

The digitalization of health care paves the way for improved quality of life?

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Abstract

The digitalization of health care is really a game changer for developing health care. This article gives an overview, discuss opportunities and reflects on methodological issues in this new era. Important issues discussed include: Could digitalization offer the right chemistry between evidence based medicine and individualization of health care. Does Big Data imply long tail health care? How could patients be co-creators of health care? And, methodological pros and cons with different sources of “evidence”.

Keywords: Digitalization, health care, evidence, big data

Introduction

A life without variation would, without doubts, be unbearably boring. Fortunately, our everyday life offers endless variability for which we should be grateful. The crucial challenge is however to learn how to live with and handle uncertainty which come along with variability. According to the great mathematician and philosopher Bertrand Russel studying philosophy might do the trick: “To teach how to live without certainty, and yet without being paralyzed by hesitation, is perhaps the chief thing that philosophy, in our age, can still do for those who study it” [1]. Another discipline dealing with uncertainty is statistics, which can be described as (phrased by the statistician Stephen Senn): “Statistics tells us how to evaluate evidence, how to design experiments, how to turn data into decisions, how much credence should be given to whom to what and why, how to reckon chances and when to take them. Statistics deals with the very essence of the universe: chance and contingency are its discourse and statisticians know the vocabulary. If you think that statistics has nothing to say about what you do or how you could do it better, then you are either wrong or in need of a more interesting job” [2].

Occupations that definitely has to deal with uncertainty, and where statistics and information play an important role, are occupations within health care. Medical care used to be described as “the art of making decisions without adequate information” [3]. Historically this “form of art” has been left to the individual physician, who has to judge the amount of research evidence needed, and how to merge this with other circumstances and personal beliefs and experience. As flaws with this approach became apparent in research, a cure, a strategy, started to

take shape, which turned into the evidence based medicine crusade. Evidence based medicine (EBM) was mentioned in research 1992 [4] and could be regarded as an umbrella definition stating that decisions, guidelines and policies in health care should be based on evidence. Evidence based medicine has certainly been influential for the development of health care, but it has also been criticized, e.g. for stereotyping medicine and neglecting individual patient characteristics.

The question is, if something even “bigger” is going on? The digitalization of health care, patient participation and the “Big data” era offer new possibilities of generating knowledge in order to improve health care. The primary aim with this article is to give an overview, discuss opportunities and to reflect on methodological issues related to the digitalization of health care. Main issues include:

- What opportunities are offered by the digitalization?
- Could EBM and individualization of health care go hand in hand?
- The relation between “real life data” and “scientific data”
- The information systems of tomorrow

EBM and levels of evidence – a matter of design

Since “evidence based” is a rather imprecise concept much effort has been focused on defining what actually is demanded before anything could be declared as “evidence based”. Are there different levels of evidence? Is there a threshold - a minimum requirement? These issues are in general not black or white, it is very seldom that something could be stated as proven to be either 100% true or false, it is rather a matter of “level of evidence” or “strength of evidence”. One important aspect, perhaps the most import one, when discussing the strength of evidence is how the data was obtained, how the study was designed. Different designs have different pros and cons and design issues have for a long time been taking into consideration when judging the quality of a study. In 1989 Sacket suggested a hierarchical system for classifying level of evidence due to the study design [5]. In that system a large randomized controlled trial (RCT) corresponds to the highest level of evidence – I, a smaller RCT: level II, cohort and case-control studies: level III, historical cohort and case studies: level IV and case series and studies with no controls as the lowest level V. Since

the original suggestion of level of evidence various modifications have been done by different organizations and journals. The hierarchical systems of today, for instance the system suggested by the Oxford Centre for Evidence-Based Medicine are much more comprehensive and have separated different types of research questions, i.e. therapeutic, prognostic, diagnostic or economic [6].

For therapeutic studies randomized control trials are still the “gold standard” and a systematic review / meta-analysis of such trials are given the highest level of evidence. Followed by case-control studies, observational studies, and case series and at the lowest level expert opinion. It is also shown that studies at the highest level of evidence are the most cited studies, and overall the suggested hierarchical system of study designs seems to correspond to citation impact [7].

A randomized control trial certainly has its scientific strengths. The randomization guarantees an objective and unbiased allocation to treatment and control groups and creates comparable groups. But, on the downside a RCT, due to safety reasons, usually have rather constraining inclusion and exclusion criteria's. As a consequence only a part of the population may be possible to study. For instance, in asthma studies only 4-6% of the patient population may be eligible for a RCT due to inclusion/exclusion criteria's [8]. Another criticism against RCT is that the surrounding conditions during the trial are different compared to standard clinical praxis. Non representative samples studied in a clinical context different from standard clinical practice infers that the external validity, i.e. possibility to generalize the results beyond the studied sub-population and study-conditions may be low, even though the internal validity, i.e. comparison between active treatment and control group within the context still may be high. Randomized controlled trials are also limited in time and number of patients, which means that adverse effects, especially long term side effects, will have low probability of being detected.

An observational study may have higher external validity, but at the same time, the studied variables may be confounded with other factors, which basically is the most important reason why RCT in general outperforms observational studies. Research based on comparisons between RCT and observations studies reports frequent differences in magnitude of effect which cannot be attributed to chance [9].

