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Cross-disciplinary methodologies for whole-person research – insights from EMPOWER2024

Check for updates

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Modern medicine is shifting towards integrative, whole-person research to understand multi-scale complexities of health and disease. However, disciplinary silos, a lack of shared frameworks, and fragmented data hinder progress. The EMPOWER 2024 workshop concluded that the future of whole-person research requires a cultural and methodological shift. This involves embracing interdisciplinarity, sharing ethical data and analysis tools, and educational innovation to translate fragmented data into actionable, holistic health solutions.

The promise and challenges of whole-person research

State-of-the-art medicine has long been constrained by reductionist approaches[1] that study individual organs or diseases in isolation, often overlooking the complex dynamic interplay between biological systems, psychological factors, and environmental influences. Whole-Person Research (WPR) seeks to overcome limitations of singular concepts by integrating multi-scale data, from molecular pathways to organ networks and socio-environmental determinants, to build a more comprehensive understanding of health and disease[2]. This paradigm shift is driven by the recognition that conditions like cancer, neurological disorders, and cardiovascular diseases cannot be fully explained by examining each component in isolation[3–6]. Instead, they emerge from genetic and environmental factors that lead to dysregulation across scales, altered dynamic interactions across inter-organ axes[7,8], or stress-induced immune dysregulation[9,10].

The landscape of integrative approaches to modern biology and medicine has evolved rapidly over the past decade, and now includes not only WPR, but other terms, such as systems medicine, network medicine,

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Table 1 | Overview of common terms to describe non-reductionist approaches to clinical research and practice, with their key differentiators and domains of use

Term	Primary focus	Scale	Key features	Applications to human health	Example
Applied Systems Biology[40,41]	Mechanistic insights of biological networks	Micro (Cells, Molecules)	Computational modeling	Translational. Build useful biological systems.	Using a computational model of a bacterium's metabolic network to genetically engineer it to overproduce insulin or an anticancer drug.
Global Health	Health issues that transcend national boundaries to achieve equity in health worldwide	Communities, Regions, Nations, Global systems	Policy, economy, environment, breadth at the population level	Public health program.	Studying the burden of cancer in European countries focusing on incidence, mortality, and years of life lost, based on national cancer registries, World Health Organization and International Agency for Research on Cancer data, and using statistical modeling to fill data gaps.
Network Medicine[42]	Interconnected disease and molecular networks, disease-centered	Micro (Molecules, cells)	Subfield of Systems medicine relying on graph theory, disease classification	Basic science. Discover disease modules and drug targets.	Creating a graph-based representation of statistical associations to infer protein-protein interactions and discover that a seemingly unrelated set of genes all interact in a specific module that, when disrupted, causes a particular heart disease.
Network Physiology[3,6,7]	Interactions across physiological systems; emergence of states, functions, clinical conditions from dynamic networks	Integration across sub-cellular, cellular, organ and organism level	Temporal dynamics, complexity, nonlinear coupling, synchronization, causality, time delays, adaptive networks, integration	Basic science. Network-based biomarkers. Multi-system disease characterization. Clinical.	Investigate real-time interactions and causality among the cardiac, brain, respiratory, renal, locomotor systems, and blood, hormonal and metabolic assays to track the evolution and breakdown of physiological networks with e.g., heart disease, multiple organ failure, sepsis, coma, neurodegenerative disorders. Quantify systems/ network response to treatment; assess survival outcomes in critical conditions and chronic disease based on dynamic network maps.
One Health	Interconnections among human, animal, and environmental health	Individual, local (community level), regional and national, and global	Multispecies and ecological	Addressing the full spectrum of disease control. Contribute to global health security.	Studying the antimicrobial resistance across humans, livestock, and the environment to determine whether resistant strains circulate between humans, animals, and the environment.
Systems Medicine[43–45]	Clinical applications of systems biology	Micro to Macro: Molecules to organs	Multi-omics, P4 medicine, patient stratification	Direct clinical. Personalized diagnosis and treatment.	Using a dynamic computational model of a cancer patient's tumor signaling network to predict which combination of drugs will be most effective while minimizing side effects, rather than using a standard one-size-fits-all chemotherapy.
Whole-Person Research[2]	Entire individual across biological, psychological, social, and environmental domains	Micro to Macro, up to a person in her/his environment	Holistic, integrative, multiscale, lifestyle-inclusive	Direct clinical. Personalized health strategies.	Studying how a subject's stress levels (psychological), social support (social), diet (behavioral), genetic predisposition to inflammation (biological), and air pollution (environmental) interact to trigger an asthma attack

