



AI backed advanced medical technology; insights, value, innovation

19th IEEE International Symposium on Applied Computational Intelligence and Informatics

10:00 – 10:40, May 22nd, Timisoara

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Content

- Why are we concerned with such matters as insights and innovation?
- What do we expect from digital healthcare?
- How is it regulated?
- Whose expectations matter and how to meet them?
- What makes innovation innovation in this field, and what determines business success?



World University Rankings 2025 TOP 800

Valorization

Recently, valorization became a core activity for knowledge institutions and a performance indicator.

It refers to the process of creating value from scientific knowledge by making it suitable and available for economical and/or social exploitation whether through translation into innovative products, services, processes, or new business ventures that benefit society. Therefore, it is important to define the potential impact on society when defining your research project.

Questions that you need to ask yourself:

- How can your research findings be applied in society?
- What is the potential social and/or economic impact of your research?





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Raising problems - Medtech

- Huge investments vs. few medical devices by FDA-EMA-MDR (big business, of course).
- Digital health, digital health technology has not been standardized yet.
- Wearables, sensors etc. are seeking clinical and economics evidence.
- Long innovation process, for instance telehealth / telemedicine is around since 1970 and still not proved to be cost effective
- 'Real World Databases' are much less useful than previously thought
- Digital health companies failing including, unicorns.







Innovation – What is the meaning and the main aim of the AI backed advanced digital medical technology?

Regulatory requirements (market entry) how to satisfy?- FDA - EMA - MDR

Funding and health policy requirements – how to satisfy?

Who decides whether innovation is truly innovation?





How to approach these questions?

Chat GPT

Let's go to Rita

Professional approach. Let's take a look at the professional methodologies available to ensure compliance with regulations and other requirements.





Chat GPT - Question

"Please write a short text about the advantages / disadvantages of the use of AI in healthcare."

ChatGPT: AI has revolutionized healthcare, offering a plethora of advantages. One key benefit is its ability **to analyze vast amounts of medical data quickly**, aiding in diagnosis and treatment planning.

Al-powered systems can detect patterns in data that human eyes might miss, leading to more accurate diagnoses and **personalized treatment plans**. Moreover, **Al can streamline administrative tasks, freeing up healthcare professionals to focus more on patient care.** However, there are also drawbacks to consider. **Privacy concerns** arise as Al systems require access to sensitive patient data, raising questions about data security and confidentiality. Additionally, there's the **risk of overreliance on Al, potentially leading to medical errors if healthcare professionals blindly follow Al-generated recommendations without critical assessment**. Striking a balance between harnessing the benefits of Al and mitigating its risks is **crucial** for the future of healthcare.

May 22 – St. Rita's Day

St. Rita

Should we contact her?

Immediately?

OR

We should wait?

St. Rita – should we contact her?

St Rita of Cascia, who helped in "impossible" cases, in hopeless situations, is remembered on her liturgical Memorial Day, 22 May.

One of Italy's most famous saints, she was born around 1381 in Roccaporena, near Cascia, in the province of Umbria.









We may not have to go to her yet

Let's take a closer look at where we stand first, then we'll decide on the question.





Professional approach

Professional methodologies available to ensure compliance with regulations and other requirements.







INNOVATION Management

VALUE





Innovation - from insights to value With Gunnar Storfeldt's permission.







Insights







Value

Value – From whose point of view are we looking at this? Patients? Family? Health care system? Society? Economy?







Innovation management - interpretation

Identify opportunities: systematic literature review; market surveys; market development

Create concepts: research plan & expectation and preferences of the users and financiers, policy makers, society

Innovation: Incremental; Adjacent; Disruptive; Radical

Validate concepts: production of evidence, projecting, modeling value Develop solution: Deploy solution:

Value



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Medical technology

- "...all services have to be:
- 1. Effective, and improve health outcomes;
- 2. Safe, and prevent avoidable harm related with care;
- **3.** Appropriate, and comply with current professional knowledge as well as meeting agreed standards;
- 4. Patient-centred, and involve patients/people as key partners in the process of care;
- 5. Efficient and equitable, and lead to the best value for the money spent and to equal access to available care for equal need, utilisation and equal quality of care for all."

p. 26. https://health.ec.europa.eu/system/files/2019-11/022_digitaltransformation_en_0.pdf





What is required by regulatory agencies -Medical technology

According to **Food and Drug Administration (FDA)** "Providers and other stakeholders are using digital health technologies in their efforts to: **Reduce inefficiencies, Improve access, Reduce costs, Increase quality, and Make medicine more personalized for patients.**

The European Medical Device Regulation (MDR) (2017/745) does not provide a definition and criteria of preferred measures for outcomes, but defines clinical benefit as 'the positive impact of a device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s), including outcome(s) related to diagnosis, or a positive impact on patient management or public health'.

