Scope and new horizons for implementation of m-Health/e-Health services in pulmonology in 2019

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Abstract

The reason for this review based on the results of many meta-analyses is the great assessed difference in the methods of most studies in e-Health, telemedicine and tele-rehabilitation. It consists of different understanding of new terms, using different hard- and software, including criteria, different methodology of patient's treatment and its evaluation. This status suggests that first of all m-Health/e-Health requires a unique ontology of terms using and methodology of studies comparing. In this review we try to describe shortly the most significant points of modern e-Health field of medicine. The basic parts include methodology of review formation, tele-communication implementation results, tele-education, interactive questioning, tele-consultation, telemedicine diagnosis, tele-monitoring, rehabilitation and tele-rehabilitation, gamification, acceptability of mobile electronic devices and software in e-Health and planning studies. At the end of the review the new ontological structure of digital medicine is presented.

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Introduction

The questions of m-Health/e-Health have become the most interesting in the last two decades and fast progressed [1,2]. Implementation of new technologies presented a possibility to construct new healthcare programs. The most significant result was revealed in the field of modification and automation of patients' rehabilitation. The scope of scientific publications has been growing. They present modern tendencies in this field of medicine [3]. So we have gradation of telemedicine techniques into tele-monitoring, tele-communication, interactive questioning, tele-rehabilitation, telemedicine diagnosis, "decision-making support", tele-consultation and some others. Thus, we have many publications including different key words that change the results and create a problem of incomparable data. Possibly, all of digital technologies decrease the number of patient's visits to the clinics, medic's visits to a patient, increase medical care availability in far districts and in cases of patient's self-care inability and severe disease course, improve patients-medics compliance, patient's skill in medical devices using technique and results of self-care rehabilitation. But not all studies revealed improvement of rehabilitation's results by using m-Health/e-Health [4]. The main problems arise because of the devices variety and the differences among the software and programs used. Actual tasks of modern period of progress are to standardize basic principles of m-Health/e-Health techniques using, to make new terms of m-Health/e-Health more understandable [5] and to confirm effectiveness of the new medical technologies.

Methodology of review completing

This review is devoted to finding relevant ideas in the wide field of mobile and electronic medicine. Following this task we do not use meta-analysis to prevent closing information resource due to restricted key words and databases. We try to describe more points of view in very difficult and recent problem of modern healthcare. The questions we have to discuss are the following: What ontology of m-Health/e-Health is more perspective to use in trials planning? The same question relates with definitions we have to use. Is "Telehealth" the most common definition among others or not? Are tele-monitoring, tele-consultation and teleconference parts of tele-rehabilitation or this point of view is not appropriate? To find the answers we constructed our review as a summary from PubMed, NCBI and e-library and of most interesting to our mind different ways in digital medicine science using tele-communication, tele-education, interactive questioning, tele-consultation, telemedicine diagnosis, rehabilitation and tele-rehabilitation, gamification, acceptability of mobile and electronic devices and software terminology. The result of this description presents as planning studies and conclusion.

Tele-communication

Communication using electronic devices is the most simple and attractive for young specialists and many patients. This possibility can be realized by phone, e-mail, skype, WhatsApp, any messengers and social networks [3,6-10]. However, the declaration of human rights requires to keep confidential status of personal information in healthcare practice. So we have to recommend these methods in confidential tool only and do not use any social networks or other simple techniques [11]. In many countries (Canada, Australia, Denmark, USA and others), different communication channels are available for the patient-physician interactions. They are phone-communication, internet connection or a digital television. All these technologies allow us to provide psychological and technical support to the patients and reduce a number of exacerbations, patient's visits to physician office, improve life quality. A very important task of the tele-communication is sharing the decision-making process [5]. Tele-conferences are often used to provide care to the patients in remote districts in difficult clinical cases or in specialists examination of different specimens or assessment of methods of visualization results. Consequently, medical communication is an important part of tele-consultation and tele-medicine and it should be provided through closed information canals-secured network.

Tele-education

Many patients demonstrated their interest in receiving a decreasing amount of information about their condition. It was evaluated that 51% of them were ready to receive information *via* computer [12]. The goal of tele-education is to encourage the patients in self-management, to increase compliance between doctors and patients, to improve the effectiveness of tele-rehabilitation, prevent exacerbations and hospitalizations, promote quality of life and increase life-expectancy.

However, patient's tele-education is characterized by some problems. First of all not all patients are able to fully understand medical terms and other specific information. The patient's problem is associated with lack of vision, loss of memory, depression which influence information intake. Sometimes the difficulty can be explained as following: "I have a problem switching on my computer", "I cannot read the text on the screen because the letters are so small", "It is difficult to find the required information on the web-page or web-cite". So the information for COPD patients can be presented only on special planforms and in appropriate manner. The amount of information presented to the patients should be limited. The group of COPD patients can be subdivided into two categories: compliant to receive tele-education and not. The last require individual approach.

