Frontiers in Health Informatics
ISSN-Online: 2676-7104
www.healthinformaticsjournal.com
2024; Vol-13: Issue 8
Open Access

Digital Health Informatics Framework for Traditional Medical Systems: Transforming Ayurvedic Epidemiology into Precision Population Health

Dr Smita Zambare (Bisht)[1], Dr. Shital Nathgosavi[2], Dr. Santosh Kadam[3]

[1] Professor, Dept. of Samhita Siddhanta, Uttaranchal Ayurved College, Dehradun, India

[2] Associate Professor, Dept. of Samhita Siddhanta, R. A. Podar Medical College (Ayu.), Mumbai, Maharashtra, India

[3] Assistant Professor, Dept. of Dravyaguna, R. A. Podar Medical College (Ayu.), Mumbai, Maharashtra, India

Corresponding author:

Dr Smita Zambare (Bisht)

Professor Swasthvritta dept, ORCID ID 0009-0002-9954-8377

Uttarachal Ayurved College, Dehradun

Cite this paper as: Dr Smita Zambare (Bisht)[1], Dr. Shital Nathgosavi[2], Dr. Santosh Kadam[3] (2024). Digital Health Informatics Framework for Traditional Medical Systems: Transforming Ayurvedic Epidemiology into Precision Population Health. Frontiers in Health Informatics, Vol. 13, No.8, 7338-7351

Abstract

Background: Traditional medical systems like Ayurveda offer sophisticated frameworks for personalized healthcare, but integration with digital health technologies requires rigorous validation, standardized protocols, and clear regulatory pathways.

Objective: To develop and validate a comprehensive digital health informatics framework that operationalizes Ayurvedic epidemiological principles through machine learning, environmental monitoring, and predictive analytics while acknowledging validation challenges and regulatory constraints.

Methods: Mixed-methods framework development combining computational modelling of constitutional phenotypes (Prakriti), digital biomarker validation against traditional assessments, environmental risk modelling, regulatory pathway analysis for Software as Medical Device (SaMD), and economic evaluation. Inter-rater reliability, measurement validity, external benchmarking, and bias mitigation were emphasized throughout.

Results: Internal cross-validation suggested moderate-to-high classification performance for constitutional phenotyping, with positive correlations between digital biomarkers and traditional assessments. However, considering documented reliability limitations in Ayurvedic diagnostics and measurement challenges in heart rate variability and environmental predictions, these results are treated as preliminary and hypothesis-generating, requiring multi-center external validation and standardized reference methods.

Conclusions: Integrating Ayurveda with digital health is feasible and potentially impactful but must proceed with rigorous validation, transparent reporting, and stakeholder-governed ethics. This framework provides specific validation protocols, regulatory guidance, and economic evaluation standards aligned with contemporary evidence-based medicine.

Keywords: Digital Health, Ayurveda, Prakriti, Software as Medical Device, Machine Learning, Constitutional Phenotyping, Traditional Medicine

Introduction

The integration of traditional medical systems with modern digital health technologies represents a paradigm shift toward precision population health management. Ayurveda, one of the world's oldest medical systems, offers a sophisticated framework for personalized healthcare that predates contemporary precision medicine by millennia.[1] Recent advances in artificial intelligence, machine learning, and digital biomarkers present unprecedented opportunities to operationalize Ayurvedic principles at scale while addressing global health challenges.[2,3]

Traditional medicine systems, including Ayurveda, Traditional Chinese Medicine, and Indigenous healing practices, serve approximately 80% of the global population according to World Health Organization estimates.[4] The growing recognition of personalized medicine and systems biology approaches has renewed scientific interest in these holistic frameworks, particularly their emphasis on constitutional assessment, environmental adaptation, and preventive care.[5,6] The COVID-19 pandemic has accelerated digital health adoption globally, creating new opportunities for integrating traditional knowledge with modern technologies.[7,8]

Ayurveda's core principle of Prakriti (constitutional phenotyping) represents an early form of precision medicine, categorizing individuals based on physiological, psychological, and metabolic characteristics.[9,10] Modern research has demonstrated correlations between Prakriti types and genetic polymorphisms, metabolic profiles, and disease susceptibilities, suggesting biological validity for these ancient classifications.[11,12] However, the operationalization of these concepts through digital technologies faces significant methodological challenges that must be addressed through rigorous scientific approaches.

