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Direct to consumer laboratory testing (DTCT) – opportunities and concerns

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ARTICLE

Direct to consumer laboratory testing has the potential for self-empowerment of patients. However, the Direct to consumer laboratory testing (DTCT) uses loopholes which are related to the particular situation of healthcare: While advertisements and claims for medical usefulness are very high regulated in healthcare, essentially no regulations safeguard the consumers in DTCT. The same is true for the quality of testing services since quality regulations are only mandatory in healthcare. Another problem is the lack of medical interpretation of test results. Besides being very risky for the consumers, healthcare professionals relying on test results obtained by DTCT must be aware about the risks of these data.

INTRODUCTION

With the advent of point of care testing as well as with the self-empowerment of patients ("P4-medicine") [1] and the availability of some disruptive technologies, there is no need to send all patients' specimen to a medical laboratory for testing and result reporting. One argument for increased Direct to consumer (DTC) access has come from the so-called "quantitative self-movement" which argues that increased data collection and subsequent analysis may fundamentally improve the ability for individual patients to understand and predict the state of their health [2]. Some Direct to consumer laboratory testing (DTCT) data can be analyzed by swarm intelligence or by big data analysis which allows new observations not possible with previous methods of healthcare. However, the focus on patient autonomy allows the selection of data and will introduce a significant bias to the conclusions. E.g., when DTCT is used for infectious disease testing and the positive results are excluded from the database because of fear of discrimination, analysis of these data will grossly underestimate the disease prevalence.

These new technical possibilities challenge the definition of healthcare and the legal regulations which are necessary to protect patients' wellbeing. These definitions – despite being universal – are rather complex and even differ between countries. Internet technologies will make country borders become invisible. Related to the "world-wide marketplace of laboratory tests" are attempts to blur the difference between laboratory testing for healthcare and for lifestyle purposes. The first being highly limited and regulated, the latter with very little regulation to allow free trade and the rules of the marketplace. In particular in genetic testing, in some countries such as Austria, Switzerland and Germany very strict laws protect the patient and the relatives [3]. The background of these legislations is the idea of genetic data exceptionalism and regulates in particular inaccurate promises, the discrimination of persons according to their genotype and an elaborate data protection for the results of genetic analyses [4]. If samples are sent to other countries and particular if treated as lifestyle tests, the impetus of these laws can be easily circumvented.

A challenge in laboratory testing (in vitro testing) is the impossibility of the patient to judge the quality of the Clinical Pathology service obtained: the direct contact will occur in exceptional situations only and the patient must rely on the intrinsic hurdles such as self-declaration, legal regulation and supervision by the authorities and often marketing buzz. Legal regulations in particular for in in vitro diagnostic differ substantially between health systems: E.g., in the US the FDA approves test kits for use in healthcare and CLIA approves medical laboratories individually on a regular basis. In Germany, the focus is on structural quality of medical laboratories and on performance quality (internal quality control and external quality assessment) which is regulated by the RiliBÄK (Guidelines of the National Physicians Chamber) [5]. Test kits are regulated by EU legislation similar to FDA approval (called "CE-marking"). However, for laboratory testing outside of healthcare (such as for lifestyle testing or for DTC), there are essential no quality qualifications or formal approval to be met. For lay persons, it will be nearly impossible to detect fraud by counterfeited FDA or CE markings on reagents.

Particular targets of novel testing formats are healthy subjects, obviously to access new markets and generate profits. Laboratory testing is offered to these persons "to guide their lifestyle". Numerical values such as those obtained in Clinical Pathology as well as by wearable computers ("wearables") are used to assist these persons [6]. Mostly, it remains unclear whether the purpose of this laboratory

testing is only lifestyle coaching with automatic "canned comments" (=lifestyle) or whether in fact this testing should better be regarded as regular healthcare with individual diagnoses and recommendations. The situation gets even more complex in genetic testing, not only due to ease of deducing the genotype of a person from genetic test results performed in relatives. In the US, strict regulations are in place for medical genetic tests, however, the FDA allows genetic lifestyle tests in general. It is obvious, that – rather unpredictable – some "innocent" genetic markers used for lifestyle purpose to a later point in time might become strong genetic markers with severe health implications for the patient and even his relatives. Examples are the ε3 and ε4 genotypes of APOE, which have only very little effects on lipoprotein metabolism [7] but became one of the most important markers for Alzheimer's disease [8]. Genetic counseling starts before testing with the "right of not-knowing". This right is non existing when in DTCT testing can be performed without genetic counseling. In fact, actionable action will occur based on the genetic test results even only by the interpretation of the patient himself, by using internet resources, or by medical counseling [9].