Interactive questioning

This method is based on electronic platform and requires special software. Expert councils provide recommendations to develop questionings. For example, Clinical COPD Questionnaire (CCQ), exacerbations of chronic pulmonary disease Tool (EXACT), patient-reported outcome (PRO), St. Georges Respiratory Questionnaire (SGRQ), Paediatric Asthma Quality of Life Questionnaire (PAQLQ), Asthma Control Questionnaire (ACQ) and a variety of ad-hoc questionnaires for COPD and asthma [13].

In addition to patient's surveys which were used in monitoring the symptoms, interactive questionnaires were suggested and underwent clinical investigation in Russian Federation [14]. About 3000 patients with different health status and diseases were included in the numeral shot studies in 2011-2018. After positive results were revealed the system was implemented in regional Unique electronic health system and is recommended now for every patient's visit with respiratory diseases before routine clinical examination done on-line. Effectiveness of bronchial obstruction syndrome diagnosis of this system was published previously. Sensitivity of method consisted of 87% and specify was 97%. For parenchymal lung damages (pneumonia cases) sensitivity was 90% and specify – 95% [15].

Another possibility for patients' symptoms monitoring appears due to automated clinical registers formation based on automated program's syndrome diagnostics. This software let to complete the electronic medical card of every patient automatically and to construct electronic dynamic register for automated control for personal patient's treatment result [16-18].

Well-designed website presented electronic resources in Canada [8]. They are including laboratory information system, diagnostic imaging repositories, drug information systems, telehealth and some other properties. The basis of this system is the Electronic medical records system. It can collect all individual medical information to support a physician to analyze previous information or so-called anamnesis data and to compare vital parameters changes in disease course.

To improve the tele-monitoring technique and the effectiveness of tele-rehabilitation a special electronic system was created in UK. It included the so-called electronic patient's symptom diary accompanied by pulse oximetry, pulse rate and pulse wave form registration [19]. Unfortunately, the authors did not describe the patient's diary for self-monitoring completely. It included a number of questions for vital signs recording (for every day completing) and emotional/well-being/anxiety-depression symptoms (once a month recording). The average time of diary completing consisted of about 2 hours, but the alarm system included only 40 parameters. This reasonably means that the number of questions was so much, and, perhaps, that they need to be corrected. However, the results of the initial study demonstrated good COPD patient's compliance.

We can confirm that interactive tele-questioning is the cheapest method for patient's symptoms monitoring that can be accompanying by different tele-monitoring systems.

Tele-consultation

As usual medical consultation using electronic devices is a modern equivalent of physician's patient's examination, but with no physical methods application [11]. So the information for physician decision is less than by conventional mode. The most publications are devoted to not primary but secondary electronic diagnostics – evaluation of disease severity and symptom's dynamics. This task is solved by interactive or phone questioning and additional remote monitoring devices using (oximetry, pulse rate calculator, BP-monitor, *etc*.) [20,21]. All these methods can be accompanied with the televisual medic's contact to a patient.

Tele-consultation can be provided as specialist/physician consultation or as a nurse's, or technician advice in different health-related questions. In patients receiving oxygen supply or home mechanical ventilation the problems related with the equipment use are more common. The same problems relate with other devices for vital function monitoring. It is a valid way to prevent general practitioner's calls and additional workload to specialist. It introduces another term, "tele-assistance" [22].

It is very important that tele-consultation is needed in the proving with evidence-based methodology because it presents us patient's examination without conventional physical methods and many traditional diagnostic criteria are lost. So, the new model of diagnosis making is based on small number of clinical thresholds and potentially characterized by low accuracy. It seems that tele-consultations are very important to support a patient in technical problems or in cases of not severe exacerbation, if the diagnose is made previously.

Telemedicine diagnosis

In 1998 the review of publications in the field of Clinical Decision Support System (CDSSs) development and implementation led to conclusion that the process will well for the future of improving the effectiveness and efficiency of clinical care. But at that time there was a limited range of clinical settings in which CDSSs have been tested and proved [23].

In 2013 European Commission presented results of the study "Benchmarking deployment of eHealth among General Practitioners II" funded by Unit F4 of DG CONNECT. The method of study included General practitioner's survey about e-Health technology adoption. The main enclosure consisted of that their access to, and using of, basic ICT (a computer connected to the Internet) in the consultation room had become almost universal in all countries (97% of the sample). For more advanced features such as Electronic Health Records (EHR), Health Information Exchange (HIE), Telehealth, and Personal Health Records (PHR), however, the data had shown that more progress is needed. This result seems to confirm what several general practitioners (GPs) had lamented during the focus groups examination and that e-Health was being pushed more for administrative purposes than for clinical ones. The sub-dimensions of the health information exchange (HIE) composite had indicated the same result. On average HIE had remained mostly at a transactional level, and was yet far from supporting information sharing across healthcare tiers. There was a quite sizeable usage gap for HIE (percentage of GPs having access but not using functionalities) suggested either lack of awareness or of interest (usefulness) [24].

