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EVIDENCE-BASED MEDICINE, PITFALLS AND ALTERNATIVES.

Michał Myśliwiec[1,2]

[1]*Medical Institute*
Lomza State University of Applied Sciences, Łomża, Poland
[2]*Department of Nephrology and Transplantation*
Medical University of Białystok, Białystok, Poland

E-mail: mysmich@poczta.onet.pl

Abstract: The aims and value of evidence-based medicine (EBM) are reviewed. Pitfalls of EBM and an array of alternatives are presented, from non-scientifically proven healing through medicine based on: preventative care, seeding trials, accelerated approval, surrogates, selection of patients, ghost-writing, marketing, disease mongering, regulations, advertisement, self-defence, hospitalizations, value, extraordinary measures and innovations. Post-progress medicine, e.g. extending the lives of very old people at all costs is critically discussed. A real EBM renaissance which is based on evidence, professional expertise and individual patient's needs (personalized medicine) is a new promising direction for medical care.

Key words: EBM, alternative medicine, compassion, marketing, defensive medicine, value in medicine, innovations, postprogress medicine, EBM renaissance, personalized medicine.

„Doctors are those who prescribe medicine of which they know little, to cure diseases of which they know less, for human beings of which they know nothing".

Attributed to Voltaire.

The idea of evidence based medicine (EBM) was developed by Sackett and Guyatt in McMaster University, Ontario, Canada in 1988, but generally Scottish epidemiologist, Arche Cochrane, is considered as a founder of the concept [1].

Definition

Evidence-based medicine is the conscientious, explicit, judicious and reasonable use of current, best evidence in making decisions about the care of individual patients, EBM integrates clinical experience and patient values with the best available research information and should be followed by doctors, nurses and lawyers (evidence based on systematic review and practice). It aims at increasing the use of high quality scientific research in clinical decision making and in writing practical guidelines for different diseases, which are continuously being updated [1]. EBM reduces the value of intuition, non-systematic clinical experience and pathophysiology to a sufficient basis in making clinical decisions and emphasizes the value of evidence obtained by clinical research. According to EBM clinical experience and intuition are of great help but should not be the main basis of decision-making. On the other hand, knowledge must not kill wisdom.

Medical knowledge advances very quickly, so it is very difficult for a busy practicing physician to follow the newest scientific information, not to mention appraising it. This creates a gap between research and practice. Most patients visit the family doctor with poorly defined and variable complains and symptoms, often unspecified (a „grey zone"). Additionally, often there are no EBM based guidelines for all diseases. Thus, a doctor must use traditional medicine, based on his personal knowledge; he has gained during medical studies, conferences and courses or from more experienced colleagues. In any case it is crucial to weigh the potential harm vs. the benefits, and take a decision in partnership with the patient, based on knowledge and individual clinical experience. The key difference between EBM and traditional medicine is that EBM demands better evidence, based on systematic review and on well-performed meta-analyses of well-designed multicenter randomized controlled clinical trials (RCT) [2].

However, EBM is not a „cookbook" but a basis for contemplation, whether to apply it to the individual patient, aiming at the benefits of optimal and cost-effective health care.

There is a difference between EBM and evidence based health care, which is a broader concept that includes a populational advanced approach to understanding the patients', families' and doctors' beliefs, values and attitudes. EBM helps health technology assessment agencies and the ministry of health in negotiations with the pharmaceutical industry and patient organizations. It is also indispensable

in taking reimbursement decisions, particularly in application of new, very expensive methods of treatment.

Classification of EBM

Evidence-based medicine categorizes different types of clinical evidence and ranks them according to the strength of their freedom from various biases:

1a Evidence obtained by meta-analysis of several RCT.
1b Evidence from only one RCT.
2a Evidence from well-designed controlled research.
2b Evidence from one quasi experimental research.
3 Evidence from non experimental studies (comparative research, cross-sectional study, case studies), according to some, for example textbooks.
4 Evidence based on the opinion of experts and clinical practice.