Box 1 | Interconnectedness of terms for systemic and holistic medicine approaches as per Table 1. Imagine a patient with heart failure, then

Applied Systems Biology might be used to engineer the bacteria that produced the drug the patient is taking.

Global Health could investigate a multinational cohort to examine differences in heart failure outcomes and access to guideline-directed medical therapy across low-, middle-, and high-income countries.

Network Medicine might identify a module of genes that predisposes a patient to a particular condition.

Network Physiology would study, for example, how the failing heart disrupts its communication with the kidneys (leading to fluid retention), the brain (leading to nervous system imbalance), respiration (leading to breathing and sleep disorders), discoordination in circulation, locomotor control, hormonal and metabolic functions.

Systems Medicine would integrate the genetic and physiological data to build a personalized model of the patient's disease and predict the best treatment.

One health would study whether chronic exposure to urban air pollution contributes to structural heart changes and heart failure in both humans and companion animals living in the same environment.

Whole-Person Research would also consider the patient's psychological state and degree of social support as critical factors affecting their ability to adhere to treatment, integrating them into the care plan.

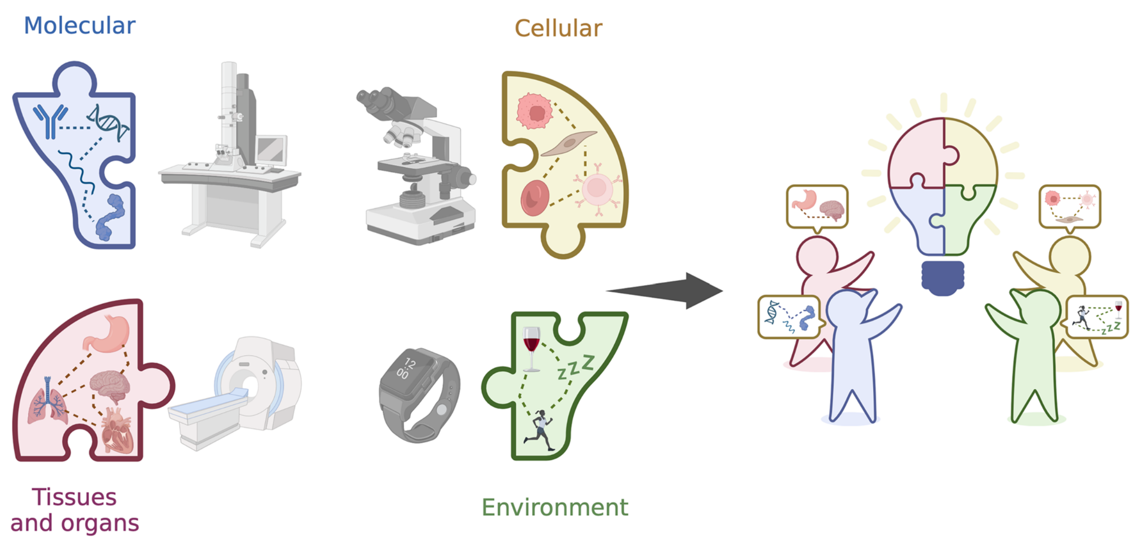

Fig. 1 | Transforming health research into whole-person research. Transforming health research into whole-person research (WPR) by interlocking the puzzle pieces each of which provides partial insights across scales of health and disease. Created with BioRender.com.

or systems biology (Table 1). The terms "Global Health" and "One Health" even go beyond the subject and cohort level: "Global Health" concentrates on improving health understanding and health outcomes across nations and populations, thereby prioritizing transnational issues, health equity, policy, and systems strengthening at a worldwide scale, while "One Health" focuses on interconnected health of humans, animals, and ecosystems.

