Achievements, Milestones and Challenges in Biomedical and Health Informatics
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50 Years of Achievements and Persistent Challenges for Biomedical and Health Informatics and John Mantas' Educational and Nursing Informatics Contributions

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Abstract. Biomedical and Health Informatics (BMHI) have been essential catalysts for achievements in medical research and healthcare applications over the past 50 years. These include increasingly sophisticated information systems and data bases for documentation and processing, standardization of biomedical data, nomenclatures, and vocabularies to assist with large scale literature indexing and text analysis for information retrieval, and methods for computationally modeling and analyzing research and clinical data. Statistical and AI techniques for decision support, instrumentation integration, and workflow aids with improved data/information management tools are critical for scientific discoveries in the -omics revolutions with their related drug and vaccine breakthroughs and their translation to clinical and preventive healthcare. Early work on biomedical image and pattern recognition, knowledge-based expert systems, innovative database, software and simulation techniques, natural language processing and computational ontologies have all been invaluable for basic research and education. However, these methods are still in their infancy and many fundamental open scientific problems abound. Scientifically this is due to persistent limitations in understanding biological processes within complex living environments and ecologies. In clinical practice the modeling of fluid practitioner roles and methods as they adjust to novel cybernetic technologies present great opportunities but also the potential of unintended e-iatrogenic harms which must be constrained in order to adhere to ethical Hippocratic norms of responsible behavior. Balancing the art, science, and technologies of BMHI has been a hallmark of debates about the field's historical evolution. The present article reviews selected milestones, achievements, and challenges in BMHI education mainly, from a historical perspective, including some commentaries from leaders and pioneers in the field, a selection of which have been published online recently by the International Medical Informatics Association (IMIA) as the first volume of an IMIA History WG eBook. The focus of this chapter is primarily on the development of BMHI in terms of those of its educational activities which have been most significant during the first half century of IMIA, and it concentrates mainly on the leadership and contributions of John Mantas who is being honored on his retirement by the Symposia in Athens for which this chapter has been written.

Keywords. Biomedical Health Informatics, Scientific-Technological Evolution, Historical Achievements, Open Persistent Informatics Challenges

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1. Introductory Overview: Biomedical and Health Informatics as Evolving Art, Science, and Technology for Inclusive, Equitable Digital Healthcare

On the occasion of honoring John Mantas in Athens for his contributions to Biomedical and Health Informatics (BMHI), it seems appropriate to start by quoting, in Chaucerian English translation, an original Greek aphorism ascribed to Hippocrates, the father of humanistic healthcare practices: "The life so short, the craft so long to learn." [1, p 251]. BMHI has evolved over the past 50 years into an interdisciplinary endeavor that has radically transformed healthcare and its underlying biomedical research leading to life-saving scientific, clinical and public health advances [1,2,3,4,5,6,7]. Yet, this modern cybernetic, digital health craft is indeed very long to learn. Being an exceptionally broad umbrella discipline that draws on the diversity of scientific, technological, and humanistic approaches to health, BMHI is necessarily guided by an equally broad set of goals and expectations that push the boundaries of what is scientifically and practically achievable through art and science [8]. And, when technologies are prematurely or poorly implemented they can lead to harm [9], referred to as e-iatrogenesis as an unintended consequence [10].

From its inception, BMHI has sought, through its interdisciplinary education professional initiatives [11,12], to synthesize the many informatics insights in order to improve scientific understanding of the wide range of connected ecologies of life from molecules to populations [13,14], and serve as a bridge that translates these understandings into best practices based on evidence from "bench to bedside" [15]. In so doing, a great challenge for system designers and users alike is to adhere to the Hippocratic ethical dictum usually summarized as "First, do no harm" in helping care for individual patients [16] while also developing general methods for biomedical and health informatics, clinical and management advances and preventive healthcare policies around the world [17,18]. Problems of diversity, equity, and inclusion have become more recognized over the past decade [19,20], and calls to action have become more urgent as disparities in care for underserved and vulnerable populations have become more obvious than ever as result of the COVID -19 pandemic [21,22].

Technological and scientific achievements in BMHI have been many and largely reliant on human ingenuity and creativity in exploiting a happy juncture of practical and theoretical informatics insights derived from the underlying mathematical, basic sciences, and engineering source disciplines. In contrast, the persistent and often frustrating informatics challenges - which also provide many exciting and provocative opportunities - have arisen largely from scientific limitations on matters of research and education, as well as the complexities of fraught human social and psychological constraints for matters of clinical care, management and preventive digital health. The intersections of practical clinical arts with the sciences and technologies of information, therefore present a uniquely rich and fruitful source of problems for scientific inquiry in the biosciences with its information sciences. However, these complex intersections can also prove to be frustratingly and ethically difficult sources of problems for the cognitive and social sciences. These are needed to deepen our understanding with humanistic insights of what can be developed as "best" healthcare practices for patients and consumers in rapidly evolving techno-societies where surveillance is ubiquitous [23] and cybersecurity dangers are pervasive [24,25].