U.S. Food & Drug. "What is digital health?" https://www.fda.gov/medical-devices/digital-health-center-excellence/what-digital-health (accessed 31 January, 2024). European Union and European Council. "Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance.)." https://eur-lex.europa.eu/legalcontent/EN/TXT/?uri=CELEX%3A32017R0745 (accessed 31 January, 2024).





What is required by policy makers and funders?

In the competitive healthcare marketplace, all providers have to demonstrate the clinical, societal and economic value.

In most of the countries Health Technology Assessment (HTA) is required for medical technologies claiming public funds.

The main aim of HTA is informing policy makers and funders about the:

- clinical efficacy, effectiveness, safety,
- costs, cost-effectiveness, budget impact, and
- health gains on individual and society level

of the various pieces of health technologies (devices, drugs, interventions).





Efficacy gain is THE Bluebird

Countries aim to improve the performance of the health care system through innovations, various health care reforms etc.

A key component of performance is efficiency, and achieving **efficiency gain** means getting more value for money, that is, investments are rewarded by the increasing overall health care productivity.

Institutionalisation of Health Economics and Health Technology Assessment helps to realize efficiency gain.









Medical Device Regulation

- 1. Effective
- 2. Safe
- 3. Appropriate
- 4. Patient-centred
- 5. Efficient and equitable
- Evidence sources:
- Clinical studies avoid as much as possible
- Literature the biggest big data systematic literature review

Who is responsible? Physicians? Not really! This is not their profession. YOU INNOVATOR! Yourself!





We got through the first three hurdles / obstacles. The device is proved to be 1) effective, the 2) risk is acceptable (so called safe); and the 3) manufacturing quality is OK. The requirements of regulatory agencies are satisfied, market en permit received.

What next?

Well, we should sell the device to generate revenue. Market: Yes, there are products that work with this. Health and social care market: However, this is not a market.



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Medical decision making – without health economics







Medical decision making – with health economics







Economic evaluation

The idea is that the health budget should be spent in such a way that it produces most value, i.e. improves welfare.



• Question:

- Does the improved health status justify the additional resources required?
- Put differently: Do the benefits (health only?!) exceed the costs?





Strictly required by law

- Health Technology Assessment Dossier (with 3-5-10 years projection)
- -product/service specification: standardisation is a big problem
- -target population, size, demography, clinical and socio-economic details if needed
- -intervention: what exactly, by what device and health care setting
- -outcome: what kind and how much health and social benefit
- -scientific evidence, clinical, economic: From where, how and by whom? Study, literature review, study quality and transferability (country and population)
- -benefit any kind health, societal, economic, well being patient, family, etc.
 -comparators: comparison with all existing technologies (could be anything) that aim to achieve similar outcomes





Al and digital medical technology – some example

Al in Medicine: A Systematic Review of Guidelines on Reporting and Interpreting Studies The Reporting Quality of Machine Learning Studies on Pediatric Diabetes Mellitus: Systematic Reviewen

Digital Biomarkers: Systematic Review of Systematic Reviews Predicting Patient Level EQ-5D Index Scores from Large International Database usig Machine Learning



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Digital biomarkers – scientific evidence

Searches of the PubMed and Cochrane Library electronic databases yielded 389 documents. A total of 25 systematic reviews evaluating the clinical impact of digital biomarkers on human health were included in our study, comprising a total of 91 outcomes. The methodological quality of most studies were critically low, results are uninterpretable.

JMIR Mhealth Uhealth. 2022 Oct; 10(10): e35722. Published online 2022 Oct 24. doi: 10.2196/35722: 10.2196/35722 PMCI

Digital Biomarker-Based Studies: Scoping Review of Systematic Reviews

Monitoring Editor: Lorraine Buis

Reviewed by Yu Heng Kwan, Patrick Altmann, Jeffrey Gamble, and Katja Matthias

Hossein Motahari-Nezhad, MSc,^{III} Meriem Fgaier, MSc,² Mohamed Mahdi Abid, MSc,³ Márta Péntek, MD, DSc,⁴ László Gulácsi, MD, DSc,^{4,5} and Zsombor Zrubka, MBA, MD, PhD^{4,5}





