MOS), electrochemical cells (EC), field effect transistors, tuning fork arrays, and nanomaterials. The most commonly used ambient sensors at this time are MOS and EC sensors, available for carbon monoxide (CO), ozone (O_3), nitrogen dioxide (NO_2), ammonia, hydrogen sulfide, and total volatile organic compounds (TVOCs). In MOS sensors, gas diffuses into the porous material, changing the conductivity upon reaction with an oxidizing or reducing gas. This change can be measured and related to the gas concentration. Humidity can interfere with the sensitivity of metal oxide sensors (Wang et al., 2010) and air temperature can also affect the sensor response. In electrochemical cells, reaction with a gas produces an electrical current that is proportional to the gas concentration. These sensors also suffer from cross sensitivities to other gases, in particular, NO_2 EC sensors can be quite sensitive to ozone interference. It has been suggested to attenuate gas interference using O_3 scrubbers (for NO_2 sensors) or charcoal

[1] http://mimobaby.com/
[2] http://mysensiblebaby.com/

filters (for CO sensors) (Everyaware Project, 2012). Another solution may be to simultaneously monitor O_3 and NO_2, and then generate a correction factor for NO_2 using O_3.

Besides cross sensitivities and interferences by external conditions like humidity, sensors also need regular calibration and are subject to drift and decreased sensitivity over time. While some published literature is available for field testing of sensors in non-occupational exposure measurement situations, much of this information is still in the gray literature, and consists primarily of laboratory testing or field validation with stationary reference monitors. Sensors' performance can be quite variable between instruments and their long-term reliability is unknown. Sensitivity to rapid changes in temperature and humidity make MOS and EC sensors more applicable to stationary area monitoring, rather than mobile personal monitoring, where movement between indoors and outdoors can result in fast changes in these conditions. Although temperature and humidity corrections could be done, these must be measured such that the response times correspond with the gas sensors. It is recommended that the temperature and humidity sensors be located such that any heat generated by the device does not interfere with these sensors. Thus, at this time, MOS and EC gas sensors may be best used in an extended fixed location network of sensors or for indoor or outdoor monitoring.

Particulate matter mass can be measured directly by changes in frequency of an oscillating sensor element or indirectly based on light scattering technology. Particle sensors generally count the number of individual particles passing through a sensing volume using light scattering or some other metric such as the time particles are detected in the sense volume. The light source is either provided by a photo-diode (e.g. Shinyei monitor[3]) or a laser (e.g. Dylos), with the former having poorer sensitivity (Holstius et al., 2014). These instruments may be effective for indoor monitoring, particularly when a strong source is present, such as cigarette smoke (Northcross et al., 2013; Semple et al., 2013). While promising, further testing in indoor environments, including those without smokers, and using more conventional gravimetric methods would be useful in terms of determining whether the Dylos can provide a low-cost alternative to current particle measurement methods in epidemiological studies.

Noise. Noise levels can be measured in occupational and environmental settings using hand-held sound meters, which measure noise at fixed locations, and noise dosimeters, which are worn on a person to measure personal noise exposure. International standards for both types of instruments are available, specifying performance standards such as frequency weighting requirements and tolerances at various frequencies. According to the IEC 61672 standard, Class 1 sound level meters must fulfill stricter requirements than Class 2, with a tolerance of +/- 1.9 dB vs. +/- 2.2 dB at 1 kHz. Sound level meters and noise dosimeters that meet standard specifications can be expensive, costing over a thousand Euros, making them inaccessible to the general population. Now, however, smartphone noise measurement apps are available, many for free, although these do not comply with the standard specifications. Most microphones in phones are aligned to the human voice (40-60 dB) rather than standard specifications.

