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How can we ensure that self-measured data is usable?

Private individuals as collectors of their own data for biobank research

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Contents

Summary

This paper discusses the opportunities and challenges of collecting data for biobank research using self-measurement methods. We will explore the scientific, ethical, legal and societal aspects which are important to obtain and use data that has been collected by the participants themselves. We have taken a mixed-method approach to this, comprising interviews with researchers who use self-measurement methods or are pioneering this approach, a focus group discussion and a literature study.

This exploration resulted in a set of recommendations, including:
- making a 'weighted' choice of the measurement method based on the parameters to be measured and the set requirements for this;
- aiming to work in partnership with the participant at all stages of the process;
- using a dynamic interface for explicit and transparent consent and information exchange;
- aiming for privacy-by-design for the entire concept of data collection in which a minimum dataset has to be the norm;
- creating a FAIR data plan for all users, including the participants, as part of the consent; and
- reviewing the entire concept of data collection using self-measurement methods by an ethical review committee which also has expertise on it in the fields of IT and data management.

Following the exploration we will discuss self-measurement in the context of developments in society and the role played in this by research organisations, government bodies and the general public. We say that self-measurement can bridge the gap between the need felt by many people in society to have more control over their health and health data, on the one hand, and keeping those people involved in research, on the other hand. To be successful the parties concerned must be able to rely on each other as the citizens that are committed, the research organisations that provide steering and the government authorities that regulate and monitor the frameworks for this. Our conclusion is that biobank studies offer a suitable vehicle for the use of self-measurement methods because the expertise and conditions necessary to safeguard aspects such as privacy, control and participant interaction are already there. Biobank research (and other types of research) can in turn benefit from self-measurement methods. Repeated or even continuous measurements can provide missing data and patterns and thus new insights useful for the prevention and treatment of complex chronic disorders. Self-measurement also strengthens the longer term commitment of participants and the interaction with them. This interaction can be provided for with suitable interfaces, such as participant and patient portals, or Personal Health Environments (PGOs), with dynamic functions for consent and exchange of information.

In this new partnership with the participant who collects his or her own self-measured data, the research organisation concerned will continue to play a steering role in the responsible collection and use of this data. This will ensure that the sensors, apps and interfaces used meet the correct standards with regard to matters such as protecting privacy, data management and ownership. The use of self-measurement methods therefore does not diminish the role of biobanks and other research organisations, but changes it. To be able to determine whether or not it would be more cost-effective or efficient to use self-measurement methods, it is important first to consider the additional financial and personnel resources required for this relative to the benefits.

Introduction

From blood sugar monitoring in diabetes to step counting, or simply keeping a record of your fitness: sensors, apps and other measuring devices by which you can measure for yourself various aspects of health and sickness, have become a trend. The technology for collecting data is becoming more readily available and cheaper. Medical and scientific research makes use of measured data from patients and participants which is collected at the research site or in the normal healthcare setting. Now that it is becoming increasingly easier to collect and process data digitally, it is worthwhile to investigate the extent to which the collection of research data can be assigned to the participants themselves and how efficient and cost-effective that is.

The purpose of this White Paper is to consider the options, the conditions to be met and what needs to be taken into account when participants provide self-measured data for biobank research. Biobanks hold samples of body tissue together with the related data that has been systematically collected. Setting up and maintaining research sources of this kind requires considerable financial resources and organisational effort. Over the years the Netherlands has developed considerable expertise and an extensive infrastructure in this field under the umbrella of BBMR-NL[1] (Biobanking and BioMolecular Resources Research Infrastructure), that in the context of BBMRI-ERIC, works closely with other BBMRI umbrella organisations elsewhere in Europe. The question is: should we be adding data to these carefully constructed systems that has been measured by people who are neither researchers nor physicians? What requirements does this impose on self-measured data, measuring equipment and the interaction with the participants? To what extent should research organisations be steering this process and how should they do that?

This paper explores the requirements to be met in order to ensure that self-measured data is also usable for research. Everyday practical experience will be included and we will also look at possible future developments. This White Paper aims to provide a guide for individual researchers, as well as medical and scientific organisations when deciding whether and how they want to incorporate and use self-measured data in biobank and other research. Particularly when self-measurements are carried out by patients, they can be used for both science and healthcare. We will discuss the various aspects of self-measurement in the light of current developments in society and set out as complete a picture as possible of the challenges and concerns about the use of self-measured data in research.

Who is this White Paper intended for?

In the first instance, this White Paper is intended for researchers who wish to include and use self-measured data in their biobank or database. This paper further aims to provide insight in the widest sense to medical and other researchers who wish to use self-measured data to answer their research questions. Finally, this paper may also be useful for policymakers, IT staff and data managers in organisations that wish to use self-measured data for healthcare and research purposes.

1 As the national umbrella organisation BBMRI-NL makes participant (largely patient) biomaterials, images and data retrievable, accessible and exchangeable for medical and scientific research on the prevention, diagnosis and treatment of diseases.

Self-measurement methods in all shapes and sizes

Today there are a great many ways in which data about lifestyle, health and disease can be collected digitally. Self-measurement methods are offered on a commercial basis and with a view to improving care. Therefore it can be either the care provider or the private individual who takes the initiative to use self-measurement. Some methods are primarily aimed at managing your disorder, while others focus on getting better or keeping healthy. This paper is concerned with methods where the self-measured data can be made available online for research purposes.

There are also innovative sensors available for measuring certain parameters which may be built-into devices that are intended to be easy to use or comfortable to wear, such as sensors in clothing, smartphones and watches (wearables), sensors that can be swallowed (insidables) and tattoos with smart functions (Koydemir and Ozcan, 2018). Questionnaires completed online, possibly using an app, are an important method of self-measurement for other parameters, such as psychological well-being and nutrition. Information from biomaterials can be obtained at home by analysing faeces or blood (see text box). Because we now have ever smaller and better sensors available, in the future we will be able to monitor users' psychological and physiological state continuously (Sawka and Friedl, 2018). The Nictiz database[2] contains more than 700 examples of different self-measurement methods and the parameters they can measure.

Many self-measuring devices send the measured data to an app, smartphone or tablet, or it can be uploaded to a computer (Figure 1). The data can then be forwarded to the supplier's permanent data storage environment. Usually the user has access to the data in the permanent storage environment, as do authorised third parties, such as a medical research organisation. The supplier of the sensor or app generally also has access to the data.

According to the Multiscope Smart Health Monitor 2016, 34% of the Dutch population uses apps, wearables or other devices to monitor health and lifestyle (Renders et al., 2016). This takes place mainly in the categories of sport & exercise (20%), weight & nutrition (18%), followed by bodily functions (12%) and mental health (4%). The starting point for measuring and recording bodily functions is often when illness or a chronic disorder develops. The eHealth monitor, compiled by Nictiz and Nivel, shows that in 2017 more than half of those with a chronic illness (55%) and half the vulnerable elderly (50%) had independently measured health indicators (Wouters et al., 2017). This is consistent with the fact that the elderly monitor their bodily functions more often than young people. Among healthy and younger people there has been an increase mainly in the use of activity trackers that monitor their lifestyle.

2 http://sharing.nictiz.nl/meetjegezondheid/

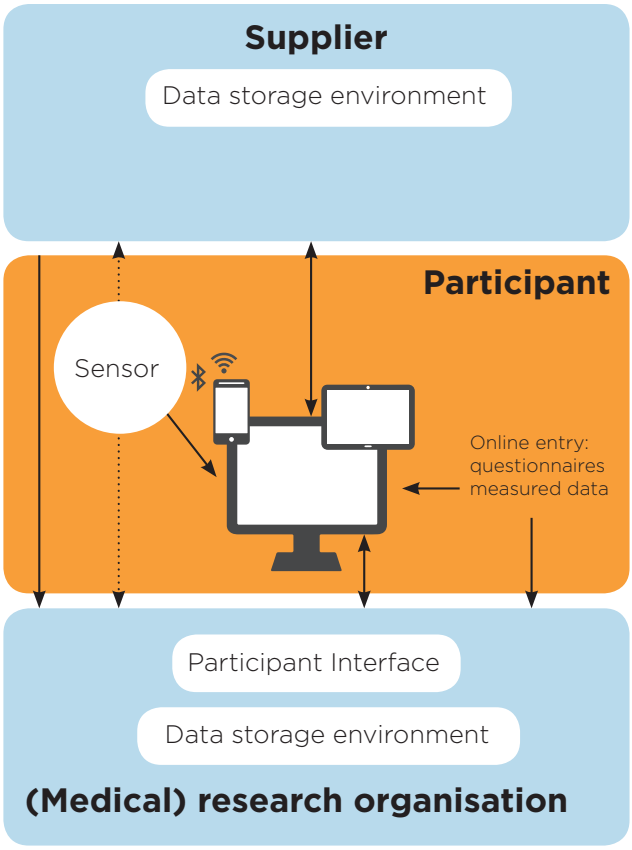

Figure 1. Data flows for self-measurement methods.