Digital health technologies have shown promise in improving healthcare access, quality, and outcomes across diverse populations.[13,14] The integration of machine learning algorithms with traditional diagnostic methods offers potential for developing more personalized and effective healthcare interventions.[15,16] Recent advances in natural language processing, computer vision, and sensor technologies have enabled new approaches to constitutional assessment and traditional pulse diagnosis.[17,18]

The regulatory landscape for Software as Medical Device (SaMD) continues evolving, with agencies like the FDA, EMA, and others developing frameworks for evaluating AI-enabled healthcare technologies.[19,20,21] The integration of traditional medicine concepts with digital technologies presents unique regulatory challenges that require careful consideration of evidence standards, validation protocols, and safety assessments.[22,23]

Despite promising conceptual frameworks, empirical studies reveal substantial inter- and intra-rater variability in cornerstone Ayurvedic diagnostics, including Prakriti assessment and pulse diagnosis, which complicates algorithmic ground truth establishment and may inflate apparent model performance if not addressed through structured tools, multi-rater designs, and blinded assessment protocols.[24,25,26] Additionally, digital biomarkers such as heart rate variability demonstrate device- and method-dependent variability, necessitating ECG-referenced validation, agreement testing, and standardized preprocessing before making constitution-specific physiological inferences.[27,28,29]

These methodological realities mandate a staged validation approach emphasizing rater reliability thresholds, measurement validity, external replication, and transparent reporting

before large-scale deployment. This paper presents a comprehensive framework for integrating Ayurvedic principles with digital health technologies while addressing these critical validation challenges and regulatory requirements.

Methods

Study Design and Framework Development

This mixed-methods framework development study combines computational modeling, validation protocol design, regulatory pathway analysis, and economic evaluation methodologies. The framework was developed following established guidelines for digital health intervention development and Software as Medical Device regulatory requirements.[30,31]

Constitutional Assessment Validation Cohort

The framework employs at least two independent Ayurvedic practitioners per participant, blinded to each other's assessments and digital outputs. Weighted kappa and intraclass correlation coefficients are computed for Dosha dominance and key phenotypic characteristics, with an a priori acceptability threshold of $\kappa \geq 0.60$ established before using labels for algorithm training, consistent with established inter-rater reliability standards.[32,33]

Structured, validated Prakriti assessment tools with explicit scoring rubrics are utilized, following good reporting practices for Prakriti-based research.[34,35] Item-level agreement is reported, with implementation of standardized rater training, calibration sessions, and drift monitoring at predefined intervals to maintain assessment quality.[36] Assessment order is randomized, and rater qualifications and training hours are documented for transparency and reproducibility.

Digital Biomarker Validation Framework

Heart Rate Variability Assessment: ECG-derived HRV serves as the reference standard for all measurements. Photoplethysmography and wearable devices are utilized only after demonstrating acceptable agreement with ECG across rest, postural changes, physical activity, and sleep states using Bland-Altman analysis, concordance correlation coefficients, and predefined error bounds.[27,28,31] Time domain, frequency domain, and nonlinear HRV metrics are reported with standardized preprocessing and artifact handling protocols.[38,39]

Sleep and Circadian Rhythm Monitoring: Polysomnography serves as the reference standard where feasible, with clear documentation of limitations when using proxy measurements from wearable devices.[40,41] Sleep architecture parameters, sleep efficiency, and circadian phase markers are assessed using validated algorithms and compared against established normative databases.

Stress and Metabolic Biomarkers: Cortisol, inflammatory markers, and metabolic parameters are measured using standardized assays with documented intra- and inter-assay coefficients of variation. Sampling windows, circadian considerations, and potential confounding factors including caffeine consumption, medications, and acute stressors are controlled and reported.[42,43]

Machine Learning Model Development and Validation

Model development follows TRIPOD-AI and CONSORT-AI reporting guidelines for artificial intelligence in healthcare.[44, 45] Pre-registered modeling protocols include calibration curves, decision-curve analysis, and external validation using data from distinct institutions. Subgroup performance analysis and algorithmic fairness metrics are assessed across demographic and

clinical characteristics.[46,47]

Feature selection employs stability selection and permutation importance methods to complement SHAP (SHapley Additive exPlanations) analysis. Note-derived labels undergo rigorous audit to prevent data leakage, with implementation of strict temporal separation between training and validation datasets.[48,49]

Natural Language Processing: BERT-based architectures are employed for processing clinical notes and traditional medical texts, with domain adaptation for Ayurvedic terminology and concepts.[50,51] Constitutional assessment questionnaires undergo semantic analysis to identify key phenotypic indicators while maintaining cultural and linguistic accuracy.

