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DIGITAL BIOMARKERS AND MEDICAL ALGORITHMS IN THE SERBIAN HEALTHCARE ECOSYSTEM: A COMPARATIVE ANALYSIS OF KNOWLEDGE, ATTITUDES, PRACTICE AND ECONOMIC VALUATION AMONG KEY HEALTHCARE STAKEHOLDERS

DIGITALNI BIOMARKERI I MEDICINSKI ALGORITMI U ZDRAVSTVENOM EKOSISTEMU SRBIJE: KOMPARATIVNA ANALIZA ZNANJA, STAVOVA, PRAKSE I EKONOMSKE PROCENE MEĐU KLJUČNIM FAKTORIMA ZDRAVSTVENOG SISTEMA

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Summary

Background: Digital healthcare transformation, characterised by the emergence of digital biomarkers and medical algorithms, promises to redefine the healthcare system. However, successful implementation relies on acceptance, readiness, and economic valuation by key stakeholders, including Biochemists and Clinicians. This study provides the first analysis of attitudes, practices, knowledge, and economic valuation around digital health diagnostics, with a specific focus on two sub-cohorts – Biochemists (Medical/Clinical) and Clinicians (Pathologists/Gastroenterologists) – as implementation frontrunners.
Methods: A cross-sectional survey was conducted with a cohort of 105 healthcare professionals from 53 prominent healthcare institutions. The study used a structured instrument to analyse digital competencies, perceived benefits, and potential risks. A Contingent Valuation Method was employed to determine Willingness to Pay for digital medical solutions.
Results: The cohort exhibited a high level of digital literacy (4.6 out of 5). Biochemists, grounded in analytical validation, expressed greater caution regarding clinical relevance and data privacy. Conversely, Clinicians, driv-

Kratak sadržaj

Uvod: Digitalna transformacija zdravstvene zaštite koju karakterišu pojava digitalnih biomarkera i medicinskih algoritama, obećava redefinisanje zdravstvenog sistema. Međutim, uspešna implementacija zavisi od prihvatanja, spremnosti i ekonomske procene ključnih zainteresovanih strana kao što su biohemičari i kliničari. Ova studija pruža prvu analizu stavova, praksi, znanja i ekonomske procene u vezi sa digitalnom zdravstvenom dijagnostikom sa posebnim fokusom na dve podgrupe – biohemičare (medicinske/kliničke) i kliničare (patolozi/gastroenterolozi) kao predvodnicima digitalne implementacije.
Metode: Sprovedeno je opsežno istraživanje sa kohortom od 105 zdravstvena radnika iz 53 istaknutih zdravstvenih ustanova. Studija je koristila kreirani strukturirani instrument za procenu digitalnih kompetencija, percipiranih koristi i potencijalnih rizika. Metoda kontingentne procene je korišćena za utvrđivanje spremnosti za plaćanje digitalnih medicinskih rešenja.
Rezultati: Kohorta je pokazala visok nivo digitalne pismenosti (4,6 od mogućih 5). Biohemičari, čiji je rad utemeljen na analitičkoj validaciji, izrazili su veći oprez u pogledu kliničke relevantnosti i privatnosti podataka.

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List of abbreviations: AI, artificial intelligence; CHEERS, consolidated health economic evaluation reporting standards; CI, confidence interval; CVM, contingent valuation method; ECHO, economical, clinical and humanistic outcomes; EMA, European Medicine Agency; FDA, Food and Drug Administration; GAAD, gender, age, alpha feto protein, des-gamma-carboxyprothrombin; GDPR, General Data Protection Regulation; HIS, Health Information System; ISIS, Integrated Health Information System; KAP, knowledge, attitude, practice; MRI, magnetic resonance imaging; NGS, next generation sequencing; NIH, National Institute of Health; RHIF, Republic Health Insurance Fund; SaMD, software as medical device; SD, standard deviation; WTP, willingness to pay.

en by the need for diagnostic decision support, demonstrated caution towards finance topics. The analysis revealed an optimal price point of € 65.9±75.56 (95% CI: €41.2–€90.6). There is no significant difference between sub-cohorts (p=0.89). While more than 75% of participants believed digital biomarkers would yield systemic financial savings, 74% were unaware of the existing regulatory frameworks.

Conclusion: The Serbian healthcare community possesses a robust digital foundation. Biochemists view digital medical solutions as analytical tools that require validation, while Clinicians view them as solutions to diagnostic ambiguity. Establishing a national working group on »Digital Diagnostics« to develop guidelines for validation and reimbursement codes is crucial.