While these approaches are interconnected – and frequently supporting each other - they use different methodologies depending on the scale of the systems being studied, and the directness of the applications in human health (Box 1).

It can be argued that the foundations for the concept of WPR were laid with the concept of Network Physiology (Box 1) over a decade ago[3]. As a field, Network Physiology has built the methodological and theoretical framework to study complex interactions among diverse systems from the sub-cellular to the organism level in a time-varying manner. This research field models the mechanisms through which physiological systems integrate as a network of networks to generate whole-body states and functions[6], and as such can be regarded a physiological and methodological backbone on which WPR builds (Table 1).

By considering the dynamic interplay of many aspects of human life, including physical, psychological, and social factors, as well as epidemiology, WPR provides a macro-scale perspective and can identify new areas of research and treatment paradigms that may be missed by traditional reductionist approaches (Fig. 1).

Integrating multiple scales of analysis enables a more comprehensive understanding of health and complex diseases and could facilitate the identification of strategies to maintain fitness and health, as well as effective interventions that address the root cause of the disease, leading to improved treatment outcomes.

However, despite its transformative potential[11], WPR faces significant challenges, including the lack of documentation of key variables, fragmented datasets[12], disconnected methodologies across disciplines [https://files.nccih.nih.gov/exsum-methodological-approaches-for-whole-person-research-workshop-summary-508.pdf?_gl=1*1lj9lyr*_ga*MTEzODUwMzQ5OS4xNzY3ODE1Mzc2*_ga_N38PWG04DD*czE3NzAyMDkwOTgkbzIkZzEkdDE3NzAyMDkzNTIkajYwJGwwJGgw], and a lack of shared frameworks to connect insights from genomics, imaging, and clinical medicine, to name a few[6]. To begin with, current PhD programs are largely siloed: much of the medical curriculum is organized by organs and their diseases. Further, students get exposed mainly to a narrow range of experimental and computational methods, which does not enable them a priori to appreciate the benefits and importance of WPR. Naturally, not every student needs to be a WPR scientist, but we must establish effective educational programs that train a subset of them to think WPR. The persistence of siloed expertise, as supported in many ways by our existing training programs, and fostered by our current