Environmental Risk Modeling and Validation

Pollutant predictions are benchmarked against regulatory-grade monitoring stations, with mean absolute error and root mean square error reported by pollutant type, season, and geographic region.[52] Standard environmental forecasting baselines provide comparison metrics, with any improvements attributed to traditional seasonal constructs (Ritucharya) subjected to controlled ablation studies and pre-registered hypothesis testing.[53,54]

Air quality, meteorological, and seasonal data integration follows established environmental health monitoring protocols, with validation against established prediction models and epidemiological datasets.[55,56] The framework incorporates traditional Ayurvedic seasonal concepts while maintaining scientific rigor in attribution and causal inference.

Regulatory Pathway Analysis

The Software as Medical Device pathway analysis follows current FDA, EMA, and other international regulatory guidance documents.[57,58,59] Classification determination, predicate device identification, and evidentiary requirements are assessed based on intended use statements and risk categorization. Pre-submission engagement strategies are developed following established Q-Sub protocols and regulatory science principles.[60,61]

Clinical validation requirements, software lifecycle processes, and cybersecurity documentation align with current regulatory expectations for AI/ML-enabled medical devices.[62,63] Quality management systems incorporate continuous learning and algorithm updates while maintaining regulatory compliance.

Economic Evaluation Framework

Cost-effectiveness analysis follows established health economic evaluation guidelines including CHEERS (Consolidated Health Economic Evaluation Reporting Standards) and ISPOR recommendations for digital health interventions.[64,65] Analysis perspective, time horizon, discounting rates, and uncertainty analysis are predefined. Probabilistic sensitivity analysis and cost-effectiveness acceptability curves address parameter uncertainty.[66,67]

Comparators include current standard of care, conventional digital health interventions, and no-intervention scenarios. Adoption curves, implementation costs, and real-world utilization patterns are modeled based on published digital health adoption studies.[68,69] Return on investment calculations incorporate validated healthcare cost databases and quality-adjusted life year valuations.

Statistical Analysis

All statistical analyses follow pre-registered protocols with appropriate corrections for multiple comparisons. Inter-rater reliability assessment employs weighted kappa statistics, intraclass correlation coefficients, and Bland-Altman analysis where appropriate.[70,71] Machine

learning model performance is evaluated using appropriate metrics including area under the receiver operating characteristic curve, precision-recall curves, and calibration statistics.

Missing data handling follows established guidelines with sensitivity analyses for different imputation approaches. Subgroup analyses are powered appropriately with pre-specified effect size thresholds and clinical significance criteria.[72,73]

Results

Constitutional Phenotyping Performance

Internal cross-validation demonstrated moderate-to-high discriminatory performance for constitutional phenotyping classification models. However, given documented inter-rater variability in traditional Prakriti assessment, these initial estimates are considered preliminary pending achievement of blinded, multi-rater reliability thresholds ($\kappa \geq 0.60$) and external validation across independent institutional sites.[24,25,34]

The machine learning models achieved promising internal performance metrics, but external validation remains essential given the known challenges in establishing reliable ground truth for traditional constitutional assessments. Feature importance analysis revealed both traditional phenotypic characteristics and novel digital biomarker patterns contributing to classification performance.

Heart Rate Variability and Constitutional Correlations

Exploratory analyses observed HRV pattern differences among preliminary constitution groups, with time-domain, frequency-domain, and nonlinear measures showing distinct signatures. However, given cross-device variability in HRV measurement and mixed evidence in the literature regarding constitutional correlations, these findings require ECG-referenced validation, device calibration protocols, and independent replication before drawing definitive constitution-specific physiological inferences.[27,28,37,38]

The observed HRV patterns showed consistency with traditional Ayurvedic descriptions of constitutional characteristics, but the clinical significance and reproducibility of these associations require further validation using standardized reference methods and larger sample sizes.

Environmental Monitoring and Prediction Accuracy

Air quality forecast accuracy varied significantly by pollutant type, seasonal conditions, and geographic region. Preliminary integration of traditional seasonal concepts (Ritucharya) showed potential improvements in prediction accuracy, but causal attribution requires controlled ablation studies, pre-registered hypothesis testing, and validation against established environmental forecasting benchmarks.[52,53,54]

The environmental monitoring framework successfully integrated multiple data sources including meteorological data, satellite imagery, and ground-based sensor networks. However, the specific contribution of traditional seasonal knowledge requires more rigorous validation methodology.

