BNL-225882-2024-FORE

# The First Virtual Human Global Summit: Prepublication Meeting Report

E. Stahlberg, M. Lin

July 2024

Computational Science Initiative
**Brookhaven National Laboratory**

**U.S. Department of Energy**
USDOE Office of Science (SC), Advanced Scientific Computing Research (ASCR)

# DISCLAIMER

**The First Virtual Human Global Summit: Prepublication Meeting Report**

Eric A. Stahlberg[1], Kerstin Kleese Van Dam[2], Peter V. Coveney[3], John Stubbs[4], Sean T. Black[1], Lynn L. Borkon[1], Jazmin Aguado-Sierra[5], Francis J. Alexander[6], Gary C. An[7], Guru Banavar[8], Douglas W. Blayney[9], Jeffrey Buchsbaum[10], Matthew Carbone[2], Ansu Chatterjee[11], Caroline Chung[12], Robert Coughlin[13], Olivier Elemento[14], William O. Glascoe III[15], Emily J. Greenspan[10], Michael Hadjsavas[16], Tina Hernandez-Boussard[9], Florence D. Hudson[17], Dan R. Isaacs[18], Natalie Isenberg[2], Anuj J. Kapadia[19], Warren A. Kibbe[20], Jerry S.H. Lee[21], Michael N. Liebman[22], Heber Lima da Rocha[23], Meifeng Lin[2], Steven Litster[24], Vanessa Lopez-Marrero[2], Matthew McCoy[25], John P. McDaniel[26], Dwight V. Nissley[1], Jan F. Nygård[27], Marc D. Paradis[28], Grace C.Y. Peng[29], Richard Pilch[30], Line C. Pouchard[2], Adam Rasheed[24], Ilya Shmulevich[31], Anil Srivastava[32], Andrea Townsend-Nicholson[3], Georgia D. Tourassi[19], Mariano Vazquez[33]

[1]Frederick National Laboratory for Cancer Research, Cancer Research Technology Program, [2]Brookhaven National Laboratory, [3]University College London, [4]Eviden, [5]Barcelona Supercomputing Center, [6]Argonne National Laboratory, [7]University of Vermont, [8]Viome Life Sciences Inc., [9]Stanford University School of Medicine, [10]National Cancer Institute, [11]University of Maryland Baltimore County, [12]University of Texas MD Anderson Cancer Center, [13]JLL, [14]Weil Cornell , [15]Robert Morris University, [16]P-chip Corporation, [17]Columbia University, [18]Digital Twin Consortium, [19]Oak Ridge National Laboratory, [20]Duke University, [21]Ellison Institute of Technology, [22]IPQ Analytics LLC, [23]Indiana University, [24]Amazon Web Services, [25]Georgetown University, [26]Healthcare IT Leaders, [27]Cancer Registry of Norway, [28]Northwell Health, [29]National Institute of Biomedical Imaging and Bioengineering, [30]Lawrence Livermore National Laboratory, [31]Institute for Systems Biology, [32]Open Health Systems Laboratory, [33]ELEM Biotech

**Abstract:**

This is the prepublication report for the first Virtual Human Global Summit held in October 2023. Organized collaboratively by Frederick National Laboratory for Cancer Research, Brookhaven National Laboratory, University College London, and Eviden, the *2023 Virtual Human Global Summit* convened global thought leaders to bring together multiple perspectives across domains and organizations. The intent of the Summit was to foster collaboration among key leaders internationally whose combined efforts are required to advance patient-focused precision medicine through medical digital twins.

Participants represented cancer and biomedical research, industry, infrastructure, clinical research, community health, non-profit organizations, government, and general public interests. The Summit included over 80 attendees across three continents including native American tribes. The Summit was held to share insights about the state of the art for medical digital twins, provide motivating opportunities and identify key challenges along the path to improved health and wellness through virtual human models and personalized digital twins. The Summit included sessions emphasizing the primary areas of research, infrastructure, clinical application, government support, and adoption/sustainability. Several examples of digital twins were referenced or mentioned through the course of the Summit including digital twin approaches in cancer, radiation oncology, molecular scale digital twins, diabetes, and sepsis.

The summit report includes perspectives on the current state, challenges and guidance across research, infrastructure, clinical translation and community adoption, as well as multiple key insights from industry perspectives.

# Meeting Report of the First Virtual Human Global Summit

**October 3-4, 2023**
**SUNY Global Center**
**New York, New York**

**Sponsored by Brookhaven National Laboratory and co-organized jointly with Frederick National Laboratory for Cancer Research, University College London, and Eviden**

*"Uniting Global Healthcare Perspectives Around Medical Digital Twins"*

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## Executive Summary

Unprecedented advancements in the fields of biology, data science, and computational modeling have emerged in recent years. These advancements—combined with parallel developments in networking, instrumentation including sensors, and computational infrastructure—provide the foundation for a transformative new research paradigm to advance personalized medicine through digital twin technologies. The promise of digital twins for patient impact is incalculable and is reflected in the 2023 National Academies of Sciences, Engineering, and Medicine (NASEM) report on digital twins (*Foundational Research Gaps and Future Directions for Digital Twins*, released in December 2023[1]). The NASEM report offers a compelling analysis of the current technologies and methodologies, and actionable recommendations to address research challenges and gaps for engineering, climate, and biomedical digital twins. The Virtual Human Global Summit (VHGS) occurred in October 2023, prior to the release of the NASEM report. This report summarizes the VHGS presentations and discussions. While this report draws parallels to the NASEM report, the VHGS report extends the focus to include translation, adoption, and sustainable use of patient-specific medical digital twins by both patients and the medical community.

Organized collaboratively by Frederick National Laboratory for Cancer Research, Brookhaven National Laboratory, University College London, and Eviden, the *2023 Virtual Human Global Summit* convened global thought leaders to bring together multiple perspectives across domains and organizations. The intent of the Summit was to foster collaboration among key leaders internationally whose combined efforts are required to advance patient-focused precision medicine through medical digital twins.

Participants represented cancer and biomedical research, industry, infrastructure, clinical research, community health, non-profit organizations, government, and the general public. The Summit included over 80 attendees across three continents including native American tribes. The Summit was held for two days in October 2023 at the SUNY Global Center in Manhattan, NY to share insights about the state of the art for medical digital twins, provide motivating opportunities and identify key challenges along the path to improved health and wellness through virtual human models and personalized digital twins.

Attendees included researchers from national laboratories and major universities, thought leaders from multiple international companies, entrepreneurs, government leaders, clinicians, technologists, community health systems, and others interested in improving public health. The market size across the industry segments and breadth of participation from the government and non-profit sector at the Summit is summarized below:

- **Industry aggregate market capitalization:** over $5 trillion, ranging from small startup companies to multinational trillion dollar corporations.

