

SANTORIO SANTORIO – THE PIONEER OF EVIDENCE
BASED MEDICINE

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ABSTRACT

In everyday clinical practice there is a constant need for valid information about diagnosis, prognosis, therapy and the prevention of a variety of diseases. But there could be a disparity between the physician's diagnostic skills and his clinical judgment if he relies only on traditional sources of information. In 1992, a group of scientists from McMaster University in Ontario, Canada attempted to integrate individual clinical expertise with the best external evidence. They proposed a process in which systematically finding, appraising and using contemporaneous research were the basis for proper clinical decisions. They called this integration of research evidence with personal clinical knowledge "Evidence Based Medicine" and since then, interest in this field has grown exponentially. Interestingly, it is the case that some 400 years before this important concept; a young physician named Santorio Santorio emerged from Koper in what is now Slovenia (1561–1636). He argued that a doctor should first rely on experience, then on reasoning, and only lastly on authority. Besides his numerous medical inventions, Santorio was the first to attempt to justify his practice by using some vital connection between measured parameters and a person's state of health. He therefore could be credited as one of the earliest individuals to embrace modern concepts of science or a pioneer in the field of EBM.

Keywords: Santorio Santorio, evidence based medicine

SANTORIO SANTORIO – ZAČETNIK NA DOKAZIH TEMELJEČE MEDICINE

IZVLEČEK

Vsakodnevno klinično delo zahteva ažurne in natančne podatke, ki nam pomagajo pri postavitvi pravilne diagnoze, prognoze in terapije pri preprečevanju določenih bolezni. Uporaba zgolj tradicionalnih virov informacij ne zadostuje sodobnim zahtevam medicinske stroke in lahko privede do neustrezne klinične presoje. Zato je skupina kanadskih znanstvenikov iz McMasterjeve Univerze v Ontariu (Kanada) leta 1992 poizkusila združiti zdravnikovo klinično znanje in izkušnje z uporabo izsledkov iz sodobne literature. Predlagali so postopek, s katerim sistematično iščemo, ocenjujemo in uporabimo izsledke kakovostnih raziskav pri odgovoru na konkretno klinično vprašanje. Tovrstno združitve klinične presoje in raziskovalnega znanja so poimenovali »na dokazih temelječa medicina«. Zanimanje za tovrstni pristop in njegova uporaba sta kmalu doživeli nesluten razmah. Vendar je že okoli 400 let pred uveljavitvijo tega koncepta mlad koprski zdravnik Santorio Santorio (1561–1636) menil, da mora zdravnikova odločitev temeljiti na izkušnjah, razmišljanju in šele nazadnje na mnenju medicinskih avtoritet. Poleg iznajdbe številnih medicinskih naprav gre prav njemu pripisati zasluge, da je kot prvi uporabil in opisal povezavo med določenimi merljivimi parametri in človekovim počutjem oziroma zdravjem. Santorio Santorio tako ostaja eden od začetnikov sodobnega koncepta na znanosti oziroma na dokazih temelječe medicine.

Ključne besede: Santorio Santorio, na dokazih temelječa medicina

INTRODUCTION

More than half a century ago, Sir Sydney Burwell, Dean of Harvard Medical School (Boston, USA) stated that his students were dismayed when he said to them that half of what they were being taught would be shown to be wrong. »And the trouble is, that none of your teachers knows which half« he added (Pickering, 1956). This situation of rapidly changing knowledge and the growing amount of published medical literature is the catalyst for a continuous need for medical education. It is estimated that the volume of published medical papers doubles every 10 to 15 years (Hook, 1999) and that more than seventy articles about clinical trials and ten systematic reviews are published per day (Bastian, Glasziou & Chalmers, 2010). A doctor of internal medicine would need to read about seventeen articles daily to remain a committed physician (Davidoff, Haynes, Sackett & Smith 1995).

For most physicians, the amount of time available to search for relevant medical information is quite limited and it decreases rapidly after graduation. On average, a student spends 90 minutes per week reading papers related to a pertinent patient, a

resident spends 45 minutes while a senior consultant spends only 20 minutes per week. A worrying 40% of consultants reported that they hadn't read any scientific papers in the last week (Sackett, 1996)!

In spite of this, older and experienced physicians are generally believed to have accumulated medical knowledge and clinical skills throughout their years in practice so as to deliver high-quality care. But evidence suggests that there is an inverse relationship between the number of years spent in practice and the quality of care provided by the physician. A systematic review of 62 reports on the performance of physicians during their professional lifetime done by Choudhry, Fletcher and Soumerai (2005) showed that 52% of the studies found a decrease in performance with increasing years in practice for all the assessed outcomes and 21% for some outcomes. Only 2% of the studies reported an increase in performance with increasing years in practice for some and all outcomes, respectively.