Diagnosis making process is a Real challenge. It is characterized as not absolutely achieved task today and is tried to be solved by several approaches. Telecommunication let clinicians to introduce interactive discussion as one of decision making manner. The real problem of this approach consists on measurement of every physician's recommendation and mathematic methodology construction for diagnosis calculation and automatically formulation based on presented clinician's opinions. So several soft wares were suggested and developed [25]. Unfortunately, many ethics' questions not give a permission to implement this method in official clinical practice [11].

One well known method consists of extraction of needed data from non-structured texts as, for example, electronic or personal medical record [26,27]. In 2001, a group of Russian researchers patented the "System of Automated Medical Preventive examination" (SAMPO) [28]. This automated program is aimed at detecting adaptation disorders, preclinical stages of diseases, stress resistance reduction and various risk factors both in practically healthy subjects and in different groups of patients. Personalized recommendations on preventive interventions for health professionals and for the subject are created as a result of automated evaluation of different health parameters. SAMPO was used in different clinical studies [29-32].

The other decisions presented in machine learning approach for program training to make a clinical decision. Machine learning works by i) defining goals, ii) exploring data and iii) training, refining and validating models. In tele-medicine task the machine learning process explore classification algorithm. Common classification algorithms for supervised learning in the healthcare field include artificial neural networks, decision trees, random forests, Bayesian networks, k-nearest neighbors, support vector machines, linear discriminant analysis, k-means clustering and logistic regression [13,27].

Different mathematical decisions can improve individual rehabilitation program after remote monitoring of respiratory muscles strength. In Vladivostok's scientific group study the strength indicators of expiratory (MEP) and inspiratory (MIP, SNIP) respiratory muscles were registered by means of the MicroRPM device (CareFusion, Basingstoke, UK). MEP, MIP and SNIP informational value was determined by means of logistic regression models. A decrease of expiratory and inspiratory respiratory muscle strength in COPD and bronchial asthma patients was recorded. The expiratory muscles dysfunction predominated in asthma, and the diaphragm dysfunction – in COPD and in patients with combination of asthma and COPD signs (ACO). Correlation analysis showed that respiratory muscle strength depends on the severity of bronchial obstruction, lung hyperinflation, skeletal muscle mass, body mass index, respiratory discomfort and functional status of patients. The comparative analysis of several regression models showed that the MEP/MIP ratio proves the feasibility of its use as an additional tool for verifying various clinical variants of bronchial obstruction [33-35].

Also it was shown that the transformation of regression model development cardiovascular diseases difficult for apply in practical medicine into a more simplified version of scale was shown. This included the determination of disease predictors; categorization and inclusion in the regression model with optimal scaling and coefficients for subsequent calculation of importance; plotting regression dependence of theoretical probability investigated variable; selection of threshold value [36,37].

To solve the problem of early preliminary clinical diagnosis making we constructed the model of multi-approach multilevel diagnostic system based on detailed interactive patient's survey [14-16,38]. This electronic system consists of 7 modules, including respiratory, oncologic, cardiovascular, renal, vertebrae/joint's, haematological and women diseases. It takes only 5-10 minutes to answer the questions of one module, and characterizes of high accuracy for preliminary syndrome diagnosis (average 80-90% in different problems). The system is characterized by two levels. The first presents syndrome diagnosis detecting and the second – nosologic form. Additional functionality includes syndromes automatically clinical registers formation and monitoring assessment of different symptoms. So, there is evidence of effective decision making systems effectiveness that can help a physician to provide as primary diagnosis as symptom monitoring after exacerbation and construct clinical registers to improve individual rehabilitation plan and healthcare system.

Tele-monitoring

There is a controversial attitude to tele-medicine and tele-monitoring. On the one hand, this approach has to improve healthcare system and make it better for many patients in remote districts, encourage them into self-related proved medical care. On the other hand, it is cost expensive manner, more than vaccination, smoking cessation program, bronchodilator using and even rehabilitation in traditional mode [39,40]. But high economic expenses mainly include too much devices using for severe/very severe COPD patients and may be decreased in mild/moderate severe patients. The aims of tele-monitoring are: reducing the impact of exacerbations through the early recognition of symptoms and prompt treatment may reduce the risk of hospitalization, improve health-related quality of life (HRQoL) and control the burden of COPD [13].

The best decision of functional parameters monitoring is wireless equipment to control oximetry, pulse rate, blood pressure, breathe rate, some respiratory functional tests. These parameters will be 24-hours collecting in cloud electronic system and analyze by computer and software in physician office. More promoted system consists of inhaler, connected with wireless appliance that measures the inhale flow rate during inhalation of remedy. If an inhale force will be failed the signal will send to physician office computer and call the patient's attention. There are many similar devices produced by some industries (GlaxoSmithCline (Ellipta), Propeller, 3M™ Intelligent Control Inhaler, *etc.*) [41].

Remote patient's monitoring stimulates the theory of tele-treatment methodology birth. It is actual task for those patients who use an oxygen therapy, CPAP or BiPAP, and other methods of ventilation support. If the oximetry will include in the electronic system will change the ventilator parameters in according to present oximetry, deep and rate of patient's breathing [42,43].