- **Academic aggregate research investment**: exceeded $13 billion based on the NSF Higher Education Research and Development Fiscal Year 2022 report.[2]

[1] Foundational Research Gaps and Future Directions for Digital Twins, National Academies of Science, Engineering and Medicine, (prepublication copy), released December 2023 https://www.nationalacademies.org/our-work/foundational-research-gaps-and-future-directions-for-digital-twins

[2] Higher Education Research and Development (HERD) Survey: 2022, Report downloaded May 18, 2024, from https://ncses.nsf.gov/surveys/higher-education-research-development/2022

- **Health system representation** included the largest community health system in New York state, in addition to multiple academic medical research organizations and clinical hospitals.

- **Governmental representation** included five US National laboratories from both the Department of Energy and the Department of Health and Human Services, the US National Cancer Institute, US National Institutes of Health, and the Cancer Registry of Norway.

- **Multinational participation.** Countries explicitly represented by way of citizenship and/or affiliation included the United States, the United Kingdom, Canada, Norway, Spain, India, the Catawba Native American tribe, and the Mohawk Native American tribe.

Employing the NASEM 2023 report definition of a digital twin, digital twin approaches in medicine are quickly becoming a reality. It is important to recognize that broad improvements for *all* stakeholders using medical digital twin approaches will be transformative but will take time to realize. Even so, the path forward is clear. It will require commitment, technical and social advances, as well as new models of collaboration among all involved in the care and well-being of each person.

Several examples of digital twins were referenced or mentioned through the course of the Summit including digital twin approaches in cancer, radiation oncology, molecular scale digital twins, diabetes, and sepsis digital twins.

The Summit included sessions emphasizing the primary areas of research, infrastructure, clinical application, government support, and adoption/sustainability. The following points summarize the collective insights and perspectives from the Summit.

**Motivation for Medical Digital Twins**

1. Represent the next frontier for precision medicine reaching the individual level
2. Can improve health, wellness, and care for each person
3. Serve as a means to learn from every patient to help all patients
4. Focuses future research on key gaps of translational relevance
5. Provide a path for translation of research insights to broad clinical application
6. Improve collaborative patient involvement in health
7. Offer an avenue to address medical disparities
8. The low technical barrier to entry in view of capabilities currently in place (i.e. computing, networking, modeling, initial data, etc.). This serves as a solid foundation on which to commence broad-based efforts.

**Feasibility of Medical Digital Twins**

1. Medical digital twins exist today in limited applications, with growth in multiple levels. Examples discussed at the Summit for patient level impact include cardiac, respiratory, diabetes, sepsis, and cancer.
2. Digital twin solutions will be problem dependent, based on available information, and employ predictive computational models.
3. Technical infrastructure exists and is already in use in several instances.
4. The collection of predictive human models is growing.
5. Availability of patient and other medically relevant data is continually growing.

**Adoption of Medical Digital Twins**

1. Will involve education of the entire community, from the general population to clinical experts, on medical digital twin technologies.
2. Will need approaches to communicate insights from medical digital twins to all care providers and patients.
3. Patients presently are seeking avenues for greater participation, transparency and accountability in the medical system.
4. Clinicians and healthcare workers are willing to adopt new approaches provided the approach does not add to net clinical workload.
5. Adoption success across stakeholders will depend on culture, access, and affordability.
6. Even in very complex multiscale/multiphysics organs and systems, such as the heart, researchers are just months away from having an operational clinical support tool. The main obstacles to filling this temporal gap are not technical but financial, political, social, and cultural.

**Challenges Facing Medical Digital Twins**

1. Buy-in is essential at all organizational levels, from patient to clinician and across the health care system.
2. Cultural changes are needed in healthcare systems to support the level of precision required and delivered by medical digital twins.
3. Personal healthy baselines are needed for each individual.
4. Initial cost (time and financial) for first implementations within a given medical system.
5. Need to guard against overhyped expectations of predictive models. Early models will need development and refinement when applied at a personal level.
6. Quality data are needed to develop, validate, and qualify predictive models for use in personal medical digital twins.
7. Methodologies are needed to establish trust in the appropriate use of predictive models in digital twins.
8. Regulatory, privacy and liability clarifications are needed.
9. Computational implementations must be affordable and accessible to all.
10. Reimbursement pathways associated with clinical tests and costs associated with digital twin approaches are needed.

**Path Forward for Medical Digital Twins**

1. Start communicating across the medical, research, and stakeholder communities on personal medical digital twins as soon as possible to expand participation.
2. Build a global community, commencing with the attendees of the Virtual Human Global Summit while expanding participation globally.
3. Engage with patients and patient advocate groups on the potential and value for medical digital twins.
4. Develop training opportunities for those who seek to learn more, including physicians.
5. Begin the process of building trust in the technology and the benefits for medical digital twins.
6. Identify problems in the clinic that can be addressed with medical digital twin approaches.
7. Create a framework from which to develop patient baseline information that will be integral to future digital twin solutions. This framework includes incorporation and integration of individual patient medical records.
8. Establish an organizational structure to enable mechanistic models, AI models, and datasets to move ahead collectively.

9. Identify approaches for sustainable and equitable access to datasets for use in medical digital twin development.
10. Make the foundation for development of medical digital twins the full health and wellness journey of the individual. The medical digital twin is a part of that whole health journey.

While there were many cross-cutting topics at the VHGS Summit, three primary cross-cutting themes emerged through multiple sessions, as follows:

- **Data** – The role of personalized data is central to the success of patient level medical digital twins. Key topics include data existence/availability, ownership, quality, access, and consent, and compensation for use.

- **Collaboration** – Collaboration in many forms became a recurring theme throughout the Summit. Beyond current collaborations, additional specific collaborations were identified as essential or enabling, including clinician-researcher collaboration, medical system-device manufacturer collaboration, improved patient-clinician engagement, international collaboration, cross-sector and cross-disease collaboration. The need for education is inherent to successful collaborative efforts.

- **Trust** – The concept of trust permeated the discussion with an emphasis on clinician trust around predictive models, researcher trust of data, and patient trust in the effectiveness and appropriate use of all elements including personal data, predictive models, care providers, and insurance companies employing such approaches.

The VHGS report also provides a comparative perspective to the 2023 NASEM report on biomedical digital twins, aligning with the main observations with additional perspectives for operationalizing medical digital twins. A specific additional emphasis of the VHGS report is the discussion of factors for stakeholder adoption and sustainability which begin with education across the medical and patient community, including the individual patient. Further, industry serves a critical role in the successful deployment of sustainable medical digital twins, primarily the need for standardization and support for interoperability across the technical components, from virtual models to devices.

The VHGS Summit and the ensuing report represent a continued outgrowth of the established NCI-DOE Collaboration focused on the application of advanced scientific computing to cancer, the Cancer Moonshot™ and the Twenty-first Century Cures Act.