The formulation of clinical questions for an individual technology should follow a scheme of PICO (population, intervention, comparators, outcome).

Sources of EBM information

There are various sources of EBM information, but one of the most universal and unbiased is Cochrane Library, founded in 1992 by Sir Iain Chalmers. This is an international not-for-profit and independent organization, which is dedicated to collecting up-to-date, accurate information about the effects of healthcare readily available worldwide. It produces and disseminates systematic reviews of healthcare interventions and promotes the search for evidence in the form of well-conducted clinical trials and other studies of interventions. The major product of the Collaboration is the Cochrane Database of Systematic Reviews which is published quarterly as part of The Cochrane Library. Other prestigious sources of knowledge are UK National Institute for Health and Clinical Excellence (NICE), UpToDate, MEDLINE, EMBASE and Centre for Reviews and Dissemination etc., available on the web. There are other internet sources or books in dependence of a medical speciality. They should be revised at least once a year.

There are 3 levels of strength in recommendations:

- Strong (an intervention „should" be done). High quality of evidence and/or other considerations support a strong guideline.
- Moderate (an intervention „should be considered". Moderate quality evidence and/or other considerations support a moderate guideline.
- Weak (an intervention „is suggested"). Low or very low quality evidence; predominantly based on expert judgment for good clinical practice.

Pitfalls of EBM

Evidence is mounting that even publications in a peer-reviewed journals do not guarantee a study's validity. Generally, EBM does not hold in the case of the elderly, who are frequently excluded from clinical studies [3]. Many studies of health care effectiveness do not show the cause-and-effect relationship they claim. Sometimes the results of RCT are contested or proven wrong in the subsequent trials. Additionally, we should avoid the six most dangerous words in EBM „There is no evidence to suggest" [4]. Very often in clinical practice there are no RCT for a particular state or they are inconclusive; therefore, scientific evidence is lacking or dubious, and clinical decisions must be taken using common sense, experience and expert opinions.

There is a problem with the trustworthiness of publications. Up to June 2016 in the US in the program of Continued Medical Education there was a topic entitled: „How do you know which health care effectiveness research you can trust?" [5].

Very often a study's quality is poor due to problems with [6]:

- poor hypothesis, considering surrogates, e.g. biochemical parameters instead of patient-oriented medicine that matters – POEMS;
- clinical material variability or limitation, e.g. „unrepresentative" patients, too small or inadequately powered trial (larger number of patients needed to show equivalence, as compared to non-inferiority design);
- poor design, including the judicious use of design flaws to give a flattering picture of the drug, e.g. use of a comparator in too low a dose or use a placebo instead of a currently used effective therapy;
- inconsistency of the results (sometimes „massaging" data, to gain a „proper result" or presenting negative results in a positive light);
- causal associations, due to confounding factors, too short trial, early stopping when benefits are noticed or measuring too many parameters (one out of 10 improved simply through chance);
- indirectness and quality of evidence, e.g. relative risk reduction of 50% (from 4% to 2%), whereas absolute risk reduction is actually 2%;
- incorrect outcome e.g. measuring uninformative outcomes, added to a composite end point, which dilutes, harms and makes it look as if a whole group of outcomes improved;
- imprecision of conclusion (evaluating per protocol, instead of intention to treat, ignoring drop-outs, changing the main outcome after finishing RCT, switching the primary outcome);

- early stopping (within 11 years up to 2008 a number of oncologic trials stopped early and only reached 86% completion);
- statistics may be biased in order to rich a desired conclusion. JAMA would no longer accept industry-funded studies unless they had an independent statistician analysing the results. Calling a difference significant does not automatically means that this is of clinical value, and cannot be a substitute for reasonable thought. Many „significant" findings cannot be reproduced. Particularly dangerous are non-statistical significances, when they are taken for granted in the conclusion, and used as advice to follow in clinical practice. Doctors may read only the summary which is often misleading;
- number needed to treat (NNT) for gaining an effect may be higher than supposed. To prevent 2 myocardial infarctions 100 people must take statins over 5 years, to prevent one death with statin 222 patients should be treated;
- publication bias (50% of RCT are unpublished, mainly of unfavourable or negative results).