The awareness of this “slippery slope” of deteriorating performance during a physician's professional career is lower than expected. A comparison between self-assessment and the estimation of one's external competence showed that there is little or no relationship between the physician's perception of his clinical abilities and an objective measurement of these abilities. A number of studies found the worst level of accuracy in self-assessment among physicians who were the least skilled and those who were the most confident about their knowledge (Davis et al., 2006).

The mismatch between a high level of self-appraisal in doctors and their low “de-facto” performance is unfortunately reflected in their everyday practice. A European survey which aimed at exploring the knowledge and attitudes of European general practitioners found significant gaps between the general practitioner's level of knowledge and his or her practice (Brotons et al., 2006). For example, 40% of the general practitioners involved in the study answered that they provide screening for lung cancer to their patients despite the fact that there is no evidence that screening is effective. On the other hand, only 20% of them support a screening program for colorectal cancer although it has been proven to be very cost-effective. If this is indeed the case, why is it that the use of available medical evidence is so sparsely used in everyday practice?

A possible answer is that most doctors have never been taught how to learn. Until some twenty years ago, acquiring new medical knowledge was a complex process which included an understanding of the pathophysiological mechanisms responsible for the disease and the use of common sense to find an appropriate therapy. After years of experience, the physician became an “expert” and over time, an unquestionable authority in the field. In the 1990's a group of Canadian researchers led by David Sackett and Gordon Guyatt from McMaster University in Toronto, challenged this concept. They proposed the judicious use of the best available data in decision making regarding the care of a single patient (Evidence-Based Medicine Working Group, 1992). An individual's clinical expertise remained important but was integrated with the best available clinical evidence from systematic research and with the patients' specific medical conditions and wishes in mind (Sackett, Richardson, Rosenberg & Haynes, 1996). This new approach was named *Evidence Based Medicine* (EBM). Its principles were soon

emulated by many other scientists working in the field of health and social sciences, changing its name to *Evidence Based Practice* (EBP) (Dawes et al., 2005).

The core issue of EBM was identified as being how to acquire relevant clinical evidence regarding a concrete problem. Traditional sources of medical information were found to be inadequate since they were usually out-of-date (textbooks) (Antman, Lau, Kupelnick, Mosteller & Chalmers, 1992), frequently wrong (experts) (Oxman & Guyatt, 1993), ineffective (continuing medical education) (Davis, Thomson, Oxman & Haynes, 1997) or too overwhelming in their volume and too variable in their validity (medical journals) (Haynes, 1993). Therefore, the architects of EBM proposed novel strategies to efficiently track down the validity and relevance of new medical evidence (Sackett et al., 1996). For this purpose they designed and founded new organizations which provide up-to-date, accurate and readily available medical information worldwide. The largest – the Cochrane Collaboration is an international, independent, not-for-profit organization made up of over 28,000 contributors from more than 100 countries. Its goal is to produce systematic reviews and concise summaries of healthcare interventions, known as Cochrane Reviews, which are published online in The Cochrane Library (The Cochrane Library, 1999). EBM is also popularized through evidence-based journals which publish only 2% of the available clinical articles which should be scientifically flawless and ready for practical use (ex. ACP Journal Club, Evidence-Based Medicine, Evidence-Based Health Policy and Management, Evidence-Based Cardiovascular Medicine etc.). The availability of these up-to-date medical resources was made possible by the evolution of an information system capable of bringing the latest information to users in only seconds. In this way, an effective tool for life-long learning is available to doctors and helps them to improve their clinical performance (Cochrane Effective Practice and Organisation of Care Group, 1999).

The principles of EBM are quite straightforward and include five steps (Dawes et al., 2005):

1. Formulating an answerable question about the clinical problem we are interested in.
2. Finding the best evidence (literature, consultations) which could help answer that question.
3. Critically evaluating the evidence for its validity, impact and applicability.
4. Integrating the critical appraisal with our clinical expertise and with our patient's unique biology, values and circumstances.
5. Evaluating the effectiveness and efficiency in executing all four steps and seeking ways to improve them.

Every step is crucial and should be accomplished before the next is started. Systematic evaluation and validation of the obtained evidence is also mandatory. Information is best derived from randomized controlled trials (RCT) systematic reviews and meta-analysis. But even with this high-quality evidence one should be aware that a poorly executed systematic review or meta-analysis may give misleading results. It is therefore important to critically appraise every paper (Akobeng, 2005).

Ironically, there is little evidence that the implementation of EBM improves the outcome for patients. However, it would be ethically questionable to perform a rando-

mized trial in which the doctor of a control group would not be allowed to search for the best available evidence regarding the treatment of his patients. In fact no such study is really needed, because population-based “outcome research” has repeatedly documented that those patients who do receive evidence-based therapies have better outcomes than those who don’t (Jernberg et al., 2011). Changing the pattern of medical decision-making from a personal-experience model to an evidence-based model doesn’t mean the abolition of clinical expertise but rather a more conscious and informed decision-making process in which the clinician must still decide whether the external evidence applies to the special needs of his patient.