Thus there seems to be a huge obstacle with different designs with discrepancies in results. It seems like we have to choose, either between the more scientifically controlled situation with high internal validity but possibly lacking external validity or with empirical information closer to clinical practice but with lower internal validity. Couldn't we get the best of both worlds? Well, a step closer to this was possible due to the development of propensity scores, suggested by Rosenheim and Rubin 1983 [10]. This groundbreaking

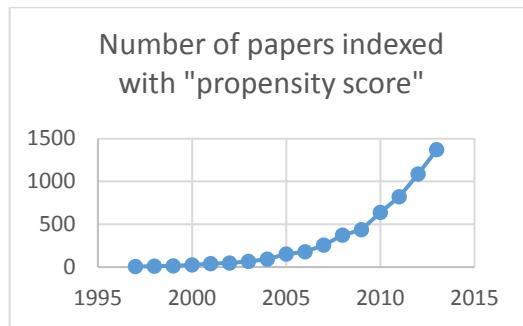
technique is based on the idea to develop a model which include important factors that affects the propensity for a patient in an observational study to be in either the “treated” group or not. An assumption is that patients with roughly the same propensity score are comparable, i.e. have the same profile regarding background factors – confounders. Whether patients with a certain propensity belongs to the treatment group or not may not depend on the factors included in the model, instead it depends on other factors not included in the model and random. A comparison between treated and not treated patients with the same propensity, gets closer to the comparison between randomized groups.

For instance, let's say that we want to study if there is a gain in using electrocardiograms (ECG) in the ambulance for a patient with suspected acute coronary syndrome, based on an observational study and patient case records. Some of the patients (most likely the majority) in this population have received an ECG in the ambulance but not all. It would not be a good idea to compare the health outcome for patients who received the ECG versus patients without ECG. For instance, patients who have a short transportation time may be left without ECG (due to lack of time), but will receive intensive care at hospital rapidly and are therefore more likely to come out well, and actually better than patients with a longer transportation time (but likely an ECG). Comparing ECG versus no ECG would also mean comparing patients with shorter versus longer time to hospital care. Obviously, time is a confounding factor which may affect the study result and give a result in opposite to the expected. Using propensity score in this situation means that factors that are related to receiving ECG or not, e.g. time to hospital, strong suspicion of acute myocardial infarction, etc. will be included in a model for estimating propensity. Thereafter patients with or without ECG but with the same propensity are being compared. This comparison is now adjusted for the factors included in the propensity model, and hopefully the reasons for why a patients receive an ECG or not, beyond the factors in the model, is due to chance, i.e. mimicking a randomized trial. Obviously, the downside with this technique is that the propensity model may have excluded important confounders, but hopefully the bias due to confounding is at least decreased substantially.

Just as there is research comparing observational studies with RCT, there is research comparing observational studies analyzed by using propensity with RCT. In a study focusing on treatment of acute coronary syndrome it was found that observational-propensity studies showed higher treatment effects than corresponding RCTs but the differences were rarely significant [11]. In a critical care study with mortality as endpoint, comparing 21 observational-propensity studies with 58 RCTs, it was shown that the observational studies did not produce any systematically higher (or lower) treatment effect than found in the RCT. However, there were differences of more than 30% in effect in around one third of the

comparisons [12]. Thus, it was concluded the two designs generally were consistent but that there may be occasional differences impossible to predict.

In short, it seems like propensity score has increased the evidence level of observational studies, even though propensity cannot reach the same level regarding internal validity as a RCT. Anyway, the use of propensity score is successively increasing, graph 1 illustrates the exponential increase in number of published papers indexed with propensity score, from 1997 to 2103 [13].



Patient centered care and new outcomes

Another era in modern health care is patient centered care (PCC). According to the international alliance of patients' organizations the essence of patient-centered healthcare is that: "The healthcare system is designed and delivered to address the healthcare needs and preferences of patients so that healthcare is appropriate and cost-effective. By promoting greater patient responsibility and optimal usage, patient centered healthcare leads to improved health outcomes, quality of life and optimal value for healthcare investment." (<https://www.iapo.org.uk/>). Research shows that PCC can improve health status and increase the efficiency of care by reducing diagnostic tests and referrals [14]. Another important ingredient in modern health care which goes hand in hand with PCC is the use of patient reported outcomes (PRO) [15]. Patient reported outcomes could be single symptoms but also multidimensional outcomes like health related quality of life. Much efforts have been made to develop valid and reliable instruments for measuring such multidimensional abstract phenomena's. These instruments could be more or less generic. For instance instruments like short-form 36 (<http://www.sf-36.org/>) , EQ-5D (<http://www.euroqol.org/>) are completely generic and could be used for all health conditions. For oncology a generic instrument (EORTC) for all kinds of cancer is suggested by the European organization for research and treatment of cancer (<http://www.eortc.org/>). But, this organization has also suggested a number of more specific instruments e.g. questionnaires suitable for colorectal cancer.

Are EBM and patient centered care compatible?

That medicine should be based on facts – evidence, that the patient should be put in center, and that patient reported outcome should be used together with classical clinical measurements in order to get a holistic view, certainly sounds desirable in modern health care. But, the question is if EBM and PCC are compatible? Evidence based medicine is sometimes criticized for being "cook-book medicine" and opponents argue that standardized procedures creates "one-size-fit-all" medicine. This would imply that EBM could not be further away from individualization and patient centered care [16]. The obvious risk is that EBM leads to standardization instead of individualization.