Examples of self-measurement of biomaterials

- **Measuring blood glucose with the iHealth Align.[3]**
  This is directly plugged into the smartphone. One drop of blood on a test strip is placed in the glucose meter which then calculates the glucose level. The measured data is collected by an app on the smartphone.
- **Measuring calprotectin with the CalproSmart[4] from Calpro to detect chronic inflammation of the bowel (IBD)**
  Patients hold a 'straw' in their faeces and, following a lateral flow immunoassay specifically for calprotectin, a colour code appears which can be scanned with an app on their smartphone. This data can be transmitted automatically to a supplier's portal from which it can then be forwarded to the medical practitioner either in the context of the treatment or for research.

The promise of self-measurement methods

There are now enough practical examples which demonstrate that self-measurement can contribute to improving health, coping with a disorder and providing care (Veenstra et al., 2015). Ideally, self-measurement gives people more control over their health. This coincides with the political move towards a civil society in which the general population becomes more involved with their own healthcare. Even in government circles self-measurement is seen as a means to support self-reliance, self management and self-administered healthcare, as shown by the letter to Parliament from the former Minister of Health, Welfare and Sport, on "eHealth and improving care"[5].

3 https://ihealthlabs.com/mobile-apps/
4 https://calpro.no/wp-content/uploads/2015/10/PI_CalproSmart.pdf
5 Letter to Parliament

Data which is collected and stored using self-measurement methods can also be very useful for medical and scientific research, particularly when it can be combined with other data and biomaterials. It could offer a cheaper and more efficient way of collecting data for biobanks. Participants can also make measurements more often which means that more data and data over a longer period could become available for research than is the case with the way it is traditionally collected for biobanks and databases. Certainly when measurements can be taken continuously, useful data can be obtained which would otherwise be lost; different patterns for different individuals can also be identified (Li et al., 2017). For example, self-measurement could provide new insights for the prevention and treatment of chronic complex disorders such as Alzheimer's and Parkinson's (Silva de Lima et al., 2016; Marais et al., 2016).

Taking measurements in familiar surroundings, such as at home, could also help to ensure that the data is even more reliable than with intermittent measurements in an out-patient clinic or research environment. Blood pressure readings are an example of this where a hospital environment does not always provide a realistic picture.

At the moment, in practice, biomaterial and data are collected at infrequent intervals in biobank studies. Depending on the type of study and its duration, healthy participants may be invited once or just a few times a year to visit the research site. Patients come to visit their physician in the context of their treatment. In the future these meetings will increasingly take place online if the data can be obtained by the participants themselves. There are currently various studies in progress to gain experience with this.

Data collections

Lifelines is a national three-generation biobank and cohort study which is following participants over a period of more than 30 years. Participants visit the site once every five years. Online questionnaires are completed every two years. Sub cohorts are seen/complete questionnaires in the intervening period. The LifeLines NEXT[6] study (began October 2016) makes use of a sub cohort of pregnant female LifeLines participants. The participants and their babies are followed from the third month of pregnancy until the end of the first year of life. The Lifelines NEXT participants are also asked if they are willing to take part in the **Newborn project**[7], in which information is generated for scientific research, and about devices (and device improvements) which also serves as a testing ground for developing new applications to improve health. In association with Philips, the participants are asked to test the devices on themselves and at home. These are devices which provide insight into health or which could contribute to better health, such as smart toothbrushes, weighing scales and health watches, baby monitors, sensors in nappies or particulate/dust meters to monitor the air quality of the surroundings.

6 https://www.lifelines.nl/deelnemers/onderzoek/aanvullend-onderzoek/NEXT
7 https://www.lifelines.nl/deelnemers/nieuws/nieuw-onderzoek-van-start-newborn

Taking part in the **PRIDE (PRegnancy and Infant Development)**[8] of the Radboud University Medical Centre, a pregnancy study, mainly involves that the participant completes a short questionnaire online (three times) during the pregnancy, and again two and six months after the due date. They may also be asked to provide a blood sample. An experiment with self-measured data provided via the REach[9] platform, developed by the REshape Center, is being conducted among a small group of those taking part in the PRIDE study. This is mainly questionnaire data, but there is also interest in data on the number of steps taken, weight and heart rate, where this data is uploaded to the Apple HealthKit.
Since 1987 the **Nederlands Tweelingen Register** (Netherlands Twin Register) has been collecting longitudinal data on twins and their family members, using online questionnaires completed every two to three years. Among specific groups of participants this data collection has been widened using other tools in which self-measurement is increasingly being used. In recent years various aspects of heart action have been measured over a period of 24 hours in which, after placing the Amsterdam University Ambulatory Monitoring System (VU-AMS, Neijts 2015), the selected group of participants continue with their normal daily routine. In another Netherlands Twin Register study participants measured their physical activity for a week using motion sensors placed on the hip. At the end of the study the participants returned the measuring equipment by post.

Exploration

We have explored various aspects that need to be into account in the selection and application of self-measuring methods for biobank and other research. We limited ourselves to those aspects which contribute to the usability of the self-measured data from the legal, ethical, societal and scientific viewpoints. To provide the basis for this investigation we interviewed medical and scientific researchers who use self-measurement methods, or aspects which could play a part in this, for their biobank or other research (see Annex 1 for the questions and a list of those interviewed).
We will discuss our general findings here and illustrate them with examples taken from the interviews. We presented this topic to the Maatschappelijke Adviesraad Biobankonderzoek[10] (Patient and Public Advisory Council) which is made up of a wide representation of interested and involved private individuals, patients and stakeholder organisations invited to take part by the BBMRI-NL. The viewpoints which were put forward in this context have been incorporated in this White Paper.

Selecting a suitable method for self-measurement

In our view the selection of a self-measurement method for biobank and other scientific research will always be the result of weighing multiple factors. To be able to arrive at that choice it is vital that the end-users of the method (participants and researchers/ healthcare professionals) are as closely involved in the set up of the study as possible.

8 https://pridestudy.nl
9 http://radboudreshapecenter.com/portfolio/reach/
10 https://www.bbmri.nl/elsi/discussieplatform-voor-biomedische-onderzoeksinfrastructuur/

Parameters

Which parameters are really relevant to be able to answer the research question? Not infrequently the self-measurement methods available measure several parameters. It is tempting to start collecting data for all those parameters. But it is not always efficient and does not meet the requirement for data minimisation as laid down in the legislation (Personal Data Protection Act (WPB)) and the future European General Data Protection Regulation (EU GDPR).

Weighted requirements and the method

Once the suitable parameters have been established, a selection has to be made from the very wide range of self-measuring methods available for those parameters. The usefulness of the self-measuring method will be determined by weighting the requirements (per parameter) which are considered to be important.
From the interviews it became clear that the following requirements for self-measuring methods are considered to be most important:

- Validity (see next paragraph)
- Reliability/precision (deviations over time)
- Price and durability of the equipment
- Ease of use
- Ability to exchange and link the data

By rating a self-measuring device according to the degree to which it meets a particular requirement and multiplying that by a weighting factor for that requirement, a total score can be calculated for products which may be eligible (Verkerke and vd Houwen, 2008). A self-measurement method suitable for the study can then be selected on the basis of this weighted score.
W = Weighting of requirements
Ps = Product score on compliance with requirements
Tsx = Total score/product/requirementx = W x Ps
Σ Tsx = Total score/product

Reliability/precision

An important advantage of self-measurement is the availability of data over several repeated measuring moments, compared with the few measuring moments on site. In this way self-measurement can provide previously unknown data and patterns of disease to help clarify unanswered questions about health. In the selection of the measuring method it is therefore necessary to determine what deviations may be expected in the measured results over time and what this means in terms of the reliability of conclusions drawn on the basis of that data.

Financial considerations

In practice the decision to use a wearable or another self-measurement method often depends on what is available or what can be provided by suppliers of sensor equipment. This may not always be the best choice for the purpose. Other stakeholder organisations can also play a steering or leading role in the selection, such as health insurers or non-profit organisations that support research into and the treatment of certain disorders. They often contribute to the financing of the self-measuring methods, certainly if they will be used for diagnosis and treatment purposes (Geesink et al., 2016).

- **Accessibility of devices**

Another important factor involved in the set up of the study and the choice of self-measurement method, is the participants' capacity to undertake the self-measurement. Not everyone can deal with the selected sensors and apps, due to technical or practical obstacles. This is certainly a factor for the elderly and chronically sick. In the future such obstacles related to mobile devices will increasingly become less of a problem, partly due to technological advances and partly because the number of people who can deal with and have access to a suitable sensor or mobile device will increase. Besides technical obstacles there may also be other aspects which limit the diversity of the participant population. In some studies self-measurements can only be carried out with an iPhone (Ata et al., 2017). A sensor or app which works on all smartphones would be the ideal solution, making it accessible to as wide a population as possible and on a device which more and more people always have with them.