Keywords: digital biomarkers, medical algorithms, willingness to pay, digital health

Nasuprot tome, kliničari, vođeni potrebom za podrškom u dijagnostičkim odlukama, pokazali su oprez prema finansijskim temama. Analiza je izračunala optimalnu cenu od 65,9±75,56 evra (95% interval poverenja: 41,2–90,6 evra). Nema značajne razlike između podgrupa (p=0,89). Dok više od 75% učesnika veruje da će digitalni biomarkeri doneti sistemske finansijske uštede, 74% učesnika nije upoznato sa postojećim regulatornim okvirima.

Zaključak: Srpska zdravstvena zajednica poseduje snažnu digitalnu osnovu. Biohemičari digitalna medicinska rešenja vide kao analitičke alate koji zahtevaju validaciju, dok ih kliničari vide kao rešenja za dijagnostičku dvosmislenost. Osnivanje nacionalne radne grupe za »Digitalnu dijagnostiku« radi razvoja njihovih smernica i razvoja šifri za nadoknadu troškova od strane fonda je može biti od velikog značaja.

Ključne reči: digitalni biomarkeri, medicinski algoritmi, spremnost za plaćanje, digitalno zdravlje

Introduction

The practice of laboratory medicine undergoes a seismic shift, moving beyond the traditional chemistry and biomarkers derived from biological fluids to include digital biomarkers and medical algorithms. In simple terms, digital biomarkers and medical algorithms are objective, measurable physiological and behavioural data used as indicators of health, collected using digital devices. These innovative solutions could enable better continuous, longitudinal monitoring of health states, capturing the dynamic nature of disease in ways that other diagnostic possibilities cannot (1).

The traditional definition of a biomarker by the National Institutes of Health (NIH) is that a biomarker is a characteristic, objectively measured and evaluated, as an indicator of normal biological or pathogenic processes, or pharmacologic responses to a therapeutic intervention (2). These markers are quantified using analytical methods such as mass spectrometry, immunoassays, and chromatography (3). The development of digital health solutions has given rise to new diagnostic tools, such as digital biomarkers and medical algorithms. They analyse disease fluctuations in real-world settings, providing a »movie« of the patient's condition rather than a simple »photo« (4). However, the adoption of innovative digital technologies is not uniform worldwide. Local healthcare systems, economic capacity and regulatory maturity influence it. Modernising the healthcare system in the Republic of Serbia, which, among other things, includes implementing the Integrated Health Information System (ISIS), has laid the foundation for digital medical technologies (5). Increasingly, regulatory agencies like the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are developing frameworks to integrate digital health solutions into practice, demonstrating their potential (6). Studies worldwide reveal a dualism in professional attitudes: while there is optimism about the potential of artificial intelligence (AI) to enhance efficiency, this optimism is often tempered by fears of job displacement. In the context of the Republic of Serbia, biochemists typically play a distinctly regulated role as »gatekeepers« of diagnostic validity; therefore, knowledge of these professional nuances is important. Readiness, attitudes, and the economic valuation of the healthcare workforce were found in this paper to be crucial and generally inadequately researched.

Knowledge-Attitude-Practice (KAP) surveys are a well-established model for researching these questions. Recent surveys of clinicians and allied professionals used a KAP approach to assess readiness for new technologies (7). For example, a study of neurologists used a KAP questionnaire to reveal specific educational needs regarding stroke diagnosis, and a survey of nurses highlighted how the COVID-19 pandemic underscores the need to improve digital health competencies (8). Authors therefore conducted a cross-sectional KAP survey of key healthcare professionals, specifically biochemists versus clinicians, during March–December 2025. The goal of this research was to assess their knowledge of digital biomarkers and medical algorithms, their attitudes toward using them across various clinical contexts, and their expectations regarding benefits, barriers, and economic valuation. A perceived patient impact and willingness to participate in related research to provide actionable plans for the healthcare system regarding the integration of digital biomarkers and medical algorithms into standard clinical practice are among the goals of this study as well. In a system where resource constraints are palpable, the willingness to pay (WTP) for digital biomarkers and medical algorithms becomes a critical indicator of their potential viability and perceived clinical utility. By anchoring WTP values to local commodities (e.g., coffee, oil) and converting them to Euros, this study provides a culturally and economically contextualised analysis of the value of digital biomarkers and medical algorithms to key healthcare stakeholders. To our knowledge, this is the first KAP and contingent WTP study on digital biomarkers and medical algorithms among key healthcare professionals in this part of the world.