LABORATORY SETTING

Laboratory testing can be performed in different settings: The conventional testing is performed in medical laboratories; some testing is performed as POCT (point of care testing). This testing is also part of healthcare and the testing is mostly performed by medical professionals. Another type of testing is DTC (direct to consumer testing). In DTC, medical professionals are often not involved at all. The consumer (the term patient is avoided intentionally) buys either the testing device or submits his sample to a (nonmedical) laboratory and is the direct recipient of the test result [6]. Typical examples are home urine pregnancy testing, lactate testing for fitness purposes or the submission of body fluids by the consumer himself for quantitative testing or for genetic testing via mail. A recent application is self-testing for SARS-CoV-2 Antigen testing from oral fluids [10]. New techniques challenge the clear separation in particular with another layer of differentiation: in healthcare, only tests with a proven medical use may be used (evidence-based medicine). In dealing with consumers, these restrictions are not in place and the rule of marketplace allows offering tests without proven use and even with potential harm to the consumer. When different testing scenarios are listed, some tests might even fall within all of these categories. For example, the continuous glucose monitoring in patients with insulin-dependent diabetes mellitus is a medical evidence-based method [11]. However, it is performed at the point of care setting or even at home. Only some medical supervision is needed so that in most of the time the patient is the direct recipient of the testing results and will adjust insulin dosages directly from the reading of the meter. Other tests such as food stuff related IgG4 are offered by sending capillary blood drawn by the patient by mail to a central laboratory. In this case, this will be named DTC despite the testing is performed in a laboratory: there is no medical evidence for this kind of testing and the testing is only performed to satisfy the patients' curiosity (and to generate revenue for the provider of these tests). Other tests such as borrelia testing in ticks are tests neither related to healthcare nor to DTC: in this case, only non-human samples (=ticks) are analyzed. Again, there is complete lack of any medical use for this kind of commercial testing. SARS-CoV-2 Antigen testing as DTCT will erode the restriction for testing certain contagious diseases by physicians only (as defined in the Medical Act and the Quacksalver Act such as the "Heilpraktiker Gesetz" in Germany) and

will also cease the notification of public healthcare bodies since this notification is mandatory for physicians only.

CHANCES AND CHALLENGES OF DTC

One challenge is to define the purpose of laboratory testing in apparently healthy subjects: in essentially all situations, the customer (patient) is not interested in the numeric results of a test but wants an answer to possible personal consequences of testing, the medical interpretation of the testing results. It is challenging to give this individual answer to the patient when the testing may be performed only beyond healthcare* (**In essentially all countries there is a restriction of healthcare to physicians. Healthcare encompasses the diagnoses of illnesses, the prescription of diagnostic examinations, the use of invasive and/or risky diagnostic techniques, the determination of medical treatment, the prescription of medications, the clinical monitoring of patients, giving pregnancy care and deliveries and decision about isolation measures in contagious diseases*). Therefore, it is not unexpected, that the providers of DTC use rather confusing and contradictory descriptions of the services delivered. In short, in their advertisements they offer individually tailored comments and personal recommendation to the testing results but in the fine print they stress that the services offered are for wellness purposes only and may not substitute medical treatment.

Another challenge is the clear definition of medical use of tests performed in Clinical Pathology. Only very few – if any -- tests offered are clearly without any medical use. Especially many esoteric tests can be beneficial in highly selected patients and it could not be justified to ban these tests because of their limited use. However, medical knowledge is essential to restrict these tests to patients who might benefit from them. If the selection of these tests has to be done by the consumer himself, chances are very high that tests are not used to increase the consumer's / patient's benefit. There is even a very high chance that the tests produce only medical, psychological and economic harm to the users of the tests and even on society as a whole [12]. In the concept of medical commons, the resources of healthcare are limited and therefore it is the responsibility of the healthcare professionals to respect the needs of society as a whole and to use the resources in healthcare with caution [13]. If unnecessary laboratory tests are ordered, chances are very high that even under state-of-the-art conditions numerous abnormal (=out of the reference range limits) test results will occur just by chance. If medical tests with little medical meaning or / and even insufficient performance of the testing procedure are used, even a remarkably high percentage of all test results will be abnormal and will confuse the customer. A similar situation is present for genetic tests when – driven by curiosity – testing is performed in the absence of a medical questions and the high number of genetic variants (many of them with unknown meaning) or of testing errors will lead to extensive follow-up procedures. In most case, the costs for the follow-up medical procedures (such as additional laboratory testing, invasive procedures, psychological support) has to be covered by the society (such as public health insurance) even when the impetus of testing was the sole curiosity of the customers [12]. Given the concept of reference ranges with 5% of the results being "abnormal" and the long list of tests available on the background of the current health illiteracy of the population, the contralateral damage of DTC is of extremely high impact. When the real performance of DTC is monitored, the rate of abnormals is even much higher (about four times higher than regular laboratory tests) [14]. In average, a testing panel of only 5 tests will result in one false abnormal result!