It is very actual task to make medical standard (guideline) for needed clinical parameters to be controlled. From systemic review of 11 studies analyzed tele-monitoring systems for COPD and asthma patients some of these parameters were presented. They are some symptoms, forced expiratory volume in 1 second (FEV1), peakflow (PEF), forced vital capacity (FVC), pulse oximetry (SpO2), heart rate (HR), weight, respiratory rate (RR), body temperature, physical activity measured by electronic device [13]. Many other publications described author's view to the best registered parameters configuration [26,44-48]. But today we do not have any universal validated and proved approach for this purpose in many clinical cases.

We also have experience in tele-monitoring using regular interactive questionnaire and some electronic devices. But based on modern clinical recommendations, spirometry is the best diagnostic manner for COPD diagnosis and monitoring. Implementation of this method demands well-skilled professionals and sometimes presents great variability in consequent measurements. There are many intelligent systems for basic spirometric parameters calculation and some of them are not validated [48,49]. To improve this problem we suggested electrical impedance method of spirometry [50,51]. This approach is characterized by a simple technique and does not need forced expiration but performs on spontaneous breathing. The principle of this technique consists of registration of resistance and a phase angle of mild alternative low frequent current which spreads through the bronchial mucus and depends on airflow. As an additional property this method let to diagnose heart failure in COPD patients. The advantage of electrical spirometry used in tele-health system consists of simplicity using by self-manage manner at home.

Some studies were devoted to the perception of modern tele-monitoring in comparison to conventional approach. It was confirmed that the new method is an acceptable alternative to a more traditional home nursing visit model for monitoring community-based patients with COPD following their discharge from hospital [52]. It revealed quick adaptation and availability of monitoring systems [19]. But some questions demand future developing and stimulate new studies on medical electronic devices acceptance principles investigation. They are confidence of individual medical information, accuracy of the results of telehealth technologies, cost-effectiveness and easy-to-use interface improving.

So, tele-monitoring of COPD patients requires special simplest equipment for self-managing at home and connected with electronic monitoring system for machine analysis and professional control.

Rehabilitation and tele-rehabilitation

Many of described previously (tele)electronic medical system are usually combined in rehabilitation office in order to make the process of rehabilitation effective and cheap [53,54]. Recently, it has been demonstrated that a 2-month rehabilitation after hospitalization is more effective in COPD exacerbation prevention than conventional route [4]. Before electronic technologies the methodology of early rehabilitation after hospitalization included one-two physician's and up to 8 nurse's visits to whose patients which characterized by severe course of COPD and excessive dyspnea in 8 weeks was successfully used [55]. New methodology is based on electronic m-Health technique characterized by one physician's, 1-2 nurses and 1-2 technical specialist's visits [52,56,57].

The reason for using rehabilitation programs for COPD and idiopathic pulmonary fibrosis patients was confirmed by many trials [4,58-62]. Mostly the efficacy of rehabilitation connected to improvement in dyspnea (in severe COPD patients the first), exercise capacity and walk distance increasing in both mild/moderate and severe patients. Rehabilitation decreases exacerbation's rate, number of hospitalizations, length of hospitalization stay and results in financial benefit to the health service. Recommended methods consist of education program, respiratory muscle training, lower extremity training. It is known that severe COPD patients demand longer rehabilitation than mild/moderate patients, up to 6 months.

The modern definition of pulmonary rehabilitation (PR) is as follows: PR is "a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors" [55].

Physical training is the main therapeutic factor in the COPD patients via rehabilitation program. Not all specialist confirm that COPD can be included in the list of diseases where rehabilitation effectiveness is approved [63]. The mechanism of physical training influence on COPD patients is not yet clear. The basic theory consists of the spiral progression of functional disability of patients due to progressive dyspnea which appears during physical exercises following by decrease motivation to physical training. As a result inspiratory muscles impairment is progressed and a patient suffers from shortness of breath. So regular physical training may potentially cut this pathological circle and improve life quality, dyspnea and exercise tolerance in COPD patients [64]. Rehabilitation program has to be accompanying by previously performed physical patient's status assessment including pulmonary function testing, arterial oxyhemoglobin saturation based on direct arterial oxygen saturation (SaO_2) or indirect peripheral oxygen saturation measured by pulse oxymetry (SpO_2), and dyspnea monitoring using the Borg scale. A cardiopulmonary exercise test including ventilation and gas exchange assessment and a standardized ramp protocol may be used too. Submaximal exercise testing (smaller increments, slower progression) may be indicated depending on the rationale for the test and the patient's clinical status. The 6-minute walk test is often used for assessing functional exercise capacity in patients with more severe pulmonary disease and/or in settings lacking exercise testing equipment. The minimal period of physical training which is needed to improve physical tolerance is 8 weeks. Improvements in functional exercise capacity seem to plateau after 12 weeks of exercise training. It includes cycle physical activities, muscle resistance trainings and flexibility training as an additional recommendation. Endurance training is more proved for best results achievement. Today there is limited evidence to support the inclusion of breathing strategies such as pursed lip breathing, yoga breathing, and computer aided breathing retraining. The rehabilitation program can be based on SpO_2 monitoring during exercises and controlled on the level of 88-90% of this parameter. If it is required either oxygen supply or CPAP therapy is recommended to support the oxygenation and physical tolerance improving.