Only 29% of completed clinical trials conducted by the faculty at major academic centers were published within 2 years of completion, and only 13% reported results on ClinicalTrial.gov [7].

In the mid-1990s, an international group of different specialists developed consolidated standards of reporting trials (CONSORT); however, reporting of RCTs remains suboptimal [8].

There is also growing problem with flawed trials, sometimes deliberately done.

Alternatives for EBM

EBM based on well systematized knowledge is a new paradigm for medical practice and one of the greatest discoveries in medicine; however, its implementation on an individual patient is an art. William Osler wrote that Medicine is a science of probability and an art of uncertainty. According to Andrzej Szczeklik, a great Polish physician and humanist, medicine is trapped in a dichotomy between an objective science and a subjective truth. There are many barriers to the application of EBM: difficulty in teaching and training, lack of physicians' time and desire to implement, and misinterpret ad hoc collected website information.

Additionally, there are no RCT and no good evidence for the most clinical conditions. In such circumstances there are a lot of alternatives which make medicine a combination of science and art.

Isaacs and Fitzgerald present 7 amusing alternatives for EBM [9].

Eminence based medicine in which experience prevails over evidence; is usually practiced by white haired or bald doctor.
Vehemence based medicine – substitutes of voice volume for evidence;
Eloquence (or elegance) based medicine is based on the smoothness of the tongue and good nap of the suit.
Providence based medicine is based on a level of religious fervour.
Diffidence based medicine is based on the level of gloom and amount of sighs.
Nervousness based medicine is led by fear of litigation for malpractice.
Confidence based medicine is restricted to surgeons.
There are several real alternatives for EBM, which will be discussed below.

Alternative medicine

Alternative medicine is any practice supposed to have healing effects but not proven by scientific methods and, therefore, without scientific evidence. Unproven technologies include traditional Chinese medicine, homeopathy, naturopathy, chiropractic, energy medicine, dog therapy etc.

Alternative technologies may be apparently effective, mainly due to the placebo effect which in EBM is close to 40% for several drugs, particularly in psychiatry. The success of therapy depends as much on the enthusiasm of the therapist as upon the faith of the patient. William Osler said that a desire to take medicine is perhaps the great feature which distinguishes man from animals [10].

According to Topol over 40% of US citizens believe in alternative medicine [11].

Compassion-based medicine

Alternative medicine has been flourishing because of the increasing lack of compassion in relations with patients. Compassion-based medicine as a mystery and majesty of medicine has been lost in the noise of high-tech, profit driven medicine [12]. Nowadays, the doctor-patient relationship, which begins with careful listening to the patient, has been weakened and seen as unrewarding for a busy doctor. Since it is uneconomical to spend much time with patients, diagnosis is performed by exclusion, which opens floodgates for endless tests and procedures.

Now CARE has been replaced by CURE and TREATMENTS [3]. Lown considers it as the lost art of healing as well as a characteristic for a sick health care system. Most chronic diseases, whatever the organ involved, have no definite cure, but they are made more tolerable if the patient is treated with respect. Even small overtures of kindness by a doctor are long remembered, although the era of paternalistic but at the same time autocratic medicine has ended.

Human touch and compassion can never be trumped by technology, but the patient must remain autonomous. Litigation against a compassionate physician who invests time with patients and is engaged in sympathetic listening is exceptionally rare [12].