The fact is that most research studies generates results valid in terms of an average pattern in the population under study. For instance, when two treatments are being compared it is rather conventional to calculate the average difference between the two treatments. Let's say that treatment: A lowers the diastolic blood pressure with 8 mmHg in average, while treatment: B lowers BP in average with 7 units. For hypertensive patients, treatment A seems to be superior, at least on a population level, i.e. if you must choose one of the two treatment for the whole population, it looks like A would be the best choice. But, this doesn't mean that treatment A is superior to B for all patients. Also assume that the standard deviation for treatment A is 8 units, while treatment B's standard deviation is only 1 mmHg. This would mean that some patients on treatment A will get no effect at all or even a rise in blood pressure. Treatment B seems to be working more or less equally effectively for all patients since the variability is extremely low. Considering the fact that the average difference is relatively small, only 1 unit, one may wonder if not B should be considered as the superior drug since it is more robust and seems to be invariant to patient characteristics? To spice up the example with an even more extreme situation, just add the assumption that treatment A with an average of 8 mmHg gives every second patient no blood pressure reduction, and every other second patient a reduction of 16 mmHg. This is 8 mHg in average, but half of the patient are without effect and half may get too much of a good thing (assuming that patients are mildly hypertonic). In this extreme situation it is clear that providing the treatment that on average is superior will actually be the worse choice, both for each single individual and for the population on the whole.

Instruments, i.e. questionnaires, for patient reported outcomes, e.g. QoL, discussed above, are also rather standardized, based on population studies, including questions that in population studies has shown to be important. Questions that may be of importance only for very few patients are usually excluded in such instruments.

To adjust health care based on cultural diversity and respecting the individuals' beliefs and attitudes about health is called cultural competence in medicine, aiming

at more individualized health care. But, when dividing patients into different cultural subpopulations, it may be an oversimplification and breed stereotypes.

Obviously, it is not an easy task to acknowledge diversity. It is pointed out that we are in a desperate need of research to examine the intersection between EBM and cultural competence in medicine [ibid], i.e. studying if EBM and PCC can be compatible.

Digitalization and big data in health care

The amount of digital data in health care is enormous and continuously growing and to put figures on this gigantic volume in bytes we need prefixes like peta, zeta or even yotta [17]. Smart use of all this data has the potential to make health care more efficient and improving diagnoses and treatments. For instance, just by using electronic patient records, important information about common diagnoses, treatments, outcomes and costs could be analyzed in order to support management decisions. Or, by using digitalized research articles it is possible to search for all papers including some specified symptoms and identify health conditions connected with these symptoms, this kind of association is used in smart diagnostic tools like “Isabel” [18]. Big data could also give valuable information for population health e.g. predict or quick identification of a pandemic outbreak.

The volume of data and the number of included patients gives the possibility to overcome some of the shortcomings with RCT. The data are most often collected in real life situation and in real time, which may be a good complement to the lack of external validity in a RCT. Furthermore, the volume of the data allows identification of also rather rare adverse events from treatments or combination of treatments, and by using electronic expert systems regarding potential drug related problems, e.g. drug-to-drug-interactions, clinically relevant information could be provided to the physicians, which in turn actually generates a change in care [19].

From a methodological point of view, there are a number of potential vulnerabilities with big data analytics. To start with the quality of the data, “garbage in – garbage out” is still a valid expression which cannot be compensated by volume. Secondly, one must be aware of the fact that data driven analyses, without guidance from a priori theoretical justifications, may sometimes lead to patterns and associations that actually were just due to chance. The chance of finding spurious relationships increases with the number of analyses done . This problem, called “mass significance”, “significance fishing” or “data dredging” is well-known, but worth pointing out in the era of efficient software that can produce tons of analyses within seconds, quoting the British economists Ronald Coase: “If you torture the data long enough, it will confess”. A pedagogic illustration of this problem is given by an experiment where a study object was shown pictures of humans in social situations with a specified emotional valence. The

study object was asked to judge the emotion shown, and this task gave significant changes in the brain according to functional neuroimaging data. Considering the fact that the study object was a dead salmon, it would clearly be an understatement to say that this brain activity was surprising. Clearly, the significant changes was only due fact that as many as 130 000 voxels (three dimensional pixels) was analyzed in these images and some of them were significant just due to chance – random noise [20]. Another amusing example of an association found by combining different data sets is between the number of people who drowned by falling in swimming pools and the number of films that Nicolas Cage appeared in. During 1999-2009 the correlation were 0.67, a strong positive correlation
[http://tylervigen.com/view_correlation?id=359].

Correlation is not the same as causation. Confounding factors must be taking into account when making big data analyses. But, making more and more information digitalized also means better possibilities to adjust for at least some of all potential confounders.

The problems described above are classical and have always been present even before the access of gigantic data volumes. But, big data, offers a much wider paved way for these problems. Another issue that is more common in a big data situation is that even very weak and irrelevant relationships will turn out to be statistically significant. A statistical significance, i.e. a low p-value, is basically a ratio between the strength of the relationship found divided by the amount of randomness. The amount of randomness is related to the sample size, and with really big data sets, the random term becomes very small and consequently even a really weak relationship could be statistically strong in comparison. Thus, one should always bear in mind that, a relationship that is statistically significant doesn't have to be of any practical significance. In “small data” situations, a study could be underpowered and the opposite could occur, i.e. relevant relationships turn out to be statistically not significant.