[3] http://www.sca-shinyei.com/particlesensor

Due to variability between different brands and models of phones and phone microphones, these apps do not perform similarly with different hardware, especially outside the human voice ranges (Kardous and Shaw, 2014). Other issues include a lack of calibration for many versions, although some allow for the user to do their own calibration (e.g. the iPhone apps SPLnFFT Noise Meter and SoundMeter); not all apps use the recommended A-weighting, or provide any weighting options; and they lack frequency analysis capability. Nonetheless, these apps have proved useful for citizen science projects such as Noisetube, which used Nokia phones for participatory noise mapping. The NoiseWatch app allows users to upload noise data to the Eye of Earth public information site. Smartphone noise apps are not usually calibrated. In an evaluation of 10 iOS apps and 4 Android apps, Kardous and Shaw (Kardous and Shaw, 2014) found several iPhone apps that met occupational relevancy criteria (according to US ANSI requirements). They also found that these apps were consistent between iPhones of the same generation, although they performed differently depending on the microphone type. Android phones, on the other hand, had more variability with the same apps on different devices, possibly because Android phones are made by different manufacturers, while iPhones are all made to the same specification.

Characterization of noise is missing in most apps. The type of noise (caused by e.g. music, traffic) and people's noise sensitivity influence potential health outcomes (Schreckenberg et al., 2010). Therefore, health related noise measurements with Class 1 or Class 2 devices are generally combined with observations/interviews/questionnaires to characterize the type of noise. The WideNoise Plus/+ app available for IPhone and Android combines short term noise measurements with questions about the type of noise measured. Furthermore, measurements are maps based on GPS, resulting in a noise map with other measurements. The WideNoise Plus/+ app was evaluated within the European FP7 project EveryAware (Everyaware Project, 2012).

For the most part, noise apps on smartphones only allow measurement while the app is in the foreground, and only a few allow exporting of data or calibration with a sound level meter. Noise apps would be a much cheaper alternative for an exposure study than a noise dosimeter, but the app would have to be able to record while running in the background and should have the ability to be calibrated. Another issue with using smartphone apps for personal noise measurement is that the phone would need to be exposed to the noise source, i.e. not in a bag or other holding device that might obstruct the microphone.

Food. Research studies have used food frequency questionnaires, daily diet logs, and recall questionnaires to assess people's food intake. Studies have also used online questionnaires as a means of gathering data, with somewhat mixed but promising results for the use of web-based food frequency questionnaires or 24 hour recall for assessing dietary data compared with non-web-based methods (Forster et al., 2014; Liu et al., 2011; Matthys et al., 2007; Ngo et al., 2009; Touvier et al., 2011; Vereecken et al., 2008). Computerized questionnaires, especially online and on mobile devices, have an added advantage of convenience for the user, as they may complete the questionnaires after meals or at some other convenient time. Data entered can then be automatically linked to a database, reducing the need for additional data entry by researchers. Online food diaries and weight-loss or fitness apps allow people to log their food intake each day, and some also provide bar code scanners for ease of entry. Given the presence of a number of these methods for the general public to keep track of their food intake, these may provide a useful tool for assessing dietary intake and modeling exposures to contaminants in food, and they should be evaluated within research studies and compared with existing questionnaires used in exposure studies. While online diaries

and apps may allow for daily recording of dietary intake over many more days, researchers must consider how much value an increased number of daily diet data adds over a single food frequency questionnaire. In addition, currently most online diaries and apps are geared towards adults and adolescents. For research studies, child-oriented questionnaires are filled out by parents or children, if they are old enough. It may be that some of these can be adapted for online or wireless use.

Personal exposure through the identification of eating behaviors could be greatly facilitated by the use of sensors for data acquisition as an input to exposure models. First-person point-of-view (FPPOV) images taken by wearable cameras can be used to better understand people's eating behaviors. Combined to image pattern recognition, these will provide additional information for the structure of a food behavior (and eventually consumption) database. Although this is still only an emerging technology, the results of the Thomaz et al (2013) study were pretty encouraging. In a feasibility study with 5 participants over 3 days eating moments were recognized with 89.68% accuracy, based on 17,575 images collected in total.

3 Discussion

There are many possibilities for using wearable sensors, mobile apps and other devices for exposure assessment. There are still challenges to be overcome in using these technologies to quantify the external exposome for scientific study, and at this time, a combination of sensors, conventional environmental monitoring, and modeling would be the most sensible strategy for exposome studies. Researchers and developers should continue collaborations to address the challenges identified in this paper. Some of the key issues that we have found to limit the ability of sensors to define the external exposome are summarized below.