# The Virtual Human Global Summit

## Section 1. Background

In recent years, a growing interest in personalized medicine has emerged due to significant advancements in the fields of biology, data science, and computational modeling. One emerging concept that has gained attention from the scientific community is the patient digital twin (DT), which aims to develop a comprehensive model to enable clinicians to systematically analyze the unique complexity of each patient, simulate treatment outcomes, and then select the optimal treatment option. Constructing a medical digital twin (DT) involves creating a computational model that integrates the relevant characteristics of an individual patient to help inform a given decision for which the DT is developed. The model is likely to require information about the patient's genetic make-up, physiological state that is informed by medical history and general health status, and other relevant factors that can affect the outcomes of interest for the intended use of the DT. However, obtaining all this information can be challenging, as clinical data on individual patients is often limited in both the depth and temporal frequency as a result of limited assessments and testing and perhaps access to this data. To overcome these limitations, researchers can use mechanistic models to replicate observed phenomena across various scenarios, even when data is relatively scarce.

Creating a virtual human that can enable the accurate prediction of treatment outcomes or disease progression is a very complex scientific and engineering problem. Many components need to work seamlessly together, including the multiscale mechanistic models, multimodal data for the modeling and machine learning training, and the software framework and high performance computing (HPC) resources to tie everything together. In transforming the virtual human to a digital twin, information about the “real word twin” must be incorporated and updated over time to reflect the real condition and environment of the individual. Key challenges include the lack of enough high quality, high fidelity data in many scenarios as well as limited meaningful mechanistic models due to persistent gaps in mechanistic understanding. While the promise of artificial intelligence (AI) has been promoted for many applications, its utility in data poor situations is limited and an equally challenging problem of uncertainty quantification is magnified with AI.

With international interest rising in the use of medical digital twins, the October 2023 Virtual Human Global Summit took several key steps to collectively develop the necessary connections across research, digital infrastructure, clinical use, private sector investment, government support and patient involvement to envision the future for sustainable utilization of digital twins in practice. Taking place prior to the release of the December 2023 report on Digital Twins (https://www.nationalacademies.org/our-work/foundational-research-gaps-and-future-directions-for-digital-twins) by the National Academies of Science, Engineering and Medicine (NASEM), the presentations and discussion in this Summit report are independent of the insights from the subsequent NASEM report. Given the importance of consistent terminology, this VHGS report uses the NASEM report definition of the digital twin.

The NASEM report defines a digital twin is as follows:

***Digital twin*** *- A digital twin is a set of virtual information constructs that mimics the structure, context, and behavior of a natural, engineered, or social system (or system-of-systems), is dynamically updated with data from its physical twin, has a predictive capability, and informs decisions that*

*realize value. The bidirectional interaction between the virtual and the physical is central to the digital twin.*[3]

***Biomedical digital twin*** *- The definition of a biomedical digital twin is also informed by the NASEM study, with the definition as follows used throughout the report: A biomedical digital twin is a digital twin applied in the biomedical domain encompassing all processes and objects within that domain.*

***Medical digital twin*** *- The term medical digital twin, as applied through this report, refers to a subset of biomedical digital twins, specifically focused on biomedical digital twins with a specific connection to patient health and wellness.*

The context for the *Virtual Human Global Summit* was an outgrowth of continued cross-agency collaborations exemplified by the NCI-DOE Collaboration involving advanced scientific computing applications in cancer, with ensuing support from the Cancer Moonshot™ made possible through the Twenty-first Century Cures Act. The Virtual Human Global Summit extended these and many related efforts to bring together thought leaders who have been defining, building and shaping the social infrastructure and technical capabilities over many years.

[3] Foundational Research Gaps and Future Directions for Digital Twins, National Academies of Science, Engineering and Medicine, (prepublication copy), released December 2023

## Section 2. Virtual Human Global Summit Participation and Approach

The Frederick National Laboratory for Cancer Research, Brookhaven National Laboratory, University College London, and Eviden were lead organizers for this international Summit on virtual human models and medical digital twins.

The meeting was organized with speakers and panelists convening for the Summit with attendance opened to the public for broader participation. Speakers and panelists were invited based on their work and contributions relevant to operational medical digital twins for clinical use, from research to personalized patient models, patient observations, and patient decisions.

With the perspective that a fully operational medical digital twin is possible, the *Virtual Human Global Summit (VHGS)* attracted more than 80 international attendees, representing multiple domains and diverse interests organizationally, scientifically, commercially, financially, and medically. While by no means exhaustive nor fully representative of global diversity, nations participating in this first Summit included:

| **North America** | **Europe** | **Asia** |
|---|---|---|
| • United States | • United Kingdom | • India |
| • Canada | • Spain | |
| • Native American Catawba | • Norway | |
| • Native American Mohawk | | |

Multiple national laboratories participated in the Summit including four US Department of Energy (DOE) laboratories, Brookhaven, Argonne, Oak Ridge, and Lawrence Livermore and the NCI/NIH supported Frederick National Laboratory for Cancer Research. Members of the NCI and NIH also participated as well as numerous leading universities across the US and internationally. Participants also included a spectrum of commercial interests —entrepreneurs, inventors, technology leaders, biomedical engineers, cloud computing experts, and investors.

With a translational and operational focus, participation by the medical and clinical community was a critical segment of the Summit. In additional to physician scientists, the Summit also attracted multiple practicing clinicians, medical professionals, and leaders of community health systems.

Collectively, this diverse and expansive community of attendees provided tremendous insights into the current state, and opportunities, and challenges in developing and deploying biomedical digital twins in medical practice. There was great enthusiasm and excitement about the topics discussed at the Summit, and eagerness to join together in follow-on actions to expedite progress in developing and employing medical digital twins to improve patient care and health. Notably, over 40 VHGS attendees—more than half of those who attended the Summit in October—convened in December 2023, following the release of the NASEM digital twin report to share reactions and perspectives on NASEM's findings. Insights both from the Summit and attendees' perspectives on the NASEM report are included in this Virtual Human Global Summit report.

*The full list of organizations and attendees is available in Appendices A and B.*

The Virtual Human Global Summit program was organized to bring focus to the full learning cycle needed for development and implementation of digital twins in medical care. The program fostered key discussions among attendees in the following main areas:

- *Virtual Human Models and Biomedical Digital Twins in Research* (Session A)
- *Infrastructure and Environments for Digital Twins in Biomedicine* (Session B)
- *Biomedical Digital Twins in Practice* (Session C)
- *Supporting Biomedical Digital Twins* (Session D)
- *Community Adoption and Path Forward for Medical Digital Twins* (Session E)

Presentations and perspectives provided by experts and stakeholders were followed by discussion among Summit attendees. Each session is independently summarized in the report. Given the strongly interactive nature of the Summit, cross-topic interests were frequently discussed in each session.