2. History of some of BMHI's Early Milestone Achievements and their Evolution

The main precursor achievements and milestones leading up to the founding discipline of Medical Informatics that preceded the more general BMHI we know today, can be traced to several major workshops, conferences and proceedings volumes and a key scientific journal paper starting over 60 years ago in the late 1950's. All involved the then emerging applications of computers, communications, and control (to which the name Cybernetics coined by Norbert Weiner was frequently applied based on his 1948 book of that title [26]) in medicine using computer programs implementing statistical and mathematical simulation methods to analyze data for various types of biomedical problems. The leading US computer company at the time, IBM, had its scientists and engineers collaborating with physicians at the Cornell Medical School in New York, investigating the feasibility of using computers for clinical data analysis. In 1959 they begun an annual series of IBM Medical Symposia [27], demonstrating, among other biomedical data analysis applications, the potential of using computers to implement medical diagnostic logic. This can be taken as a precursor to the more recent applications of computers with machine learning for the analysis of big data in biomedicine [28].

It was in the same year of 1959, however, that a widely known scientific publication event occurred that can be considered as the first major milestone for BMHI advances, setting the field on a path of investigating how to model medical reasoning and provide clinical decision support for practitioners using general, well recognized, though often controversially interpreted statistical methods for handling uncertainty and risk in decision-making. The publication involved was an article by Ledley and Lusted which appeared in the prestigious US journal Science entitled Reasoning Foundations of Medical Diagnosis [29], and introduced for the first time, a formal logical probabilistic framework- that of rational utility theory - for representing clinical reasoning with a mathematical model. The Bayesian statistical methods they proposed had the virtue of being able to update subjective prior probability estimates that a physician might have about a sick patient's disease using the probabilities of observed clinical evidence derived from previous studies of similar patients. These methods still remain the most frequently used formal methods for computationally modeling of inferencing for clinical diagnostic reasoning and many epidemiological applications today [30] within the commonly used hypothetico-deductive frameworks for decision-making.

However, many fundamental open scientific questions around scientific statistical inferencing methods in biomedicine still persist today and are related to some of the difficulties being encountered in applications using Artificial Intelligence and machine learning algorithms and data-driven inferencing especially [31]. These include problems of coming up with subjective probability estimates which are clearly agent-and-context specific in medicine, healthcare, and most other psychological/cognitive science and social science problems, together with the frequent misuse of probabilistic independence assumptions for complex evidence and hypothesis definitions and relationships. Underlying ontological assumptions about illness and disease, their etiologies and processes are complicated in populations with high degrees of diversity arising from environmental, genetic, cultural and other factors and for all species. Modern insights into the complicated but still poorly understood interactions with microbiomes and other ecological factors at all scales adds to the open scientific problems at both the ontological and epistemological levels. As result, practical methodological disagreements and debates about the applicability of statistical models for arriving at inferences about specific individuals is extremely fraught since ethical issues about responsibility of both

patient and practitioner are involved. Scientific epidemiological inferences about groups or populations, involving very different levels of abstraction for decisions in biomedicine are likewise the subject of much debate. Consequently, alternative statistical analytical approaches based on hypothesis testing using either the Fisher, Neyman-Pearson or other paradigms for null hypothesis significance testing (NHST) are still major competitive inference reasoning candidates across BMHI applications today [32,33].

Historically these likelihood-based methods for probabilistically modeling medical diagnostic and automated multiphasic screening were the preferred statistical inference approach [34] of another key founding member of medical informatics in the USA, Dr. Morris Collen. His contributions to, and leadership roles in BMHI internationally have led to him being called the "father of medical informatics" [35]. After taking leadership of many international and educational initiatives in medical informatics, and sponsoring an award for research excellence through the Academy for Medical Informatics (ACMI), he wrote a very detailed history of the field in the USA with quite a few references to worldwide activities in healthcare informatics. An updated version, co-edited with Marion Ball, was published in 2014 after Collen's death at the age of 100 [36].

Yet, during the first full decade of early or precursor work on the fundamentals of computer information processing it was the more general encyclopedic textbook by Robert Ledley from 1965 entitled Use of Computers in Biology and Medicine that became the first comprehensive book encompassing the main informatics subjects of the time – the logical, statistical, and other algorithmic methods for problem-solving in the biomedical sciences and medical care more generally [37].

A different, yet even more significant early achievement for the field of BMHI was the founding of the first scientific journal covering medical documentation and statistical methods - Methods of Information in Medicine by Gustav Wagner published in German in 1962 [38,39]. This journal switched to being published in English and became the official journal of IMIA when the international association was founded in 1979.