Data quality. Sensor devices need rigorous testing to ensure that the data generated satisfy pre-determined data quality objectives. It is likely that sensors do not meet reference instrument or "gold standard" criteria, but it is possible to set secondary data quality objectives that are more easily attainable which allow sensors to be used as complementary data collectors and thereby increase data quantity. For example, air quality or water sensors could be used more widely to increase the spatial and temporal range of existing official monitoring systems. To do this, however, the sensors must be able to demonstrate good reliability and appropriate precision between devices (i.e. in side-by-side tests) and over time. This should apply not only to devices made by the same company but also to devices made by different companies and, for mobile applications, across different operating systems. They should also demonstrate a consistent relationship with reference methods, so that even if the sensors do not record values as accurately, they may be corrected for any bias.

For environmental sensors, some may not be as sensitive to environmental levels as reference methods, which are often more expensive and more cumbersome. This has particularly been an issue for air quality sensors, although sensitivity has been improving. Improved sensor detection limits would make these devices more useful for environmental health studies. Since personal sensors of environmental pollution would not be used for monitoring regulatory compliance their performance has to be assessed in the frame of the overall uncertainty allowed in exposome studies. They key question that needs to be answered in this context is what is the overall uncertainty introduced by the use of ubiquitous

personal sensors against the uncertainty resulting from the temporally and spatially deficient regulatory monitoring networks.

Similarly, sensors/apps for physical activity or location should show comparability with more established research methods. For collection of dietary data, apps and sensors have the potential to improve upon methods typically used in the past, such as food frequency questionnaires or recall surveys. Allowing a person to search for their food items in a database or scan barcodes may improve the specificity of reported foods, although these methods are still subject to user forgetfulness and error in estimation of portion sizes or approximation of foods not in the database.

Overall, studies on the reliability and validity of sensors and apps and how they compare to gold standards are needed before sensors can be used in environmental health studies. Data quality objectives should be defined *a priori*. Any errors, even within acceptable limits, and correction algorithms should be transparent.

Data quantity: A second key issue is related to storage, processing and analysis of the huge amount of data which can be collected with these sensors. Considering the multitude of exposures to be measured to characterise the exposome, it is critical to have a system that can manage and integrate a large amount of data. Sensor technologies, for example, are generally based on real time measurements, and the use of multiple devices to assess a person's external exposome could be linked to an online database. This will result in a large amount of data to be stored and processed so that it can usefully be retrieved for later analysis. Consideration needs to be given to the averaging time of continuous measurements and the frequency of non-continuous readings necessary to adequately characterize an individual's exposome. For example, a data reading collected every second already leads to 86,400 data points for a single 24 hour period and 604,800 points for a week for a single individual. A study of 10 people leads to over 6 million data points for a single measurement type alone. All this data must be stored, processed, and analyzed. This is not a small matter for an exposome study, which seeks to measure many things.

In addition, the timeframe of measurement needs to be considered, with respect to the frequency and duration of monitoring. Different measurements may be monitored for different timeframes. For example, a physical activity monitor might be used to collect data over a longer period of time than an air quality monitor. The main issues here relate to the convenience of carrying the monitoring device, the amount of intervention needed by the subject to ensure reliable data collection, and the expected exposure variability.

Data processing. The data acquired by individual sensors need interpretation (e.g. human behaviour recognition). This requires statistical advances, sophisticated data mining techniques, computing power as well as a careful sharing of data sources while also maintaining privacy protection for personal data. Big data is difficult to be used with classical relational databases, desktop statistics and traditional visualization packages. They require instead "massively parallel software", on several servers. Without significant advances in this area the analysis of the wealth of data threatens to become the new limiting factor in further progress (Sarigiannis and Gotti, 2014).

Ethical issues. The use of wireless devices and storage of information on the internet also leads to potential security concerns. Furthermore privacy and ethical issues are raised when these technologies are applied for assessing exposure to environmental stressors.