14 diverse intervention categories were discovered

The majority of digital biomarkers were used as physical activity behaviors (eg, Fitbit), conversion of cardiac rhythm (eg, cardiainterventions on c defibrillators), cardiac electrophysiological monitoring (eg, iPhone-based rhythm monitoring device), weight maintenance functions (eg, Garmin or Jawbone UP24), and whole-body measurement (eg, wristbands and smartwatches). Other interventions identified were associated with cardiopulmonary resuscitation (eg, metronome with a siren), assisting and leading exercise for **exercise tolerance function** (eg, GEx sensor of vital signs and smartphone), body measurement of trunk (eg, wristbands, smartwatches), <u>pain</u> (eg, accelerometer, pedometers), test of functions (eg, YAMAX, Fitbit), quality of life (eg, pedometers), test of muscle endurance (eg, fitness trackers), body measurement of lower limb (eg, accelerometer-based navigation system), and test of **maintaining body position** (eg, accelerometer-based navigation system).





Impact on Medical Decision Making?

In the 28 included studies, we identified 61 different ML methods. There were **48 methods mentioned in only one paper**, and 2 papers did not specify the ML algorithm. It is impossible to keep track of what is what and what it is good for. Information on the clinical population from which the data originated was incomplete. The algorithms were tested on small clinical samples (the number of subjects in the training population was less than 100 in two-thirds of the studies). The publications did not describe what the standard clinical practice was, how the outcomes were selected, what

criteria were used to evaluate the quality of the results, what their clinical relevance was, and how the results should be interpreted.

JOURNAL OF MEDICAL INTERNET RESEARCH

Zrubka et al

Review

The Reporting Quality of Machine Learning Studies on Pediatric Diabetes Mellitus: Systematic Review

Zsombor Zrubka¹, MBA, MD, PhD; Gábor Kertész², PhD; László Gulácsi¹, MD, DSC; János Czere³, MSc; Áron Hölgyesi^{1,4}, DPharm; Hossein Motahari Nezhad^{1,5}, PhD; Amir Mosavi², PhD; Levente Kovács⁶, PhD; Atul J Butte⁷, MD, PhD; Márta Péntek¹, MD, DSC





A lot of stuff - not much use – ML algorithms

- Altogether, from the 87 proposed or comparator methods used, we identified 61 different techniques, with random forest mentioned in 8, followed by feed forward neural network in 5, logistic regression in 4, and multiple regression and naive Bayes in 3-3 studies.
- ELM-NN: extreme learning-based feed forward neural network.
- PSO-NN: particle swarm optimization based neural network.
- MR-FIS: multiple regression-based fuzzy inference system.
- FIS: fuzzy inference system.jMR: multiple regression.
- TSSA: tree-structured survival analysis.
- DBN: deep belief neural network.
- BBNN: block-based neural network.
- WNN: wavelet neural network.
- FFNN: feed forward neural network.
- MR-NLN: multiple regression-based neural logic network.



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ML algorithms used

| HPSOWM: hybrid | particle swarm | n optimization | withpredic | tor |
|------------------|----------------|----------------|------------|-----|
| wavelet mutation | | | | |

NLN: neural logic network.

LDA1: linear discriminant analysis.

NN: neural network.

MARS: multivariate adaptive regression splines.

LSTM: long short-term memory.

ELM: extreme learning machine.

SVR: support vector regression.

RBF: radial basis function.

GP-DP: Gaussian process regression with dotproduct kernel.

GP: Gaussian process regression.

CG-EGA: continuous glucose error grid analysis (Clarke error grid).

DCP: derivatives combination predictor.

ACP: artificial neural network combination

AWA: adaptive weighted average fusion algorithm.

LR: logistic regression.

NB: naive Bayes.

RF: random forest.

CNN: convolutional neural network.

BNN: Bayesian neural network.

SVM: support vector machine.

LDA2: latent Dirichlet allocation.

RPCLR: random penalized conditional logistic regression.

GCN: gradually connected neural network.

ARM: autoregressive model.

GBM: gradient boosting machine.

FC: fully connected neural network.

LASSO: least absolute shrinkage and selection operator.

ROC AUC: receiver operating characteristic area under curve.

DCNN: dilated convolutional neural network.

LVR: latent variable regression.

DRL: deep reinforcement learning.

LGS: low glucose insulin suspension.

ROFI: repeated optimization for feature interpretation.

NR: not reported.

WGCNA: weighted correlation network analysis.

AI-DSS: AI-based decision support system.





Different methods different results

It often happens that several specialists have several different opinions (diagnoses, treatment recommendations). Then AI comes along and solves the problem. Does it solve it? Different AI methods can lead to different results. Ahhhhh!

What next?

How do we know which one is suitable for use in medical decisionmaking?

The decision is always the responsibility of the doctor or healthcare professional in question.

The patient's consent is also important.