In the 1960's another precursor milestone achievement for BMHI was the publication by Donald Lindberg of the book The Computer and Medical Care in 1968 [40] which for the first time covered most of the principal applications of computers in healthcare from clinical rather than formal mathematical or technological and computational perspectives. Lindberg was a pioneer in computer methods for laboratory medicine who rapidly became a leader of medical informatics in the US, envisioning early the future of the field as revolutionizing library operations through computerization of information retrieval and informatics methods. As Director of the USA's National Library of Medicine (NLM) from 1984 until his retirement in 2015, he turned the NLM into the main sponsor of BMHI research and development both in-house in the National Institutes of Health, by funding academic and professional educational programs across the US, and internationally by his close connection and active participation in IMIA activities. It would be hard to overstate Lindberg's and the NLM's contributions to the dramatic worldwide expansion of BMHI and the catalytic role they have played in biomedical research discoveries, and their impact on the practices of medicine and healthcare [41]. This is most especially true for the emerging translational medicine achievements, which NLM's informatics infrastructure is critical in supporting, just as it did the Human Genome Project, which led to the genomic and other -omic biomedical advances. The NLM produced powerful indexing and literature search capabilities open to all without cost long before online commercial search engines and software like Google were envisioned. The development of a Unified Medical Language System and support for Natural Language Processing, together with biomedical research databases

and knowledge bases of all kinds, expert systems and the Visible Human Project were all major achievements for BMHI which have transformed the life sciences, biomedicine and healthcare over the past 50 years. The educational impact of NLM's informatics breakthroughs in biomedicine and informatics has been likewise incomparable to that produced by any other institution. A contributed volume describing Lindberg's major contributions to BMHI written by his colleagues and collaborators entitled Transforming Biomedical Informatics and Health Information Access: Don Lindberg and the U.S. National Library of Medicine has been recently published by IOS Press [42].

Returning to the first decade of BMHI achievements, Lawrence Weed proposed a ground-braking change in how medical records could be organized – and oriented towards patients' medical problems, in order to guide and teach practitioners and patients alike, rather than just following traditional difficult-to-understand practitioners' notes of clinical encounters [43]. His articles and book on the Problem Oriented Medical Record had great influence on how researchers and practitioners looked at the structures for recording information about patients [44] and continues to be relevant today [45].

During the first decade of BMHI in the 1960's researchers in what was to become medical informatics were active in Europe as well as the USA and Canada. In France, the physician and biophysicist Francois Grémy taught university and medical school courses on the subject, and he took the initiative of founding the first international professional organization for medical informatics under the aegis of the International Federation of Information Processing (IFIP) Societies [46]. The success of the IFIP-Technical Committee 4 for Medical Informatics described next in this article contrasted with the relative ineffectiveness of an earlier and excessively theoretically-oriented international organization for Cybernetic Medicine [47], and followed soon after a most productive first international meeting in Ellsinore, Denmark, under the shadow of Hamlet's castle [48]. This meeting brought together many of the early leaders in what was to become medical informatics, and effectively demonstrated that practical computer information systems for hospitals and other clinical and biomedical research and educational purposes would be a more promising future direction for the field – which proved true historically [49].

As one can see from the above, the groundwork for educational directions in BMHI was being laid even before the word informatics (derived from the French "informatique" thanks to Grémy's role in the formation of IFIP–TC4) came to denote the disciplines involved, which did not start to happen until the 1970's and even the 1980's when it gradually started to replace the earlier strictly computational, statistical, or documentation emphases used to characterize the emerging medical informatics field.

3. Early Historical Milestones in the emergence of Medical Informatics professional organizations

The major accomplishment and milestone in the history of Medical Informatics as a discipline was its establishment with its own professional organization. As mentioned above, the Technical Committee 4 (TC-4) of the International Federation of Information Processing Societies (IFIP) was organized by Francois Grémy in 1968. That same year he also established the French Association for the Applications of Informatics in Medicine (AIM). In the following years he became the promoter and organizer of a number of workshop conferences on different medical informatics topics such as information processing for medical records in Lyon in 1970, the analysis of biomedical

signals for ECG and VCG in Hanover in 1972, and health informatics education in Lyon in 1974 under the aegis of TC-4 [50,51,52,53]. A number of European countries led in the early organization of national medical informatics societies. In Denmark, a society for medical informatics associated with the Danish medical societies was established as early as 1966, while the Swedish Society for Medical Information Processing was founded the next year. In the Netherlands, the VMBI was founded in 1970, and the Norwegian and Belgian (MIM) society were both established in 1974. Other major European countries such as Germany and the UK, had scientific or technological professional societies like the GMDS (covering informatics, biometrics, and epidemiology) and the British Computer Society's Health Informatics Specialist Groups, taking responsibility for the professional organization of informatics in their countries [54].

BMHI can be said to have reached a milestone of international recognition as a distinct discipline in its own right after the success of the first World Congress or MEDINFO held in Stockholm in 1974. This was the first official milestone for BMHI using the word informatics in a major conference that coalesced people with their ideas about how medical information was being processed by computers and shared widely in an interdisciplinary manner. This first MEDINFO generated enthusiasm among the participants who became aware that the time was ripe to carry out the organizing and planning for not only national, but also regional and international societies for medical and health informatics. These included COACH (Canadian Health Informatics organization) in 1975, the European Federation of Medical Informatics (EFMI) in 1976, and the International Medical Informatics Association (IMIA) in 1979 when it became independent from IFIP, though still in association with it.