Issues of data ownership and data protection need to be clarified and structured to allow ubiquitous environmental health monitoring to become an everyday reality.
Many devices and apps noted in this article are available to the public, and people agree to terms and conditions regarding their privacy associated with use of these products. By participating in a study using such items, they are also agreeing to the same terms and conditions, along with agreement to provide researchers access to the information collected. Researchers must make these conditions clear to the participants as part of the informed consent process, and note that a participant not only agrees to allow researchers access to their information, ***but that the company whose product is being used may also have access to the same data***. This may affect the selection of devices and apps for studies or the development of apps specifically for studies. As with all wireless device and cloud storage, there are concerns that unauthorized parties may hack into systems and access the data. This provides a challenge to researchers, who are usually required to ensure safe storage and encryption of participant data. Harmonization of data handling and standardization of data privacy and confidentiality procedures are needed to support the wider use of personal sensors in this context.

Behaviour modification. There is a risk that the use of some of the devices and apps mentioned in this manuscript will affect the behaviour of the user. Some of these devices and apps, such as fitness monitors and diet apps are designed with the idea of influencing people's choices and actions. On the other hand, in previous exposure studies, one can argue that the need to wear a monitoring device, whether small or large, could also have led to behaviour modification compared to days with no monitoring. The hope is that with newer technology, there will be less burden on the individual and therefore less potential for measurement error. Any positive aspects of behaviour changes, such as a greater awareness of activity and diet, may also be longer lasting than the duration of a study and thus be considered a benefit.

Cost. Many wearable sensors are still expensive, although they may be relatively cheaper than conventional monitoring equipment. The increasing availability of MEMs that anyone can buy online has made do-it-yourself devices more possible for technically savvy general users, and these are often relatively affordable. Commercially available devices are still too expensive for widespread use by all members of the population. For an exposome study, the need for many different sensors means that costs can increase quickly. Another issue for mobile applications is that they often require the latest and most expensive smartphone or tablet. For greater accessibility it would be useful for versions of applications to be available for several models, including older devices.

Practicality. Although more study subjects may be monitored for longer periods of time, there is still a burden on the subject. Some sensor devices are still not well designed for personal use in everyday life, and many devices require personal interaction or maintenance. For example, personal air monitors are still not sufficiently small or unobtrusive to carry around, which often include the need for a smartphone with apps running in the foreground, and require frequent recharging. An exposome monitoring system built around a smaller set of sensors, supplemented by data from stationary or publically available sources is much more feasible at this time. For example, activity monitors such as the Fitbit are easy to carry around and many people will have a mobile phone with location abilities. If not, GPS units are relatively inexpensive and small. We may be better able to generate reliable air pollution data via models, validated by reference networks and supplemented by lower cost sensors or other methods, which can then be combined with the subjects location and activity data to

provide estimates of personal exposures. Sensors can also be placed in homes, where climate conditions are less variable, to provide information on indoor exposures, which can be used to complement the ambient exposure data in modeling, for example, noise or air quality.

In addition, participants still have to be motivated to wear and collect data. For example, they must be willing to keep diet logs, answer other question periodically, or sync and charge their devices. Compliance over the long run may dwindle, as people may forget or find it inconvenient to continue to use their devices. Researchers must be careful in designing studies to maximize the timeframe and amount of data to be collected. Although constant monitoring may be difficult, it is still possible to gather much more data longitudinally than in the past.

4 Conclusions

The exposome, or the “totality” of a person’s lifetime exposure is a vast concept, which exposure science is still trying to resolve. The rapid advance of sensing and wireless technology has opened up a new and exciting frontier for exposure science, by providing means to measure across time and space, and perhaps in the future across many different aspects of the exposome. These possibilities also open up new questions as to whether and how sensor based data can be used for better understanding the health impacts of the environment, while assuring the privacy of the participants. As research and development progresses, scientists, product developers, computer scientists, human interaction designers, and ethicists will need to work together to push forward and manage this era of sensor technology and big data. In the meantime, exposome projects will need to balance the possibilities of new sensor technologies with more conventional and well-tested methods of data collection.