The correlation between physical activity of COPD patients and time to the first hospital admission was established and minimal important difference was investigated [65]. It was between 600-1100 steps per day. Those patients who had improvement of more than 600 steps per day, characterized by decreased frequent exacerbations. This study demonstrated high efficacy of physical rehabilitation program on COPD exacerbation frequency. The other questions are how physical rehabilitation may influence a dyspnea, and what is the ratio between rehabilitation and medication in COPD patient's dyspnea treatment? It is assumed that bronchodilators improve dynamic hyperinflation in COPD patients and decrease sensation of shortness of breath. But the effect of short-acting beta2-agonists is lower in patients who do not have dynamic hyperinflation due to the reduced abdominal compartmental lung volume, increased abdomen effort to pump the lung in a case of increased pleural cavity pressure and as a Valsalva maneuver decreased cardiac output and the blood shift from trunk to extremities formation [66]. This problem may be solved by physical rehabilitation in addition to pharmacological treatment. But the best decision consists of individual assessment of patient's physical exercise tolerance and its change during physical training.

The most famous test for physical tolerance in COPD patients is 6-MWD test. However, the equivalent and more comprehensive is Glittre ALD test [67,68]. The Glittre ALD test consists of the following: while wearing a backpack with a load of 2.5 kg for women and 5 kg for men, subjects start from a sitting position, walk on a flat 10 m course, ascend and descend two steps (17 cm high x 27 cm wide) located in the middle of the course, face two shelves upon arrival at the end of the course, in which the upper (shoulder height) contains three 1 kg objects; the objects are to be moved one by one to the lower shelf (waist height) and then to the ground, after which they must be placed again on the lower shelf and then on the higher shelf; the individual then returns, following the course to the original position and another lap immediately follows as described above. A total of five laps must be completed in the shortest possible time. Maximal time is 2 min for completing this test for healthy individuals without violating the protocol. Most COPD patients might perform test for about 4 min. It was proved that Glittre ALD test presents the same information and can be used instead 6-MWD test to control functional COPD patient's status.

We can add that Glittre ALD test seems to require less time and space to be performed than a 6-MWD test, more comprehensive for functional patient's status assessment, useful for rehabilitation center, but it is not available for self-manage control at home. Recently simpler test was assumed. A so-called Time to Up and Go test (TUG) consists of standing up from a chair, walking a distance of 3 m at a comfortable and safe pace, turning and walking back to the chair to sitting down again. This test has been used for the assessment of functional mobility, walking ability, dynamic balance and risk of falling in subjects with a variety of conditions. It was changed seconds in the group of COPD patients. If it was more than 11.2 seconds, had good sensitivity (0.75) and specificity (0.83) for identifying patients with a baseline 6-minute walk distance <350 m. TUG time improved after physical rehabilitation ($p<0.0001$) and a change of 0.9-1.4 seconds was identified as clinically important. COPD patients with a baseline TUG time >11 seconds showed poorer health outcome measures but were more responsive to PR in terms of the performance on the TUG [69].

As a result of our overview of COPD patient's rehabilitation we have to confirm that most studies and meta-analyses proved the effectiveness of rehabilitation programs which include educational programs, physical training, individual monitoring and medication, oxygen or ventilator supply. The best results depend on individual risk factor assessment such as late COPD stage, comorbidities, severe respiratory failure required ventilation support, severe exacerbations with hospitalization, and lower functional exercise capacity. Today's task is to solve the problem of guideline development in according to evidence based recommendation for different rehabilitation programs to different patients and for standardization of patient's health status assessment and classification as well as standardization of rehabilitation approach [37,70-73].

The results of several studies devoted to efficacy of tele-rehabilitation programs have been published only in a last few years [74]. Not all of them confirmed the better outcomes in patient's health status and in economic factors [13,75,76]. But there were not unique methodology of evaluation procedure and rehabilitation programs. One of the evolution theories speculates the perspectives of different tele-rehabilitation implementation in according to predictive benefit. This differentiation suggested to be automatically using predictive software model.

In the Dutch study [77] the good effectiveness of predict mathematics model was reported. Data from 553 COPD patients based in the North Denmark Region were analyzed and used as predictors for four multiple linear regression models. The models were trained and evaluated for their abilities to predict individual patient's future health- and cost-related developments, with and without tele-healthcare. The polarity of predictions was similar for both tasks across models in 82.05% of all cases.

The other publication from Denmark presented the results of the TeleCare North Cluster-randomized Trial included 1225 patients, 578 patients receiving tele-healthcare and 647 the usual care. The aim of the study was to investigate if it is possible to use predictive algorithms to help stratify tele-healthcare for COPD patients in a way that maximizes the patient-level cost-effectiveness ratio. The authors revealed more significant data for linear support vector machines model. The accuracy of the model was 79.1% and the AUC was 0.89 [78].