In the USA, the earliest professional society precursor to informatics was an offshoot of the American Hospital Association (AHA), which evolved into the Health Information and Management Systems Society in 1966. More technically oriented was the Society for Advanced Medical Systems (SAMS) formed in 1967, while the more clinically oriented Society for Computer Medicine (SCM) was organized in 1971. These were to merge in 1982 to form the American Association for Medical Systems and Informatics (AAMSI). It took until 1989 for AAMSI to merge with the Symposium on Computer Applications in Medical Care (SCAMC), founded in 1976, and the American College of Medical Informatics (ACMI), the honor society founded in 1984 for them to all join, and establish the integrated focus for academic healthcare informatics in the US - the American Medical Informatics Association (AMIA) [36]. Internationally, most countries, like the US, did not develop scientific and academically oriented informatics societies until the decades of the 1980's or beyond, encouraged by IMIA's activities to spread worldwide through the regional associations that followed EFMI: IMIA-LAC for Latin America and the Caribbean, APAMI for the Asia-Pacific, HELINA for Africa, and MEAHI for the Middle East.

Nursing Informatics (NI) has had a very different beginnings and evolutions than medical informatics, with their organizations founded by members of the nursing profession who were interested in tackling the challenges and dealing with the opportunities of information processing and computer systems, as they started to be introduced clinically by hospitals and clinical institutions beginning in the decade of the 1970's [55]. This circumstance in great contrast to medical informatics, where most practicing physicians were able to largely ignore information technology (IT) developments until the late 1980's, leaving the early evolution of medical informatics to just a few visionaries and enthusiasts among practitioners usually collaborating with

interested scientists, mathematicians, computer scientist/informaticians or engineering technologists. Nurses became very aware early that the "lack of standards for clinical language and data limited the functionality and usefulness of early applications"[55]. It is not surprising then, that for its first decades, most nursing informatics activities were devoted to education and connected to medical and health informatics organizations as special interest groups or working groups. Later, practitioner oriented professional organizations have arisen as computer and information systems became more prevalent, and the TIGER initiative was developed to promote nursing informatics educational reform through technologies [56]. A very comprehensive overview of nursing informatics today can be found in [57].

4. Overview of Educational and Nursing Informatics and the Contributions of John Mantas.

The world-wide impact of research and practices in BMHI has been highlighted by the recent publication of an eBook by the International Medical Informatics Association (IMIA) [58], which in its first volume online details the personal stories of a number of pioneers and leaders in the field, including John Mantas.

Since the present book and this chapter is designed for the Symposia held in Athens on October 29, 2022 to honor John Mantas on the occasion of his retirement, it is appropriate to highlight his contributions to the discipline of BMHI, especially in the fields of education and nursing, where his teaching, insights and collaborations have developed the educational practices and perspectives that have significantly advanced the field [7,11,17]. In [58] Mantas says: "What we are, what defines us, is mostly the accumulation of the efforts of others who influence us", reflecting for nursing education, the epitome of caring approaches that support the health and lives of others. This in many ways explains Mantas' choice of nursing informatics and his focus on educational activities of BMHI as an academic specialization. He describes his professional journey and the influence that Arie Hasman and Rolf Engelbrecht had on him to join the EFMI Working Group on Education, and his appreciation for Reinhold Haux who introduced him to the broader international informatics community of IMIA, where he led the Task Force on Educational Recommendations [11] which were subsequently updated and led to an IMIA Accreditation Program [59]. Mantas goes on to describe his efforts to introduce health informatics into the curriculum of medical and nursing schools in Greece, which resulted in the "first time in the literature that we encounter an official use of the term for a course, which was accepted very late in the 1990's and beginning of the 2000's as the appropriate generic term reflecting our field" [58, p. 142]. Mantas also recounts how a serendipitous invitation to represent Greece to the European Commission in Brussels for the announcement of the new program of Advanced Informatics in Medicine (AIM) led to his collaboration with many European colleagues such as Engelbrecht, Stefanelli, De Moor, and Rector. Shortly afterwards Mantas also joined another EC program on education in Health Informatics at the M.Sc. level – the Erasmus Inter-University Cooperation Programme, which drew 35 lecturers from across Europe from 1990 to 1997. During this time, Mantas was the principal investigator and coordinator of the NIGHTINGALE (Nursing Informatics Generic High-level Training in Informatics for Learning and Education) project, also funded by the EC from 1995, which convened workshops across the continent and developed a nursing informatics curriculum and the compilation of a textbook [7].