- **Ability to exchange and link data**

To be able to use data easily and effectively for research it is also important to check that manufacturers' sensors and apps have an API (Application Programming Interface). An API essentially determines how the data can be used and combined; it usually comprises a set of technical files, documentation and other support. An API enables systems to be connected to one another. If an API is not accessible (i.e. it is not 'open') then the requirement of interoperability will not be met. Using an open API, sensors can be linked to an app, for example, as well as to other databases and systems. This allows the measured data to be interpreted and displayed.

The websites of software suppliers still do not provide sufficiently clear documentation on APIs. However, more and more smart devices have an open API. It is worthwhile to look at lists of smart devices with an open API[11],[12]. Steps are being taken in various quarters to make APIs more readily available, accessible and usable, e.g., in the Open API Initiative[13] and the SmartAPI project[14]. In its letter advising the former Minister of Health, Welfare and Sport, Edith Schippers, entitled 'Implementatie van eHealth vraagt om durf en ruimte' [Room and risk acceptance necessary for the implementation of eHealth], the Council for Health and Society (RVS) provided an analysis of the obstacles to innovation in IT and made a number of recommendations for the wider and more rapid implementation of eHealth (Prins et al., 2017). This would enable an 'eHealth Highway' to be created that would make it easier and cheaper to exchange data. The use and linking of data from consumer self-measuring devices and consumer platforms should be included in this highway.

Measuring methods

The purchase of a smartwatch (with accelerometers) linked to an app to be used in an international cohort of more than 900 people with Parkinson's disease was funded by the Michael J Fox Foundation for Parkinson's Research (MJFF). The participants use their own mobile phone on which the app is installed.

11 https://www.programmableweb.com/
12 https://medium.com/@mr_moodnode/27-smart-devices-that-have-open-api-11698813b474
13 https://openapis.org/about
14 http://smart-api.info

The decision to use this method of data collection meant that data could be collected worldwide and brought together on one platform for research on Parkinson's disease **(ParkinsonThuis)[15].**
For the self-measurements in the **LifeLines Newborn** project a set of self-measuring equipment offered by Philips will be used in the context of research on 'the health development of the child in relation to pre and postnatal genetic and environmental factors'.
With the aid of accelerometer data combined with modern blood tests (metabolomics), the **Leiden LangLeven[16]** study (Leiden Longevity Study) looks at whether it is possible to say anything about the health of the elderly and how this relates to their lifestyle. The project team itself selected this type of movement monitoring device.
The **PRIDE** study uses the REach platform developed by the REshape Center. The self-measured data for this study comes from the Apple HealthKit and is data that was previously uploaded by the participants via a link with self-selected sensors or wearables. Here the researcher is bound by the choice of the participant in order to obtain data.
The **Nederlands Tweelingen Register** (Netherlands Twin Register) uses the VU-AMS monitor which was developed in-house because there were no instruments available which could measure the electrocardiogram (ECG) at the same time as the impedance cardiogram (ICG) in real-life situations. This ECG/ICG combination is ideal for measuring the autonomic nervous system and its effect on the heart action. Software was developed for this to link heart action to parallel motion recording with an accelerometer.

Validity, before and during measurements

In our view there is still too little overview and control over the validity of self-measuring methods. For biobank and other research however it is essential that validated equipment that can be used in a controlled manner is used. This means that investment and sufficient personnel resourses are needed on the part of the (medical) research organisation, both in the acquisition and validation of the self-measuring equipment, as well as in the form of personal guidance.

When self-measurements are carried out only for personal use to gain an overview and some control over the personal health and lifestyle, responsibility for the selection and use of the equipment rests with the individual concerned. There is no legislation concerning the introduction onto the market of self-measuring devices, including when these measure health parameters. As soon as the self-measured data is collected at the request of a physician or researcher, responsibility for the validity of the data and the conclusions drawn from that rests with him or her. The validity of the data will be determined largely by the chosen measuring method and how it is used by the participants. The physician or researcher has to select a valid method of self-measurement very carefully. It must be clear whether the device measures what it is intended to measure and what algorithms are being used, particularly if the sensor data is no longer raw but processed. The CE labelling for medical applications cannot be used as a guideline for the validity of the measuring method.

15 http://www.parkinsonthuis.nl
16 http://www.leidenlangleven.nl/nl/home

This label only guarantees that the product meets the European product requirements and does not guarantee the quality of the recorded data or any assessment of that data (Hengst et al.; 2015; Incentiz, 2016). Stakeholders are working on tools for selecting a valid method of self-measurement. In January 2016 the Royal Dutch Medical Association (KNMG) published a report intended to help with the assessment of medical apps: de Medische App Checker [the Medical App Checker] (KNMG, 2016). This looked at the reliability and quality of an app and the degree to which personal data is protected, among other things. The GGD AppStore (GGD and GHOR Nederland, 2016) provides a list of apps that have been tested by GGD (Municipal Health Service) professionals. More and more validation studies are also appearing in the literature on self-measuring equipment, as shown by the rapidly growing database of validation studies for activity trackers, e.g. Fitabase[17].

Validity and reliability

The self-measuring equipment selected in the practical examples investigated was to some extent determined by the supplier (because the equipment was provided free of charge) or by the body providing funding for the study. The validity and reliability of most the wearables and apps used in the studies investigated is still being further determined in ongoing research.

The accelerometer data in the **Leiden LangLeven** study was difficult to interpret. The algorithms for this device were constructed on the basis of measurements in young test persons in a laboratory setting (on an exercise bike, for example). Because it was not clear which activities precisely the measured data recorded in the elderly people, an additional validation study was conducted and new algorithms built. Thirty-six older test subjects wore a set of wearables and carried out labelled activities in everyday situations (Growing Old Together Validation, GOTOv). This study will be published.
Self-measured data was used in the **PRIDE** study which had already been collected before the start of the study with measuring equipment chosen by the participants themselves.
The in-house developed VU-AMS monitor was validated in the **Netherlands Twin Register** against standard measurements in controlled laboratory conditions and against alternative measurement methods, such as echocardiography.

Besides the validity of the measuring equipment, the instructions for its use are also important. Even while the actual collection of the self-measured data is taking place, it is still important to monitor the use of the equipment by the participants. How often and how much depends on the intended duration and frequency of the measurements and the user-friendliness of the devices. Here too, some responsibility rests with the medical or research organisation.

It often turns out that wearables and apps which according to the manufacturer can be used in research or care situations do not provide reliable and valid data; because the wearable is not user-friendly, for example, or the battery life is much shorter than stated, or the data is not transmitted if the Wi-Fi network is not available (Breteler, 2016)

17 https://fitabase.com/research-library/

The measured data from self-measurement methods which have not (or not yet) been validated or which differ within one study (because the participants chose the method themselves) are not necessarily unusable. In the context of personalised health the data is useful for the individual participants. But if you want to use data from individual participants for biobank or other research which you can compare over longer periods of time or between different participants, of if you want to link that data to other data, then the medical or research organisation has to assume joint responsibility for the self-measuring method and its correct use over the entire measurement period.

Support

In the **LifeLines Newborn** project specially assigned staff is used to install the self-measuring equipment in the participants' homes and to provide instruction during the measuring periods.
In the **ParkinsonThuis** study the participants were given a smartwatch and the Mobility Monitor on loan for a single period of 3 months with the option of extending this period. These were sent to the participants by post together with a manual. If the participants had problems with setting up the smartwatch and installing the app on their own mobile phone, they could call the study help. The help desk could help the participant remotely with the correct set up of the smartwatch. At the end of the study period both devices were returned by post. An evaluation questionnaire also included questions about how user-friendly the system was perceived to be.
For **the Netherlands Twin Register** the VU-AMS monitor was installed by staff, usually in participants' home but sometimes as part of a project at the University of Amsterdam. Participants then received instructions on how to disconnect and re-attach the sensors when necessary, before starting their daily routine.

"We see it primarily as the task of the physician/researcher to explain to the participants what is expected of them and what is safe for them to do. This also applies when assessing whether commercially-available self-measuring equipment, apps and devices can be used for research purposes. We would have more faith in this than simply looking for something in an App store ourselves.". *Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] - BBMRI-NL*

Participant interaction

In our view appropriate interaction with participants is essential if the collection of self-measured data for research is to be successful and collected with the intended frequency. Interaction that is based on a partnership between the participant and the research organisation is preferable, because this creates added value for both parties. Consistent with such a partnership, an interface should be provided with functionality tailored to the control and information needs of the participants, along with a consultative forum which enables participants and their representatives to be involved in such matters as study organisation, design and providing feedback.

We divide self-measurement for research purposes into three phases: the initiation phase, the operational phase and the prolongation phase (see Table 1). All three should, as far as possible, be set up together with the participants (or their representatives), taking into account the specific needs of a role in medical research and the information and communication associated with this. Not everyone wants to be involved in research or self-measuring or is even asked to do that.