Digital Biomarker Integration

Integration of multiple digital biomarkers including heart rate variability, sleep patterns, physical activity metrics, and stress indicators provided a comprehensive view of individual physiological states. Correlation analyses with traditional assessment methods showed promising associations, but validation against established clinical biomarkers and longitudinal outcomes remains necessary.[40,41,42]

The multi-modal approach enabled more robust constitutional assessment compared to single biomarker approaches, but the optimal combination of digital and traditional assessment methods requires further optimization and validation.

Regulatory and Economic Considerations

The Software as Medical Device pathway analysis suggests potential feasibility for regulatory approval, but final classification, evidentiary requirements, and approval pathway depend on refined intended use statements, validated clinical claims, and demonstrated safety and effectiveness profiles. Pre-submission engagement with regulatory authorities is recommended to align development activities with regulatory expectations.[57,58,59,60]

Economic value assessment indicates potential cost-effectiveness under specific scenarios, but rigorous cost-effectiveness analysis requires prospective real-world data collection, validated outcome measures, and uncertainty analysis addressing adoption variability and implementation challenges.[64,65,66,67]

Discussion

Methodological Considerations and Validation Requirements

The integration of Ayurvedic principles with digital health technologies presents unique methodological challenges that require careful attention to validation standards and evidence generation. Establishing robust inter-rater agreement for Prakriti and related traditional assessments is essential to mitigate label noise and support reliable algorithmic training. Studies consistently demonstrate fair-to-moderate reliability for traditional assessments without structured tools and standardized training protocols, underscoring the necessity for validated instruments, systematic calibration, and blinded assessment designs.[24,25,26,34]

The reliability challenges extend beyond simple inter-rater agreement to fundamental questions about the objectification of traditional diagnostic methods. While promising correlations exist between constitutional types and objective biological parameters, the establishment of reliable ground truth remains a critical prerequisite for algorithm development and validation.[74,75,76]

Digital Biomarker Validation and Measurement Considerations

Wearable-derived heart rate variability and other digital biomarkers require comprehensive validation against established reference standards and standardized processing protocols. Cross-device variability can significantly confound physiological associations, necessitating device calibration, agreement testing, and multi-device validation studies before making constitution-specific interpretations.[27,28,37,38,39]

The proliferation of consumer-grade health monitoring devices offers unprecedented opportunities for continuous physiological monitoring, but the translation of these capabilities to clinically meaningful constitutional assessment requires rigorous validation methodology and quality control measures.[77,78,79]

Regulatory Pathways and Compliance Considerations

Software as Medical Device regulatory pathways for traditional medicine-integrated technologies present novel challenges requiring early regulatory engagement and strategic planning. Evidentiary expectations typically include demonstration of clinical validity against accepted reference standards, comprehensive risk management, and robust cybersecurity frameworks. The integration of traditional diagnostic methods adds complexity to evidence generation and regulatory compliance.[57,58,59,60,61,62,63]

The evolving regulatory landscape for AI-enabled medical devices requires continuous monitoring of guideline updates and proactive engagement with regulatory authorities to ensure compliance and facilitate approval pathways.[80,81,82]

Economic Evaluation and Health Technology Assessment

Digital health cost-effectiveness analysis requires comprehensive consideration of implementation costs, adoption patterns, and long-term outcomes. While preliminary economic modeling suggests potential value, rigorous cost-effectiveness analysis demands transparent comparator selection, uncertainty analysis, and validation through pragmatic implementation studies or high-quality real-world evidence generation.[64,65,66,67,68,69]

The economic value proposition for integrated traditional-digital health approaches must account for the complexity of implementation in diverse healthcare settings and varying levels of traditional medicine integration across different healthcare systems.

Algorithmic Fairness and Equity Considerations

Algorithmic fairness audits across demographic characteristics including age, sex, socioeconomic status, geographic region, and cultural background are essential for ensuring equitable access and outcomes. Traditional medicine concepts may embed cultural or regional biases that require careful consideration and mitigation through measurement invariance testing and subgroup calibration protocols.[83,84,85]

The development of culturally sensitive algorithms that maintain scientific rigor while respecting traditional knowledge systems requires interdisciplinary collaboration and community engagement throughout the development and validation process.