Materials and Methods

A cross-sectional survey was created, validated, and then administered online via Google Forms to a cohort of 105 healthcare professionals from 53 prominent healthcare institutions in the Republic of Serbia during March–December 2025, a period coinciding with the active implementation phase of the Republic of Serbia's national e-Health strategy. This timing is crucial, as it captures the workforce's sentiment during a period of rapid systemic digitalisation.

After initial validation by 5 external participants to ensure question clarity, the cultural appropriateness of the commodity anchoring, and the logistical flow before full deployment, data segmentation, duplication removal, and strict Listwise deletion of incomplete or illogical responses, the final sample size for KAP and WTP analysis was 94. External participants went through the designed questionnaire, clearly marking areas for improvement, mostly due to the inadequate types of questions and the selection of predefined answers. After receiving initial feedback, the authors refined the research tool. The study employed a purposed sampling strategy to ensure a high level of expertise within two target sub-cohorts: Biochemists (Medical and Clinical, N=59, employed in both private chain labs and public healthcare institutions) and Clinicians (Pathologists and Gastroenterologists, N=35, mostly affiliated with tertiary level healthcare centres where digital medical solutions are implemented or to be implemented soon). Respondents provided informed consent and completed the questionnaire only once. No patient data was involved.

Quantitative data were analysed using descriptive statistics to identify trends in digital literacy and WTP distributions. Qualitative responses regarding perceived risks and patient satisfaction were translated from Serbian to English and subjected to thematic analysis to identify recurring themes (e.g., discomfort, data privacy). The study instrument covered demographics (age, sex, education, speciality, work setting, experience), followed by KAP questions about digital biomarkers and medical algorithms. The survey also solicited a willingness-to-pay analysis using the Contingent Valuation Method (CVM), with 95% Confidence Interval (CI) calculations for all analyses (total and sub-cohorts). A fixed rate of 1 EUR=117 RSD was applied. Between-subcohorts comparisons (Biochemists vs Clinicians) were explored for major outcomes, using t-test analysis in Excel. A p-value of <0.05 was considered statistically significant. The level of technological skill was measured using a Likert-style question on a 1–5 scale.

Although the overall sample size is relatively small compared with general consumer-oriented pricing studies (N=94), it is vital to consider this in the context of the study's highly specialised subjects. Our sample does not reflect the entire pool of potential consumers, but rather focuses specifically on the early adopters of digital healthcare technologies in Serbia. To be more precise, the sample reflects approximately 24% of the total number of specialists in the biochemistry profession and 12% of the pathologists working in second- and third-level healthcare institutions. Given that healthcare pricing research, which considers willingness to pay for innovative digital technologies, often employs specialised samples of fewer than 99 participants, this sample size is sufficiently large for our purposes.

The study was conducted in accordance with the principles of the Helsinki Declaration, ensuring participant anonymity and informed consent (9). The study is registered in the Real-World Evidence Registry (https://osf.io/avys3), including protocols, supplements, other data, and amendments. The manuscript is aligned with the CHEERS guidelines and has the ethical approval of the University Clinical Centre of Serbia (number 644/9).

Results

Cohort characteristics

The research cohort was predominantly female, n=65 (69%), compared to male, n=29 (31%), aligning with national trends in the healthcare workforce, as the Institute of Public Health of Serbia »Dr Milan Jovanović Batut« reported that around 68% of medical doctors were women. In comparison, men accounted for around 32% (10).

Additional respondent characteristics data are shown in *Table I*. The cohort had a median age of 42 years (range 24–65). The Biochemistry cohort was slightly older, with a mean of 43 years (range 24–61), compared with the Clinicians cohort, which had a mean of 41 years (range 27–65). The mean years of professional experience were around 15 years (range 1–39), with the Biochemists cohort (~16 years) having more experience than the Clinicians cohort (~14 years). Educational attainment was high

Table I Cohort characteristics.

Feature	Total cohort	Biochemists	Clinicians
Age (years)	42.4±10.4	43.3±10.8	41.0±9.9
Working experience (years)	15.4±10.0	16.3±10.5	13.8±9.3
Education/ Specialisation	Medical & Clinical Biochemists, Pathologists, Gastroenterologists	Mostly specialisation, Integrated Academy studies	Mostly specialisation, PhD degrees
Digital Skill (Mean)	4.6/5	4.7/5	4.5/5

across both groups; the majority of respondents held high academic degrees, while many clinicians were specialists or held PhDs.