Moving back to opportunities with Big Data, the potential applications described in the beginning of this section was focused mostly on analyses made of data that formerly was available in hard copy form, and analyses on population level. Analyses that have been done also previously but with much more effort. These analyses could contribute to evidence based medicine and the understanding of diagnoses and treatments. In other words, Big Data can contribute to EBM. Now, let's focus on patient centered care and discuss the potential value of Big Data.

Well, Big Data could be used for analyses that accounts for patients characteristics. With rich data it is possible to provide more diversified segmentation of analyses. For instance, it would be possible to identify sub-populations with an increased risk of developing future health conditions (e.g. diabetes or cardiovascular events). It would also offer better possibilities to make segmentation

regarding suitable treatments. Related to the discussion in a previous section regarding treatment effect (A vs B), Big Data analytics could focus on calculating the expected treatment effect for A compared to B given patient characteristics. This could simply be done by identifying all patients in the data set with the same characteristics and exploring and optimizing treatment options. In a study of ambulance allocation, a computer supported decision system was shown to improve the allocation of patients (triage) to different prioritization. The system was designed for patients with chest pain, one of the most common reasons for calling the alarm central. The patient's gender, age, the answers to a few crucial questions and the dispatcher's suspicion, was used as predictors in a model based on thousands of previous patients [21].

Using multivariate models, statistical regression, neural networks, decision trees, etc have for a long time been possible to use for finding more tailor-made models for diagnoses and treatment regimens. But, Big data offers an increased possibility to make this kind of individualization.

Is Big Data just about enhanced possibilities of making rather traditional analyses, that was much more tedious or in practice impossible to realize? Well, another essential difference regards who collects the data. Very much research and the examples above are based on information and data that the care providers and researchers have collected. But, the game changing situation in big data is that the care taker or potential care taker plays an active and important role.

Digitalization and patient participation

According to a nationwide (U.S) survey done in 2013 including roughly 3000 adults, as many as 59% of U.S adults have looked for health information during the last year, 35% have used internet for diagnostic purposes (their own or another person's condition), roughly half (53%) of the "online diagnosers" discussed their findings with a clinician and 41% got their initial online diagnosed condition confirmed [22]. The same study also indicates interest for peer-to-peer healthcare, e.g. 26% have read or watched someone else's experiences of a health condition during the last year [ibid].

There is undoubtedly an interest in health information and peer-to-peer interaction via social media. There are different types of potential support that such social interaction could provide, e.g. emotional support ("being there", listening, empathizing) or informational support (providing guidance and advice), even though there is a need for more evidence regarding benefits for the patients [23]). One of the largest peer-to-peer forums for patients is "patients like me" attracting more than 400 thousand patients and ranging over more than 2500 health conditions, it has been reported that patients have identified several benefits belonging to this community

[24]. The patients reported an increased understanding of their disease and their treatment options.

From a methodological point of view, peer-to-peer discussions are as a matter of fact revolutionizing. As pointed out previously much effort have been used for finding valid and reliable instruments (questionnaires) for patient reporting outcomes, e.g. quality of life. With the ambition to include as relevant questions as possible most of these instruments include deep interviews. Even though such a scientific approach has the advantage to get deep understanding, exploring and identifying dimensions important for the patients, it is de facto a situation between the "dependent" patient and the authority – the care giver. And, there are several potential sources of bias. For instance; a desire to "answer correct", patients may not want to discuss sensitive issues (like sexuality), patients may feel that their bothers are too trivial to mention, or in some problems may not be discussed since the patient doesn't believe that it is a matter for the care giver, or that the care giver actually don't have the right competence. In short, the situation may be somewhat artificial and dimensions crucial for the patients may not be discovered or may not get the relevant prioritization. As always, we cannot study reality as it is, only reality as it appears by the way we study it.

The point is that peer-to-peer discussions actually gives a valuable and easy access source of data that can contribute to completely new knowledge with high real life validity. The peer-to-peer discussion is free from the authority situation described above. One interesting and important research objective is to explore which dimensions of the disease that are being discussed and which dimensions that seems to be the most important from a patient perspective. Are these dimensions the same, and in the same order, as the dimensions and order found by using instruments developed by health researchers? Are information provided via patient-to-patient discussions a more valid source of information and knowledge related to patient centered care, than information found by using instruments developed by health researchers? If a health platform offers both peer-to-peer discussion and the possibility to raise questions to health professionals, it will certainly generate interesting information, not as a substitute to classical research studies, but definitely as a valuable complement.

Concerns of health is an important part of our lives, and "care of self", have always been important to humans. The old saying "listen to your body" are nowadays refined into "quantify your body and analyze". The phenomena "quantified self" is starting to be mainstream [25]. Quantified self means tracking physiological, psychological, behavioral or environmental data. There are more than 500 tools (<http://quantifiedself.com/guide/>) that could assist with measuring and/or keep record of the data and assist with different analyses. These tools may include both classical quantitative variables like, weight, heart rate, etc and more qualitative variables like mode

and emotions. Wristband could automatically measure a number of variables, e.g. motion (steps walking or running), heart rate and sleep. One of the potentials with quantified self is that self-tracking could contribute to better understanding of personal health and illuminate and increase awareness of important factors for individual well-being. And, when self-tracking data sets are used jointly the aggregated data could be used for more population based analyses. For instance, consider research about correlation between sleep and the lunar cycle. A study from 2014 included more than 1000 individuals which is in a scientifically context considered to be a large study [26], keeping in mind that previous studies was based on 30-50 individuals. But, from a Big Data and Quantified self-perspective, thousands of patients is not that impressive. Considering that Fitbit® (manufacturer of wristbands, with roughly one third of the market for wearable trackers) alone has nearly ten millions active users who are collecting data about their sleep (duration and quality of sleep) among other variables. The pros with this situation is that the data is collected under rather natural circumstances (assuming that the individual have been used to wear the wristband as a natural thing) and an enormous sample size. The cons is that the lack of scientific rigidness and circumstances are beyond control. How accurate does the wristband measure sleep? How about other circumstances affecting the sleep?