Mantas is a Full Professor at the National and Kaspodistrian University of Athens, where he is Director of the Health Informatics Laboratory. He has presented talks, and written and edited a number of very comprehensive articles about the history of educational efforts in BMHI – with the most detailed one being a 2016 article in the IMIA Yearbook of Medical Informatics [60] entitled Biomedical and Health Informatics – the IMIA Years. This provides a systematic overview arrived at from a literature search of title and abstracts of papers written in English beginning with the founding of IMIA. The results were an analysis of the educational topics covered by a wide range of curricular developments and course offerings, with their sources and durations of educational activities, and special attention paid to the international dimensions and impacts of the work. The IMIA Yearbook review was based on an earlier paper, which proposed a five-stage evolutionary framework for describing the history of BMHI education [61].

Most recently John Mantas has contributed to the ongoing inquiry by international experts in BMHI into research strategies that can lead to thought-provoking critical proposals that will encourage scientific debate on the nature of good research in medical informatics [62]. It is fitting to end this section on the accomplishments of John Mantas with such a forward-looking and constructive prospect – which bodes well for a productive retirement.

5. Conclusion: Historical Greek origins of rational, altruistic healthcare - inspired by Mantas' speech to the General Assembly of EFMI on his election as President

Upon his election as President of EFMI in 2010, Mantas made an acceptance speech to the General Assembly and Council of the Federation at their meeting held in Athens, which is both unique, and most elegant. It uses Greek-derived English words exclusively (except for articles and pronouns) to thank the "Panethnic Synod" or General Assembly of EFMI for his election! Mantas in this way reminds his audience – and us - of just how much medicine and healthcare owes to its mythical founder Asclepius, in Ancient Greece, whose daughters Hygieia (Healthiness), Iaso (Healing), Aegle (Good Health goddess), and Panacea (goddess of universal remedy) continue to join with him in inspiring the healing practices today, with Asclepius' staff or rod enduring as the main symbol of medicine [63]. Empirical clinical observation and rationality in searching for the etiology or causes of illnesses in the practice of healing was introduced about a century later by Hippocrates of Ionia, whose book Of The Epidemics [64] is especially relevant in the present age of emerging pandemic infectious disease [65], and whose Oath still guides the ethics of medicine [66]. Five hundred years after Hippocrates, Galen of Pergamon, another Greek healer from Ionia, became the personal physician of the Roman philosopher-emperor Marcus Aurelius, and compiled the most extensive and influential medical and pharmacological texts which were translated first into Arabic and later into many European languages, preserving and transmitting the healthcare lessons from antiquity to the Islamic and Western civilizations [67]. Another key contribution to modern healthcare - the organization of hospitals - can trace its origins to the later Greek cultural sphere of the Byzantine Empire, where hospital institutions arose to charitably and altruistically help alleviate the suffering of patients during the many epidemics that had become a documented recurring and almost global scourge during medieval times [68] – still relevant as the COVID-19 pandemic continues to evolve today. As suggested

by the title of a 2016 article [69] by distinguished colleagues who were the founding editors of the IMIA Yearbook of Medical Informatics - that John Mantas has contributed to so often and well - a renewed promise of medical informatics would be to mitigate such tragic threats to human life and health.

The contributions of Greek science, medicine and healthcare across the centuries emphasizes the distinguished practical cultural heritage that John Mantas has brought to his professional career in Biomedical and Health Informatics. His academic and professional leadership are reflected in John's many accomplishments and the responsible positions of societies and institutions that he has been entrusted with – as President of EFMI, Dean of the School of Health Sciences at the University of Athens, and Vice-Rector of the Cyprus University of Technology.

May he enjoy a healthy, relaxingly productive, and well-earned retirement!

References:

[1] Oxford Dictionary of Quotations, Third Edition. Oxford: Oxford University Press, 1980.
[2] Hersh W. editor. Health Informatics: Practical Guide, Eighth Edition. Pensacola, FL: Lulu.com. 2022.
[3] Hubner UH, Wilson GM, Morawski TS, Ball MJ. editors. Nursing Informatics: A Health Informatics, Interprofessional and Global Perspective, Fifth Edition. Springer Nature Switzerland AG, 2022.
[4] Shortliffe EH. Cimino JJ, editors, Chiang MF co-editor. Biomedical Informatics: Computer Applications in Health Care and Biomedicine. Fifth Edition, Springer Nature Switzerland AG, 2021.
[5] Venot A Burgun. A Quantin C, editors. Medical Informatics, e-Health: Fundamentals and Applications. Springer-Verlag, London, 2014.
[6] Coiera E. editor. Guide to Health Informatics, CRC Press – Routledge Taylor & Francis Group, 2015.
[7] Mantas J, Hasman A. editors. Textbook in health informatics – a nursing perspective. Amsterdam IOS Press; 2001.
[8] van Bemmel JH. Medical Informatics, Art or Science? Methods Inf Med 1996; 35:157-72.35 (Suppl. 03) 157-172.
[9] Coiera E, Aarts J, Kulikowski C. The dangerous decade. J Amer Med Inform Assoc 2012;19(1):2-5. https://doi.org/10.1136/amiajnl-2011-000674.
[10] Weiner JP, Kfuri T, Chan K, Fowles JB. "e-Iatrogenesis": the most critical unintended consequence of CPOE and other HIT. J Am Med Inform Assoc. 2007 May-Jun;14(3):387-8; discussion 389. doi: 10.1197/jamia.M2338. Epub 2007 Feb 28. PMID: 17329719; PMCID: PMC2244888.
[11] Mantas J, Ammenwerth E, Demiris G, Hasman A, Haux R, Hersh W, Hovenga E, Lun KC, Marin H, Martin-Sanchez F, Wright G. Recommendations of the International Medical Informatics Association (IMIA) on Education in Biomedical and Health Informatics. First Revision. Methods Inf Med 2010; 49:105-120, doi:10.3414/MES119.
[12] Kulikowski CA, Shortliffe EH, Currie LM, Elkin PL, Hunter LE ,Johnson TR, Kalet IJ, Lenert LA, Musen MA, Ozbolt JG, Smith JW, Tarczy-Hornoch PZ, Williamson JJ. AMIA Board white paper: definition of biomedical informatics and the specification of core competencies for graduate education in the discipline. J Amer Med Assoc 2012 19(6): 931-938. https://doi.org/10.1136/amiajnl-2012-001053.
[13] Kulikowski CA. The Micro-Macro Spectrum of Medical Informatics Challenges: From Molecular Medicine to Transforming Health Care in a Globalizing Society. Methods Inf Med 2002;41:20-4.
[14] Kuhn KA, Knoll A, Mewes HW, Schwaiger M, Bode A, Broy M, Daniel H, Feussner H, Gradinger R, Hauner H, Höfler H, Holzmann B, Horsch A, Kemper A, Krcmar H, Kochs EF, Lange R, Leidl R, Mansmann U, Mayr EW, Meitinger T, Molls M, Navab N, Nüsslin F, Peschel C, Reiser M, Ring J, Rummeny EJ, Schlichter J, Schmid R, Wichmann HE, Ziegler S. Informatics and medicine--from molecules to populations. Methods Inf Med. 2008;47(4):283-95. PMID: 18690362.
[15] Murphy SN, Mendis ME, Berkowitz DA, Kohane I, Chueh H. Integration of clinical and genetic data in the i2b2 architecture. AMIA Annu Symp Proc. 2006:1040. PMID:17238659.
[16] Doherty RF. Ethical Dimensions in the Health Professions. St. Louis: Elsevier, 2021.
[17] Mantas J. editor. Health and Medical Informatics in Europe, Amsterdam: IOS Press, 2000.
[18] Geissbuhler A, Kimura M, Kulikowski CA, Murray PJ, Ohno-Machado L, Park H-A, Haux R. Confluence of Disciplines in Health Informatics: an International Perspective. Methods Inf Med 2011; 50(06):545-555. DOI: 10.3414/ME11-0600005.