Even when someone starts taking part, it is by no means guaranteed that they will continue. Twelve per cent of the Dutch population has used self-measurement in the past, which shows that some users lose interest (Multiscope, 2016). Self-measurement can be successfully deployed for as long a period as possible by giving participants (or their representatives) a designated role in the research organisation, for example, on an Advisory Board. This will enable participants (or their representatives) to contribute valuable experience and insight both for the preparations during the initiation phase and for the evaluation of the self-measurements during the prologation phase.

Cooperation is also required when performing the self-measurements during the operational and the prolongation phases. This requires a **partnership** between researchers and participants which adds value for both parties, particularly when self-measurement is to be carried out over a long period of time, as with biobanks.

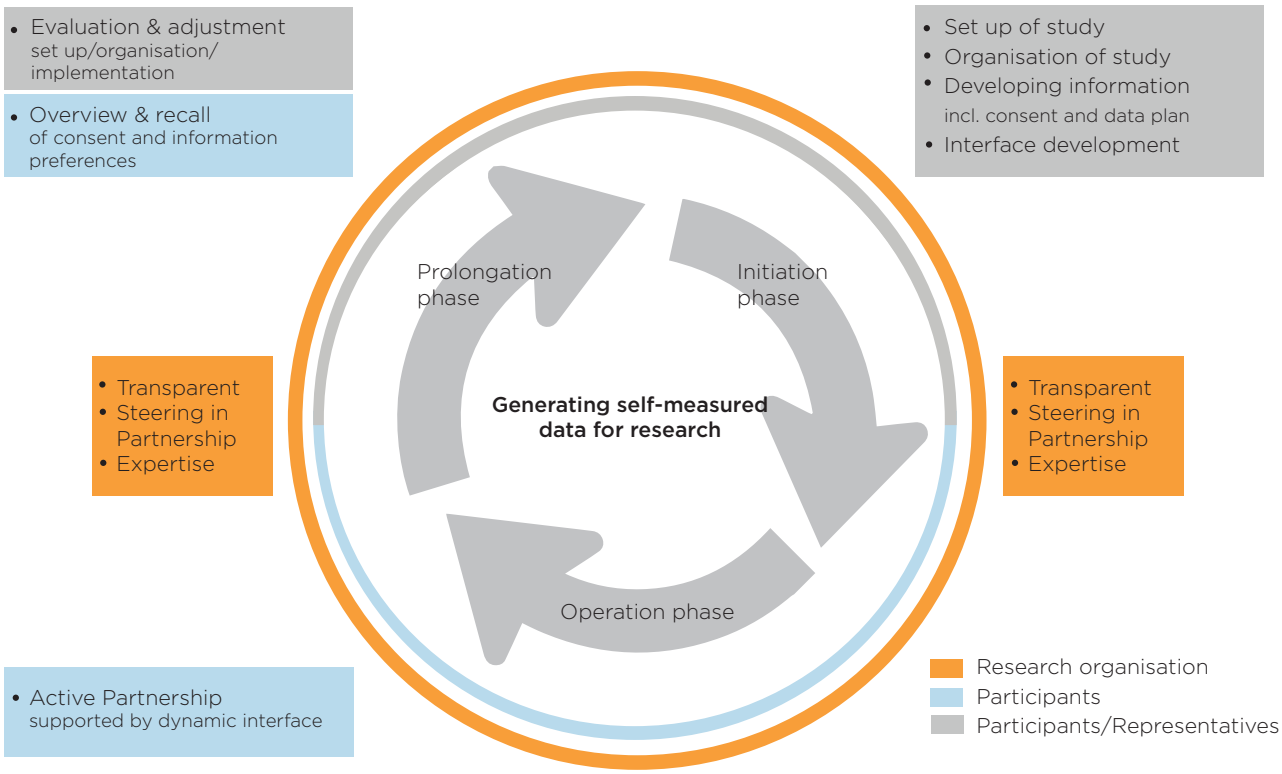

Figure 2. **Phases in self-measurement for research purposes and interaction with the participants (or their representatives) at each stage; through an advisory forum and in active partnership with the participants performing the self-measurements during the study.**

The contact not only has to be made and maintained but throughout the entire period that participants are generating self-measured data for research, matters related to privacy, control and providing information need to be addressed and implemented in concert. Biobanks already have considerable knowledge and expertise in this area (Boeckhout et al., 2014) which can be utilised in a long-term partnership between researchers and participants. Biobanks are ideally placed to provide a framework which can easily combine data collection using modern technology with gaining the commitment of healthy volunteers and patients (Trinidad et al., 2011).

"... information should be written together with participants/patients in order to ensure that is readily understood." *Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research]/BBMRI-NL*

A suitable vehicle, such as an online interface, has to be set up to enable such a partnership to be created. A participants' portal of a biobank or cohort study, or a disease-specific patient portal, can be set up in a way that facilitates such matters as providing information about the research, consent and feedback about the results. Other meaningful interaction with patients or participants can also take place there. The medical or other research organisation will be largely responsible for these portals and their management. A Personal Health Environment (PGO) (see below) may be a better option for extending the partnership into this area, because it will be managed by the patient him/herself with the support of the medical research organisation, if required.

eHealth tool 'Mijn IBD-coach'

The eHealth tool 'Mijn IBD-coach'[18] [My IBD Coach] is a disease-specific interface (de Jong et al., 2017a). This tool gives the medical professional direct communication with his or her IBD patients in which information, advice, and health-related data (such as self-measured calprotectin in faecal matter) can easily be exchanged. Before the tool was developed the need for such an eHealth system was first surveyed among the various stakeholders, including patients. The patients were then expressly involved in the development, testing and evaluation of the tool in an iterative process (de Jong et al., 2017b). Patients ensured that communication with the healthcare organisation and tailored information related to their disorder, medication and care were also specifically included in the tool. Apart from its use in care, the data from the IBD Coach is also linked to the databases of the biobank studies. "By linking the data from the IBD Coach to the databases of the Parelsnoer Institute[19] and the LifeLines study, we now have a wealth of information. Not only about patients going through a flare up of the disease but also those who are experiencing a quiet period. What risk factors are found in their genes, their diet or their immediate environment? This provides new information about the impact of various factors on the development and course of IBD" (interview with Professor G. Dijkstra [20]).

18 http://www.sananet.nl/mijn-ibd-coach.html
19 www.parelsnoer.org
20 https://kennisinzicht.umcg.nl/paginas/online-coach-bij-chronische-darmziekte.aspx

Nevertheless in general we see that biobank studies and other studies that make use of self-measurement or self-reporting by participants have created few opportunities for online interaction. Where self-measurement is used in research too little consideration is given to the participant's needs. Continual communication and interaction motivates participants to continue to be involved with the study (Coathup et al., 2016; Boeckhout et al., 2014).

In the studies looked at we see that the participant often has an app on his or her smartphone or tablet which shows the measured results produced by a sensor, or which he or she has entered. The app also sometimes offers extra functions for the researcher/ physician to add a questionnaire and for the participant to provide self-reporting functions, e.g. on medication use. Initial information about the study is still often provided in a letter or presented on a website as static information. The website is also where feedback related to the study itself takes place. Usually no individual results are provided as feedback other than the measured data shown on the display of the sensor or app.

Information exchange

Those taking part in the **Nederlands Tweelingen Register**[21] receive an information leaflet and information is also provided on the NTR website. Facebook and Twitter are used at a global level to provide feedback on results and to reach participants. The participants' portal is used to provide reminders relating to questionnaires that still have to be completed. In the future this will become increasingly personalised, while information and feedback will be provided in the personal and secure online environment.
In the **ParkinsonThuis** study feedback of individual information is provided, e.g. calculated activity level, tremor activity and night-time activity, using an app. The patient can also record in the app when the medication was taken and this is also shown in the activities chart. The participants find this feedback very motivating. Information about the study is communicated in a bi-monthly newsletter and on the website, and feedback is provided in the form of research results for the patient population as a whole. The app and the website are not linked.
The aim of the **LifeLines Newborn** project is that the participant interaction will take place largely online in the future. It is being considered whether a Personal Health Environment (PGO) would be a suitable platform for this. At present the exchange of information and participant interaction for the LifeLines population as a whole takes place through various channels which will only grow in number. It is believed that combining all of these into a single online channel would neither work for all the participants nor be useful to them.
In the Leiden LangLeven study information is provided on the website, through newsletters and at participant gatherings. The results of the study itself and other associated studies can be communicated in this way. There is no feedback of personal results unless this is requested or arranged for by the GP or the specialist providing treatment.

The interaction related to self-measurement for research could be seen as an opportunity that could quite easily be introduced in the context of the changing expectations related to people taking more responsibility for and control over their own health and disease (Kooiker and Hoeymans, 2014).

21 http://tweelingenregister.org

Consent

In our view if data from self-measurement is to be used by people other than the participants, transparency about this use and consent for this should be mandatory, in accordance with the legislation (Personal Data Protection Act (WPB) and from 2018 the General Data Protection Regulation (GDPR)). Ideally, providing for these requirements online is preferable as this best facilitates the partnership between the research organisation and the participants.