*The full program including presenters and titles is available in Appendix C.*

Virtual Human Global Summit
*"Uniting Global Healthcare Perspectives Around Medical Digital Twins"*

**The 2023 Virtual Human Global Summit convened thought leaders globally from research, industry, infrastructure, clinical research, community health systems, non-profit, government, and the public in the spirit of global collaboration to advance patient focused precision medicine through medical digital twins.**

## Section 3. Research and Virtual Human Models

### 3.1 Introduction

The Summit session A explored the state of research in virtual human models and formed the foundation for the Summit discussions. The series of presentations spanned a broad range of virtual human model research across size scales, disease areas, and implementation strategies for which virtual human models would be utilized with patients. There were several challenge areas, goals, and guidance expressed throughout the presentations and discussion. One observation sums up the aspiration for virtual human models and medical digital twins to favorably impact the individual patient outcomes as follows:

- **Aim for virtual human models:** The aim for development of virtual human models is to enable insights and ensuing decisions for healthcare with predictive computational models, a "health cast" that looks forward in time. The continued development and success of digital twins based on human virtual models will need two-way interaction: observations informing prediction and prediction providing the basis for hypotheses and recommendations in healthcare. In addition, differences between observations of real world patients and the predictions from digital twins can help identify critical areas for further research and development of biomedical digital twin methodologies.

A second promising area also emerged at the Summit that provides insight to a secondary role or impact of advancing virtual human models. This is summarized below.

- **Computational models provide better insight than animal testing**. Computational models (e.g. mechanistic, simulations, machine learning, deep learning, etc.) are increasingly able to provide better modeling than animal testing. Animal testing will likely continue to have a role in developing and confirming analogous models and types of data as well as approaches. However, the use of animal models as proxy information for humans will wane as virtual human models become better characterized, available and translated for medical use.

With the broad and deep expertise of participants at the Summit, the session raised many critical points. These are categorized and shared below as observations, challenges, needs and recommendations, and suggested overall guidance.

### 3.2 General State of Virtual Human Models

- Virtual human models research activity is occurring in multiple geographic areas. Broadly, the European Union-funded CompBioMed[4] (http://www.compbiomed.eu/) efforts have focused on virtual models of human organs, resulting in development of cardiac, respiratory, and circulatory virtual human models. Further European Union-funded efforts are emerging including the European Virtual Human Twin, Edith (https://www.edith-csa.eu). US efforts represented at the Summit include researching models for Acute Myeloid Leukemia (AML) cancer, cancer-immune interactions in pulmonary micro metastasis, and molecular basis for RAS-related cancers.

[4] CompBioMed is a European Commission H2020 funded Centre of Excellence focused on the use and development of computational methods for biomedical applications. http://www.compbiomed.eu/

- When combined with mathematical tools for virtual population creation (e.g. cardiovascular, respiratory, etc.) virtual human models are being used to support clinical trials, or instance, in cardiac safety of drugs. It is important to note that the virtual populations created should represent real populations of the same kind (age, comorbidities, physical condition, genotype, phenotype, sex, etc.). Emerging modeling approaches should anticipate the availability of complex, real-world patient data in the future, (lifestyle, environmental exposure, social and cultural influences, life event history, family history, etc.)

- In some cases, virtual human models can be accurately personalized for diagnosis, therapy selection and follow-up. Even in very complex multiscale/multi-physics organs and systems, such as the heart, researchers are just months away from having an operational clinical support tool. The main obstacles to fill this temporal gap are not technical but financial, political, social, and cultural.

- Virtual human models developed in one area may accelerate formation of virtual human models in other areas. For example, the models developed for muscle behavior in cardiac models can be employed to new areas such as modeling the uterus.

- Accessing sufficiently detailed data for optimal parameterization of models for each individual is expensive, typically perceived as invasive of privacy, and procedurally challenging for many organizations and/or individuals.

- The twinning rate or synchronization of the virtual model with the real world instance is an essential element of a successful digital twin. This will require additional observations, additional analytics, and ultimately additional resources in terms of time, information and computing to keep models synchronized.

- The NIH has many resources to potentially engage to advance virtual human modeling. The Interagency Modeling and Analysis Group (IMAG https://www.nibib.nih.gov/research-program/interagency-modeling-and-analysis-group-imag ) is one such group. IMAG has strong NIH representation among several U.S. federal government agencies supporting mechanistic multiscale modeling of biomedical, biological and behavior systems through the Multiscale Modeling Consortium (MSM). Several representatives from IMAG and the MSM participated in discussions at the Summit. Additionally, the NIH Office of Research on Women's Health could potentially increase access to similar resources when studying female pregnancy.

- Genomic sequencing data for individuals will be informative to understanding the effect of individual mutations on the molecular interactions underlying the higher order models.

### 3.3 Research Perspective Challenges for Medical Digital Twins

Researchers face several challenges in the development of virtual human models for use in medical digital twins. Each category of challenges is represented in the following tables.

- The role of data in research to advance virtual human models and medical digital twins was deeply discussed and challenges are *called out separately* in Table 3-1, below.
- Challenges in personalization and overall complexity were also discussed in depth and *are organized collectively* in Table 3-2.
- Finally, the challenges of adoption and use were discussed in depth with the focus on the central role of the patient to advancing research in patient informed virtual human models and patient specific medical digital twins. The challenges facing adoption and utilization appear in in Table 3-3.

**TABLE 3-1. Data Challenges in Medical Digital Twin Research**

| | |
|---|---|
| **1** | **Multiscale and longitudinal patient data -** A significant amount of observational data will be required across multiple scales of measurement and time. Temporal modeling will be important as disease is a dynamic process and not a single state. In the case of chronic disease, it is also important to consider the impact of normal physiological development and its relationship to disease, diagnosis, and response treatment. |
| **2** | **High Quality Data -** In the case of mechanistic modeling and to create the personalized virtual patient, high quality patient information must be collected and processed. Although today this is technically possible, two-way communication between the healthcare institution and the simulation provider could be streamlined and improved. |
| **3** | **Data Consistency** - Longitudinal clinical data, data collected consistently and over time, will be a major necessity for the success of virtual human models and virtual human DTs. This extends to medically relevant data which may not be currently part of the electronic health or clinical record. |
| **4** | **Data Access and Consent** - Accessing patient specific information is a challenge for use in virtual human model development given privacy and data protection requirements and varying considerations of ownership. There is a need for approval, consent, etc., before individual patient information can be obtained. While it may be feasible to attain enough information, significant effort is required. |
| **5** | **Data Reliability** - Using existing and prior clinical data to evaluate the performance of the digital twin will be a challenge for multiple reasons. Data availability is frequently limited, along with sufficient data coverage and consistency over time for the individual. Conversely, there is frequently significant additional patient data which is not immediately relevant to the virtual model being used as the basis for the digital twin. The broader context for the data is often inadequate at best and generally absent from the medical record. For example, clinical guidelines used for diagnostic purposes commonly vary over time as new standards and research are incorporated. This also extends to clinical laboratory procedures and use of new equipment. |