Prophylaxis based medicine

Prophylaxis in general meaning is health promotion and disease's prevention. It has been proven that prophylaxis is more rewarding than treatment, particularly in elderly. However, there are different approaches to prophylaxis, from a healthy style of life to testing for early diagnosis. It is postulated to attach much weight to exercise, proper diet and BMI normalization, as they may lower MI by 70% and delay dementia in elderly by 7 years. Despite of those generally accepted facts, most people prefer testing. About 50% tests in the US are routine tests. Another approach to prophylaxis vigorously advertised on TV is taking vitamins and diet supplements. According to Topol 50% of the US citizens take vitamins. It may be even dangerous as 16 out of 40 diet supplements contained pesticides in a toxic dose [11].

There is a big mess with prophylactic examination aiming at early diagnosis of several malignancies in the general population. Mammography doesn't lower mortality in breast cancer, and only 5 women over 50, will benefit out of 1000 examined yearly for 10 years. In 600 of them it would be a false alarm with a biopsy in 2/3 and in some of them unnecessary surgery or radiation therapy with high expense and untold emotional costs. Switzerland and Denmark have stopped mammographic screening in the general population, as it is unrewarding.

Prostatic carcinoma screening is reasonable only in high risk men. The same deals with lung carcinoma. The US Preventive Services Task Force recommends that all current and former smokes 55-80 years old should have annual lung CT scan. It will save the life of 1 patient out of 300 examined. In 25% of patients examined the result will be falsely positive, prompting unnecessary procedures, like a lung biopsy.

Seeding trial based medicine

The design of a trial is geared towards marketing rather than answering a meaningful clinical question. It involves many centers and few patients per center, but the drug starts to be more widely known. They are designed with marketing in mind in order to lure leading physicians, who are opinion leaders, to prescribe a drug [6].

Accelerated approval based medicine

This deals with new or emerging drugs for incurable and devastating diseases.

Formerly, approved by FDA in December, as the performance of that institution was measured by how many drugs were approved in each calendar year. In the accelerated approval programme FDA demanded continuation of a study and presentation of compelling results, but post marketing studies are often neglected. Between 1992 and 2008 90 drugs had been given accelerated approval, while 144 RCTs were promised by pharma. In 2009 one in every 3 of those RCTs was still outstanding; interestingly no drug was taken off the market, as it is hard to reject the drug when you are facing with moving life—and-death testimony of a single patient (often sponsored by the firm) [6]. From 1992 to 2010 FDA granted accelerated approval of 35 cancer drugs designated for 47 new disease indications [3].

Surrogate based medicine

Surrogate outcomes are based on a selected parameter, like cholesterol, blood glucose or blood pressure, instead of patient-oriented outcomes, like morbidity or mortality.

Most of drugs for COPD (7/9 – 78%), diabetes (26/26 – 100% and glaucoma (9/9 – 100%) were approved by FDA based on surrogates. It has been postulated that patient-centered outcomes should be chosen whenever possible, e.g. macro or micro vascular events in diabetes instead of blood glucose, as rosiglitazon was associated with unexpected higher risk for cardio-vascular events [13]. Now the FDA requires drug companies manufacturing diabetes drugs to provide data on cardio-vascular outcomes and to continue monitoring the drug safety in post marketing studies.

Selective patients based medicine

Clinical trials are based on very carefully selected patients with specific characteristics of health and disease. Out of 179 patients with asthma only 6% were eligible for a trial which was the basis of the international consensus guidelines for treating asthma. Therefore, most of real-world patients with asthma would have been excluded [14] In another RCT on depression treatment only one patient out of 8 was eligible. Similarly, only one patient out of 7 with osteoporosis was eligible for the study of bisphosphonate. Such selectivity makes those trials on non-representative patients completely irrelevant to the real-world population [6].

Ghost writers based medicine

Ghost authorship is particularly common in presenting RCTs [6].