The self-measured data will often ultimately be held in the permanent storage environment of the sensor or app supplier and can be streamed to a server where the physician/researcher has access to the data. These are all 'processes'. All processing[22] of data which can be traced to a person, personal data, is subject to the Personal Data Protection Act (WPB)) and from May 2018, the European privacy legislation, the General Data Protection Regulation (GDPR). Self-measured data is often linked to information such as IP address or location information which makes it traceable. Self-measured data will generally be covered by Article 9 of the GDPR (processing of special categories of personal data), as it could contain information related to someone's health. The processing of sensitive personal data is prohibited. The GDPR states that this ban does not apply in a number of situations, including where the individual (whose personal data is involved) gives his or her consent for the data to be processed. This means that the express consent of the participants must be obtained in order to collect, store and use their self-measured data, or there must be other grounds for doing so. The GDPR is much stricter than the previous legislation concerning the validity of informed consent. The consent must be voluntary, unequivocal and specific, and must be based on complete information about what the processing will be used for and to whom the data will be provided (Witt, 2015). Acceptance of the general terms and conditions of the supplier is not sufficient. The participant must also give their consent in the form of an 'affirmative action' which the party processing the data must also be able to prove.

With conventional, largely offline, biobank research, the collection of biomaterials and data generally takes place during personal contact with the patient or participant. He or she is provided with written and verbal information, and written consent is requested for the use of biomaterial and data for scientific research. In an era where more and more online data is self-measured the question is how control by the participant can best be safeguarded? Participants can and increasingly want to decide for themselves when and what health data will be used and for what purpose. This requires a dynamic online approach in consultation with the participants.

The researchers working for the REshape Center are in favour of a 'personal consent flow', a continual process in which a participant decides online who may see and use what information and for how long (Rake et al., 2017). In the UK too, research is being done on the use of the dynamic consent principle to be able to keep pace with technological advances in the area of online data collection for research (Budin-Ljøsne et al., 2017; Kaye et al., 2015). In this case the consent forms part of a coherent technological platform on which all online interaction between the researcher and the participants is arranged in a flexible and dynamic manner.

22 Personal Data Protection Act (WPB), Section 1b: processing of personal data means: any operation or set of operations which is/are performed upon personal data, including in any event the collection, recording, organisation, storage, adaptation, alteration, retrieval, viewing, use, disclosure by transmission, dissemination or otherwise making available, combining, linking, as well as blocking, exchanging, erasing or destroying of data.

Participants can indicate on the platform which parties may or may not use the health data and which data, how often they are willing to be approached and what for. In the Netherlands we see more and more initiatives in which a form of online consent for the use of uploaded data (self-measured or otherwise) is integrated into more complex interfaces, such as for research purposes in the stations and personal lockers in the Personal Health Train[23] project of the Dutch Techcentre for Life Sciences (DTL) and the REach platform of the REshape Center, and for wider applications in the Personal Health Environments (PGOs) previously referred to (e.g. MedMij).[24]

Informed Consent

The studies examined still often included a written Informed Consent form for the use of certain specific self-measured data. Those taking part in the **ParkinsonThuis** study provide Informed Consent online for the collection, storage and use of the sensor information from the wearables (continual readings). The participant is sent an information letter first, by post or by e-mail. A week later the researcher calls the participant to answer any questions that he or she may have. The link is sent to the participant by e-mail 48 hours later. The participant gives his or her consent online via this link.
In the **Netherlands Twin Register** study participants can notify by post or by e-mail that they do not wish to be approached to take part in research (temporarily or permanently, or for specific types of research). There are also plans to include the Informed Consent in the MijnNTR portal.
The **PRIDE** study uses an app that is part of the REach platform to communicate with participants about self-measurement. For the questionnaires the consent request forms part of the questionnaire itself and the consent is formalised with an answer in the affirmative. There is also a separate question in the online questionnaire requesting consent to read out the HealthKit data. This consent is then given by moving a slider. In the case of biomaterials, such as saliva, participants are provided with a separate consent form on paper with additional information on the rear. They can then still decide whether or not they wish to provide that. “This is, in fact, a very simple form of dynamic consent.” Changes are taking place in the area of dynamic consent on the REach platform. The platform includes a separate module for consent. Participants can sign by placing a fingerprint on their telephone to give consent. The consent is held separately from the other data as a PDF to prevent the possibility of any personal data being linked to data in the questionnaire (Rake et al., 2017). Work is also being done on making selection menus more dynamic and creating more distinction between prospective studies and sharing past information.

With an account on a personal interface the participant can find whatever information he or she wants in one place, collect and view his or her health data and give consent for this to be shared. However, people do not always regularly visit ‘their environment’; it depends on what it gives them. Organisations that wish to make use of the data with, and for the benefit of private individuals, need to take this into account. They are also responsible for checking at regular intervals whether a consent is still valid. An overview of the consents given should be provided with the option of adjusting or withdrawing individual consents given online.

23 https://www.dtls.nl/fair-data/personal-health-train/
24 https://www.medmij.nl

By providing participants with more control and by being transparent about the purposes of the research, people will be more willing to share - and continue to share - their data (Geesink et al., 2016). A balance does need to be found between participants' freedom of choice and the usability of the measured data for research purposes. Not least because this sort of 'freedom of choice' in consent could lead to a wider variation in how individual datasets may be used and for how long. This could make research more difficult. Studies on dynamic online consent, like that of the REshape Center, may provide useful guidelines for this.

Privacy

In our view particular attention needs to be devoted to the privacy aspects of self-measured data for biobank and other research, in addition to what has already been laid down for standard data collection and use. Particularly in a period in which many things are still unclear and new, stricter legislation is being introduced. Other than in the standard situation, with self-measuring there is often a supplier of equipment or data storage capacity involved, ownership of the data is not always entirely clear, and there will be other data environments and linkages involved. The privacy-by-design principle should be applied to the entire concept of data collection, and to each separate part. Safeguarding privacy and transparency along every step of the self-measurement process adds to participants' confidence and the ability to undertake successful research using their data.

Privacy is when an individual is aware of the collection and the use of his or her information and has a certain degree of control over that (Goodwin, 1991). The Personal Data Protection Act (WPB) provides privacy protection also for self-measured data (that may be directly or indirectly derived or coded). People need to be informed about the collection, processing and storage of this personal data and their consent for this is required. Most organisations where data and biomaterial is collected for medical research are set up to comply with those requirements. Nevertheless, when self-measuring methods are used, privacy could come under threat. Suppliers of measuring devices or apps often have access to the measured data which has been stored on a smartphone or in a cloud environment. Through the use of unclear terms and conditions manufacturers can also process the data themselves or sell it for marketing purposes.

The new European legislation on privacy, the General Data Protection Regulation (GDPR), provides additional protection. This imposes stricter standards on the technology and the security of the device so that privacy aspects become part of its engineered design (i.e. privacy by design) and data can only be obtained anonymously (in no way traceable) by unauthorised parties to whom the individual has not given his or her consent. People must also be able to object to the use of personal data for targeted marketing. The Article 29 Working Party, WP29[25] , the independent advisory body of European data protection authorities concerned with privacy matters, has set out in guidelines how various aspects of the GDPR should be applied in practice.

25 http://ec.europa.eu/newsroom/just/item-detail.cfm?item_id=50083

Not uncommonly the self-measuring devices collect other data in addition to the parameters they are intended to measure for the study, such as GPS data on a smartwatch. This is very privacy-sensitive data which provides a lot of information about someone's lifestyle. The GDPR provides for a data minimisation requirement, i.e. that only the data necessary for the purpose may be processed. When the processing (or some part of it) is done by the supplier of the self-measuring equipment, under the GDPR some transparent agreement must be made between the researcher and the supplier which lays down who is responsible for the processing (data controller): the researcher, the supplier or both, and how that will be done in a way which is compliant with the provisions of the GDPR (Article 26 GDPR). The content of the agreement should be made available to the participant and included in the Informed Consent. The participant's consent given for data to be processed by the researcher for a particular purpose therefore does not automatically mean that consent has been given for the supplier to do the same.

Once the self-measured data has been stored in the data storage environment of a medical research organisation, or if that data is accessible to the organisation by means of an interface, that organisation is responsible for ensuring that this self-measured data, along with other personal data, is stored and used in such a way that the researchers can only have access to the pseudonymised data. This must safeguarded along the entire path that the data travels, as well as for the links that have to be provided for this. The question that constantly needs to be asked is: who is responsible for the data processing? Who is entitled to use the data and for what purposes and under what conditions? It is recommended that a Data Protection Impact Assessment (DPIA) should be carried out, which may even be mandatory in some situations under the new legislation. Article 35 of the GDPR states that where a type of processing is likely to result in a high risk of infringement of the rights and freedoms of natural persons, the data controller must conduct a DPIA on a regular basis. The Article 29 Working Party has formulated nine criteria in its guidelines to be able to determine in practice whether or not a DPIA needs to be carried out, BBMRI-NL has had a GDPR Register, DPIA & Compliance Tool[26] specially developed, which includes a DPIA function, for the purpose of processing personal data for scientific research.