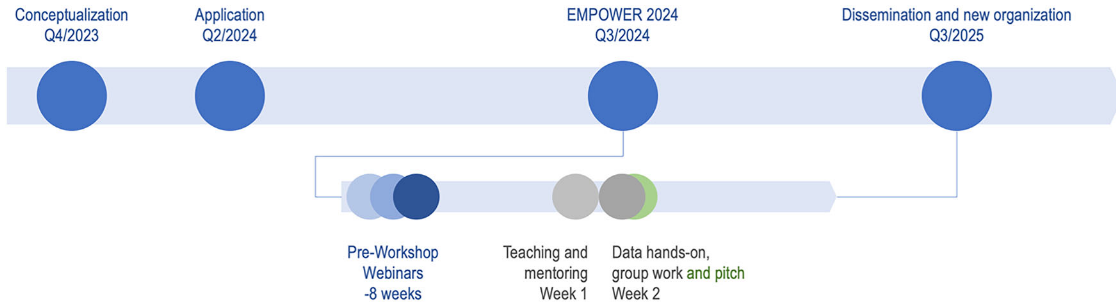

Fig. 2 | Structure of the EMPOWER 2024 workshop. The genesis and structure of the EMPOWER 2024 workshop as an example of a novel concept[46] for providing a platform for WPR activists. Following a gestation phase (ideation, application, funding decision), a series of webinars preceded the 2-week workshop. Webinars were centered around knowledge transformation on key domains of WPR and introduction to the multimodal data sets to be used during the workshop. Also, webinars provided a low-level entry to community and trust building. Workshop weeks 1 and 2 were focused on training/mentoring and data analysis, respectively. Data hackathons were geared towards presenting tangible results and lessons learned during a science slam session open to the non-registered audience on the last 2 days of the event. Dissemination of WPR activities were envisaged with regards to novel manuscripts on the data in use, perspectives on insights from the different workshop activities, word-of-mouth, and following applications for continuous funding.

research award schemes - within national variants - further separates clinicians, molecular biologists, imaging specialists, computational biologists, and behavioral scientists.

Today's funding mechanisms and academic incentives, for the most part favor hypothesis-driven research over integrative approaches (they are not mutually exclusive), which slows the adoption of WPR. Siloed funding support also hinders the development of large, consistent multimodal datasets[13–15], and it restricts the number of diverse domain experts working jointly on a common project.

Notwithstanding first efforts towards developing funding schemes and infrastructures that break this silo mentality[16,17], parallel activities must be initiated to broaden the mindset of researchers and healthcare stakeholders to embrace and engage in the concept of holistic whole-person approaches to patient care and health research. With this ambition in mind, we set out to create a forum for WPR advocates that would address some of the key barriers (e.g., lack of communication, disjointed vocabulary, shortage of multimodal data cohorts, multitude of directions and objectives) in a pilot approach, that – if proven successful – could be repeated and grow.

The Genesis of EMPOWER 2024

Whole-person research demands cross-disciplinary expertise and the willingness to transcend academic disciplines despite operational and individual barriers. Recognizing this gap between disciplines, approaches and methodologies in addressing fundamental questions related to the mechanisms and principles of integration of systems and sub-systems across levels and scales in the human body under health and disease, the International Summer Institute on Network Physiology (ISINP)[18] was established in 2016. The U.S. National Center for Complementary and Integrative Health (NCCIH) convened a pioneering workshop in 2021 to explore methodological synergies for systemic health research[19]. Among its participants were future co-organizers of EMPOWER 2024, who highlighted the potential of total-body positron emission tomography (TB-PET) imaging to quantify multi-organ interactions at the human scale[20]. Subsequent meetings in Edinburgh (2022) and Vienna (2023)[21] further refined these ideas, but deep collaboration remained limited by time and disciplinary boundaries, so that participants often spoke *past* each other instead of *to* each other.

Building on this momentum, Institut Pascal[22] supported an application for the EMPOWER 2024 workshop to translate theory into practice. EMPOWER 2024 aimed to transform fragmented insights into actionable frameworks for WPR (Supplementary Table S1). Unlike prior events, our concept included hands-on problem-solving by interdisciplinary teams comprised of imaging and data scientists, mathematicians, physicists, immunologists, biologists, and clinicians, working on multi-scale data from PET, MRI, genomics, blood markers, and wearables, to name a few. To address the limited readiness of attendees for WPR, we structured the workshop program to spark curiosity across domains.

To that end, EMPOWER 2024 was designed as an intensive 2-week program [www.empower2024.org] to maximize interdisciplinary collaboration while accommodating professional schedules of the participants (Fig. 2). After extensive deliberation, the organizers invited expert speakers from key WPR domains: blood markers (ctDNA, etc), pathology, electrical signals (EEG, MEG), genomics, bioinformatics, spatial biology, immunology, metabolism, microbiota, system biology, mathematical biology, chronobiology, epigenetics, neurology, cardiology, oncology, complex systems, and data science.

In addition to expert speakers selected from the above WPR fields, registration for this workshop was open to young researchers with a PhD or postdoctoral experience in WPR domains. The junior participants came mainly, but not exclusively, from the speakers' laboratories. They had to apply with their CV and a letter of motivation, and 20 applicants were selected by the core organizational team (IB, SRC, RDB, TB, LKSS, EA) and were given the opportunity to present their WPR-related work during poster sessions.