In 2011 important clinical papers, published in 6 leading medical journals, were searched by contacting the corresponding author. It appeared that 8% of all articles had ghost authorship (12% of research articles, 6% of reviews and 5% of editorials) [15]. There is every reason to believe

that this is an underestimate, as it seems closer to 30% of crucial reports from RCT were produced by industry writers) which is consistent with testimonies of editors in chief of top medical journals, interrogated in the US Senate in 2010 [6]. The first author of a basic paper on Vioox (withdrawn from the market due to cardiovascular side effects) pleaded that the producer designed the trial and wrote the paper [6]. Even a textbook for physicians confirmed by 3 academics, had ghost authorship, and was paid for by pharma. Richard Smith – editor of prestigious the British Medical Journal testified that he came across a dilemma „whether to publish a trial that brings 100 000 pound profit (from ordered reprints) or meet the end-of-year budget by firing an editor" [6].

Marketing-based medicine

While EBM is a noble ideal, marketing-based medicine is the current reality. Internal documents from the pharmaceutical industry suggest that the publicly available evidence base may not accurately represent the underlying data regarding its products. The industry and its associated medical communication firms state that publications in the medical literature primarily serve marketing interests [16]. Suppression and spinning of negative data and ghost-writing have emerged as tools to help manage medical journal publications to best suit product sales, while disease mongering and market segmentation of physicians are also used to efficiently maximize profits.

„Disease mongering" refers to the practice of expanding the recognized boundaries of a disease entity to encompass subclinical, borderline and normal range symptoms in order to increase prescriptions and sales for a drug or therapy [17].

All too often industry's interests trumps the patient's, including flawed clinical trials followed by the suppression of unfavourable results, poor regulation, diseases invented purely for profit, swollen marketing budgets, doctors and academics in the pay of pharma [6]. A very popular group of these drugs are used to treat depression. It is surprising that the name Selective Serotonin Reuptake Inhibitor (SSRI) was developed not in a scientific but in marketing department of a pharmaceutical firm, to distinguish their antidepressant drug from the blockbuster product of another company [18]. It is interesting that there is no blockbuster which is a lifesaving drug. They all are lifestyle or risk management drugs [18].

Disease mongering medicine

Disease mongering reveals a name for an unknown and widely distributed disease or widens the definition of a known one, e.g. depression. Monger has the same meaning as dealer, which explains the purpose of mongering diseases, which is the increase of drug sales or the development of new drugs for a newly named disease. The examples are osteopenia or female sexual dysfunction [18], although there are more amusing: latrophobia (fear of doctors, ergophobia (fear of work), coro (shrinking penis in elderly) and asneezia (inability to sneeze) [10].

Regulations-based medicine

Generally, regulations direct the processes of diagnosis and treatment, which are decided mostly not by doctors, but by clerks responsible for their reimbursement. There are also tricks which may influence the reimbursement. A very expensive antileukemia drug was going to finish its patent in 2011, which would allow it to put on the market at almost 50% cheaper priced generics. However, the firm modified its molecule by attaching fluorine in 2006 and successfully applied to EMA for prolonging the patent for both substances up to 2017. This made ready generics illegal until 21.11.2017. An attempt to replace the original drug with generics in Poland engendered patient protests.

Advertisement-based medicine

Poland is an exceptional country in Europe where drug advertizing is allowed. A particular target group are the elderly who at the same time are the most vulnerable to advertising . On Mondays, pharmacists are accustomed to elderly people providing lists of „wonderful preparations" which were advertised on TV during the weekend. According to the Main Statistics Agency mean survival in 2014 in Poland of women is 82 and men is 74. However, a 67 year old woman's life expectancy is 19.2 years, and man of the same age is 15 years, so the problem will continue to increase. In order to protect elderly people from misleading information, I would postulate to:

- ban drug advertisement in the mass media (radio, TV, press, internet) and leave it to pharmacists who are competent in providing advice to patients),
- forbid the use of misleading names for diet supplements, e.g. Naturfuragin, Teraflu, Insulan etc.,
- ban the offer of any product to elderly people by telephone, or door to door selling,
- allow manipulated deals to be cancelled within a month.