From a previous little study it is known that tele-healthcare could be cost-effective for COPD patients [79,80]. The presented above Dutch studies used so called machine-learning techniques. It is known that machine-learning methods is recommended to predict outcomes for some patients and is eligible for tele-healthcare [3]. However, the opposite point of view is presented as well [81]. The reports mentioned above suggested that the reason of cost-effectiveness ratio improving consists of determination of the special group of COPD patients, which is perspective for rehabilitation program. But discussion about this question directs to the methodology of effectiveness studding. First of all it is connected with the initial level of patient's health status and healthcare economic costs. But to our mind it can be based on collecting clinical features which are the initial material of mathematical model. In both Dutch studies, presented above the similar clinical features were included. They were systolic and diastolic blood pressure, pulse rate, body mass index, percentage of expected forced expiratory volume in one second, percentage of expected forced vital capacity, marital status, highest education, duration of COPD, job status, number of persons in household, smoking status, evaluation of quality of life using three scales, and healthcare related expenditures in last year (intervention costs, hospital-, medicine-, and primary sector costs, cost to practical help and care at home, home based nursing care, and rehabilitation) – 32-39 parameters at all. But we don't understand is the significance of all these parameters the same or not? Our own experience presented other conclusion and suggested that we have to use more detailed clinical features to characterize patient's current health status [15]. So, in this question the decision to recommend tele-rehabilitation as a cost-effective procedure to improve patient's status seems to be reasonable. The other question consists of the kind of rehabilitation program that is recommended for tele-rehabilitation. For example, it can be based on interactive interviewing of patients only or includes any monitoring devices, or even oxygen concentrator using, or CPAP. So, the cost-effect ratio still needs to be studied for different rehabilitation modes in different groups of COPD patients.

The same problems are presented in a UK study, which did not confirm the effectiveness of tele-rehabilitation [82]. First of all different methods of tele-rehabilitation were combined. The second problem consists of that the authors included three groups of patients with Diabetes mellitus, COPD and heart failure. Any detailed information about clinical status of COPD patients was not presented. As the result of this study slight improvement of physical component scale (SF-12) was achieved. But there were not specific symptoms and clinically significant parameters for COPD patients. Because PCS (SF-12) is composed of four scales assessing physical function, role limitations caused by physical problems, bodily pain, and general health [83]. It is possible that effectiveness of m-Health/e-Health techniques in rehabilitation program depends on choosing of needed health status parameters to be monitoring. Now we can say that we don't understand what electronic devices need to effective monitoring of CORD patients, because the program used in clinical trials was based on several physical data which were collected from physicians review and national registers.

Positive results of tele-rehabilitation program implementation were based on evaluation of shuttle walk test time, self-efficacy, Chronic Respiratory Disease Questionnaire total score and Physical health assessment [76]. Another positive result's study used the 6-min walking test (6MWT), Medical Research Council (MRC) scale and Saint George's Respiratory Questionnaire (SGRQ) as well as the results of monitoring via oximeter, steps-counter, bicycle, remote control and interactive TV software as an addition to questionnaire [53]. These data confirm our point of view about requirements for recommendation on evaluation battery tests using for tele-rehabilitation efficacy, feasibility, adherence to and satisfaction determination.

Consequently, we can conclude that tele-rehabilitation efficacy needs to be confirmed in large trials using closed including criteria and defined control tests.

Acceptability of mobile, electronic devices and software

A very important part of many investigations devoted to Information received by the participants. Comfort and effectiveness of electronic devices and tele-monitoring using depends on patient's age, education and health status, social and economic features. The involved patients need the instruction manual, contact telephone numbers for different purposes, reviewed information about the technology, service, diseases mechanism and curative methods. The most problem character was revealed in cases of health status deterioration. If a patient requires an emergent support to make a decision he is distressed and presents many questions. His respect to the telehealth service will be destroyed. The actual problems of a patient are poor vision, disorientation in touch screen, web-page or device's buttons using, poor understanding of his own symptoms and effective treatment plan [5,52].

Presented data need to be confirmed in large trials and risk factors of probable complications have to be revealed.

Gamification in e-Health

Gamification is a new approach in medicine that helps to involve a person in performing certain diagnostic or therapeutic actions through the game process. It is based on the application of game elements to nongame fields to motivate and increase compliance. Despite the fact that gamification has been used for a long time in many areas of marketing and sales, its use in medicine is only at initial stage. We know that developing a framework for gamification that is based on providing personalization of content, is beneficial for intrinsic motivation, which in turn increases long-term engagement needed for adherence. First and most important scope of gamification is pediatrics. It can change the way youth perceive health management by inviting them to collaborate in their health. This may improve disease management and in perspective may become a stimulus for more significant goals in treating asthma [83].