[19] Southerland WM, Swamidass SJ, Payne PRO, Wiley L, Williams-DeVane C. The diversity and disparity in biomedical informatics (DDBI) workshop. Pac Symp Biocomput. 2018;23:614-617. PMID: 29218919; PMCID: PMC5964987.
[20] Bakken S. Toward diversity, equity, and inclusion in informatics, health care, and society. J Am Med Inform Assoc. 2020 Nov 1;27(11):1639-1640. doi: 10.1093/jamia/ocaa265. PMID: 33202019; PMCID: PMC7671629.
[21] Hirko KA, Kerver JM, Ford S, Szafranski C, Beckett J, Kitchen C, Wendling AL. Telehealth in response to the COVID-19 pandemic: Implications for rural health disparities. Journal of the American Medical Informatics Association. 2020 Nov;27(11):1816-8.
[22] Cohen-Cline H, Li HF, Gill M, Rodriguez F, Hernandez-Boussard T, Wolberg H, Lippa J, Vartanian K. Major disparities in COVID-19 test positivity for patients with non-English preferred language even after accounting for race and social factors in the United States in 2020. BMC Public Health. 2021 Nov 18;21(1):2121. doi: 10.1186/s12889-021-12171-z. PMID: 34794421; PMCID: PMC8600352.
[23] Zuboff S. The Age of Surveillance Capitalism: The Fight for a Human Future at the New Frontier of Power. Profile Books, 2018.
[24] Argaw ST, Troncoso-Pastoriza JR, Lacey D, Florin MV, Calcavecchia F, Anderson D, Burleson W, Vogel JM, O'Leary C, Eshaya-Chauvin B, Flahault A. Cybersecurity of Hospitals: discussing the challenges and working towards mitigating the risks. BMC medical informatics and decision making. 2020 Dec;20(1):1-0.
[25] He Y, Aliyu A, Evans M, Luo C. Health Care Cybersecurity Challenges and Solutions Under the Climate of COVID-19: Scoping Review. J Med Internet Res. 2021 Apr 20;23(4):e21747. doi: 10.2196/21747. Erratum in: J Med Internet Res. 2021 Apr 28;23(4):e29877. PMID: 33764885; PMCID: PMC8059789.
[26] Wiener N. Cybernetics: or Control and Communication in the Animal and the Machine, Wyd. Hermann & Cie & Camb. Mass, 1948.
[27] Proceedings of the 1st IBM medical symposium. Endicott, NY: IBM, 1959
[28] Greene JA, Lea AS. Digital Futures Past - The Long Arc of Big Data in Medicine. N Engl J Med. 2019 Aug 1;381(5):480-485. doi: 10.1056/NEJMms1817674. PMID: 31365808; PMCID: PMC7928218
[29] Ledley RS, Lusted LB. Reasoning foundations of medical diagnosis; symbolic logic, probability, and value theory aid our understanding of how physicians reason. Science. 1959 Jul 3;130(3366):9-21. doi: 10.1126/science.130.3366.9. PMID: 13668531.
[30] Spiegelhalter D. The Art of Statistics: How to Learn from Data. New York: Basic Books, 2019.
[31] Kulikowski CA. Beginnings of Artificial Intelligence in Medicine (AIM): Computational Artifice Assisting Scientific Inquiry and Clinical Art – with Refllections on Present AIM Challenges. Yearb Med Inform 2019; 28(01):249-256. DOI: 10.1055/s-0039-1677895.
[32] Mayo DG. Statistical Inference as Severe Testing: How to Get Beyond the Statistics Wars. Cambridge: Cambridge University Press, 2018.
[33] Perez Gonzalez JD. Fisher, Neyman-Pearson or NHST? A tutorial for teaching data testing. Front Psychol. 2015 Mar 3;6:223. doi: 10.3389/fpsyg.2015.00223. PMID: 25784889; PMCID: PMC4347431.
[34] Collen MF. Multiphasic screening as a diagnostic method in preventive medicine. Methods Inf Med. 1965 Jun;4(2):71-4. PMID: 5829292.
[35] Safran C. Celebrating Morris F. Collen (1913-2014). Yearb Med Inform. 2015 Jun 30;10(1):2–4. PMCID: PMC4587066.
[36] Collen MF, Ball MI. editors. The History of Medical Informatics in the United States. Second Edition, Springer-Verlag, London, 2015.
[37] Ledley RS. Use of Computers in Biology and Medicine. New York: McGraw Hill; 1965.
[38] Oberhoffer G. Report on an international seminar for medical documentation and statistics. Methods Inf Med. 1962;01:27–31.
[39] Haux R, Aronsky D, Leong TY, McCray AT. Methods in year 50: preserving the past and preparing for the future. Methods Inf Med. 2011;50(1):1-6. doi: 10.3414/ME10-05-0005. PMID: 21229185.
[40] Lindberg DAB. The Computer and Medical Care. Springfield, IL. Charles C. Thomas; 1968.
[41] Kulikowski CA. Donald A.B. Lindberg: Inspiring Leader and Visionary in Biomedicine, Healthcare, and Informatics. Yearb Med Inform 2020:253-8. http://dx.doi.org/10.1055/s-0040-1701972.
[42] Humphreys BL, Logan RA, Miller RA, Siegel ER. editors. Transforming Biomedical Informatics and Health Information Access: Don Lindberg and the U.S. National Library of Medicine. Amsterdam: IOS Press, 2022.
[43] Weed LL. Special article: medical records that guide and teach. N Engl J Med. 1968; 278(12): 593- 600.
[44] Wright A, Sittig DF, McGowan J, Ash JS, Weed LL. Bringing science to medicine: an interview with Larry Weed, inventor of the problem-oriented medical record. J Am Med Inform Assoc. 2014 Nov-Dec;21(6):964-8. doi: 10.1136/amiajnl-2014-002776. Epub 2014 May 28. PMID: 24872343; PMCID: PMC4215056.