Defense-based medicine

There is a growing risk of a lawsuit resulting from not performing a test which a lawyer considers very important. Avoiding the possibility of legal liability prompts doctors to order a lot of unnecessary tests and to prescribe a drug for every symptom. It is a very difficult task to change a

general paradigm that every disease, which is named, should be automatically treated. Testing too much may lead to over diagnosis – as broader disease definitions. Such medicine may be wasting resources and bad for the health of an individual client, and cause clients to easily change into patients, due to the abnormality of some tests. It creates a „patient paradox": over testing healthy people and not enough care of the truly sick, who are left with confusing options, as they have several diseases which do not fit the procedures contracted and reimbursed in that particular facility [19].

Patients who sue doctors or hospitals consistently say that the prime reason is a perceived lack of caring. Another reason is the impression that a doctor was unavailable when needed or abandoned them. A common reason is also ignoring patient's concerns and failing to consider his or her perspective. It appears that litigation resulted more from miscommunication than malpractice per se. Every doctor is vulnerable to a malpractice suit, irrespective of competence and care. Besides purchasing liability insurance, doctors have been practicing a defensive medicine. There are two consequences of such practice: it maximizes procedures fraught with potential complications and sets up every patient as a potential adversary. Defensive medicine distorts professionalism and dehumanizes medicine. The patient, instead of working with a friendly and caring physician, encounters disinterest and hostility [12].

Hospital-based medicine [12]

Hospital should be reserved for the sickest patients, as this is the most expensive form of treatment, and the costs of hospitalization are burgeoning (in the US over 4000 USD/day, in France 853 USD, less than 500 USD in the Netherlands). Additionally, hospitalisation may harm patients, and it is considered to be the third top killer in the US due to nosocomial infections and medical errors. The average infections rate is 4% a day; one out of every 9 patients with hospital acquired infection dies although 1/6 of deaths are potentially preventable. With the Affordable Care Act US Medicare reimburses less for hospital stays, but it may be estimated a 40-50% excess of beds in hospitals.

Digital medical technology may reduce the need for hospitalizations. It has been expected that a patient centered design of hospital room could reduce infections, falls, errors and ultimately costs. At the present time in Denmark remote monitoring and video conferences play a large role in end-of–life care. Such facilities have created a situation where now over 92% people die at home in Denmark.

A remarkable example of shifting chronic treatment from hospitals to ambulatory supervision was recently opened the Montefiore Medical Center in the Bronx, NY City. It has $\sim$100,000m^2, 11 stories, 12 operating rooms, 4 procedure rooms, an advanced imaging center, laboratory and pharmacy service and only ICU, operating and emergency rooms. There are no beds whatsoever for chronic diseases [11].

Value based medicine [11]

Value-based medicine is important for taking decisions on reimbursement. Of course, EBM is a basis of efficiency, effectiveness and cost control [3].

Very high spending for medicine (18% GDP in the USA; 2.8 trillion of USD, which is almost 8 times more than Polish budget for medicine) should be reasonably distributed. The top 1% accounts for 21.4% expenditures (87,850 USD per patient). Almost 80% of the total medical US budget is spent on chronic diseases and 30% on the last 6 months of life. With the Affordable Care Act US Medicare reimburses less for hospital stays, but pays for the effective care according a rule „no outcome – no income", instead „fee for service". There is a strong tendency in US to increase the amount of doctors taking fee for value [11].

Extraordinary medicine

It uses not routine measures at present time and may be essentially an experimental medicine. Sometimes referred to as the „more is better" approach to medicine (not EBM), including extremely high doses of drugs, or aiming at „target" level of blood pressure or „normalization" of a biochemical parameter, e.g. LDL. Sometimes it may be dangerous, particularly in elderly patients. A border between enough and too much is difficult to define, particularly in relation to prolonging life of a very old and suffering patient. Extraordinary medicine may become ordinary due to gaining evidence from RCT, often by churning out „statistically proven" as highly effective, e.g. by using relative risk or multiplying publications in top medical journals. Evidence may result in gaining reimbursement, which forces the desire of patients and families to use that technology and press the doctor to prescribe it. When a medical technology is evidence based and reimbursed, it appears to be ordinary, desirable, ethically necessary and difficult to refuse [3].