An advantage with the quantified self is that it allows analyses on an individual level, sleeping data collected over several lunar cycles could be used to analyze if this specific individual have a correlation between sleep and the phase of the moon. But, also on an individual level there may be methodological aspects to consider. For instance, if a person, a priori, believes in worse sleep during full moon, it could cause a self-fulfilling prophecy. But, for a person who has never considered lunar cycle to be of any importance for sleeping quality, collected data could give an unbiased correlation. Among all users and all possible correlations to make between sleep and all possible variables, it is expected to find spurious correlations and certainly a lot of persons will find relationships which are pure random productions, which will be disguised if the analysis is repeated.

For making analyses there is always a possibility to download data and use standard software like excel. But, a next step would be to arrange public databases were health information could be shared and aggregated for research purposes. For instance zenobase.com is a health data platform where you can analyze your data, e.g. correlate sleep with other variables, and share data with others. However, data quality and data privacy are two important concerns regarding such platforms.

I argue that data from quantified self also has the potential to be revolutionizing. Laboratory variables and reference intervals are claimed to be the most frequently used tool in the diagnostic work-up [27]. However,

researchers in laboratory medicine struggles with variability, i.e. variability between individuals, within individuals and measurement error. Reference intervals are suggested for large populations, even though partitioning by gender and age are common, and there is always a risk that individual changes, even rather dramatically ones, are being left without notice since the value still is within the reference interval. For instance, my own Hemoglobin value has always been rather high, close to 160 g/L. If my value is decreased heavily, say by 25 units, my value will still be within the reference interval (roughly 130-160 g/L for adult males) and if I or my clinician was unaware of my previous history with values close to 160, this lower value may have been left without further notice. For diagnostic purposes, it would be optimal if it was possible to use the patient as its own reference. Quantified self has the potential to facilitate this possibility, which for a long time only has been a utopic dream among researchers in diagnostic theory and laboratory medicine.

Revisiting the question: Are EBM and patient centered care compatible?

As defined in the introduction, EBM means that provided health care should be based on evidence. Patient centered care means that the care should be individualized and adjusted due to patient characteristics. Assuming that there exists evidence regarding which health care that is optimal given the patient characteristics, then there would be no conflict between EBM and PCC, it would be possible to make an individually adjusted evidence based care. But, as mentioned previously, the vast majority of all research is providing evidence only on a population level, or at some sub-populations at best. Given that a RCT is large or that data is comprised by a joint data base with all clinical information regarding a new drug, it is certainly possible to analyze the variability of the drug. It is possible to analyze and identify sub-populations with various degrees of benefits from the treatment, e.g. to find sub-populations were the treatment is ideal or sub-populations who would benefit more from other choices of treatment.

But, instead of relying on large scale RCT, digitalization, patient participation and Big Data may do the trick. Just as online business has made it profitable to also offer small scale items, the so called long-tail economy, it is also possible to discuss long-tail health care. With access to big data also rare health conditions may be detected and small information about small sub-populations may be discovered. And, patients may actually play an important role in this situation. Assume that a patient has a rather rare health condition, meaning that the responsible clinician maybe will encounter a few number of such patients during the entire career. The clinician may have access to evidence based information, e.g. review articles and general recommendations. But, assume that the patient has been active in peer-to-peer discussions via social media and has identified a number of peers with the similar characteristics and that these

peers together has identified some important behavioral factors or a specific treatment that seems to be optimal given these characteristics. Given all available information at internet, and the possibility to interact with others (who interact with their care providers), it is actually reasonable that the patients becomes more of an expert of the health condition than the clinician, at least regarding knowledge about the health condition for patients with the same characteristics as the patient self. If a number of patients share the data on a platform like patientslikeme.com it is possible to more systematically make analyses like this, i.e. study rare conditions and small sub-populations and variation between patients.

In a situation with a health condition with great variability, i.e. high degree of uncertainty, and with a knowledgeable engaged patient it is reasonable and in PCC spirit to partner and make shared decision making regarding the care of the condition [28]. Thus, Big Data gives the possibility to make more individually adjusted health care, also for rare conditions and for small sub-populations. And patient participation and peer-to-peer discussions may act as one important source of information, generating valuable findings and hypothesis. Patients could have a much more proactive role.

Several chronic diseases, e.g. Multiple sclerosis and Parkinson's disease may vary much between patients and it is important to make individual considerations when providing care, using knowledge described above. Moreover, these diseases are also examples of conditions that not only vary much between patients, but also vary much within a patient. There may be a variation in symptoms and degree of symptoms over time and the dosage of treatment may have to be adjusted over time. For being able to surveil such within-patient variability, self-tracking and using tools, quantified self, may be extremely valuable and a necessity for PCC and shared decision making.

Well, the answer to the question addressed (if EMB and PCC are compatible) is: yes indeed, and digitalization of health care plays an important role. My point is that there is no conflict between EBM and PCC as long as the health care provider doesn't suffice with population based research, but instead also adopt big data, patient participation and quantified self.