This approach makes possible to adapt the various programs of rehabilitation and treatment for the elderly, which make up the bulk of patients with COPD [84]. Consequently, only few of the available games today specifically target the elderly population especially patients with chronic conditions. Moreover, we know very little regarding what motivates elderly patients to engage in gaming and what games they would like to play. Hereafter, we should provide highly individualized and intelligent feedback approaches, while gamification strategies could increase motivation [85]. Usage of active video games in many age groups and clinical conditions has been demonstrated as an enjoyable form of pulmonary rehabilitation. For this purpose, it can be used either video games designed specifically for this purpose or it could be commercial games designed for recreational exercise that has been adapted for use in rehabilitation. Future studies should explore the differences between these two approaches (game consoles and individual games) to enable the creation of the most effective gaming interventions for use in pulmonary rehabilitation [86].

Gamification is a promising direction not only in treatment and in diagnosis of respiratory diseases but also in smoking cessation. There are already developed some programs that provide a game-based approach to smoking cessation tailored to their individual situation [87].

Thus, there are many ways of using gamification both for diagnostic and therapeutic purposes and even as a method for smoking cessation.

Planning studies

As a result of our review we can conclude that Digital medicine is a more common platform for developing any directions such as telemedicine, artificial intelligence, machine learning, biomedical statistics and mathematical analysis, digital medicine diagnosis and precision medicine, medical equipment software, medical robotics, biosensors and may be some other. This article mostly describes only tele-medical technologies, subdivided into tele-communication, tele-education, interactive questioning, tele-consultation, telemedicine diagnosis, tele-monitoring, tele-rehabilitation, gamification and acceptability of mobile and electronic devices and software. Unfortunately, sometimes the same questions are published using different terminologies. This is a big problem of meta-analysis making; a unique definition of the new medical knowledge area, the digital medicine, is therefore dramatically needed. Maybe the structure on knowledge and ontology of digital medicine will be common in future publications (Figure 1).

The ontology of digital medicine will help scientist to project better meta-analysis using limited number of key words. But the presented structure is not unique because many authors describe for example tele-monitoring and tele-education as a substructure of tele-Health [3,52,81,88].

Our analysis of number of publications in this field led us putting the telemedicine and tele-rehabilitation in the center of this structure due to the prevalence of number of publications devoted to these terms. A proposed new ontology is presented in Figure 2.

The new ontology makes the focus on tele-rehabilitation as a practical task of digital technology implementation in medicine. But in fact we need telemedicine diagnosis as a central part of digital technologies progress in the future. It is because we are waiting for automatic differentiation of patients in subgroups to choose the right treatment for right patient. The common recommendations for further researches include the necessity of evaluation scales construction: i) for patient's acceptability for different digital innovations; ii) for physician's approving of digital technologies. Other efforts can be in the field of tele-education of patients to improve their understanding, adherence to treatment and health outcomes. The formations of questionnaire for determine needed medical information is an important task in this area.

Tele-communication is not an essential part of digital medicine and telemedicine but a necessary component to make digital service acceptable to patients. Instead that tele-education is real part of healthcare and the role of this approach is increasing in period of

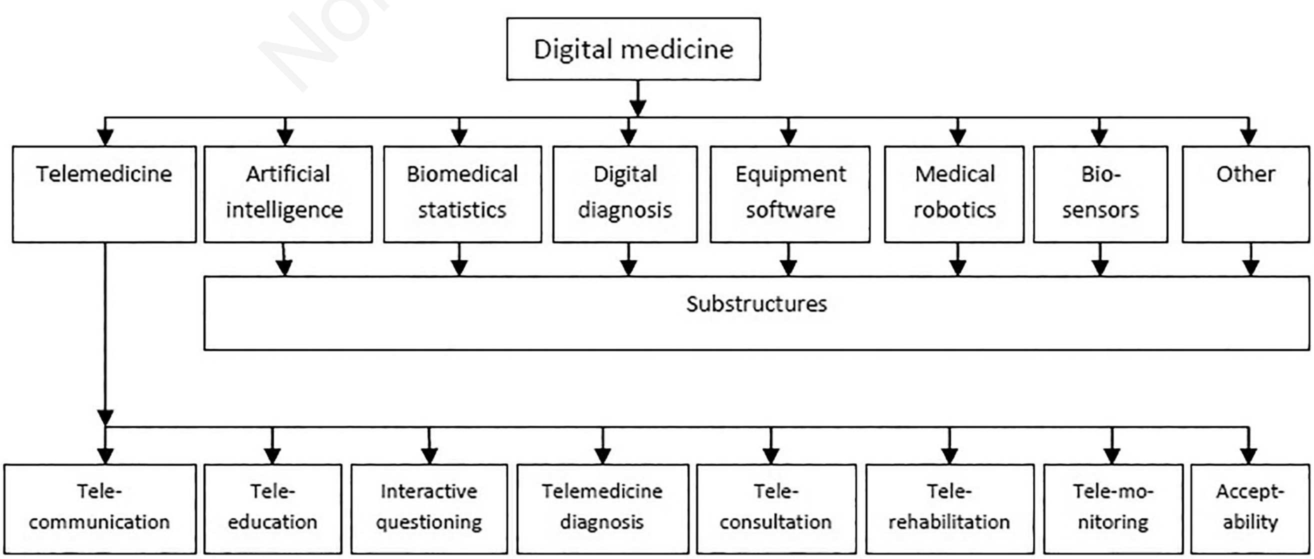

Figure 1. Ontological structure of digital medicine.