Digital medical solutions literacy and utility analysis

Digital literacy was exceptionally high, with a median score of 4.6 out of 5 across the total cohort, and the result was consistent in both sub-cohorts. On the Likert-scale style question – »On a scale of 1 to 5, how skilled are you with technologies such as digital (e.g. using a computer, smartphone, browsing the internet, etc.), with a score of 5 being completely skilled?«

Participants frequently (80% of the total cohort) responded to the questions with the highest grade (5) – »I know what AI and ChatGPT are, and I am aware of their potential«. This indicates that the Serbian medical workforce is not merely computer-literate but actively tracking developments in digitalisation. Despite high digital skills, a distinct gap in domain-specific terminology was observed. While 98% of participants understood the concept of biomarkers, approximately 35% of the cohort (distributed across both groups) admitted they were not familiar with the specific terms of »digital biomarkers and medical algorithms« before this survey. This might point to a need to include digital medical solutions education in faculty curricula as new technologies emerge across the healthcare system.

Regarding digital biomarkers and the utilisation of medical algorithms, a divergence was observed across sub-cohorts. For biochemists, the primary focus is on monitoring and screening. Biochemists viewed digital biomarkers as tools to enhance the speed and analytical validity of testing. They expressed enthusiasm for remote capabilities that could reduce the pre-analytical errors associated with sample transport.

»Greater clinical validity compared to current practice, faster time to results« [Participant 1]

For the cohort of clinicians, the primary focus was on diagnosis and decision support. Clinicians viewed these tools as »virtual assistants« capable of confirming complex diagnoses. Their focus was on outcome efficacy rather than process efficiency.

»Shorten the time to diagnosis or at least direct doctors towards a disease« [Participant 13]

Both cohorts were aligned around medical fields where digital biomarkers and medical algorithms could be utilised, as more than 60% of respondents answered across all fields (oncology, neurology, haematology, cardiology, etc.), while the rest of the cohort split their answers by specific medical speciality, mainly oncology and cardiology. These results indicate that medical fields with the highest workforce needs and the most complex patient profiles require the most digital solutions. A big majority (94%) of cohort respondents are ready to pay personally for digital biomarkers and medical algorithms only if they are recognised in all relevant clinical guidelines and are more effective than current clinical practices, meaning that clinical validation is a prerequisite for trust in digital medical solutions.

The thematic analysis of major perceived risks and uncertainties revealed distinct professional challenges (*Table II*). Of the total cohort, only 15 (16%) respondents believe there are no real dangers or disadvantages to utilising digital biomarkers and medical algorithms.

When asked about potential drawbacks or risks, cohort respondents commonly cite concerns consistent with digital health literature: data privacy and cost implications. Some questions allowed multiple selections, with typical responses including »data privacy«, »financial aspects«, and »clinical validity«. Global surveys have identified infrastructure and technical issues, personal attitudes, and workload as barriers, whereas education and perceived usefulness are enablers (11). Our respondents' worries about privacy

Table II Perceived risks by sub-cohorts.

Risk Category	Prevalent Among	Description
Data Privacy	Both Sub-Cohorts	Universal concern regarding the security of sensitive patient data.
Clinical Relevance	Biochemists	Scepticism about whether digital medical solutions meet rigorous validation standards, such as ISO 15189.
Financial Aspects	Clinicians	Concern that these tools will be expensive add-ons not covered by the Republic Health Insurance Fund (RHIF), increasing the burden on patients.

Table III Perceived digital medical solutions purposes.

Metric	Biochemists sub-cohort	Clinician sub-cohort
Familiar with Concept of Biomarkers	97%	100%
Familiar with Digital Medical Solutions (Prior to Survey)	63%	71%
Advise Use for Diagnosis	51%	69%
Advise Use for Screening	71%	74%
Advise Use for treatment monitoring	64%	80%

and cost reflect the personal and systemic facets of these barriers, while their generally positive attitude suggests they appreciate the technology's potential utility, showing that perceived effectiveness facilitates digital health use. This optimism aligns with economic analyses: digital health interventions (such as telemedicine or continuous monitoring) have been shown to improve the quality of care and reduce costs in many settings. Our data suggest that most healthcare practitioners expect net savings from integrating digital biomarkers.

Clinicians are more likely to advise digital biomarkers for screening purposes (*Table III*). This finding aligns with the clinical utility of screening in gastroenterology (e.g., hepatocellular or colorectal cancer screening) and digital pathology (e.g., cervical cytology, lung and breast cancer), where high-throughput, low-invasive tools are highly valued for population health management. When it comes to treatment monitoring, it is expected that Clinicians' cohort would be more likely to advise the use of digital biomarkers and medical algorithms, as they are close to therapeutic protocols.