As a final example on this issues, consider the health condition: overweight/obesity. There are a number of evidence based strategies for weight loss, i.e. strategies proven to give an average reduction in weight on a population level. Naturally, the basket of evidence based strategies is a good start to choose between when considering a suitable treatment. But, naturally, strategies proven to be effective in population based studies, doesn't guarantee a success for all individuals in the population. On an individual level, given the individual characteristics, preferences and environmental circumstances, it is a good idea to identify, (within the basket of evidence based regimens) to identify the

strategy that could be sustainable given the individual characteristics. A strategy that actually fits the individual, still an effect cannot be guaranteed, but the chances are at least optimized, given both general evidence and individual conditions.

Some challenges on the road

The aim with this paper was to discuss opportunities given by the digitalization of health care. Just presenting opportunities may give an over optimistic or even utopic impression. And, naturally, using the full potential of the digitalized health care is not a well paved road, it is a truly bumpy road, with a lot of stumbling block. Let's discuss some of the major challenges.

Most importantly, Rome wasn't built in a day. To build trust in new sources of information, develop patient participation and adopt shared decision making, strengthen medical literacy are all examples of cultural changes, which needs time for acceptance and implementation [29]. Promisingly, the big pharma industry seems to have a more open view today in performing more patient centric research, and regards patients as an important active partner in research and not only as a "research subject" and even though researchers have been skeptical there is a trend that several important stake holders are starting to accept health data generated by social media [30].

It has been claimed that health care is lagging behind other industries, but health is a complex phenomenon and data quality, security and ethical considerations must be allowed to take time. For instance, consider the tons of health information available on internet. How could an individual know if the provided information is valid or not? In a study the information regarding safe infant sleep recommendations, it was found that 43.5% (1300 Web sites being analyzed) provided accurate information [31]. Who is responsibility for ensuring that the information provided is adequate and correct? Should care givers take a proactive role and accredit sites? Should physicians act as information guides for their patients?

Furthermore, reading and possibly also collecting and sharing health information is also intricate matters which demands well thought trough pedagogics – an important design parameter. Furthermore, on a societal level, one might strive for higher health literacy, improving the capacity of being reflective consumers of health information with the possibility to take advantage of the benefits with e-health and increased empowerment. Consequently, pedagogics, health literacy and empowerment ought to be important concepts to adopt in health care information systems. Models for how to evaluate online health data and to further develop knowledge in credibility assessment has been suggested [32].

From a methodological point of view, there is much to do in order to increase the precision and usefulness of "Big Data". Furthermore, the value of every day, real life –

generated data must be discussed and evaluated. Today, a systematic review of RCTs is regarded as the highest level of evidence. But, even if such a review may include thousands of patients, it must be compared to big data including perhaps millions of individuals, measured continuously, even though, in a less controlled, less scientific, environment.

Just as similarities and discrepancies between RCT and observational studies, with or without propensity score adjustment have been explored, studies based on online data must also be explored in comparison to other classical approaches. Some examples of such studies already exists, illustrating that online data certainly could be valuable and informative, and that online population could reflect the clinical population, but that adjustment due to confounders and demographic differences may be needed in order to reduce bias [33-36]. For instance, the platform patientslikeme.com reports on their homepage (FAQ- What are the main limitations of PatientsLikeMe data?) that their database have some overrepresentation of white patients, females, are a few years younger, few 75+, and tends to have a higher education than the general population.

Digitalization of health care – a paradigm shift

To sum up, let's consider the major opportunities, justifying that the digitalization of health should be regarded as a paradigm shift.

Big data – a complementary nerve system: The digitalization of health care lays the ground for a knowledge revolution of a magnitude that deserves to be called a paradigm shift. For a long time computer and information systems has been complemented and empowered human characteristics, and ICT has helped us to collect, store and process data and allows us to interact and communicate. The information systems of today and all the data routinely collected gives us the Big Data society, which gives us the possibility to in real time analyze real life data, i.e. Big Data as an extra complementary nerve system who could help us control and improve our lives. Health care is no longer a matter of making decisions without adequate information. The information is available, both on an individual level and on a population level, we just have to learn how to use it efficiently.

Patients as health care developers: From a work place perspective, ICT gives enhanced learning opportunities for care givers in their everyday practice, e.g. with providing evidence based information digitally, learning by interacting with peers both in house and globally, etc. [37]. However, the radical cultural change given by the digitalization, the true game changer, is the fact that patients are given a completely new role. Instead of just being consumers of health care and study subjects in research, patients are nowadays participators. The development of health care is nowadays not only a matter for the care providers. Patients plays a central role and are

engaged both in their own and others health care. And research issues and important factors to be highlighted are driven by patients e.g. by using social media. Just as in business industry, the time is up for “co-creation” also in the health care business.

Evidence from population down to the individual: Never before has data, in that amount, been available both on a population level and on an individual level. With patients more engaged in their health (also when healthy) and self-tracking and using social media, there is nowadays a possibility to both study the vast majority and general populations health, but also to adopt “long tail health care” for studying really small subpopulations. Even a subpopulation that consists of a tiny percentage of all humans, consists of a large number of patients, since the general population is that big. Furthermore, quantified self by using either commercial devices or devices provided by the health care, gives the possibility to individualize care. Digitalization and patient engagement makes it possible to realize patient centered care in full.