[45] Aronson MD. The Purpose of the Medical Record: Why Lawrence Weed Still Matters. Am J Med. 2019 Nov;132(11):1256-1257. doi: 10.1016/j.amjmed.2019.03.051. Epub 2019 Apr 30. PMID: 31051149.
[46] Degoulet P, Haux R, Kulikowski C, Lun KC. François Grémy and the birth of IMIA. 1st IMIA/UMIT Medical Informatics Award of Excellence given to Professor Grémy. Methods Inf Med. 2005;44(3):349-51. PMID: 16113756.
[47] Masturzo A. Cybernetic Medicine. Springfield IL: Charles C Thomas; 1965.
[48] Hansen T. Proceedings of the First International Hospital Data Processing Conference. Elsinore: 1966
[49] Kulikowski CA. Historical Roots of International Biomedical and Health Informatics: The Road to IFIP-TC4 and IMIA through Cybernetic Medicine and the Elsinore Meetings. Yearb Med Inform. 2017 Aug;26(1):257-262. doi: 10.15265/IY-2017-001. Epub 2017 Sep 11. PMID: 28480479; PMCID: PMC6239242.
[50] Degoulet P, Fieschi M, Goldberg M, Salomon R. Francois Grémy, a Humanist and Information Sciences Pioneer. Yearb Med Inform 2014; 09 (01) 3-5.
[51] Anderson J, Forsythe JM. editors. Information Processing of Medical Records. Proc of the IFIP-TC4 Working Conference on Information Processing of Medical Records, Lyon, April 6-10, 1970. Amsterdam: North-Holland; 1970.
[52] Zywietz C, Schneider B. editors. Computer Application on ECG and VCG Analysis. Proc 2nd IFIP-TC4 Working Conference, Hanover 1971. Amsterdam: North-Holland; 1973.
[53] Anderson J, Grémy F, Pagès JC. editors. Education in Informatics of Health Personnel. Amsterdam: North-Holland; 1974.
[54] van Bemmel J, McCray AT. Editors. Yearbook of Medical Informatics 92: Advances in an Interdisciplinary Science. Stuttgart; Schattauer and IMIA; 13-42, 1992.
[55] Ozbolt J, Saba V. A brief history of nursing informatics in the United States of America. Nurs. Outlook. 56:199-205. 2008.
[56] Hübner U, Shaw T, Thye J, Egbert N, Marin HF, Chang P, O'Connor S, Day K, Honey M, Blake R, Hovenga E, Skiba D, Ball MJ. Technology Informatics Guiding Education Reform - TIGER. Methods Inf Med. 2018 Jun;57(S 01):e30-e42. doi: 10.3414/ME17-01-0155. Epub 2018 Jun 20. PMID: 29956297; PMCID: PMC6193400.
[57] Hubner UH, Wilson GM, Morawski TS, Ball MJ. Nursing Informatics: A Health Informatics, Interprofessional and Global Perspective, Fifth Edition. Cham, Switzerland: Springer Nature, 2022.
[58] Kulikowski CA, Mihalas GI, Greenes RA, Park H-A, Yacubsohn V. editors. International Medical Informatics and the Transformation of Health Care [Internet]. Geneva: International Medical Informatics Association; 2021. [cited 2022 Aug 29]. Available from: https://imia-medinfo.org/wp/history-book/.
[59] Jaspers MW, Mantas J, Borycki E, Hasman A. IMIA Accreditation of Biomedical and Health Informatics Education: Current State and Future Directions. Yearb Med Inform. 2017 Aug;26(1):252-256. doi: 10.15265/IY-2017-011. Epub 2017 Sep 11. PMID: 28480478; PMCID: PMC6239229.
[60] Mantas J. Biomedical and Health Informatics Education - the IMIA Years. Yearb Med Inform. 2016 Aug 2;Suppl 1(Suppl 1):S92-S102. doi: 10.15265/IY-2016-032. PMID: 27488405; PMCID: PMC5171512.
[61] Hasman A, Mantas J, Zarubina T. An abridged history of medical informatics education in Europe. Acta Inform Med. 2014 Feb;22(1):25-36. doi: 10.5455/aim.2014.22.25-36. Epub 2014 Jan 25. PMID: 24648617; PMCID: PMC3947951.
[62] Haux R, Kulikowski CA, Bakken S, de Lusignan S, Kimura M, Koch S, Mantas J, Maojo V, Marschollek M, Martin-Sanchez F, Moen A, Park H-A, Sarkar IN, Leong TY, McCray AT. Research Strategies for Biomedical and Health Informatics: Some Thought-provoking and Critical Proposals to Encourage Scientific Debate on the Nature of Good Research in Medical Informatics. Methods Inf Med 2017; 56(Open): e1-e10, https://doi.org/10.3414/ME 16-01-0125.
[63] Wikipedia [Internet]. Aesclipius. https://en.wikipedia.org/wiki/Asclepius.
[64] Hippocrates. Of the Epidemics (Adams F, Translation). Available from: http://classic.mit.edu/Hippocrates/epidemics.1.i.html.
[65] Kulikowski CA. Ethics in the History of Medical Informatics for Decision-Making: Early Challenges to Digital Health Goals. Yearb Med Inform. 2022 Jun 2. doi: 10.1055/s-0042-1742491. Epub ahead of print. PMID: 35654428.
[66] Oxtoby K. Is the Hippocratic oath still relevant today? BMJ 2016; 355:i6629. doi: https://doi.org/10.1136/bmj.i6629.
[67] Hankinson RJ, in Hankinson RJ, editor. The Man and His Work. in The Cambridge Companion to Galen, Cambridge Companions to Philosophy, Cambridge: Cambridge University Press, 1-33.
[68] Horden P The Earliest Hospitals in Byzantium, Western Europe, and Islam. J Interdisciplinary History, MIT Press, 2005; 35: 361-389.
[69] van Bemmel JH, McCray AT The Renewed Promise of Medical Informatics. Yeab Med Inform 2016, Suppl1: S12-7, http://dx.doi.org/10.15265/IYS-2016-s011. Pub online May 20, 2016.