The challenge is to start thinking about the privacy aspects together with the participants (or their representatives) as early as possible in the research process. This will help to avoid inefficiency and maintain the confidence of those taking part. All too often privacy is something which organisations still only start to think about later, or about which they make vague statements. If you consider the privacy of the client right from the outset and are transparent about that, this engenders confidence. Privacy then becomes one of the reasons why people will choose to work with you (Lavender, 2014).

In some of the studies investigated the data from the self-measuring devices (wearables and apps) ended up in the secure data centres of major providers, such as the Amazon cloud. In other cases, the data was stored in the organisation's own secure environment. This is always done in a coded or pseudonymised manner. The personal data as well as the key are stored at another location. This is stated in the consent signed by the participant. When the manufacturers also have access to the data from the measuring device, as far as is known, that is only anonymised data.

26 https://www.bbmri.nl/elsi-tools-avg-register-dpia-compliance-applicatie-in-dutch/

Privacy and security

In the **Leiden LangLeven** study data from wearables is held in the study database. The manufacturer of the measuring equipment and the researchers have access only to anonymised data. The key is held by the Leiden University Medical Centre. The same also applies to the use of the movement monitor in the ParkinsonThuis study. Each monitor has a unique ID which is known only to the study and which allows the study to link measured data to personal data. The supplier has access only to coded data.
In the **ParkinsonThuis** study accelerometer data (recorded with a Pebble Smartwatch) is first processed on the smartphone in a specially developed app to provide usable measurements of physical activity and this is then streamed together with metadata from the smartphone to the Amazon data storage environment. All the data belongs to the Michael J Fox Foundation which also manages the data and guarantees privacy when issuing requests to use the data for research.
In the **LifeLines Newborn** study the data from the self-measuring devices is stored and managed in a secure IT infrastructure which guarantees the privacy of the participants. The commercial organisations involved are only permitted to process anonymised data. Research with the data is only possible further to approval of the research. Lifelines then provides access to pseudonymised data that cannot be traced to the participants and for which LifeLines holds the key.

Ethical Review

In our view it is by no means obvious what legislation applies to the ethical review of data collection and research using data that has been measured by private individuals themselves. It is clear, however, that additional assessment criteria are needed for the technology and algorithms when reviewing research activities that make use of eHealth applications, such as self-measurement methods. People with IT and data management expertise should preferably be included on ethical review committees.

If self-measured data is used for medical research, then there also has to be an ethical review of the data to be collected and the intended research with that data. As with most medical research with data and biobanks, such research activities are generally not covered by the Medical Research (Human Subjects) Act (WMO). The methods are also too wide-ranging and several factors always have to be weighed against one another to determine whether or not this type of research needs to be reviewed by a recognised Medical and Ethical Review Committee (METC). Firstly, it has to be considered to what extent the self-measurement device may be deemed and used as a medical device (Section 13 of the Medical Devices Decree).

If apps can be used to make a diagnosis or for the treatment or relief of disorders, for example, they qualify as medical devices and therefore any research with them must be assessed by an METC. An additional criterion is whether devices are used and whether these are provided to the participants or whether the participants buy and use them for themselves. The burden placed on the participant is another important factor, although this will become less as sensors become ever smaller and more easily integrated in the future.

The medical research organisations and umbrella associations (Coreon/Federa; NFU; BBMRI-NL; Parelsnoer Institute) are currently working on the development of a joint review system for research that falls outside the scope of the Medical Research (Human Subjects) Act (WMO). The basis for this has been drawn from: Human Tissue and Medical Research: code of conduct for responsible use (Federa, 2011) and the Code of Conduct for the Use of Data in Health Research (Federa, 2004).

There is still not much known about what additional assessment criteria should be met for the collection and use of self-measured data. The sensors, apps and participant interfaces to be used, for example, would have to be assessed in relation to criteria such as the burden on and risk to the participant. The expertise of the eHealth application suppliers would also have to be taken into account in the assessment. The same applies to the scientific and medical basis for the algorithms used in the self-measurement methods and interfaces, certainly when these will ultimately be used to support decisions or even replace people, and instead of personal advice or treatment.

Any new criteria for the ethical assessment of data collection and use from eHealth applications requires new expertise on the ethical review committees, e.g., in the areas of IT and data management. This is consistent with recommendations made by the Royal Netherlands Academy of Arts and Sciences (KNAW), to set up an Ethical Review Board for Informatics to be able to assess whether personal data is being responsibly used in IT research[27].

When evaluating proposed research with self-measured data the review committee also needs to include the digital environment. In pilot studies associated with the Personal Health Train project (DTL), the infrastructure was set up so that data which originally had been collected in various different environments could be left there but still combined and made available for analysis and, in this way, guarantee privacy and security.

Review

In the practical examples investigated where self-measurements were involved, the study and the procedure for data collection were generally submitted to an Medical Ethical Review committee (METc) and assessed on the basis of the set criteria for research governed by the WMO legislation. The REshape Center is attempting to bridge the gap between the standard form of review by the METC and a form of assessment of research which is not subject to the WMO legislation in which self-measured data is collected and used for research. During the development of its dynamic consent procedure for the REach platform, the REshape Center therefore worked closely with the METc on this area which is new to both.

27 https://www.knaw.nl/shared/resources/actueel/publicaties/pdf/20160919-eng-advisory-ethische-en-juridische-aspecten-van-informaticaonderzoek-web

Data management

In our view if the (medical) research organisation is storing the data, responsibility for its management rests with that organisation and therefore the participants should be informed and give their consent for that to take place. A clear data management plan based on the FAIR principles will therefore form an essential part of the preparations and communication with participants about what will be done with their data.

Data which the participant measured for him or herself, in the first instance, is the responsibility of the participant; this is stored as agreed in the general terms and conditions of the supplier. Processing this data must be done in accordance with the GDPR and the party responsible for that must be able to demonstrate that the processing complies with the legislation. As soon as the data is measured at the request of a medical research organisation and it is held in that organisation's environment, responsibility for the data collection shifts to the organisation and it is necessary to make clear agreements with participants about its management. Even though the servers of a supplier where the data is stored lie beyond the sphere of influence of the research organisation, it is also necessary to make that route visible. In such an event it has to be established who holds processing responsibility under the GDPR and what written agreements must be drawn up for this.

The study set up can incorporate that the data management will be coordinated with the supplier and the participants. Agreements need to be part of the Informed Consent and, wherever possible, systematically incorporated in the dynamic interaction with the participant. The legal basis for this is the fundamental right that everyone has to protection of his/her personal data (Article 8(1) of the Charter of Fundamental Rights of the European Union (CFREU)). Besides the right to protection of their data, this article also gives people the right to see their data and rectify it. The GDPR, however, has created the room in certain situations to deviate from these rights for the purposes of scientific research (Article 89 GDPR).

"It is also important to maintain personal control over our self-measured data, how it is managed and what is done with it. Certainly when this data is used by third parties, possibly for commercial purposes. Researchers/medical professionals do not have carte blanche in the use of measured data.... Taking part in research should be seen as something done in cooperation with clinicians or researchers." *Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] - BBMRI-NL*

Having an understanding of what will be done with the data is an important requirement to be able to use the self-measured data for healthcare and research. It needs to be clear what data is being held where, how long the data will be kept, who is entitled to see the data and who has control of this.

"The self-measured data has to have real value for research." "Responsibility for the proper use of self-measured data rests not solely with the private individual, but with the appropriate organisations as well." *Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] - BBMRI-NL*

The major challenge in the area of data management is not whether or not all the information flows can be regulated, but to what extent this should be done to protect participants as the owners of the data and to ensure that their interests and wishes continue to be taken into account. It is not the technology but the relationship with the participant which should guide this. Application of the internationally-recognised FAIR data principles (Findability, Accessibility, Interoperability, Reusability) (Wilkinson et al., 2016) should ensure that wherever possible the data continues to be findable and reusable in the future for new research purposes, either through the research organisation or by the participant him/herself, or by third parties authorised by the participant.

Data flows

In the practical examples we considered the information flows were arranged in various different ways. In the **Leiden LangLeven** study the participant only sees the measured data on the display of the accelerometer from which the data is sent directly, unprocessed, to the Leiden LangLeven study database.
In the **LifeLines Newborn** study it has been agreed in writing with the manufacturers of the self-measuring equipment that for the collection of the data their secure data streaming processes will be set up only to send the data directly to the secure IT environment for data storage and exchange and that they then destroy the data. The women taking part in the Newborn study provide separate consent to take part in the individual trials and the collection and use of their data for that purpose. A data plan which describes which party may use what anonymised or pseudonymised data will form part of that and be reformulated for each new application.
In the **ParkinsonThuis** study the data is sent from an app to a secure Amazon environment together with data collected in other countries where the same app is also used. The management of the data rests with the umbrella organisation, the Michael J Fox Foundation (MJFF). The research team of the ParkinsonThuis study can view and use the raw data of its 'own' participants by logging-in to the secure environment. The data can only be provided to and used by third parties by submitting a request to the MJFF.