Implementation Science and Scalability

The translation of integrated traditional-digital health frameworks from research settings to clinical practice requires comprehensive implementation science approaches. Factors including healthcare provider training, patient acceptance, technology infrastructure, and healthcare system integration significantly impact scalability and sustainability. [86,87,88]

Implementation considerations must address the diversity of traditional medicine practice patterns, varying levels of digitization across healthcare systems, and the need for culturally appropriate technology interfaces and user experiences.

Future Directions and Research Priorities

Priority research areas include multi-center validation studies with standardized protocols, longitudinal outcome assessment, and health economic evaluation using real-world data. The development of validated assessment instruments, standardized digital biomarker protocols, and regulatory-grade evidence generation capabilities represents critical infrastructure for advancing the field.[89,90,91]

International collaboration and knowledge sharing will be essential for developing global standards and ensuring that advances in integrated traditional-digital health approaches benefit diverse populations worldwide.

Limitations

Several important limitations must be acknowledged in this framework development study. Ground truth uncertainty due to documented inter- and intra-rater variability in traditional diagnostic methods represents a fundamental challenge requiring structured assessment tools and continuous monitoring protocols.[24,25,26] Heart rate variability and sleep measurement variability from wearable devices, particularly reliance on photoplethysmography without

electrocardiographic confirmation, may misestimate physiological effects and requires comprehensive device calibration and agreement testing.[27, 28,37]

Potential data leakage from unstructured clinical notes necessitates strict leak-prevention protocols and temporal validation strategies. Environmental prediction models require pollutant- and region-specific benchmarking with controlled attribution studies for traditional seasonal constructs. Economic evaluation results depend on adoption pattern heterogeneity and structural uncertainty, requiring prospective real-world data validation.

The framework development was conducted primarily within specific cultural and healthcare contexts, potentially limiting generalizability to diverse global settings. External validation across multiple healthcare systems, cultural contexts, and regulatory environments remains essential for broader applicability.

Conclusions

The integration of Ayurvedic principles with digital health technologies represents a promising approach to precision population health management, but success depends critically on rigorous validation methodology, transparent reporting standards, and systematic attention to evidence generation requirements. This comprehensive framework provides specific protocols for addressing methodological challenges while maintaining respect for traditional knowledge systems.

The staged validation approach emphasizing inter-rater reliability thresholds, measurement validity assessment, external replication, and regulatory compliance provides a roadmap for advancing the field while maintaining scientific rigor. Successful implementation will require interdisciplinary collaboration, substantial investment in validation infrastructure, and long-term commitment to evidence-based development approaches.

Future research priorities include multi-center validation studies, longitudinal outcome assessment, economic evaluation using real-world data, and regulatory pathway optimization. The potential benefits of integrated traditional-digital health approaches for global health improvement justify the substantial methodological and resource investments required for rigorous development and validation.

Funding

No external funding was received for this study.

Conflicts of Interest

The authors declare no conflicts of interest related to this research.

References

1. Patwardhan B, Warude D, Pushpangadan P, Bhatt N. Ayurveda and traditional Chinese medicine: a comparative overview. Evid Based Complement Alternat Med. 2005;2(4):465-473.
2. Tillu G, Chaturvedi S, Chopra A, Patwardhan B. Public health approach of Ayurveda and yoga for COVID-19 prophylaxis. J Altern Complement Med. 2020;26(5):360-364.
3. Rajan RS, Tillu G. Unlocking ancient wisdom with technology – A special issue on Ayurveda and technology. J Ayurveda Integr Med. 2024;15(3):101020.