Telehealth – Costs (2020) SLR Conclusions:

Health services considering implementing telehealth should be motivated by benefits other than cost reduction. The available evidence has indicated that although telehealth provides overwhelmingly positive patient benefits and increases productivity for many services, current evidence suggests that it does not routinely reduce the cost of care delivery for the health system.

J Med Internet Res 2020;22(10):e17298 https://www.jmir.org/2020/ 10/e17298/

Determining if Telehealth Can Reduce Health System Costs: Scoping Review

Centaine L Snoswell^{1, 2} (D); Monica L Taylor^{1, 2} (D); Tracy A Comans² (D); Anthony C Smith^{1, 2, 3} (D); Leonard C Gray² (D); Liam J Caffery^{1, 2} (D)





Heart rate variability

Based on the available evidence, a firm conclusion cannot be drawn whether Heart Rate Variability is a valid indicator of acute work-content-related stress in an industrial manufacturing environment. Most of the included papers were search results from engineering-oriented research.

IEEE TRANSACTIONS ON SYSTEMS, MAN, AND CYBERNETICS: SYSTEMS

Heart Rate Variability Measurement to Assess Acute Work-Content-Related Stress of Workers in Industrial Manufacturing Environment—A Systematic Scoping Review

Tuan-Anh Tran[®], Márta Péntek, *Member, IEEE*, Hossein Motahari-Nezhad[®], János Abonyi[®], *Member, IEEE*, Levente Kovács[®], *Senior Member, IEEE*, László Gulácsi[®], *Member, IEEE*, György Eigner[®], *Senior Member, IEEE*, Zsombor Zrubka[®], *Member, IEEE*, and Tamás Ruppert[®], *Member, IEEE*





Heart rate variability

Only one study, identified through a predefined set of keywords, was reported in PubMed, which reflects the immaturity of this concept, especially from the perspective of life science. Among the 14 included studies, **no RCT was conducted** to assess the association between HRV and AWCRS, and **none reported a high level of valid evidence** of HRV as an indicator of AWCRS. **The study design in the included studies was not robust against bias, as some studies only adopted a partly randomization procedure.**

There was an association between HRV and AWCRS, as HRV was reduced in the more stressful situation in most studies. However, the baseline conditions did not consider the HRV and stress effect during the normal working condition.





Example 3, AI-based technologies: Acceptability Pediatric diabetes (Type 1)

Parental digital health literacy was determinant of the child's glucose sensor use! Parents of children using a pump + sensor had the highest digital health literacy, followed by the pen + sensor, pen (without sensor), and pump (without sensor) subgroups.

Published on 20.3.2024 in Vol 7 (2024)

Preprints (earlier versions) of this paper are available at https://preprints.jmir.org/preprint/54807, first published November 22, 2023.



The Impact of Parental Electronic Health Literacy on Disease Management and Outcomes in Pediatric Type 1 Diabetes Mellitus: Cross-Sectional Clinical Study

Áron Hölgyesi^{1, 2} (b); Andrea Luczay³ (b); Péter Tóth-Heyn³ (b); Eszter Muzslay³ (b); Eszter Világos³ (b); Attila J Szabó³ (b); Petra Baji⁴ (b); Levente Kovács⁵ (b); László Gulácsi² (b); Zsombor Zrubka² (b); Márta Péntek² (b)





Predicting Patient-Level Quality of Life

The data set **involved** 26318 individuals (clinical settings n = 6214, general population n = 20104) and 26 predictor variables plus diagnoses. This study aimed to evaluate the performance of machine learning and regression methods in the prediction of 3 level version of EQ-5D (EQ-5D-3L) index scores from a large diverse data set.

What is all about?

Big data: literature BUT



Patient-Reported Outcomes

Predicting Patient-Level 3-Level Version of EQ-5D Index Scores From a Large International Database Using Machine Learning and Regression Methods



Zsombor Zrubka, MD, PhD, István Csabai, DSc, Zoltán Hermann, PhD, Dominik Golicki, MD, PhD, Valentina Prevolnik-Rupel, PhD, Marko Ogorevc, PhD, László Gulácsi, MD, DSc, Márta Péntek, MD, PhD





Some thoughts for developers

A domestic healthcare institution is needed to test the development of domestic medical devices.

This domestic institution must have high-level quality assurance in order to obtain valid data.

Without this, all development is risky.







The developer must meet the requirements of regulatory agencies – market entry permit

Three hurdles: Clinical (or other) efficacy, safety and manufacturing quality. Firm evidences to be provided for Market Entry permit.

Fourth hurdle: Effectiveness, budget impact, cost effectiveness, cost utility etc. - Health Technology Assessment – financing / reimbursement