The lack of doctors prompted Mozambique officials to train nurses in performing caesarean section, which is a kind of successful extraordinary or innovative medicine [20].

Innovation-based medicine

There are new innovative technologies including new drugs particularly in oncology. Some of them are extremely expensive, e.g. immune system unblocking ipilimumab for melanoma which costs over 120 000 USD. The epitome of

innovation is a patient with 28 coronarographies and 67 coronary stents within 10 years [11].

Besides new technologies and new compounds it includes electronic teaching of medicine. The average person is projected to have 7 connected devices in 2020, with a smart phone as a hub [20]. An example of ill-innovation is apparently healthy golfer in whom intensive coronary arteries calcification was accidentally discovered. It resulted in 5 stents, 4 obligatory drugs and total destruction of his active life and sexual impotency [11].

According to Topol, a convergence of the digital world and medicine is the main way to save logistic and economical efficiency of healthcare in the situation of current giant and exponentially escalating costs. He called it a creative destruction of medicine [11]. The major role will be played by a well-informed patient, who will control his or her own health, based on genomic information and real-time data from nanosensors, smaller than grain of sand, and wireless technology incorporated in his or her personal smart phone. The system may be connected with a doctor (telemedicine), who may ask on-line for some additional information. One of the advantages of the system would be registered radiation exposure, with convergence with particular genomic variation that predisposes particular individuals even low dose radiation. Gene specific effectiveness or side effects of a drug may also be predicted. The need for hospitals will be substantially reduced and restricted to the care of the most acutely ill patients. Topol predicts that in the next years over 50% of office visits to become redundant and replaced by remote monitoring, digital health records and virtual house calls. In 2012 US National Health Service NHS (not known as the most progressive health system in the world) requested general practitioners to recommend computer applications to their patients for managing conditions ranging from DM to depression in an attempt to give them more power and reduce visits to doctors [20]. Live Health Online costs 49 USD for videoconference with a doctor, followed by a subscription for 9 USD a month. Telemedicine is allowed in the US, but a patient has to have a physical visit with the doctor before virtual consultations are allowed. It has steadily increased in the US from 12% in 2012 to 17% in 2013 (a 5% yearly increase).

A smart medical home can easily be designed with monitors and emergency response system. Patients would be remotely monitored from home [20].

Post progress medicine

Great progress in modern medical technology has caused a tendency to extend life at all costs; however, generally RCT findings for the elderly with multiple health problems are contentious and questionable. It leads to the overuse of procedures or technologies, particularly in elderly patients suffering from many diseases who can be treated using very advanced technology (implantable cardioverter-defibrillator (ICD), costing 41 000 USD or 7 times more expensive left ventricular-assisted device. Widening indications to ICD for „life threatening cardiac event or ejection fraction <35%" cause the device to be used in almost all geriatric patients. It may represent off-loading of ethical responsibility, as it touches the dilemma of extending the life span past a point that people want. The increasing use of life-extending therapies in a very sick elderly person creates a difficult dilemma where is a border between enough and too much [3].

Real EBM Renaissance

Prof. Greenhalgh is a leader of a group in London School of Medicine and Dentistry and University of Oxford, which postulates with the Lancet, a return to real EBM, by reducing waste and increasing the value in medical research and improving publishing standards [21]. They conclude that nowadays very often the patients are left confused and even tyrannised when their clinical management is inappropriately driven by spurious clinical studies, algorithmic protocols, top-down directives and population targets. They offer an agenda for a renaissance of EBM, refocusing on providing useable evidence that can be combined with context and professional expertise so that individual patients get optimal treatment (personalized medicine).

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