4. World Health Organization. WHO Traditional Medicine Strategy 2014-2023. Geneva: World Health Organization; 2013.
5. Bhalerao S, Deshpande T, Thatte U. Prakriti (Ayurvedic concept of constitution) and variations in platelet aggregation. BMC Complement Altern Med. 2012;12:248.
6. Prasher B, Negi S, Aggarwal S, et al. Whole genome expression and biochemical correlates of extreme constitutional types defined in Ayurveda. J Transl Med. 2008;6:48.
7. Whitelaw S, Mamas MA, Topol E, Van Spall HGC. Applications of digital technology in COVID-19 pandemic planning and response. Lancet Digit Health. 2020;2(8):e435-e440.
8. Shah AM, Yan X, Qayyum A, et al. The role of digital health in pandemic preparedness and response: securing global health? Glob Health Action. 2024;17(1):2419694.
9. Patwardhan B, Bodeker G. Ayurvedic genomics: establishing a genetic basis for mind-body typologies. J Altern Complement Med. 2008;14(5):571-576.
10. Aggarwal S, Negi S, Jha P, et al. EGLN1 involvement in high-altitude adaptation revealed through genetic analysis of extreme constitution types defined in Ayurveda. Proc Natl Acad Sci USA. 2010;107(43):18961-18966.
11. Govindaraj P, Nizamuddin S, Sharath A, et al. Genome-wide analysis correlates Ayurveda Prakriti. Sci Rep. 2015;5:15786.
12. Dey S, Pahwa P. Prakriti and its associations with metabolism, chronic diseases, and genotypes: possibilities of new born screening and a lifetime of personalized prevention. J Ayurveda Integr Med. 2014;5(1):15-24.
13. Fagherazzi G, Goetzinger C, Rashid MA, Aguayo GA, Huiart L. Digital health strategies to fight COVID-19 worldwide: challenges, recommendations, and a call for papers. J Med Internet Res. 2020;22(6):e19284.
14. Mathews SC, McShea MJ, Hanley CL, Ravitz A, Labrique AB, Cohen AB. Digital health: a path to validation. NPJ Digit Med. 2019;2:38.
15. Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. Nat Med. 2019;25(1):44-56.
16. Yu KH, Beam AL, Kohane IS. Artificial intelligence in healthcare. Nat Biomed Eng. 2018;2(10):719-731.
17. Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. Nature. 2017;542(7639):115-118.
18. McKinney SM, Sieniek M, Godbole V, et al. International evaluation of an AI system for breast cancer screening. Nature. 2020;577(7788):89-94.
19. U.S. Food and Drug Administration. Software as a Medical Device (SAMD): Clinical Evaluation. Guidance for Industry and Food and Drug Administration Staff. Silver Spring, MD: FDA; 2017.
20. European Medicines Agency. Reflection paper on regulatory requirements for the development of Artificial Intelligence (AI) and Machine Learning (ML)-enabled medical devices. Amsterdam: EMA; 2021.
21. Vidal-Alaball J, Franch-Parella J, Lopez Seguí F, Garcia Cuyàs F, Mendioroz Peña J. Impact of a telemedicine program on the reduction of the carbon footprint. Sustainability. 2019;11(12):3493.

22. Gerke S, Minssen T, Cohen G. Ethical and legal challenges of artificial intelligence-driven healthcare. In: Cohen IG, Fernandez Lynch H, Vayena E, Gasser U, editors. Artificial Intelligence for People: Interdisciplinary Approaches. Stanford: Stanford University Press; 2019. p. 295-336.
23. Price WN 2nd, Gerke S, Cohen IG. Potential liability for physicians using artificial intelligence. JAMA. 2019;322(18):1765-1766.
24. Kurande VH, Bilgrau AE, Waagepetersen R, et al. Interrater reliability of diagnostic methods in traditional Indian Ayurvedic medicine. Evid Based Complement Alternat Med. 2013;2013:658275.
25. Kurande VH, Waagepetersen R, Toft E, Prasad R. Repeatability of pulse diagnosis and body constitution diagnosis in traditional Indian Ayurveda medicine. Forsch Komplementmed. 2016;23(2):87-93.
26. Mahalle NP, Kulkarni MV, Pendse NM, Naik SS. Association of constitutional type of Ayurveda with cardiovascular risk factors, inflammatory markers and insulin resistance. J Ayurveda Integr Med. 2012;3(3):150-157.
27. Bellenger CR, Fuller JT, Thomson RL, Davison K, Robertson EY, Buckley JD. Monitoring athletic training status through autonomic heart rate regulation: a systematic review. Sports Med. 2016;46(10):1461-1486.
28. Shaffer F, Ginsberg JP. An overview of heart rate variability metrics and norms. Front Public Health. 2017;5:258.
29. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation. 1996;93(5):1043-1065.
30. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ. 2008;337:a1655.
31. Murray E, Treweek S, Pope C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. BMC Med. 2010;8:63.
32. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-174.
33. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155-163.
34. Kurande VH, Chopra A, Kalekar N. Prakriti-based research: good reporting practices. J Ayurveda Integr Med. 2016;7(2):69-73.
35. Prasad PV, Patil P, Todkar SS, Chopra A. Development of a clinically useful tool for Prakriti assessment. Int J Ayurveda Med. 2021;12(3):123-131.
36. Hallgren KA. Computing inter-rater reliability for observational data: an overview and tutorial. Tutor Quant Methods Psychol. 2012;8(1):23-34.
37. Plews DJ, Scott B, Altini M, Wood M, Kilding AE, Laursen PB. Comparison of heart-rate-variability recording with smartphone photoplethysmography, Polar H7 chest strap, and electrocardiography. Int J Sports Physiol Perform. 2017;12(10):1324-1328.
38. Hernando D, Roca S, Sancho J, Alesanco Á, Bailón R. Validation of the Apple Watch for heart rate variability measurements during relax and mental stress in healthy subjects. Sensors (Basel). 2018;18(8):2619.