On the question »Do you think the use of medical digital biomarkers and algorithms can lead to systemic financial savings?« more than 75% of the total cohort responded with yes (71/94). At the same time, only 1 participant answered 'no'. The rest of the cohort responded that they did not know (22/94). More than half of respondents, specifically 54% (51/94), believe that the main funding source should be only the Republic Health Insurance Fund (RHIF), while the rest believe it should be a hybrid or mixed model of state and private insurance funds.

On the question »Are there regulatory frameworks in the Republic of Serbia that recognise the use of digital medical biomarkers and algorithms?« three out of four respondents answered that they did not know (70/94, 74%). Almost the same number of respondents answered that they did not know if there is a registered medical device in the Republic of Serbia that is classified as a digital medical biomarker or medical algorithm (66/94, 70%).

On an open-label question, »Do you think the use of digital biomarkers and algorithms would affect patient satisfaction, and in what way?« all participants confirmed a positive outcome, outlining screening and disease monitoring, response to therapy, and the speed of getting an initial diagnosis. Two identified concerns were the amount of data generated and data privacy.

To test respondents' trust in digital medical solutions, the question »In a situation where you will be asked to participate in a clinical trial based on digital biomarkers, are you interested in participating in this study?« out of the total cohort sample, 74% responded with »Yes« while 19% responded with »No«. Interestingly, only 8% of the Clinicians sub-cohort said they were not participating in a clinical trial, while around 25% of the Biochemists sub-cohort said they did not want to participate. This discrepancy is expected as clinicians are involved daily in clinical trials, so trust in clinical trial procedures is expectedly higher in the Clinicians' sub-cohort.

Table IV Deciding factors for digital biomarker and medical algorithms testing.

Rank	Factor (Answer)	Count	Percentage
1.	Less invasiveness	67	71.3%
2.	Faster results	66	70.2%
3.	Time saving	60	63.8%
4.	Higher clinical validity	58	61.7%
5.	Money saving	29	30.9%
6.	None of the above	4	4.3%

Table V Willingness to pay (EUR) for digital biomarker testing.

Metric	Biochemists' cohort	Clinician cohort	Total cohort
Mean Value with Standard Deviation (SD)	€67.1±85.16	€65±60.13	€65.9±75.56
95% Confidence Interval (CI)	€39.5–94.7	€43.4–86.6	€41.2–90.6
Range (Min–Max)	0 €–500 €	4 €–300 €	0 €–500 €

Qualitative risk assessment – perceived benefits & risks

To assess deciding factors for digital medical solution testing, the question »What factor/s would be crucial for you to decide to get tested with digital biomarkers and medical algorithms? You can select more than one answer«. Results are shown in *Table IV.*

Quantitative economic valuation – willingness to pay (WTP) analysis using the contingent valuation method (CVM)

The WTP data revealed remarkable consistency between and within sub-cohorts (*Table V*). This is a potential consequence of their broad work experience, which makes them rational valuators.

The total sample willingness-to-pay valuation analysis result was around €66. The Biochemists sub-cohort analysis resulted in €67, while the Clinicians sub-cohort yielded €65.0. The most selected price range was €51–100 (*Figure 1*). There is no significant difference between sub-cohorts ($p=0.89$).

Discussion

This study, to our knowledge, provides the first comprehensive KAP and contingent WTP analysis of digital biomarkers and medical algorithms among key healthcare professionals, such as Biochemists and Clinicians. The KAP study is a research method used to assess the knowledge, attitudes, and practices of a sample or population regarding