New sources of information – new knowledge: There is some skepticism among scientists regarding the value of “big data” and data collected routinely in every day practice. This is due to the lack of scientific rigidity, e.g. the environment is uncontrolled, assessments and variables may not be scientifically validated, and devices may have questionable precision. But, on the other hand, real life data, doesn't suffer from scientific experimental situations which cannot be generalized to the real life situation. Never before has the discussion regarding the balance between rigor and relevance been more important. Naturally, “big data” can be improved by standardization and developing more precise assessments etc. And, from my point of view, real life data is gives new learning opportunities, not as a substitute to more rigid scientific studies, but as a complement. For instance, it will be extremely interesting to study if the health issues and their importance found in patient driven discussions gives the same results as found in research, using e.g. quality of life questionnaires.

The next step: creating the information systems of tomorrow

Computers and information systems could really empower us human beings. The design of information systems, has traditionally, focused on usability and usefulness, aiming at improving productivity and efficiency. This traditional view has been complemented by designing systems that encourage engagement and thereby contributes to e.g. democratization and learning opportunities. But, now it is time to take the next step. It is suggested that: “To create designing socio-technical environments that actually foster, nurture and support “Quality of Life” (QoL)” is one of the most challenging design problems in the digital age”, as stated by Gerhard Fischer [38].

In U.S. the institute of medicine has advanced the “learning health care system” [29,39], defined as “each patient-care experience naturally reflects the best available evidence, and, in turn, adds seamlessly to learning what works best in different circumstances” [40].

Final comments

Within the scientific community and evidence based medicine, it seems like observational studies are given higher credits today, due to easy access of data and refined analyses. At the same time, assessing health is nowadays much more focused on variables highly relevant for the patient, frequently reported by the patient, and not just clinical data. With other words, health research has taken a turn towards methods and variables closer to the reality for patients. Methodologically, it is a challenge to evaluate and summarize the joint knowledge from different approaches. How to evaluate and balance rigor and relevance and how to decrease the gap between research and reality is an exceptional live issue in the current progression.

The next step in this progress of getting empirical data even closer to reality, is to actually use real-life data generated routinely in the everyday reality. Developing learning systems like the ones described in the previous section, using data as continuous impulses in a “big data nerve system” in order to generate general population knowledge (evidence based general population theory) and at the same time individualizing, aligns well with the dimensions described above as a paradigm shift.

Well, the opportunities discussed doesn't seem to be over optimistic after all, as a matter of fact, we are already on the digitalized way towards better quality of life.

References:

1. Russell, B. (2013). History of Western Philosophy: Collectors Edition. Routledge.
2. <http://www.senns.demon.co.uk/DICE.html>
3. Sox, H. C., & Higgins, M. C. (1988). Medical decision making. ACP Press.
4. Evidence-Based Medicine Working Group. (1992). Evidence-based medicine. A new approach to teaching the practice of medicine. *Jama*, 268(17), 2420.
5. Sackett, D. L. (1989). Rules of evidence and clinical recommendations on the use of antithrombotic agents. *CHEST Journal*, 95(2_Supplement), 2S-4S.
6. OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>
7. Patsopoulos, N. A., Analatos, A. A., & Ioannidis, J. P. (2005). Relative citation impact of various study designs in the health sciences. *Jama*, 293(19), 2362-2366.
8. Liisspers, K., Teixeira, P., Blom, C., Kocks, J., Ställberg, B., Price, D., & Chavannes, N. (2016). Are pharmacological randomised controlled clinical trials relevant to real-life asthma populations? A protocol for an UNLOCK study from the IPCRG. *NPJ primary care respiratory medicine*, 26, 16016.
9. Ioannidis, J. P., Haidich, A. B., Pappa, M., Pantazis, N., Kokori, S. I., Tektonidou, M. G., Contopoulos-Ioannidis, D.G., Lau, J. (2001). Comparison of evidence of treatment effects in randomized and nonrandomized studies. *Jama*, 286(7), 821-830.
10. Rosenbaum, P. R., & Rubin, D. B. (1983). The central role of the propensity score in observational studies for causal effects. *Biometrika*, 70(1), 41-55.
11. Dahabreh, I. J., Sheldrick, R. C., Paulus, J. K., Chung, M., Varvarigou, V., Jafri, H., Rassen, J.A., Trikalinos, T.A., Kitsios, G. D. (2012). Do observational studies using propensity score methods agree with randomized trials? A systematic comparison of studies on acute coronary syndromes. *European heart journal*, 33(15), 1893-1901.
12. Kitsios, G. D., Dahabreh, I. J., Callahan, S., Paulus, J. K., Campagna, A. C., & Dargin, J. M. (2015). Can we trust observational studies using propensity scores in the critical care literature? A systematic comparison with randomized clinical trials. *Critical care medicine*, 43(9), 1870-1879.
13. <http://dan.corlan.net/medline-trend.html>
14. Oates, J., Weston, W. W., & Jordan, J. (2000). The impact of patient-centered care on outcomes. *Fam Pract*, 49, 796-804.
15. Deshpande, P. R., Rajan, S., Sudeepthi, B. L., & Nazir, C. A. (2011). Patient-reported outcomes: a new era in clinical research. *Perspectives in clinical research*, 2(4), 137.
16. Hasnain-Wynia, R. (2006). Is evidence-based medicine patient-centered and is patient-centered care evidence-based?. *Health services research*, 41(1), 1-9.
17. Raghupathi, W., & Raghupathi, V. (2014). Big data analytics in healthcare: promise and potential. *Health Information Science and Systems*, 2(1), 1.
18. Nash, D. B. (2010). Isabel, a New Diagnostic Aid For the 21st Century. *Pharmacy and Therapeutics*, 35(12), 651.
19. Hammar, T., Lidström, B., Petersson, G., Gustafson, Y., & Eiermann, B. (2015). Potential drug-related problems detected by electronic expert support system: physicians' views on clinical relevance. *International journal of clinical pharmacy*, 37(5), 941-948.
20. <http://prefrontal.org/files/posters/Bennett-Salmon-2009.pdf>