The workshop opened by reflecting on the participants' expectations towards whole-person research, thereby using insights from a pre-workshop survey to stir discussions (Fig. 3, Supplementary Table S2).

The first week focused on cross-disciplinary education, employing a Feynman-style learning approach: lectures built from foundational concepts to advanced topics to ensure all participants could engage. Talks paired "domain" and "enabler" experts (example: domain = metabolism, enabler = imaging), with session moderators fostering discussions to bridge knowledge gaps across fields. In addition, all faculty members were asked to begin lectures at a level accessible to non-specialists. Ample time was given to afternoon and evening engagements, both social and cultural, to foster relation building among workshop participants.

The second week focused on hands-on analysis of 3 multimodal datasets. Six interdisciplinary teams of 3 or 4 junior researchers, formed based on complementary skills, worked with a co-organizer and domain expert on real-world challenges from data fusion to experimental design. The teams then developed integrative analysis paradigms and pitched their results in a final "science slam" (Fig. 2).

To support familiarization of the teams with the topics and data used for the hands-on, workshop participants were invited to attend a series of virtual seminars preceding the actual workshop (Fig. 2). During these webinars, the principal investigators of the multi-discipline studies that were used during the workshop introduced the data domains and relevant data structures[23–27]. This activity began the process of building trust among the participants in addition to providing an appreciation for the structure and complexity of the data at hand.