39. Georgiou K, Larentzakis AV, Khamis NN, et al. Can wearable devices accurately measure heart rate variability? A systematic review. Folia Med (Plovdiv). 2018;60(1):7-20.
40. Ancoli-Israel S, Cole R, Alessi C, et al. The role of actigraphy in the study of sleep and circadian rhythms. Sleep. 2003;26(3):342-392.
41. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193-213.
42. Hellhammer DH, Wüst S, Kudielka BM. Salivary cortisol as a biomarker in stress research. Psychoneuroendocrinology. 2009;34(2):163-171.
43. Kivimäki M, Steptoe A. Effects of stress on the development and progression of cardiovascular disease. Nat Rev Cardiol. 2018;15(4):215-229.
44. Collins GS, Reitsma JB, Altman DG, Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ. 2015;350:g7594.
45. Liu X, Rivera SC, Moher D, Calvert MJ, Denniston AK; SPIRIT-AI and CONSORT-AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. Nat Med. 2020;26(9):1364-1374.
46. Chen IY, Pierson E, Rose S, Joshi S, Ferryman K, Ghassemi M. Ethical machine learning in healthcare. Annu Rev Biomed Data Sci. 2021;4:123-144.
47. Rajkomar A, Hardt M, Howell MD, Corrado G, Chin MH. Ensuring fairness in machine learning to advance health equity. Ann Intern Med. 2018;169(12):866-872.
48. Kaufman S, Rosset S, Perlich C, Stitelman O. Leakage in data mining: formulation, detection, and avoidance. ACM Trans Knowl Discov Data. 2012;6(4):1-21.
49. Kapoor S, Narayanan A. Leakage and the reproducibility crisis in machine-learning-based science. Patterns (N Y). 2023;4(9):100804.
50. Devlin J, Chang MW, Lee K, Toutanova K. BERT: Pre-training of Deep Bidirectional Transformers for Language Understanding. arXiv preprint arXiv:1810.04805. 2018.
51. Lee J, Yoon W, Kim S, et al. BioBERT: a pre-trained biomedical language representation model for biomedical text mining. Bioinformatics. 2020;36(4):1234-1240.
52. Grange L, Nguyen CC, Larkin A. Exposure to traffic-related air pollution and serum inflammatory cytokines in children. Environ Pollut. 2017;229:291-299.
53. WHO Global Air Quality Guidelines. Particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide. Geneva: World Health Organization; 2021.
54. Reid CE, Considine EM, Watson GL, et al. Associations between respiratory health and ozone and fine particulate matter during the 2008 Beijing Olympics. Environ Res. 2014;133:315-321.
55. Brook RD, Rajagopalan S, Pope CA 3rd, et al. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation. 2010;121(21):2331-2378.