In all the examples examined, in one way or another the participant can see the measured and often already processed data by means of the sensor or a linked app. The manufacturer of the sensor or app sometimes has access to anonymised data. The final destination of the data in these examples is always a server of the research organisation. The participants do not know what the precise storage locations and data streams are. However, it is usually set out in general terms in the Informed Consent form what may and may not be done with the data and by which parties.

Recommendations further to the investigation

The recommendations arising from the investigation are summarised in the table below. These could serve as a guideline when setting up and undertaking studies in which data measured by the participants themselves is collected with the aid of smart devices, such as wearables.

Recommendations from the investigation	
Initiation phase: research organisation + participants (or their representatives)	
• Selecting the method	Make a weighted choice based on suitable parameters and requirements.
• Validity	Check whether sensor data agrees with data from valid reference measurements; check algorithms behind any data processing; validate any method.
• Participant interaction	Involve participants (or their representatives) in the set up and organisation of the study and the information provided. Equip the interactive interface with dynamic functionality for consent and the exchange of information.
• Consent	Draw up a Consent that ideally is dynamic in nature with clear agreements about the data plan and privacy aspects; ensure that consent can be provided by means of an 'affirmative action' which can be demonstrated at a later date.
• Privacy	Use privacy by design as the basis, not just for the equipment but also for the entire study design; apply the principle of data minimisation and collect only data that is necessary for the goal; make specific agreements (laid down in the consent) about access to the data by researchers (pseudonymised) and about how any responsibility for data processing is divided between the researchers and the supplier. Carry out a DPIA if necessary.
• Ethical review	Include the technology, the data processing algorithms and the data handling in the review of the data collection; supplement review committees with IT and data management experts.
• Data management	Draw up a transparent data plan for the data use, storage and management. As far as possible, apply the FAIR principles concerning the accessibility and re-use of the data by researchers, and by the participants themselves.
Operational phase: research organisation + participants	
• Validity	Provide clear user instructions for the participants; possibly provide a help desk to provide support; monitor the correct use of the remote or on site self-measuring method.
• Participant interaction	Create a mutual partnership with the participants; tailor the interface so that preferences for consent and information exchange can be set and observed.
• Consent	Ensure that all privacy and data management matters are agreed in a way which is transparent and demonstrable.
• Privacy	Ensure compliance with the privacy aspects agreed to in the consent.
• Data management	Ensure that the data collection, storage and management takes place as agreed in the consent.
Prolongation phase: research organisation + participants (or their representatives)	
• Validity	Monitor use; modify if necessary further to evaluation.
• Participant interaction	Involve participants (or their representatives) in the evaluation; provide information on a regular basis about set preferences for consent and information exchange and provide the opportunity to change these.
• Consent	Facilitate and implement selected preferences (or changes).
• Privacy	As in the implementation phase; repeat any DPIA on a regular basis.
• Ethical review	Examine the protocols for the intended research with the self-measured data with a particular emphasis on the privacy and data management aspects.
• Data management	As in the implementation phase.

Table 1. Recommendations for the practical set up of the various phases of a study in which data is collected by the participants themselves using smart devices.

Discussion

Keeping up with developments in society

Given that citizens increasingly want to have control over their own health and health data but are less willing to take part in conventional population and cohort studies, self-measurement can help to involve them in this type of research, for example through their Personal Health Environment (PGO). Maintaining that involvement requires some effort. It is a matter of all the parties working together to discover what works in this new digital environment. Participants want to be involved in the research, while participation is not something which can easily be managed.

Changes in society concerning the use of data in healthcare and research form the backdrop to the major increase in the use of self-measurement. Healthcare data is becoming increasingly widespread, from files in clinics and research sites to a personal electronic (or digital) environment. The collection of data is also becoming more intensive and constant: ever more parameters are becoming suitable for continual measurement and data collection. Finally, what patients and participants expect is also changing: people are starting to attach more importance to taking responsibility for themselves and assuming control over their own health and disease. People have become increasingly more often involved in research in recent years and sometimes even conduct research and analyses for themselves using gathered data (or have this carried out) (Prainsack, 2014).

From the public perspective these developments create room for self-measurement in (biobank) research. At the same time, however, we see that people are less and less willing to take part in conventional population studies and biobanks (Buyx et al., 2017). The gap has to be bridged between traditional data collection in biobank studies and the more innovative ways which address the changes taking place in society. Self-measurement could offer a solution. If the potential for self-measurement were to be fully utilised, it could provide a suitable instrument to involve participants in research in the longer term (see Table 1). In this way self-measurement could make a major contribution to predictive, pre-emptive, personalised and participatory personalised medicine. The interactive, non-site related nature of self-measurement methods makes them ideal for this. Effective cooperation with participants or their representatives, be it in an advisory forum or as research partners is essential to be able to gather self-measured data which is useful for biobank and other research: involvement should never be presumed. Technological advances which facilitate personalised care and research must be linked to developments which make it possible for participants to make informed choices. Such choices are vital to participant involvement and will be driven by the participants' motivations and the avenues available to them (Horne, 2017).

As we have indicated, an online interface is desirable to create such a partnership in the context of self-measurement. An online interface managed by the participant and which enables him or her to regulate the cooperation with the medical research organisation would be ideal. Suitable candidates for this include the Personal Health Environments (PGOs) which are currently being set up in the Netherlands to give people more control over their healthcare. In such an environment the researcher essentially becomes the participant's guest, and through the participant the researcher gains access to his or her self-measured (or other) data. Matters related to control and the exchange of information can be arranged in the PGO.

People can easily collect and view information for themselves related to health, nutrition, lifestyle and family history and share it with others in a PGO (Kregting, 2017). This would then be medical data from the electronic patient files of the GP, pharmacist and other healthcare providers, and the data which these people collect themselves through self-measurements or other information which is important to them. At the moment MedMij[28] is being developed by the Netherlands Patients' Federation, together with Nictiz and the Ministry of Health, Welfare and Sport (VWS). This will provide a set of requirements, standards and agreements which PGOs must meet so that information can be exchanged securely and so that the electronic environment is both affordable for everyone and verifiable in terms of quality. In developing a framework for PGOs the main focus has been on the medical aspects of this eHealth application. A recommendation however is that the importance of this form of data collection for research should be recognised in the PGO development process and supported as much as possible by the MedMij programme.
The availability of a suitable vehicle for the online interaction, however, provides no guarantee that usable self-measured data will be obtained. This is an entirely new way of collecting data over which the researcher has little control. The measuring itself takes place out of sight of the researcher and depends on the participant's willingness to contribute. While the medical researcher operates the measuring equipment for conventional data collection, with self-measurement this is left to the participant. The degree to which the participant accepts the technology, to a large degree, will ultimately determine his or her willingness to take part. This acceptance appears to depend mostly on the wearability of the self-measuring device and how useful it is thought to be. Of course, there may be all sorts of personal reasons why self-measurement is considered to be useful, but in a recent study Hassan showed that most people considered contributing to medical research to be sufficiently useful to carry out the self-measurements (and continue to do so), even if this is only in the context of a wider public interest (Hassan et al. 2017, Del Savio et al., 2017).

"The self-measured data has to have real value for research." .
Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] - BBMRI-NL

It is not the case that everyone who is asked to undertake self-measurement for useful medical and scientific research is keen to do so. Research shows that not everyone can or is even willing to play an active part in their own (or other people's) health and sickness (Rademakers, 2014). The willingness to take part is determined by cognitive, psychological and social factors. The composition of the population that is able and willing to do self-measurement therefore may differ from that of the population that can be reached with conventional collection methods for data and biomaterials. This means that for the use of self-measurement for biobank and other research it is necessary to made decisions about the number of participants and the population variation.

Responsibility and confidence

To ensure the optimum and safe use of self-measured data for medical research and healthcare, there needs to be cooperation between the participant performing the measurements, the organisation steering the research and the government body providing for the legal framework and its enforcement. At present there is insufficient clarity surrounding the various roles and how they will be implemented. There is still a challenging task ahead of us which has to be accomplished in a rapidly changing digital landscape.

28 www.medmij.nl

Whether self-measured data from a separate data stream is stored in a biobank or accessed for research via a Personal Health Environment (PGO), all of the aspects discussed in the investigation always need to be carefully considered: from the measuring method itself and validity, throughout the entire data collection process, to participant interaction, privacy, consent, ethical review and data management. The degree to which this is done properly will determine the usability of the data: scientifically, ethically, legally and in the public interest. Even though the participant owns the data and should have control over the data and its use, it is unavoidable that a medical research organisation must hold joint responsibility for this together with the participant. In the above investigation we argued that the best way to do this in a way which benefits both parties is in a partnership between the research organisation and the participant, with clearly defined agreements about what is expected and using an online platform.