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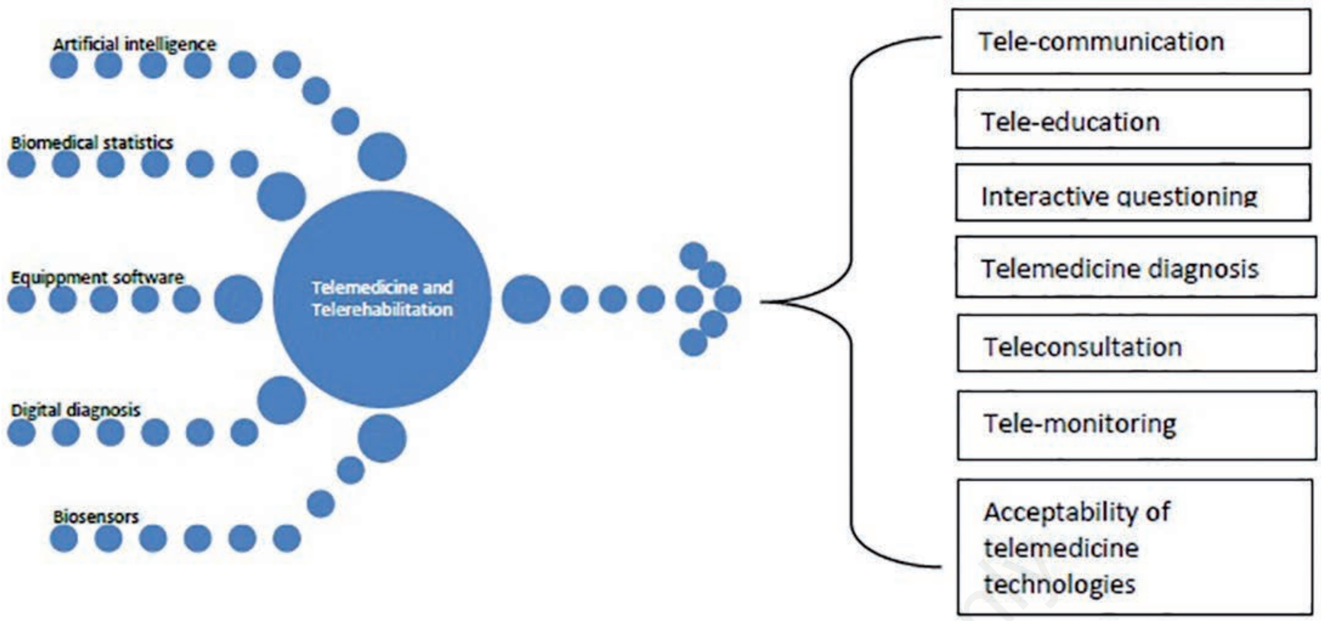

Figure 2. Proposed new ontological structure of digital medicine.

digital medicine development. The community is needed in investigation of basic principles of remote educational programs for different patients' groups in according to health status, age, natural educational level and self-ability of a patient. One of the most actual tasks is to minimize healthcare cost thinking about digital medicine. Among other techniques the interactive questioning is the cheapest method. The results of structured interactive questioning let to make primary diagnosis in well accuracy, make monitoring of a patient, construct automated clinical registers and support decision system. Future trails may be effective using well-constructed interactive techniques. The most interesting results will be presented using integrated interactive questionnaires in Unique Informative Digital Healthcare System.

Tele-consultation can be performed in different manners. The difference consists of information volume for decision making and artificial intelligence using as an essential component. So, different systems will be compared to improve this important part of telemedicine. Artificial intelligence is the most difficult part in telemedicine diagnosis making. It is absolutely proved that in an information deficit to decision making tele- and video-consultations without artificial intelligence are wrong. This part of digital medicine is very perspective to be investigated, but today the most effective variant of decision-making system based on combination of traditional and modern medical logistic and mathematical methods. Diagnosis making systems may be accompanied or separated from other components of telehealth and tele-rehabilitation.

Artificial intelligence can make a great progress in rehabilitation effectiveness and efficacy. Future studies have to answer the questions about the best monitoring parameters for different groups of patients and different complexes of rehabilitation. The significant criteria for tele-rehabilitation effectiveness are in the field of acceptability of mobile and electronic devices. The future studies are necessary to determine an appropriate model of healthcare quality control as in scientific works as in healthcare practice.

Conclusions

The main task of ERS m-Health/e-Health group in 2019 seems as spreading new knowledge about electronic based health technologies and making recommendation for their implementation in according with so called "good m-Health/e-Health practice". We have to discuss possible perspectives and difficulties of new methodologies using and try to develop international standards in m-Health/e-Health investigation and implementation.

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