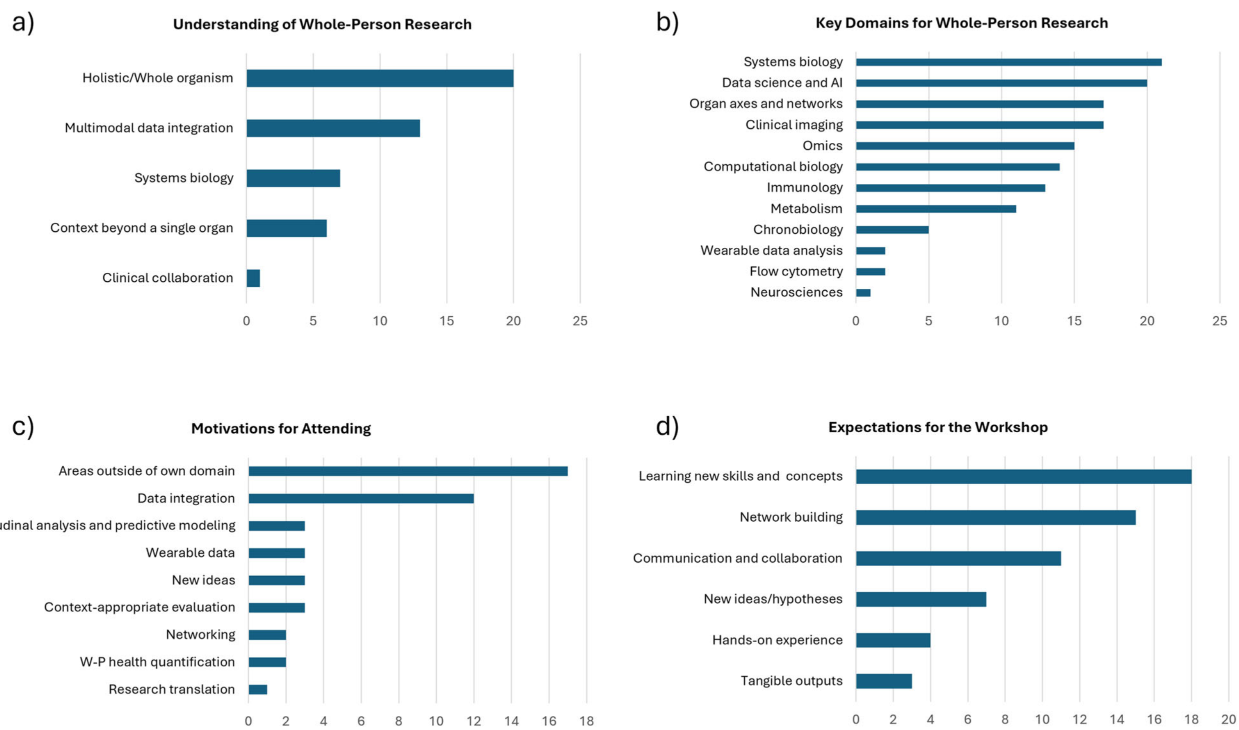

Fig. 3 | Results from a pre-workshop survey. Results synthesis from pre-workshop survey for the following summarized prompts: **a** Define what whole-person research means to you; **b** What are the key domains for promoting whole-person research; **c** What motivated you to attend this workshop?; and **d** What are your expectations for this workshop?.

In short, the EMPOWER 2024 workshop sensitized early career researchers to WPR (Table 1), through innovative teaching concepts, cross-specialty training and access to multimodal datasets. The workshop goal was later summarized by one of the co-organizers as "an open-mind-cross-disciplinary-bottom-up-everybody-is-still-learning-here atmosphere".

Insights from EMPOWER 2024

Bridging disciplines

By sparking curiosity, the EMPOWER 2024 workshop highlighted the transformative potential of interdisciplinary collaboration in advancing WPR, with presentations spanning imaging, AI, genomics, metabolism, and immunology – all as key domains of (siloed) expertise that are relevant for non-reductionist research (Table 1). Central to the conversation was that a concerted effort needs to be made to move from studying diseases of specific organs or systems in isolation, to view them as deviations from overall health. Thus, a better understanding of whole-person health will ultimately transform our approach to understanding disease[28]. All domain experts acknowledged that no single modality or discipline suffices to capture the complexity of human health. Several speakers emphasized that multi-scale imaging is crucial in understanding how molecular and biological mechanisms interact and induce effects across scales, from cells to systems.

Naturally, a central theme of the deliberations was the challenge of integrating complex, multi-scale biological data to build a holistic view of human health. While powerful, AI and computational models face significant hurdles, including the need for massive data, privacy issues related to sharing training data for robust machine learning and AI-driven prediction models, a shortage of robust and widely available analysis tools to evaluate models and ensure predictions' explainability, as well as the value of human expertise for interpretation and validation[29]. AI's dual role as both enabler and challenge was a recurring focus in several presentations. At the time of the workshop, there was an apparent preference for "accessible AI"—prioritizing clinician collaboration, data pre-processing, and domain-specific solutions over "dinosaur" foundation models. However, as a post-meeting note, foundational models are now becoming accessible for fine tuning of specific tasks, such as MedGamma1.5 that enables AI developers to fast-track applications involving both high-dimensional images and text (https://deepmind.google/models/gemma/medgemma/), attesting to the rapid progress in this field[30,31]. Their propensity to hallucinate[32] (i.e., produce plausible yet incorrect statements) poses critical risks in high-stakes applications, such as medical research. This calls for carefully designed standardized evaluation methodology to uncover their weaknesses. Open-sourcing evaluation pipelines and datasets will allow fine-tuned foundation models to be transparently benchmarked and fairly compared.

Speakers also emphasized that biological processes are dynamic, operating across intricate spatial (e.g., systemic inflammation) and temporal (e.g., circadian rhythms) dimensions. This complexity demands the documentation of new variables through new technological tools (e.g., wearable devices) and their integration within frameworks that can bridge both spatial scales, from molecular pathways to whole-organism physiology, and time scales from minutes to days and years. Ultimately, progress requires a collaborative, interdisciplinary ethos. Successful initiatives, such as HeartShare[33] illustrate the value of translating fragmented data into actionable, whole-person insights. But such success rests on the ability and willingness of people to merging diverse clinical, omics, and computational approaches within a framework built on trust and methodological rigor. For key takeaways from the faculty presentations, see Supplementary Table S3.