56. Burnett R, Chen H, Szyszkowicz M, et al. Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. Proc Natl Acad Sci USA. 2018;115(38):9592-9597.
57. U.S. Food and Drug Administration. Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. Silver Spring, MD: FDA; 2021.
58. U.S. Food and Drug Administration. Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions. Silver Spring, MD: FDA; 2023.
59. European Commission. Proposal for a Regulation on artificial intelligence (Artificial Intelligence Act) and amending certain Union legislative acts. Brussels: European Commission; 2021.
60. Sherman RE, Anderson SA, Dal Pan GJ, et al. Real-world evidence - what is it and what can it tell us? N Engl J Med. 2016;375(23):2293-2297.
61. Eichler HG, Oye K, Baird LG, et al. Adaptive licensing: taking the right turns - a conversation with regulators. Clin Pharmacol Ther. 2012;91(3):434-437.
62. U.S. Food and Drug Administration. Content of Premarket Submissions for Device Software Functions. Guidance for Industry and Food and Drug Administration Staff. Silver Spring, MD: FDA; 2021.
63. U.S. Food and Drug Administration. Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions. Guidance for Industry and Food and Drug Administration Staff. Silver Spring, MD: FDA; 2022.
64. Husereau D, Drummond M, Petrou S, et al.; ISPOR Health Economic Evaluation Publication Guidelines-CHEERS Good Reporting Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. Value Health. 2013;16(2):231-250.
65. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. JAMA. 2016;316(10):1093-1103.
66. Briggs AH, Weinstein MC, Fenwick EA, et al.; ISPOR-SMDM Modeling Good Research Practices Task Force. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-6. Value Health. 2012;15(6):835-842.
67. Fenwick E, Claxton K, Sculpher M. Representing uncertainty: the role of cost-effectiveness acceptability curves. Health Econ. 2001;10(8):779-787.
68. Snoswell CL, Caffery LJ, Whitty JA, Thomas EE, Smith AC. Cost-effectiveness of skin cancer referral and consultation using teledermoscopy in Australia. JAMA Dermatol. 2018;154(6):694-700.
69. Iribarren SJ, Cato K, Falzon L, Stone PW. What is the economic evidence for mHealth? A systematic review of economic evaluations of mHealth solutions. PLoS One. 2017;12(2):e0170581.
70. Kottner J, Audige L, Brorson S, et al. Guidelines for Reporting Reliability and Agreement Studies (GRRAS) were proposed. J Clin Epidemiol. 2011;64(1):96-106.

71. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1(8476):307-310.
72. Little RJ, D'Agostino R, Cohen ML, et al. The prevention and treatment of missing data in clinical trials. N Engl J Med. 2012;367(14):1355-1360.
73. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ. 2009;338:b2393.
74. Mahalle NP, Kulkarni MV, Pendse NM, Naik SS, Phatak MS. Development and validation of a Prototype Prakriti Analysis Tool (PPAT): inferences from a pilot study. Ayu. 2012;33(2):210-215.
75. Prasher B, Gibson G, Mukerji M. Genomic insights into ayurvedic and western approaches to personalized medicine. J Genet. 2016;95(1):209-228.
76. Patwardhan B, Mukerji M, Tillu G. Molecular targets and pathways for Ayurvedic drugs and formulations. Biochem Pharmacol. 2010;80(12):1774-1783.
77. Peake JM, Kerr G, Sullivan JP. A critical review of consumer wearables, mobile applications, and equipment for providing biofeedback, monitoring stress, and sleep in physically active populations. Front Physiol. 2018;9:743.
78. Cadmus-Bertram LA, Marcus BH, Patterson RE, Parker BA, Morey BL. Randomized trial of a Fitbit-based physical activity intervention for women. Am J Prev Med. 2015;49(3):414-418.
79. Feehan LM, Geldman J, Sayre EC, et al. Accuracy of Fitbit devices: systematic review and narrative syntheses of quantitative data. JMIR Mhealth Uhealth. 2018;6(8):e10527.
80. Clark RC, Tazbaz T, Rado O, et al. Marketing and US Food and Drug Administration clearance of artificial intelligence and machine learning enabled software in and as medical devices: a systematic review. JAMA Netw Open. 2023;6(6):e2316723.
81. Vasey B, Nagendran M, Campbell B, et al. Reporting guideline for the early-stage clinical evaluation of decision support systems driven by artificial intelligence: DECIDE-AI. Nat Med. 2022;28(5):924-933.
82. Sendak MP, Gao M, Brajer N, Balu S. Presenting machine learning model information to clinical end users with model facts labels. NPJ Digit Med. 2020;3:41.
83. Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. Science. 2019;366(6464):447-453.
84. Gianfrancesco MA, Tamang S, Yazdany J, Schmajuk G. Potential biases in machine learning algorithms using electronic health record data. JAMA Intern Med. 2018;178(11):1544-1547.
85. Chen IY, Szolovits P, Ghassemi M. Can AI help reduce disparities in general medical and mental health care? AMA J Ethics. 2019;21(2):E167-179.
86. Proctor E, Silmere H, Raghavan R, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Adm Policy Ment Health. 2011;38(2):65-76.
87. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci. 2009;4:50.

88. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am J Public Health. 1999;89(9):1322-1327.
89. Chan AW, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ. 2013;346:e7586.
90. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c332.
91. Michie S, Fixsen D, Grimshaw JM, Eccles MP. Specifying and reporting complex behaviour change interventions: the need for a scientific method. Implement Sci. 2009;4:40.