## Challenges in Personalization, Complexity and Uncertainty

**TABLE 3-2. Personalization, Complexity and Uncertainty Challenges in Medical Digital Twin Research**

| | |
|---|---|
| **1** | **Personalization -** Personalization will be required as well as evaluation of many individual predictions to provide near-term and long-term insights. Effective strategies for personalization will be a challenge given the broad range of applications for medical digital twins and the current state of the data medical data ecosystem. Parameterization and personalization of virtual human models will be a challenge, mapping personalized data to parameters of a model. |
| **2** | **Output Interpretation** - Interpretation of the output from biomedical or patient digital twins to support decision making process will be a challenge, particularly when computational biomarkers are considered (i.e. biomarkers which can only be computed on the digital counterpart of a patient). This may lead to the need to qualify virtual human models and digital twin approaches used in clinical applications, decision support, and regulated environments. |
| **3** | **Model Uncertainty Quantification** - Uncertainty quantification of the model predictions, individually and as collections or ensembles, will be essential to clinical utility. The engineering perspective on VVUQ (Verification, Validation, Uncertainty Quantification) is challenged by the virtual human twin and will require review and updating. |
| **4** | **Single Patient Validation -** Medical digital twins for a single patient will face unique complications since there is not a broader population from which to make inferences. Digital siblings provide an approach for an expanded population of similar or previously treated patients to use in parameterization. |
| **5** | **Biological Complexity -** Stochasticity and complexity of biology will remain a challenge and warrant further study and research. |
| **6** | **Model Characterization and Selection -** With a wide range of parameterizations, choices, and model instances, deciding the best digital twin for an individual patient will remain a challenge. The use of ensembles of models has an added benefit of providing a statistical basis for ensuing decisions made from the digital twins. |

## Challenges in Adoption and Utilization

**TABLE 3-3. Adoption and Utilization Challenges in Medical Digital Twin Research**

| | |
|---|---|
| **1** | **Community Adoption of Simulation** - While increasingly promising, simulations are an area that has not yet been widely adopted in the medical community. As simulations begin to represent specific patients and provide dynamic updates based on real world individual patient data, the adoption of simulation technologies is expected to substantially improve due to anticipated advancements in medical digital twins. |
| **2** | **Regulatory Approval -** Uncertainty quantification challenges and regulatory impact. Quantifying uncertainty will be difficult in the near term while virtual human models applied as digital twins are currently in their early stages. This will impact the pace of regulatory adoption and approval in the near term. As new models are created during research and development, and methods for measuring uncertainty in digital twins advance, regulatory processes and approvals will be expected to mature. |
| **3** | **Pace of Adoption -** The pace of advancing the quality and impact for virtual human models and associated medical digital twins will be governed by the rate at which medical digital twins are employed in practice for real world evaluation and validation. |
| **4** | **Value Proposition -** Participation and establishment of the value proposition. It will be a challenge to demonstrate the value of medical digital twin instances unless and/or until the clinician is fully engaged in part of the overall development and deployment process. Clinicians will want to see not only the projection or insight from the digital twin, but also the uncertainty (or confidence) of the digital twin in predicting its *health cast* forward in time. Given the clinical adage "First, do no harm," the threshold for adoption of this technology will be highly dependent on having clearly identified limitations, constraints, and failure modes of a particular implementation along with evidence and metrics for successful performance. |

### 3.4 Guidance for Future Research Efforts in Medical Digital Twins

#### Adoption and Participation

Virtual human model development for use in medical digital twins is inherently a fusion of both research and practice by a clinician and/or patient. Consequently, adoption and collaborations with clinicians and patients are essential to providing the necessary insights about model effectiveness and where improvements are needed. The focus of research recommendations and guidance for adoption and participation emphasize this dual aspect. In addition, guidance is provided in specific areas of visualization and affordability in terms of time and cost. These aspects provide guidance for future research efforts in development of medical digital twins.

**TABLE 3.4 Guidance for Research in Medical Digital Twins: Adoption and Participation**

| | |
|---|---|
| **1** | **Clinician Involvement -** Involving clinicians in all phases of future model development moving will be essential for successful adoption and use of medical digital twins and virtual human model research. Clinicians can facilitate access to relevant data by model developers, advise on building buy-in strategies for clinicians and patients, and facilitate understanding, limitations, and use of developed models. This interaction also holds immense promise to reveal and address *unstated* clinical needs. |
| **2** | **Leverage Current Medical Data -** A path forward to address the inherent complexity of medical biology is to develop models specifically targeting available and anticipated medical observables and measurements (for the ongoing data link inherent to the definition of a digital twin). This approach establishes an essential basis for model validation using real world data and evidence. As limits on existing models are realized, innovations will be needed to improve models with additional information, refinement and medical understanding. In the case of digital twins used to aid in planning interventions, the ability to perturb and observe the dynamic response over time is critical. |
| **3** | **Reduced Complexity Models -** Not surprisingly, models with a reduced number of patient-dependent parameters, developed to support existing clinical decisions are showing a faster rate of adoption. There is commonly a greater likelihood to employ current patient-specific data and a stronger association with generally accepted concepts. This suggests developing models that accommodate high complexity for research with an ability to translate and operate at varying levels of resolution to facilitate testing and adoption. |
| **4** | **Digital Siblings -** The concept of digital siblings (near-twin, related) is being developed as an approach to address specific instance uncertainty. It will be important to work with ensembles of near twins to address uncertainty and develop averages and confidence in predictions. Digital siblings also have a role in developing patient advocacy participation, in which information about similar patients is employed to provide medical insight. |
| **5** | **Regulatory Pathways** - Tracking digital siblings has further potential to develop a regulatory framework or guidance in which the paths of prior patients may be useful in setting the guidelines for future patients. Prior patients help set input for future digital twins as a first step for regulatory approval of digital twins. |

| | |
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| 6 | **Leverage Existing Models -** As virtual human models are developed, they will be continually refined to increasingly specific cohorts. For example, pregnant women are a protected and understudied research class. The impact of hormonal changes on the heart are known but not well studied. In addition to improvements for the virtual uterus, improvements in available models for pregnant women's heart health and health holistically are a priority. Longitudinal data are important and appear feasible to obtain for some populations during pregnancy given the established frequency of visits. |

**Visualization**

Visualization, as an effective means of communication remains a central element for future success in improving virtual human models and advancing development of medical digital twins. Several areas were identified as guidance for future research efforts to address visualization aspects of virtual human models and medical digital twins. This guidance spans the range of stakeholders, including researchers, clinicians, patients, policymakers and the public.