The “EBM concept” is not completely new and its authors identify some of its expression in post-revolutionary Paris (when clinicians such as Pierre Louis rejected the pronouncements of authorities) (Evidence-Based Medicine Working Group, 1992). Even earlier in history there have been individuals who doubted the concepts of “authority based medicine”. At the end of the 16th century a young Venetian doctor wrote that: “... rather than relying on authority in the first instance, (as so many of my colleagues do), one should first rely on sense experience, then on reasoning, and only lastly on authority!” (Grmek, 1975). His name was Santorio Santorio and was one of the most prominent doctors of the Venetian Republic. He was born on March 26, 1561 in Justinopolis (now Koper, Slovenia). His father was a nobleman from Friuli in the service of the Venetian Republic and his mother was from a noble family in Justinopolis. His education began in Justinopolis and then Venice and he entered the University of Padua in 1575. At the age of only 21, he received his medical degree and spent his next year working as a doctor in various eastern European countries. In 1599 he set up a medical practice in Venice and he soon joined a circle of educated men which included Galileo Galilei. In 1611 he was appointed Chair of Theoretical Medicine at the University of Padua, and he taught there until his retirement in 1624 (Castiglioni, 1987).

His great contribution to medicine was the introduction of quantitative experimentation into biological science. He constructed a large weigh scale on which he weighed his solid and liquid intake and bodily excretions. After 30 years of thorough observations, he established that the amount of the visible excreta was less than what he ate and drank. He concluded that a substantial portion of the weight of his food intake was lost from the body through his skin in the form of *perspiratio insesibilis* or insensible perspiration (Grmek, 1946). He reported his observation in his landmark text *De Statica Medica* (1914) *On Static Medicine* which has been called the first systematic study on basal metabolism (Eknoyan, 1999). Through his experiments, Santorio introduced the quantitative aspect into medical research, and at the same time founded the modern study of metabolism. He was largely responsible for the introduction of clinical observation and experimental medicine into the physician’s domain in the late sixteenth century – the very same principles which are also incorporated in the modern concept of EBM (Major, 1938).

Rather than describing the body and its functions in terms of elements and qualities, Santorio argued throughout his career that the fundamental properties were mathematical ones, such as size, position and form. He compared the human body to a complex

mechanism in which the proper interlocking of its integral parts determines the body's state of health. This was a radical break with traditional medical theory in which the mathematical properties of an object were considered incidental. Santorio made these incidental properties central to his view of medicine and was therefore regarded as the principal architect of the Iatrophysical School of Medicine (Pintar, 1960).

In his everyday medical practice, Santorio relied mainly on the Hippocratic and Galenic principles of a fluid or "humor" imbalance as a cause of diseases. However, his theoretical reasoning and his method of investigation greatly differed from classical thinking. Instead of blindly following ancient authorities he advocated sense experience and reasoning before accepting the opinion of authority. He also recognized the unique nature of every individual (Borisov, 1996).

In his book, *De Statica Medica* (section II, XLVIII aphorism) he wrote: "*Those who, in winter are afflicted by diseases caused by a fullness of humours, should cleanse their bowels with laxatives in autumn, not in spring, to weigh as they did at the beginning of summer.*" Four hundred years later this individual approach was advanced by Sackett (1996) who defined the EBM as "*the integration of best research evidence with clinical expertise and specific patient values*". The origins of this idea could be tracked down to Santorio's time when he promoted the use of clinical experience and recognized the singularity of each patient. He had very limited access to medical literature, which in his period was low in volume and poor in quality, and therefore of limited value for external evidence. However, he made a considerable contribution to renaissance medical literature. The second edition of his book *De Statica Medica* (1615; first edition 1614) was reprinted some forty times, and was translated into English (1676), Italian (1704), French (1722), and German (1736). Not only did he publish the principles of empirical methodology but he consistently applied his discoveries when working with patients. His integration of medical knowledge, experimental findings and the awareness of the patient's distinct needs make Santorio a forefather of EBM.

CONCLUSION

Evidence Based Medicine is not a cookbook on how to practice modern medicine, but rather a way of tracking down the best external evidence with which to answer a specific clinical question. It cannot replace the individual clinical expertise which is still crucial for the integrative judgment on how external evidence applies to the individual patient. Santorio Santorio was aware of the peculiarities of patients and suggested that sense experience and an empirical approach should be used in treatment. His systematic work on metabolic homeostasis together with the implication of his scientific findings in everyday clinical practice makes of him the pioneer of modern evidence-based medicine.

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