This does not mean that biobank organisations will have to relinquish their previous steering role. The expertise that they have built up over the years means that they are now ideally placed to take the lead in such matters as safeguarding participants' privacy and control, the validity of the measuring method and the measured data, as well as the data management. The expertise of the research organisation is vital if self-measured data is to be used for medical research in way which is meaningful and responsible. The participants must be able to have confidence in that expertise.

"Responsibility for the proper use of self-measured data rests not solely with the private individual, but with the appropriate organisations as well." *Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] - BBMRI-NL*

The research partner needs to perform its steering task in a way which is open and transparent. This is one of the necessary conditions to be able to use self-measured data for research, not only from the participants' point of view, but also from the legal perspective. Clear communication about what will be done with the data, carefully safeguarding freedom of choice and providing clarity about its importance will help to inspire confidence in the research organisation and ensure the continued involvement of the participants. When participants are confident that the measuring method used is suitable, that their privacy and control are protected, and that the conclusions drawn on the basis of the measured results are correct, they will be more readily persuaded that their contribution really is vitally important for healthcare research and all the more likely to be committed data collectors.

Clarity about the various roles and how they will be performed is also vital to the successful use of self-measured data. We have identified roughly three roles: the role of the involved participant, the role of the steering researcher (or umbrella organisation) and the role of the government body which sets out the legal framework and provides for its enforcement. When these roles are recognised, the attendant responsibilities can also be adequately defined and provided for.

"The Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] considers it important that self-measured data for care and biobank research is used correctly. This is seen as a shared responsibility: "there is a limit to what the private individual should exercise control over". Besides individual control over data, therefore, confidence in and the reliability of the party that processes the data (i.e. a biobank, researcher or physician) is considered to be very important - they are considered to be the most important parties responsible for the proper management of the data. This also requires proper supervision and sanctions imposed by the authorities and other bodies in the event of misuse. Reliable organisations therefore have to earn that trust and protected it with sound rules and enforcement." *Source: Maatschappelijke Adviesraad Biobankonderzoek [Patient and Public Advisory Council on Biobank Research] - BBMRI-NL*

At the moment the government has provided little in the way of legislation or regulation related to self-measurement. If we want to be able to effectively use the wealth of information offered by self-measurement for research and healthcare in the future, then agreements will have to made about how to do this safely and under whose responsibility. This is in line with the findings of a report on digital information security by the Rathenau Institute for the Netherlands' Upper House of Parliament (Kool et al., 2017). This report urges that more action be taken, beyond privacy and security, to address the blind spots in the current governance system for the digital society The institute urges, for example, the inclusion of 'open standards' in the legislation to govern the security of smart devices: in this way supervisory bodies could act on the basis of this legislation to combat unsafe IT products.

Self-measurement as a cost-effective alternative to data collection on site

The scientific and societal benefits will always have to be weighed against the organisational and financial resources required when considering the use of self-measurement for medical research purposes. As the situation stands, there is no-cut-and-dried answer to this question.

Self-measurement methods can offer considerable scientific added value. The availability of a large amount of different types of new data collected more often means that it is possible to answer other medical and scientific questions. Besides following cohorts over time, self-measurement will also make it easier to follow individuals over time and draw conclusions which result in both population and personal health benefits. Awareness is growing that the continual monitoring of participants yields vital additional information which can help clarify the underlying mechanisms and patterns of health and disease (J. Fleischer et al., 2017; Li et al. 2017). With discrete measurements, even when these are frequently carried out, there will always be a grey area between the measurements about which there is no information. To gain a better understanding of the development and course of chronic, complex disorders, such as Parkinson's and Alzheimer's, in particular, it is essential to gain more insight into the patterns of relevant parameters and underlying biomarkers. More research is needed to determine to what extent continuous measurements can be carried out in a reliable and valid way, and over what time period (Marais et al. 2016; Silva de Lima et al. 2017).

The reasons stated above for people to take part and their acceptance of the measuring method will be important factors, along with other more technical aspects (Sumalan et al., 2017; Elayan et al. 2017). Biobanks provide an important infrastructure for medical and scientific research, such as biomarker research (Hewit 2013; Liu and Pollard, 2016). By supplementing existing collections and combining them with useful self-measured data (continuous or otherwise), biobanks can fulfil that role even more effectively and make an important contribution to current developments in personalised medicine.

As we have shown above, besides this scientific benefit, providing self-measured data may serve as a useful instrument in encouraging participants to remain involved. The participant becomes more of a partner and provides a lasting 'reservoir' of reliable self-measured data in exchange for dynamic control over his or her own health data. This could be described as contributing to the societal sustainability of biobanks.

It is more difficult to answer the question of whether there are financial benefits attached to the use of self-measurement methods for biobank or other research that offer economic sustainability. It is not such that by providing the participant with a sensor and an app data which is useful for biobank research will constantly be generated of its own accord. We have shown that at all stages of the process there are conditions attached to the usefulness of a self-measuring method for research (see Table 1) and that the research organisation has a responsibility to steer the process to ensure that those conditions are met, in dynamic interaction with the participant based on a common interest. Is the measuring equipment suitable for the purpose of generating the data required? How will the participant gain access to the measuring device and the instructions for its use? Is there a vehicle available which will provide user-friendly, long-term and dynamic interaction with the participant? How will the participant's privacy and control be safeguarded? Who has access to what data? Where will the data be securely held?

The research organisation will need to be constantly involved in providing steering, not just during the period or periods when the self-measurement method is used, but beyond that as well. This means there is no guarantee that the use of self-measurement methods for research will be more cost-effective. The cost of the additional financial and personnel resources and the benefits have to be clear in advance to determine whether or not it would be more cost-effective or efficient to use self-measurement. It will also always be necessary to strike a balance between the scientific quality required, the technical feasibility and the ability to meet the ethical, legal and societal requirements.

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Annex I

People interviewed with experience of or pioneering with self-measurement methods for research purposes

Marjan Faber, neurology department, Radboud UMC;
Jules Lancee, REshape Center Radboud UMC;
Marleen van Gelder, REshape Center Radboud UMC;
Tom van de Belt, REshape Center Radboud UMC;
Jackie Dekens, Lifelines Newborn project UMCG;
Marco Berndsen, Lifelines;
Eline Slagboom, Leiden LangLeven Study LUMC;
Gonneke Willemsen, Nederlands Tweeling Register [Netherlands Twins Register] Vumc (VU University of Amsterdam);
Gerard Dijkstra, IBD Parel UMCG;

Questionnaire used for the interviews

Project information

-What parameters do you or your partners measure?
-For what purpose? Healthcare related, research project.
-What measuring method is used? Sensors, apps, etc.
-In what population are the measurements taken? Size, composition, existing/newly recruited, etc.

Participant interaction/portals;

-How do you invite/ask your participants to use the self-measuring method? (digitally/in person; at what point in the study; using what point of entry: physician, researcher, etc.)
-Do you use a participants/patients' portal (existing or otherwise)? Which portal/where?
-Can participants indicate whether or not they wish to be approached?
-Who takes the initiative in the use of the measuring method?
-What percentage of commitments do you get?
-How often are they asked?
-How is the participant provided with information about the purpose? In one direction or interactively?
-What information is provided and in what form (infographics, videos, etc.)?
-Are the measurements continuous or taken at intervals?
-Can participants indicate for themselves what data they are willing to share for research or healthcare?
-What feedback do you provide?
-What communication channels do you use for the feedback?
-How do you keep the participants involved? What is the drop-out percentage?

Consent;

-Is consent provided for the storage and use of the data?
-Is it explained what the consequences of that consent are?
-Do you use an Informed Consent form specially developed for this purpose? Which?
-How dynamic is the consent? And how is that arranged?
-Can the participant switch the 'self-management module' on or off?
-In what context is the data used? For healthcare, for research, for a healthy lifestyle?

Ethical review of the data collection and research with self-measured data;
-Is there a supervisory body which includes the collection and use of self-measured data for scientific research in its ethical review?
-What aspects are reviewed or assessed? Ethical, substantive?

Privacy;
-Do you use a TTP when using the data for research?
-Is data storage/an environment to link data used (data warehouse, workspace, health suite)?
-How do you otherwise arrange for the anonymisation/coding of the data?
-Is this stated in the Informed Consent?

Validity and selection of self-measuring methods;
-How was/is the measurement method selected?
-Who is responsible for the method and its use?
-How is validity verified and monitored?
-How is the financing/purchase of the sensors and apps arranged?
-How and how often is the participant provided with the necessary devices?

Linking with other databases inside or outside the biobank;
-Do you link the self-measured data to other data?
-How is the linking arranged and what form does it take? See Privacy?

The data management plan;
-Who has access to the data? (Fitbit, Apple and Garmin too?)
-In what form is the data available?
-Who is responsible for the data and who owns it?
-Where is the data stored?

To conclude;
-Is there anything we have not covered here?
-What interests you about the approach taken in other studies or projects?