Thus, despite their enormous potential many challenges remain to be overcome. The importance of a holistic approach to manage all aspects of the environmental exposure, and the importance of multiple exposures in sensitive groups such as children and elderly, have been recognised (Mitchell et al., 2007), and need to extend to all aspects of their personal exposure. Ultimately, these are essential for a sound exposure-based evaluation of policy interventions will most cost-effectively reduce the impacts of the environmental burden on the population as a whole and especially on the more vulnerable groups.

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Appendix 1

Table 1: Activity sensors used in research

Company/Monitor	Features
Actigraph • wActisleepBT • wGT3X-BT	wActisleepBT • total sleep time (TST), sleep latency, wake after sleep onset (WASO), sleep efficiency, • energy expenditure, MET rates, steps taken, physical activity intensity, • heart rate R-R intervals, • subject position, and ambient light levels. wGT3X-BT • acceleration, energy expenditure, MET rates, steps taken, physical activity intensity, • heart rate R-R intervals, • subject position, • total sleep time, sleep efficiency, • ambient light levels. • Used in NHANES
Stay Healthy • CT1 • RX3	CT1 • Calorie expenditure (not sure how) RT3 • Has triaxial accelerometer
MiniSun • IDEEA	• Track body motion and posture for 24 hours. • Energy expenditure analysis • 5 sets of sensors
Orient	• Includes triaxial accelerometer, 3 gyroscopes, two magnetometers •
CalFit	• Accelerometer • GPS • Android app
Senswear Armband Pro Sensewear mini	• Total energy expenditure (kcal/min) • Active energy expenditure (kcal/min) • METS • Total number of steps • Physical activity levels and duration • Sleep duration and efficiency • Lying down time • On/Off Body time • Software to analyse data
Actiheart (CamNTech)	• Heart rate monitor • Accelerometer • Can be worn with electrode or Polar chest band • Estimate energy expenditure
Zephyr Bioharness 3	• HR, R-R interval

Company/Monitor	**Features**
	• Breathing rate • Posture • Activity level • Peak acceleration • Speed and distance • GPS • Bluetooth enabled for Android devices
Zephyr BioPatch	• HR, RR interval • Breathing rate • ECG • Activity • Position and posture
Actical (Philips)	• Physical activity • Steps • Energy expenditure

Table 2: Some of the activity monitors available for general use

Company/Monitor	**Features**	**Cost***
Moves (app)	• Available for iPhone, Android • Tracks location, mode of transport, steps taken	Free
Fitbit	• One – waist, 3 axial accelerometer and altimeter, calories, distance, sleep, steps, Bluetooth sync to PC/Mac • Flex – wrist, same as One, minus altimeter, plus activity, food, water, body mass tracking, sync to mobile device	£80/€100
Vivofit (Garmin)	• Supposed to not need recharging, always on for a year • Calories, steps, can be used with heart rate monitor • Water resistant • Online community	£80/€100
Jawbone	• Steps • Sleep • Food (has barcode scanner) • Mood logger • 7 day charge	£100/€130
Nike + Fuelband	• Step, activity logger • Ambient light sensor •	£90/€115
Pulse (Withings)	• Steps, elevation, distance, calories expended • Heart rate, blood oxygen • Sleep patterns • Compatible with multiple apps	€120
Activ8 (Remedy)	• Worn around thigh • Measures posture (time spent in	€99

Company/Monitor	Features	Cost*
	various positions) and METS	
Vifit (Medisana)	• Activity and sleep tracking	€60
Sensible Baby	• Monitors position, temperature, movement • Smartphone/tablet compatible • Looks like a large button	N/A
Mimo baby	• Kimono onesie with lilypad and turtle • Measures respiration, movement, temperature, position • Smartphone/tablet compatible • Bluetooth	About $200 (€160) for a starter pack with 3 kimonos, Lilypad and Turtle

Table 3: Air sensor devices (information from developer website or technical sheets, unless otherwise specified)