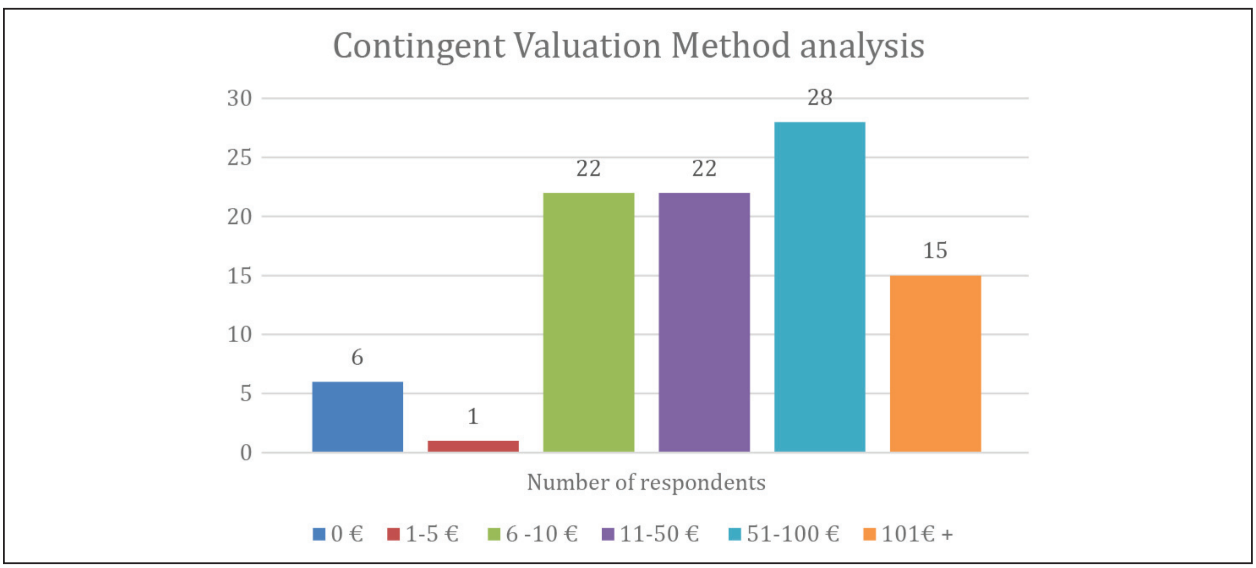

Figure 1 Total cohort contingent valuation method analysis results.

specific health topics, for example, digital medical solutions.

- Knowledge: What people know about disease, risks, prevention or another subtopic.
- Attitudes: How people feel (positively/negatively) about a health problem, treatment, prevention, or diagnosis.
- Practices: What people do (e.g. do they wash their hands, go for checkups, etc.).

The goal is to identify gaps in knowledge, negative attitudes, and behavioural barriers, as well as benefits, to create targeted and effective next steps and program suggestions. The study population was stratified into two primary focus subgroups: Biochemists – medical and clinical, represented mainly by heads of biochemistry laboratories at the tertiary healthcare level; and Clinicians, comprising heads of pathology labs, pathologists, and gastroenterologists, also predominantly from tertiary and secondary healthcare levels. Sample cohorts were carefully designed based on current experience using, piloting or learning about digital biomarkers and medical algorithms (e.g. digital pathology and related medical algorithms like Ki-67, HER2, PD-L1 and digital biomarkers in early disease stratification between non-cancer liver diseases and hepatocellular carcinoma, like the GAAD algorithm as the first practical examples of digital medical solutions in this part of Europe).

The digital literacy analysed within and between both sub-cohorts confirms that healthcare professionals in the Republic of Serbia are digitally fluent and daily engage with digital technologies. This conclusion is aligned with data from other countries, indicating rapid implementation of digital medical solutions following the COVID pandemic (12). Our cohort's familiarity with digital solutions such as ChatGPT also suggests cognitive openness to innovative solutions.