Another challenge is DTC testing performed at the interface between lifestyle testing and healthcare. This occurs if data from DTC are presented to the attending physician to guide medical therapy. This is of particular concern since DTC testing has not to be performed under the same quality standards (e.g. in Germany, quality standards are only given for testing in healthcare and not for lifestyle purposes [5]) and in the US, huge DTC companies either claimed to be exempt from FDA approval since the tests allegedly were developed and used only within the organization (under the exemptions valid for laboratory developed tests) or they failed to reach minimum performance goals over extended periods of time for critical tests such as in coagulation testing [15]. If a physician relies on the (incorrect) data presented from DTC, the liability will be with the physician primarily. It will be difficult or even impossible to charge the health-illiterate patient, the unqualified non-medical laboratory or the administrator of the hospital or the health plan who recommended the DTC laboratory since the physician is regarded to be the only one in the whole process who could judge medically the (insufficient) quality of the DTC services. A comparable situation is present when the patient himself performs the testing and the physician relies on this self-testing data only [9]. In these cases, the integrity of the data presented to the physician is another point of concern since unlike to the protected and elaborate ways of data collection in health, consumer health data are often collected by apps which can be easily manipulated by the patient or by others.

Another challenge by DTC is the concept of obtaining evidence in medicine: In DTC, the restrictions of healthcare are not valid. The medical claim of a certain test or of a panel of tests have to be judged in studies and the conclusion of these studies have been scrutinized by structured processes by peers and institutions such as in health technology assessment [16]. In DTC, often blogs and social media are used to advertise the products. Typically, the "experiences" of consumers (i.e. bloggers paid and supported by the vendor of the tests) are presented who claim improved vitality after getting the individual recommendations of DTC. These, false, claims would be illegal in health care. However, if a possible customer of a certain DTC test will do a search in the internet, essentially all comments on these tests will only be the biased recommendations of the test and scientifically-proven negative comments appear at the end of the search list only. This shows that social media and online comments offer an easy way to inject biased, incorrect, or misleading information. It is a continuing challenge of the medical and scientific community to respond to these online comments to build up a counterpart. This can be particularly challenging since the business plan of DTC companies can be severely challenged by evidence-based clarifications and the DTC companies will try to eliminate such clarification by the whole armamentarium of legal allegations [17] and 'trolls' (online harassers) [18].

Other challenges of DTC is the intense use of IT services [19]. Medical data is regarded as overly sensitive data and numerous restrictions for storage and access must be obeyed by healthcare professionals. Additional regulations prohibit the exclusive use of telemedicine in some countries such as in Germany. Critical is the intense use of external IT service providers because of the risks such as data theft, right of possession of medical data, integrity of medical data, legal issues of cloud storage and numerous other issues. If IT services become essential for the medical process, another obstacle is the general relation between a patient and his physician who becomes invisible behind the IT interface: Unlike a commercial firm, physicians may not extend their services by unlimited hiring employees or even

outsourcing medical services. E.g. in Germany, there is the obligation in medicine to render qualified services and in person (Common service law §613 (1) "BGB", Physician law: §19 (1), for patients under public insurance §32 (1) "Zulassungsverordnung für Vertragsärzte" and §15 (1) „Bundesmantelvertrag-Ärzte"). Other professions such as biomedical specialists can be employed in the Clinical Pathology laboratory, but the whole laboratory must be guided and managed by the Clinical Pathologists and may not be a huge commercial testing facility only.

CONCLUSION

DTCT bears severe risks to patients and customers relying on the results of these tests. Of particular concern is in many cases the absence of claims of medical usefulness. In addition, despite being an in vitro method, there is a very high chance of substantial medical harm as well as of severe economic impact on the users of DTC testing (psychic harm, follow up procedures) and on the society as a whole with huge negative impact on medical commons.

In addition, the negative news of large-scale wrong-doing in DTC and the replacement of evidence-based medicine by advertisements in the social media jeopardize the privileged situation of healthcare and of real laboratory testing in Clinical Pathology laboratories. Outside the laboratory, there are extremely high personal liability risks for healthcare professionals relying on DTCT data. Finally, the essential and medically-sound regulations of genetic data protection laws as well as of infection control are often leveraged by DTCT.

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