Working with complex multimodal data sets

The practical part of the workshop (hands-on exercises) was a key differentiator to other workshops with similar intent; however, it also absorbed a significant portion of the preparation time. First, the organizers pre-selected three multimodal data cohorts (Supplementary Table S4) based primarily on their own research, accessibility (including IRB approval) of the data and a desire to advance paradigms related to these data.

Pre-selecting the data, sorting and anonymization were done by team members of the PI's groups. The data varied in size between 250 GB and

Box 2 | Key barriers to whole-person health research

Methodological silos: Traditional discipline-specific approaches are poorly equipped to analyze the complex, multi-scale interactions (e.g., gut–brain axis, organ crosstalk) that define human physiology.

Lack of a unifying lexicon: There is no standardized language to describe systemic interactions across disciplines. Terms for fundamental concepts, such as inter-organ communication (e.g., "organ axes") remain inconsistent and ambiguous.

Limited cross-disciplinary collaboration: Research projects and teams are often composed of experts from one or two scientific domains, which is insufficient to address the full complexity of human health.

Inadequate data collection and integration: Most existing databases are modality- or organ-specific and may not document key variables enabling a WPR approach. The lack of large-scale, multi-omics, and multi-organ data repositories prevents a truly integrated, multi-view analysis of disease mechanisms.

Box 3 | Pathways to advancing whole-person research on health and disease

Overcoming the barriers to WPR requires a concerted effort across multiple fronts:

Fostering interdisciplinary collaboration: Developing a shared lexicon and collaborative frameworks is essential to break down traditional disciplinary silos and enable effective communication.

Harnessing technological innovation: Emerging experimental and computational methods provide unprecedented capabilities for capturing multi-organ interactions and analyzing complex, system-wide data.

Integrating multimodal data: A core principle is the leveraging of multi-type data at multiple spatial and time scales to build a more complete picture of health and complex diseases.

Merging modeling approaches: Combining mechanistic models (e.g., network theory) with data-driven approaches (e.g., AI, wearables) will be crucial for generating testable, systems-level hypotheses.

Building consensus and infrastructure: Community-wide efforts to create standards, secure interdisciplinary funding, and design large-scale studies that enable the vertical (molecular to organ) and horizontal (biological to environmental) integration of data.

Establishing transverse educational programs: Develop cross-disciplinary training to facilitate and encourage effective communication between experts from different fields.

Rethinking academic evaluation: Align promotion, tenure, and funding criteria to the realities of team science. Current career metrics reward first- and last-authorships and individual grants, thereby undervaluing shared authorships. Recognizing contributorship (e.g., CRediT taxonomy) and giving equal weight to co-lead roles is essential to sustain interdisciplinary work.

1TB. While the PIs had an in-depth knowledge of the data cohorts, workshop participants had to be introduced to the study objectives and data types as part of the pre-workshop webinars and through ongoing intra-workshop mentoring.

One key observation was that participants across all teams preferred to start analyzing the data they were most familiar with, so the analysis was informed by prior knowledge about that type of data but limited in methodological cross-fertilization during the analysis of one data type. This highlights the need for cross-disciplinary education that enables early-stage researchers to feel confident exploring a wide variety of large and diverse datasets.

Generally, the interpretation of multimodal data insights was constrained by two factors: the amount of time needed to process raw data from each discipline to extract final features, and a shortage of experts to assess their biological plausibility. The former calls for the design of well-curated and structured data collections dedicated to WPR, while the latter emphasizes the need to involve a large variety of experts to advance WPR.