Sampler/sensor/ system	**Measured factors**	**Measurement Principle/devices**	**Range/LOD***	**Cost****	**Other**
Aeroqual	Gases	Gas sensitive semi-conductor (O_3, VOC) Gas sensitive electrochemical (NO_2, CO)	O_3 (0.001ppm - 10ppm), VOC (1-500ppm), CO (1-100 ppm), NO_2 (0.005-1ppm),	~€1900	Fully charged battery runs 8 hours, dependent on sensor head NO2 vs. reference R^2 = 0.63, but temporal tracking fairly similar (Delgado-Saborit, J.M., 2012)
Dylos DC1700	Two size ranges >0.5 and <2.5 **µm**	Optical (laser) particle counter Battery operated	Lower range about 16 µg/m^3 LOD < 1 µg/m^3 Range up to 10 mg/m^3	~€380	Modifiable – additional particle bins may be requested Possible underestimation at high range (>600 ug/m3), compared with Sidepak AM510 (Semple et al., 2013) Modified version - Compared with DustTrak using mono-disperse particles, woodsmoke, ambient CA air, ammonium sulfate. R2 generally close to

Sampler/sensor/ system	**Measured factors**	**Measurement Principle/devices**	**Range/LOD***	**Cost****	**Other**
					1. (Northcross et al., 2013)
Sensaris Senspods	PM NO, NO_2, CO, O_3	Shinyei PPD42 NS (particles > 1µm) Alphasense sensors		Particles ~ €300 (EcoPM) Gases ~€ 500	All have GPS unit

Sampler/sensor/ system	Measured factors	Measurement Principle/devices	Range/LOD*	Cost**	Other
MicroPEM	PM10, PM2.5	Filter based with PM2.5 and PM10 cutpoints Nephelometer	Upper limit 10,000 µg/m^3 (lower 5) nephelometer	~€1600	Weighs < 240 g Target noise < 3dBA above background at 30 cm
GeoTech AQMesh	NO, NO2, O3, CO, SO2, Temp, RH	Amperometric gas	LODs – max range (ppb) NO - <3-2000 NO2 - <5-200 O3 - <5 -200 CO - < 5 – 5,000 SO2 - < 5 – 10,000	N/A	Stationary monitor that transmits data to cloud-based server for processing and delivery
CairClip	O_3 NO_2 VOC H_2S NH_3	Electrochemical	0-250 ppb, 20 ppb (LOD)	N/A	O3 and NO2 showed strong sensitivity to each other. O3 showed different calibration functions between lab and field, and sensitivity to temperature and power supply changes. Recommended longer averaging time (at least 11 min) NO2 also sensitive to NH3, and subject to long term drift, as well

Sampler/sensor/ system	**Measured factors**	**Measurement Principle/devices**	**Range/LOD***	**Cost****	**Other**
					as temperature and relative humidity effects. (Spinnelle et al., 2013a, 2013b)
SensorBox (EveryWhere)	CO NO2 O3 Noise T RH	WideNoise smartphone sensor CO sensors: E2V MiCs-5521, MiCs-525 (w/ charcoal filter), Alphasense CO-BF O3: E2V MiCs-2610 VOC: Applied Sensors As-MLV T, RH: Sensiron SHT 21		N/A	Overall poor performance for single gas monitors, especially in summer. Noise sensor performance varies by phone/device. Noise measures not weighted. (Everyaware Project, 2012)
microAeth	Black carbon	Light absorption	0-1 mg BC/m^3	~€6000	
Aretas sampler system	Particles NO2 O3 CO Noise	Unclear	PM: 0 to 28,000 pcs/L NO2: 0 - 20 ppm NO2 O3: 20 - 200 ppb CO: 0 - 500 ppm	N/A	NO2 resolution: 0.1 ppm NO2 O3: Accuracy: ±20 ppb, ±4.5% RH, ±0.5 °C CO resolution 1ppm

Sampler/sensor/ system	**Measured factors**	**Measurement Principle/devices**	**Range/LOD***	**Cost****	**Other**
M-dust	PM2.5	Mini vacuum pump Conical Inhaleable sampling head Particle sensing unit (light scattering)	0-116 ug/m^3	Base sensor kit €380	

*Range/LODs generally as listed on manufacturer website or published
**Costs are approximate. Interested parties should contact companies for quotations.