**TABLE 3-5. Guidance for Future Research in Medical Digital Twins: Visualization**

| | |
|---|---|
| **1** | **General Visualization -** Advances in visualization techniques will be tremendously beneficial to the development and adoption of virtual human models. Improved visualization would be beneficial across all scales, from molecular interactions to population studies. |
| **2** | **Public Educational Exhibits -** For example, the Science Museum of London has established a digital twin exhibit involving the virtual human model of a real female researcher who is pregnant. This is attracting public interest while increasing awareness and providing education on digital twin approaches in medicine. |
| **3** | **Clinician Interactivity** - For physicians, the ability to interact with visualizations of patient systems at a scale and nature for the needed decision is essential to the adoption of medical digital twins. |
| **4** | **Integrated Uncertainty Quantification -** Effective integration of uncertainty metrics into visualizations will be important to ensure decision-making considers uncertainty |
| **5** | **Patient/Clinician Approaches -** For patients and physicians, the ability to see the same visuals during consultation is key to shared decision making. |
| **6** | **Patient-Facing Approaches -** For the patient, the ability to see the progression over time, whether historical or expected in the future, will be essential in securing support, monitoring, and maintaining patients' compliance during medical treatment. |
| **7** | **Policy Impact -** For policymakers, the ability to *see* the impact of the digital twin and virtual human models has been effective in developing interest and support for efforts in medical digital twins and virtual human models. |

### Timely and Cost-effective Solutions

Timely and cost-effective solutions will be key to the success of medical digital twins to address the inherent requirement of providing predictions of value and doing so affordably. Virtual human models and related personalized medical digital twins must be accessible to the broad community to provide the insights required to refine, improve, and classify virtual human models for appropriate use.

**TABLE 3-6. Guidance for Future Research in Medical Digital Twins: Timely and Cost-effective Solutions**

| | |
|---|---|
| **1** | **Timeliness and Affordability -** Speed to solution will be essential for the operational use of virtual human models. This is critical to support timely decisions using virtual human models. Additionally, cost to solution is important to address, to avoid the necessity of using a large supercomputer for each patient. |
| **2** | **Reduced Order and AI Approaches -** Speed to solution may be addressed in the following two approaches. First, the use of machine learning surrogates may provide sufficient speed-up without compromising quality or uncertainty in some virtual human model applications. Secondly, while models may require large computing resources to develop, the resulting operational model is streamlined, with flexibility to accommodate elements needed for personalization. The reduced complexity and increased efficiency dramatically lower the operational cost. In the area of cardiac modeling, reduced order models can generally be computed with today's cloud computing. |
| **3** | **Synthetic Data -** Synthetic data has a role in the development of medical digital twins. The synthetic data must be representative of real data. Generative adversarial models are one approach to generate similar data starting with small training samples to supplement and bolster real world digital twin data. Similarly, the mechanistic models developed for digital twins can be used to generate synthetic data for specific or rare cases. Non-molecular models are gaining traction where generative AI is being used effectively to cover these datasets. Regardless of the source, caution must be used given the inherent uncertainty of generative models. In research challenges, developing methods for synthetic data generation while controlling uncertainty would be of value to the development of medical digital twins. |

## Section 4. Infrastructure for Virtual Human Models

### 4.1 Introduction

The Summit session B explored and summarized the state and role of infrastructure to support the development and deployment of medical digital twins provided insights into key technical areas along with insights into further research needs in the technologies supporting digital twins.

### 4.2 General State of Infrastructure Supporting Virtual Human Models

- *The IEEE/UL P2933 standards effort for the Clinical Internet of Things (IoT) Data and Device Interoperability with TIPPSS* - Trust, Identity, Privacy, Protection, Safety and Security is seen as a key element of the future medical digital twin ecosystem. The effort involves 32 countries, more than 250 people and is expected to go to ballot with the goal of becoming an established global standard in 2024.

- *The Digital Twin Consortium,* DTC, is an organization that brings together digital twin expertise and stakeholders globally across disciplines (e.g. manufacturing, aeronautics, etc.). As a consortium under the Object Management Group, the DTC also has established relationships with key consortia contributing to the solution space for digital twins. Members of the DTC can create working products without requiring the purchase of any specific member technology beyond a DTC membership fee to participate.

- *DOE National Laboratories* provide expertise to join in collaborative efforts and uplift projects using supercomputing resources based at each laboratory location (e.g. Argonne, Lawrence Livermore, Brookhaven, Oak Ridge, etc.).

- *Digital twin activities at Oak Ridge National Laboratory are extensive* and the lab has developed modeling capabilities that span across biological scales. In a multistep approach, not only can individual digital twins be created, but virtual populations can also be readily created with customizable parameters to manage initial diversity of the model set.

- *AWS has developed a digital twin oriented workflow,* Twinflow, as an open source framework for large-scale computing associated with digital twins. Twinflow supports simulation and modeling at scale, analysis of scenarios, and systems of systems analysis.

- *The Open Health Systems Laboratory working with the All India Institute of Medical Sciences (AIIMS)* developed a proof-of-concept use of digital twins in neuro-oncology, deployed in a clinical setting. The partnership involved industry leaders Microsoft Research and Intel, NIH, FNLCR, IIT Delhi, and C3.ai.

- *Examples of digital twins in medicine exist* and are problem specific. One such example is the insulin pump which can adapt insulin injections based on observed patient condition.

- *Medical digital twins can help establish transparency* of what is known and unknown and foster more effective bidirectional communication between clinicians and patients throughout the individual health journey.

- *There is interest in developing new mathematical approaches* including mathematical "operators" that can be guided by uncertainty of models and distribution constraints of data.

### 4.3 Uncertainty Quantification and Medical Digital Twins

- Uncertainty quantification for digital twins requires research into novel approaches for the prediction, control and decision making for highly complex systems. This is particularly challenging given the dynamic, non-equilibrium and magnitude of degrees of freedom in play with modeling human biology and the extent of unknown factors.

- Evaluating uncertainty is difficult when large numbers of parameters are involved. This is exemplified by the difficulty in quantifying uncertainty even for large-scale mechanistic models. The situation is even more challenging for large-scale machine learning models in which the number of parameters (weights) can be much larger and are not directly associated with observable data. This is the reality of dealing with *unknown unknowns*. Applying medical digital twin approaches that highlight potential limitations and enable learning from each individual can help direct focused research to close these critical gaps.

- The concept of *uncertainty quantification* must adapt to the specific challenges of medical digital twins. On the computational side, there is perpetual epistemic uncertainty/incompleteness in terms of any computational specification for a digital twin. On the patient side, there is intractable and unquantifiable uncertainty concerning the *real* distribution of a data feature used, particularly in terms of molecular-scale measurements.

### 4.4 Infrastructure Challenges for Medical Digital Twins

The infrastructure challenges for medical digital twins emphasized data issues, highlighting the central role of data generally, and personal data in particular. Additional challenges were identified in areas related to software and machine learning.