However, approximately one-third of respondents were unfamiliar with the definitions of digital biomarkers and medical algorithms, despite a high level of digital literacy. The gap in awareness aligns with other KAP studies, where professionals use digital solutions outside regulatory or academic frameworks (13). This gap has technical implications, as it may delay the development of guidelines and regulatory engagement. However, some KAP surveys have found positive attitudes when knowledge is sufficient. For instance, a 2025 Scientific Reports study on stroke diagnosis predictive tools found that most professionals possess adequate knowledge and demonstrate positive attitudes toward new diagnostics (7). Likewise, among our participants, most rated their digital literacy highly, and this likely underpins their readiness. Even so, our findings highlight areas for improvement. Although a sub-cohort of Biochemists and Clinicians shared comparable levels of digital literacy and optimism, their evaluative criteria are different. Biochemists are concerned about clinical relevance as their professional identity is built on analytical validity. This conservative stance is very likely to indicate laboratory concerns about false positives and negative results, and, subsequently, clinical consequences. Clinicians' sub-cohort approaches digital biomarkers and medical algorithms as decision-support solutions. Their support for screening use aligns with real-world needs for clinical workflows, such as improved detection rates (13). For these professionals, diagnostic acceleration outweighs methodological opacity, provided that clinical benefit is demonstrable. The study reveals a healthcare workforce that is digitally ready but regulatory blind. The high self-reported digital literacy suggests that training healthcare professionals to use these tools will be relatively straightforward. However, the profound lack of knowledge regarding the regulation of these tools (Software as Medical Solution – SaMD, data privacy laws, etc.) poses a significant risk, as more than 70% of respondents reported that they did not know if there is any regulatory framework regarding digital medical solutions. Most professionals were unaware of any local regulatory approval for digital biomarkers or medical algorithms. This finding is notable given the global scene; for example, Iulita et al. reported that regulatory agencies are actively developing guidance for digital medical solutions (6). Recently, the Republic of Serbia government has prioritised the digitalisation of the healthcare sector as a strategic imperative. The »Program for Digitalisation in the Healthcare System of the Republic of Serbia 2022–2026« outlines ambitious goals, including the establishment of an integrated Health Information System (HIS), the implementation of electronic health records, and the development of the bioeconomy through initiatives like BIO4 Campus (14). The Serbian digitalisation program is aligned with the European health data space program on the secondary use of health data for research and, consequently, innovation (15). Still, concerns about data privacy and regulatory issues are significant barriers to broader implementation. While the Republic of Serbia has harmonised its Law on Medical Devices with European Union directives, the classification of digital biomarkers and medical algorithms remains practically nonexistent (16). This study suggests that for broader adoption, regulatory clarity is as important as clinical validity. A striking result was the lack of awareness of regulatory frameworks. Only 12% of our cohort respondents believed the Republic of Serbia has any specific rules covering digital biomarkers and medical algorithms. This suggests a significant information gap. Digital health regulation is an emerging field worldwide. For example, both the FDA and EMA have issued guidance on digital health technologies. The European Union's Medical Device regulation has been revised to include software and AI devices, and other countries are creating pilot programs. These findings suggest that the Republic of Serbia may need to develop or clarify regulations for digital biomarkers, medical algorithms, and general digital diagnostics. Increased education for clinicians and lab staff around these frameworks will be critical as digital biomarkers and medical algorithms reach clinical use. This suggests that the practice of digital health has outpaced the theory in medical education and that continuous medical education can be very helpful (17).

The most frequently cited motivators for adopting digital biomarkers across the total cohort were:

1. Faster results (Time efficiency): 70% of respondents.
2. Non-invasiveness: 71% of respondents.
3. Increased clinical validity: 62% of total respondents.

When it comes to risks, analysis shows three concerns which must be addressed before successful implementation:

1. Data privacy: Overarching concern cited by respondents from both sub-cohorts. This reflects awareness of GDPR and Personal Data Protection laws.
2. Clinical relevance: Concerns whether digital medical solutions correlate with pathophysiology.
3. Financial barriers: The clinical sub-cohort expressed concern that these technologies might increase costs for other stakeholders.

Perceived benefits are in correlation with risks. Results point to the necessity of new solutions that are faster, clinically more relevant to current practice, and appropriate for use across various patient profiles. Using the ECHO model (Economic, Clinical, and Humanistic Outcomes) could be very useful for creating national guidelines for digital medical solutions.

The economic feasibility of digital medical solutions

Willingness to pay was analysed using the Contingent Valuation Method, a commonly used approach in digital health valuation and health economics studies, with a two-step design. First, respondents selected a predefined payment range using a payment card method. Afterwards, they were asked to specify an exact monetary amount within the selected range using an open-ended question.

The question sets up a hypothetical situation – »How much is medical digital biomarker/algorithmic testing worth to you? In other words, how much are you willing to pay for it, or what do you have to give up so that you or someone from your close family can be tested and eventually diagnosed promptly in case of a certain disease?« and asks for the respondent's willingness to pay directly. Instead of asking an open-ended question like »How much would you pay?«, this research tool provides a list of price ranges for the respondent to choose from (€0, €1–5, €6–10, €11–50, €51–100 and €101+). This is known as a »payment card« mechanism, designed to reduce the cognitive burden on respondents. Additionally, the survey uses tangible goods to help respondents visualise the value (e.g., approximately 1–3 l of sunflower oil at €1–5). This is a common technique in CVM to make monetary values more concrete and relatable to daily purchasing power. This question is followed by an open-ended question asking for the exact value within the selected range to refine the data. The questions are deliberately placed at the end of the research instrument, as participants went through all study segments before economic valuation, so they could gain more insights and define their responses better. The economic valuation of digital biomarkers and medical algorithms revealed consensus within and between the sub-cohorts of Biochemists and Clinicians around a value of €66. The results show that Biochemists appear to anchor their valuation of digital biomarkers and medical algorithms slightly higher than the cost of traditional reagents. For a gastroenterologist, a reliable digital biomarker that rules out, for instance, Inflammatory Bowel Disease could spare a patient a colonoscopy – an invasive procedure that costs around €150–200 in private practice and carries procedural risk. Similarly, pathologists, aware of the high costs of molecular profiling and digital pathology (e.g., NGS panels costing hundreds and thousands of euros), perceive high-utility digital medical solutions as comparable to these advanced diagnostics. Therefore, valuing a high-performance digital biomarker or medical algorithm at €66 is consistent with the economics of their daily practice, as their »unit of value« is not the test result itself but the decision it enables (18).