Catalyzing interdisciplinary collaboration through science communication

Simon Cherry's closing presentation, *"How to Talk Science"* underscored that effective communication is not just a soft skill but a critical enabler of WPR. He emphasized that conveying complex, multimodal findings requires clarity, adaptability, and audience awareness. Researchers must "speak to the whole room," translating expert knowledge into accessible narratives without diluting scientific rigor.

On that note, the following principles emerged from his presentation that we invite others engaging in WPR to consider: (1) employ structured storytelling to unify fragmented data, (2) entertain visual simplicity (intuitive graphs over dense tables) to transcend disciplinary jargon, and (3) follow a humble, engaging delivery that invites collaboration.

Just as WPR integrates diverse datasets, effective science communication must connect experts across fields—immunologists to engineers, clinicians to data scientists—by fostering trust through transparency about limitations (e.g., AI's "black-box" challenges). As WPR advances, prioritizing these principles will ensure that discoveries in multimodal data integration translate into actionable, equitable health solutions. To that end, Cherry's ultimate message aligns well with the workshop's vision: "Integrating the whole-person begins with communicating to the whole team."

A call for integrated, ethical, and collaborative whole-person research

The EMPOWER 2024 workshop crystallized a pivotal fact: the future of WPR depends on interdisciplinary integration, where imaging, AI, genomics, clinical practice, and other fields converge to transcend traditional disciplines (Box 2). Across presentations, a shared vision emerged that calls for collecting large multimodal data at scale, while continuing to address critical technology gaps, such as efficient integration tools, data harmonization and rigorous cross-site validations of AI models.

Setting up multimodal cohorts is costly and requires access to diverse equipment and groups of subjects, often spread across different sites, each governed by its own legislation on subject recruitment and data sharing. Meaningful WPR, therefore, demands collaborative networks that jointly design experiments, collect datasets at multiple sites and integrate them under shared standards.

Moving from today's fragmented approaches to integrated WPR demands bold shifts in both mindset and methodology (Box 3), replacing silos, inconsistent terminologies, and isolated datasets with shared frameworks for multimodal and multiscale data. Such efforts can draw from interoperable initiatives, such as the Fast Health Interoperability Resources (FHIR)[https://www.fhir.org/], the Observational Medical Outcomes Partnership (OMOP) common data model [https://ohdsi.github.io/CommonDataModel/], or the Open Electronic Health Record[34], which aims to standardize medical terminology and to support the creation of domain-specific medical ontologies. Progress further depends on breaking disciplinary barriers through establishing shared vocabularies, leveraging novel tools like TB-PET[35] for multi-organ imaging, and combining mechanistic models with AI-driven analytics[36]. The collection of large multimodal cohorts must be supported to deploy integrative approaches, make new discoveries and test data-driven assumptions. Crucially, this evolution requires aligning funding and policy with WPR's holistic vision, as seen in the NCCIH's strategic prioritization of research on prevention-focused healthcare[37].

In addition to novel funding mechanisms, education and academic evaluation must be reconsidered. Higher education is still organized by discipline and cross-disciplinary training remains the exception whereas WPR requires recurrent exposure to a broad variety of knowledge from different fields. Researchers are still primarily judged by single-discipline metrics, such as first/last authorship and individual grants, while equally important collaborative contributions are often undervalued. Reviewers and hiring committees often regard shared or co-lead authorships as "second tier," thereby discouraging the very cross-disciplinary efforts WPR and science in general requires. Recent analyses highlight how current promotion and tenure norms disadvantage team science and recommend explicit recognition of "contributorship" rather than position on the author list[38,39]. Therefore, aligning career incentives with collaborative practice is essential for WPR to succeed.

This workshop - EMPOWER 2024 - concluded that by fostering mindsets and environments that permit change and cater to genuine collaboration, equitable data integration, and new vocabularies, we can transform WPR from aspiration to reality (Boxes 2,3, and Supplementary Table S3). We may be rewarded by a healthcare paradigm designed around whole-person care[11].

Data availability

No datasets were generated during the workshop period.

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Competing interests

The authors declare no competing interests.

Additional information

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