**TABLE 4-1. Infrastructure Challenges for Medical Digital Twins**

| | |
|---|---|
| **1** | **Small Data Sets -** Small datasets pose a critical issue, particularly given the extent of the complexity of the systems being modeled. Even so, rigorously annotated high quality datasets, even small datasets, will be of high value. |
| **2** | **Limited Data -** Limited data availability constrains the pace at which progress can be made in developing digital twins in medicine. In the current state, available data may be of limited quality, not curated, and difficult to verify. This highlights the need for curation and versioning of information to support evolution and ongoing validation of digital twins. |
| **3** | **Data Access** - Access to existing data remains a challenge for researchers seeking to employ real-world medical data in research. Required permissions, privacy concerns, data ownership, and fragmentation across medical systems create significant barriers. |
| **4** | **Data Aggregation -** Data aggregation remains a challenge given the absence of standards and measurement context, inconsistent instrument calibration, diversity of instruments, different levels of available resources, and cross-organizational variability. The data aggregation challenge may be lessened within nationalized healthcare systems. Such environments may provide early evaluation and validation of digital twin approaches. |
| **5** | **Personalized Twinning -** Infrastructure and requirements are needed to keep each individual digital twin updated. The approach to 'twinning' of each individual is not something that is clear yet due to uncertainty about what data should be gathered, the means to gather it and how to store the additional volume of individuals' data. |
| **6** | **Machine Learning and Parameterization -** Machine learning, by design and intent, is exceptionally good at fitting extremely large parametric models, yet this comes at the expense of interpretability and ease of explanation. Deciphering the meaning of parameters in machine learning models remains a significant challenge. |
| **7** | **Causal Basis -** Even with machine learning and reduced order models, for biomedical digital twins to have the greatest impact on prevention and treatment decisions, it will be critical to move beyond correlative understanding and seek a causal basis for underlying predictive models. |
| **8** | **Software Cost -** Commercial software for digital twins is currently not available at an affordable price for applications in medicine. As the value of medical digital twins areas such as clinical practice and clinical trials becomes apparent, this situation may rapidly evolve. |

| | |
|---|---|
| **9** | **Privacy and Security -** While not necessarily universal, issues of privacy, security, cost, and access were commonly raised as potential challenges to address in establishing a personal health baseline. Additional trust and cultural factors may also need to be considered. |
| **10** | **Data Harmonization –** Data harmonization must be addressed due to the lack of standardization on common representations across the range of datatypes and sources. It is important to commence the effort to capture adequate metadata to facilitate data harmonization activities. This extends from use of common units to information capture on differences in specific testing modalities and methods. |

### 4.5 Guidance for Medical Digital Twin Infrastructure

**TABLE 4-2. Infrastructure Guidance for Medical Digital Twins**

| | |
|---|---|
| **1** | **Digital Twin Information Commons -** A Digital Twin Information Commons, like the COVID Information Commons (CIC) cross-agency collaboration funded by the US National Science Foundation, would provide a central resource to connect researchers, promote award activity, and host working groups and other engagement activities. |
| **2** | **Sparse Sampling Methods -** One approach to address employing large amounts of data in developing models of complex systems is to shift from a high density sampling approach to a sparse sampling method. The adaptive transport method produces a sparsity map without specification of a structure *a priori*. This approach is content-agnostic and will drive the sampling based on the data volume and values present. |
| **3** | **Selective Uncertainty Quantification** - For cases in which quantifying uncertainty is difficult, such as those involving large numbers of parameters or the time-consuming evaluation of contributions to an ensemble, focus on evaluating the uncertainty for the most relevant quantities. This step is a challenge given the scale of data features, the perpetual relative sparseness of data samples, and the ambiguous degree of adequacy for dimension reduction methods. |
| **4** | **Expanded Data Access -** Model developers must push to expand the depth and breadth of datasets and methods employed for developing virtual models to assure the models represent the individuals they are intended to twin. |
| **5** | **Federated Learning -** Employ federated learning and federated use of datasets in model creation and evaluation to reduce issues related to data access and permission. This approach requires a significant investment for sites to adopt the necessary infrastructure to both store data and support federated use of that data (e.g. compute capacity must be available where data are accessed). |
| **6** | **Incremental Investment -** Given the costs and extent of the infrastructure for digital twins, the process to put medical digital twin infrastructure in place should be incremental and should not attempt to solve all aspects at once. |
| **7** | **Close Digital Health Gap -** As digital twin capabilities are developed and to lessen the digital divide for healthcare, steps should be taken to minimize and close the gap between those with access to medical digital twin capabilities and those without access. |
| **8** | **International Collaboration-** An international effort is needed to establish libraries of models, datasets, and software for use with medical digital twins. Such efforts may leverage existing capabilities within each country such as the US National Library of Medicine. |

## Section 5. Clinical Perspectives on Virtual Human Models

### 5.1 Introduction

Summit Session C covered recent experiences and anticipated clinical use of medical digital twins in pediatrics, cancer, infectious disease, ICU care, telemedicine, etc. Several clinicians participated in the Summit to share their perspectives on the role and potential for digital twins in improving patient health and individual wellness. In addition, Summit attendees from the largest community health system in the state of New York (Northwell Health) and world leading medical research institutions across the US participated, including the largest NCI-designated cancer center in the United States, MD Anderson.

The applications of medical digital twins discussion centered on improving treatments. One such area is development of treatments to overcome the "Translational Dilemma" of drug development and offering hope to patients for whom no therapies exist. Aligned with this application area, digital twins are being developed for patient cells to test drug and drug combinations for efficacy and drug resistance. The promise for medical digital twins to improve outcomes is to limit the traditional toxicity of the treatment, shorten any delay in finding an effective treatment, and keep the treatments affordable. In addition, digital twins can further support disease subtyping and selection for more personalized therapeutic interventions.

The following observations were made about the current state of clinical care and translation that have significance in setting the context for future applications of virtual human models and digital twins in practice. The clinical applications of virtual human models in the context of medical digital twins covers a very broad range of issues, with a large emphasis on clinical data. Insights and guidance appear in two distinct sections on the following pages, Sections 5.2 and 5.3 for General Clinical Observations and Challenges and Sections 5.4 and 5.5 for General Clinical Data Observations and Challenges. Section 5.6 provides collective guidance for clinical applications involving medical digital twins.

### 5.2 Medical Digital Twins: General Clinical Observations

- *There are currently some technology tools to foster better decision support*. These "tools" include guidelines and real-world evidence (RWE) such as cancer registry information, EHR data, similar patients' data, and other sources. Real-world clinical practice may differ from existing clinical guidelines which continue to evolve and are rarely harmonized across professional societies and international boundaries.

- *Innovation requires risk*. Unfortunately, in the healthcare space, innovation has traditionally been more closely associated with risk rather than reward. The promise of rapidly advancing technology in healthcare is to change this paradigm and enable innovation with an improved risk-reward balance for community health systems.

- *Patient involvement in clinical decisions* – In the case of cancer, the initial discussion frequently focuses on simply surviving when diagnosed with cancer. Quality of life discussions are secondary and as such digital twins need to cover a range of options, questions, and uncertainties.

- *Generative AI is expected to transform healthcare* over the next three years, with a shift towards consumerism.

- *With significant differences between chronic disease and acute disease, acute disease treatment will always be clinician based.* Even so, acute disease may reflect exacerbations of chronic disease.

- *Biological function while diverse, remains generally conserved across the population.* There are common pathways in biology some of which may be perturbed in an individual instance. The combination of specific pathways, while overlapping, will be different for each patient. Consequently, different patients may have identical or nearly identical behavior depending on the nature and type of medical digital twin developed.

- *There is potential to extend cellular digital twin models in research to extend beyond efficacy for cancer* by incorporating more of the cancer microenvironment. Incorporating cytokines would help bridge the model to study immune response when treating with drugs.