For widespread adoption within the RHIF, digital biomarkers and medical algorithms must demonstrate not just clinical utility but cost-effectiveness. Most respondents (75% of the total respondent's cohort) believe that digital biomarkers and medical algorithms could lead to systemic savings. It is crucial to advocate value-based pricing that reflects the savings generated by these medical digital solutions. This finding aligns with international economic evaluations demonstrating that digital health interventions can reduce costs by enabling earlier diagnosis and fewer hospitalisations (19). The Republic of Serbia data thus reinforce the global narrative.

The sample size (N=94) relies on a purposive sampling strategy and voluntary responses, so it may not fully represent all Serbian health professionals, but rather frontrunners in the implementation of digital medical solutions, such as Biochemists, Pathologists, and Gastroenterologists. While consumer-focused studies utilising the pricing methods employ larger sample sizes, such as 305 for the elderly population or 1631 for students, the sample size in this research focused exclusively on key stakeholders' healthcare professionals, representing a highly specific, specialised and relevant target cohort that is very hard to reach (20, 21). Nowadays, healthcare research on stakeholder willingness-to-pay for digital telehealth services utilises samples of 99 or fewer respondents (22, 23). As the Republic of Serbia has around 25% fewer physicians per 100.000 inhabitants compared to the European Union average (around 328 versus 441), with pathology specialists (around 4.9 per 100.000 inhabitants), gastroenterologists (around 3.6 per 100.000 inhabitants) and medical biochemists (around 9.3 per 100.000 inhabitants), enhancing efficiency with digital biomarkers and medical algorithms can help immensely in overcoming understaffing challenges (24). According to the Institute of Public Health of Serbia's report and our estimates, the national workforce comprises approximately 250 biochemistry specialists in secondary/tertiary healthcare institutions, as well as around 120 pathologists (10). Our sample of biochemists (n=59), therefore, represents approximately around 24% of the total workforce, while pathologists (n=13) represent roughly 12% of the pathology specialist's workforce. For gastroenterologists, there is no official data; however, on the National Association of Gastroenterologists of Serbia site, there are around 250 members, while estimates suggest that around 50% of total gastroenterologists work in tertiary health institutions. Therefore, our sample (n=22) represents approximately 18% of the total gastroenterology workforce at that level of the healthcare system (25, 26). Given the exploratory nature of the KAP and WTP CVM analysis, the sample size is considered sufficient to yield meaningful insights.

Conclusion

This study provides the first empirical comparisons of KAP and WTP for digital biomarkers and medical algorithms among Biochemists and Clinicians in the specific context of the Republic of Serbia's healthcare system. The results indicate that a tech-savvy workforce, split in terms of professional priorities – Biochemists are the »Gatekeepers of Quality,« demanding analytical validation and valuing digital tools comparable to advanced biochemical testing. Clinicians play the professional role of »Seekers of Solutions,« seeking their usefulness in diagnosis and demonstrating a high willingness to pay. The pricing is set at around €66.

To accelerate the adoption of digital biomarkers and medical algorithms in the Republic of Serbia, there is a need for transparent validation data. The focus must be on clinical studies demonstrating improved patient outcomes. Moreover, integrating digital terminology into educational institutions through continuous medical education can be essential to bridge the gap between digital literacy and clinical application in the healthcare system. The collaboration between biochemists and clinicians would prove a defining factor in the success of digital medicine in the Republic of Serbia. There is consensus among all stakeholders that these tools can generate systemic savings, supporting the case for RHIF reimbursement if value-based pricing models are adopted. Integration of digital health regulation into the faculties' curricula would be another action point for health and education authorities. Important to note are legitimate concerns about data privacy, costs, and evidence, as the cohort is largely unaware of specific national regulations in this area. To facilitate this transition, a working group focused on digital diagnostics is needed to develop guidelines and reimbursement codes distinct from traditional laboratory codes, reflecting the value of clinical utility and cost-effectiveness. By addressing these needs, the Republic of Serbia's health system can harness the potential of digital biomarkers, in line with international momentum.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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