21. Gellerstedt, M., Rawshani, N., Herlitz, J., Bång, A., Gelang, C., Andersson, J. O., Larsson, A., Rawshani, A. (2016). Could prioritisation by emergency medicine dispatchers be improved by using computer-based decision support? A cohort of patients with chest pain. *International Journal of Cardiology* 220, 734-738.
22. Fox, S., & Duggan, M. (2013). Health online 2013. *Health*, 1-55.
23. Helgeson, V. S., & Cohen, S. (1996). Social support and adjustment to cancer: reconciling descriptive, correlational, and intervention research. *Health Psychology*, 15(2), 135.
24. Wicks, P., Massagli, M., Frost, J., Brownstein, C., Okun, S., Vaughan, T., Bradley, R., Heywood, J. (2010). Sharing health data for better outcomes on PatientsLikeMe. *Journal of medical Internet research*, 12(2), e19.
25. Swan, M. (2013). The quantified self: Fundamental disruption in big data science and biological discovery. *Big Data*, 1(2), 85-99.
26. Cordi, M., Ackermann, S., Bes, F. W., Hartmann, F., Konrad, B. N., Genzel, L., Pawlowski M., Steiger A., Schultz H., Rasch B., Dresler, M. (2014). Lunar cycle effects on sleep and the file drawer problem. *Current Biology*, 24(12), R549-R550.
27. Sasse, E. A. (1996). Reference intervals and clinical decision limits. *Clinical chemistry theory, analysis, and correlation*, 3rd ed. St. Louis: Mosby, 370-1.
28. Guyatt, G. H., Scott, I. A., & You, J. J. (2014). Patient engagement and shared decision-making. *Journal of general internal medicine*, 29(4), 562.
29. Larson, E. B. (2013). Building trust in the power of “big data” research to serve the public good. *JAMA*, 309(23), 2443-2444.
30. Sharma, N. S. (2015). Patient centric approach for clinical trials: current trend and new opportunities. *Perspectives in clinical research*, 6(3), 134.
31. Chung, M., Oden, R. P., Joyner, B. L., Sims, A., & Moon, R. Y. (2012). Safe infant sleep recommendations on the internet: Let's google it. *The Journal of pediatrics*, 161(6), 1080-1084.
32. Metzger, M. J. (2007). Making sense of credibility on the Web: Models for evaluating online information and recommendations for future research. *Journal of the American Society for Information Science and Technology*, 58(13), 2078-2091.
33. Rothman, M., Gnanaskathy, A., Wicks, P., & Papadopoulos, E. J. (2015). Can we use social media to support content validity of patient-reported outcome instruments in medical product development? *Value in Health*, 18(1), 1-4.
34. Bove, R., Secor, E., Healy, B. C., Musallam, A., Vaughan, T., Glanz, B. I., Greeke E., Weiner H., Chitnis, T., Wicks, P., De Jager, P. L. (2013). Evaluation of an online platform for multiple sclerosis research: patient description, validation of severity scale, and exploration of BMI effects on disease course. *PloS one*, 8(3), e59707.
35. Schroeder, E. B., Desai, J., Schmittiel, J. A., Paolino, A. R., Schneider, J. L., Goodrich, G. K., Lawrence, J.M., Newton, K.M., Nichols, G.A., O'Connor P.J., Fitz-Randolph, J., Steiner, J.F. (2015). An Innovative Approach to Informing Research: Gathering Perspectives on Diabetes Care Challenges From an Online Patient Community. *Interactive journal of medical research*, 4(2).
36. Nakamura, C., Bromberg, M., Bhargava, S., Wicks, P., & Zeng-Treitler, Q. (2012). Mining online social network data for biomedical research: a comparison of clinicians' and patients' perceptions about amyotrophic lateral sclerosis treatments. *Journal of medical Internet research*, 14(3), e90.
37. Vallo Hult, H., Byström, K., Gellerstedt, M. *ICT and Learning Usability at Work Challenges and Opportunities for Physicians in Everyday Practice*. Proceedings: IFIP 8.6 Conference, Ljungskile, Sweden 2016. Springer-Verlag GmbH Berlin Heidelberg 2016.
38. Fischer, G. (2015). *Faustian Bargains*” and Design Trade-Offs: Frames of Reference for Quality of Life in the Digital Age. University of Colorado, Boulder (forthcoming). http://studylib.net/doc/10508047/%E2%80%9Cf_austian-bargains%E2%80%9D-and-design-trade-offs--gerhard-fischer
39. Smith, M., Halvorsen, G., & Kaplan, G. (2012). What's needed is a health care system that learns: recommendations from an IOM report. *Jama*, 308(16), 1637-1638.
40. Institute of Medicine. *Best Care at Lower Cost: The Path to Continuously Learning Health Care in America*. Washington, DC: National Academies Press; 2012.