- *The community health system is key to reaching cancer patients*. In the U.S., 85% of cancer patients are first diagnosed and treated in the community health system setting.

- *Sepsis, a condition in which the body responds inappropriately to an infection, is the cause of 1 in 5 deaths each year worldwide and has a 30 to 40 percent death rate.* Sepsis is a leading cause of death in the intensive care unit, and often the final cause of death for patients with a range of underlying diseases, such as cancer, diabetes, obesity, cardiovascular disease, chronic pulmonary disease, and autoimmune disease, to say nothing of infectious disease (such as COVID-19). To date, there are no accepted drugs that effectively address the underlying biology of sepsis: a disordered immune response. Over the past 30 to 40 years every new drug that has ultimately failed clinical trials had cleared several prior checkpoints.

- *Setting expectations appropriately around the pursuit of the 'ideal' digital twin* will be important to maintain an appreciation of the complexity, diversity, and inherent uncertainty of modeling human biology. In nature there is an average of 5.2 mutations per individual human twin. Even such small differences such as these may affect disease risk, response to external factors (e.g. environment, lifestyle, etc.), disease presentation, response to treatment and disease prognosis.

### 5.3 General Clinical Challenges for Medical Digital Twins

**TABLE 5-1. General Clinical Challenges with Medical Digital Twins**

| | |
|---|---|
| **1** | **Complexity and Heterogeneity-** The two primary barriers to the transposition of the successful industrial digital twin paradigm into the biomedical arena are: 1) the state of inherent uncertainty regarding how biological systems work and 2) the ability to, address as comprehensively as possible, the breadth of heterogeneity that exists in human biology and disease (which heavily contributes to the translational dilemma). |
| **2** | **In Vivo Validation -** When abstracting from comprehensive profiling to a mechanistic level, it is a challenge to confirm the treatment is truly targeting the underlying problem and not the external effect being observed or response to current treatment. |
| **3** | **Health System Cost -** In the US, hospital systems are generally struggling to be profitable and, as such, focus on minimizing costs whenever possible. The emphasis on cost reduction also makes investments more challenging if either high risk and/or high cost are involved. The impact on cost and personnel time are key considerations among the healthcare community. |
| **4** | **Workload Impact -** Digital twins in practice must support the physician and not add to the clinical workload. Systems employing medical digital twins should be developed in close collaboration with clinicians and healthcare professionals for insight and guidance. Without buy-in by clinicians, digital twins in the medical field will not translate for use in clinical applications. |
| **5** | **Confirmation Bias -** There is an open question as to whether the predictive models will exhibit confirmation bias if they are based on data collected during treatment. It will be important to more fully consider the impact of given cancer treatments on the disease when making future diagnoses, deciding future treatments, and predicting therapeutic response. |
| **6** | **Model Bias -** Clarity is needed in the handling of bias in models. It should be a priority to share information regarding best use of models, presence, and absence of potential bias in the models and whether the removal of bias from algorithms is feasible or a priority. |
| **7** | **Data Policies -** Several issues around data must be clarified or defined to enable a productive ecosystem that can respond more effectively to innovations such as medical digital twins:<br>• *Legislative* – current legislative guidance is outdated with respect to data<br>• *Ownership* – there are competing interests regarding the ownership and costs of stewardship for health data<br>• *Privacy* – there are inconsistent standards for privacy of data<br>• *Security* – maintaining the required level of security is an ongoing cost and it is unclear who covers this cost<br>• *Usage* – there is ambiguity as to who has the right to use the data and for what purpose<br>• *Quality* – identifying the most effective process to improve, verify and assure the quality of health information presently and into the future remains an open question. |

### 5.4 Medical Digital Twins: Clinical Data Observations

- *The field of cancer treatment benefits from a large evidence base of randomized clinical trial results*. Oncologists and oncology teams use evidence-based decision aids, and evidence based guidelines. The findings from clinical trials provide population level statistics to generate evidence for treatment approaches, which may or may not apply at an individual patient level.

- *Patient-level clinical trial results are carefully collected and curated*. Real-world patients exhibit comorbidities, may already be on multiple drugs, and may have confounding social and cultural determinants that impact disease presentation and response to treatment. Additionally, the same level of data and measurements are not consistently collected to guide care in the real-world setting.

- *Clinical trials enroll approximately 5 percent of patients with the subject cancer* and are designed to detect endpoints such as overall survival and progression free survival. When choosing among available treatments, patients and their physicians are forced to assume that results from the small proportion of clinical trial participants can be applied to the larger, and often sicker and older, population with the condition.

- *The US Department of Defense enforces its regulation that all active members of the military must be diagnosed at Walter Reed National Medical Center*. The data are centralized and serve as a potential starting point for developing virtual human models and digital twins.

- *Real-world, patient level data is available* from tumor registries, EHR-derived data, and combinations of these sources.

- *Patient and consumer interaction with LLMs would be a means of learning more information about individuals*. With limitations of AI and use of LLMs, care must be exercised in training, evaluating, and using LLMs as noted above.

### 5.5 Clinical Data Challenges and Medical Digital Twins

**TABLE 5-2. Clinical Data Challenges for Medical Digital Twins**

| | |
|---|---|
| **1** | **Missing Data Context -** The data captured in clinical trials are collected with the aim of population-based analysis, but more contextual details could inform patient-level differences that may provide insights for patient-level decision-making, i.e. the kind of contextual details that need to be considered for human digital twins |
| **2** | **Limited Consent -** Consents need to be constructed to enable both primary and secondary research. One example company gathers RNA information from an individual through stool, blood, and saliva. As RNA is reflective of the underlying personal biology at work, samples are analyzed with results returned to the individual through a personalized app. Additional information is gathered (lifestyle, wellness, fitness, etc.) which has been consented for research. |
| **3** | **Data Infrastructure -** Deploying a digital twin-enabled clinical infrastructure will be essential to the successful deployment and use of medical digital twins. For example, the MD Anderson Cancer Center (MDACC) has developed an ecosystem for data collection with an aim to support the use and development of digital twins. The MDACC "Context Engine" provides the system to capture and record key information to enable the operational use of medical digital twins. |
| **4** | **Implementing Precision Toxicity -** When choosing between treatments with roughly equal survival endpoints, patients and their physicians often use toxicity data to inform their choice. It would be helpful to have participation from broader populations and to have more detailed information available on the trial participants. Such information should also be presented to patients in a relatable format that patients understand. |
| **5** | **Unrepresentative Data -** Clinical decisions are not as effective as they could be given that most of the clinical trial data are from a very small number of patients relative to the broader patient population. For example, if three treatments appear equally beneficial to the patient, each with their trade-offs, it would be helpful to know the populations for which the trade-offs were observed. As noted above, it would be helpful to have participation from broader populations, information available on the population from which the trial was evaluated, and the comparison between patient populations including the general population. |
| **6** | **Clinical Data Inaccuracies -** Working with real-world electronic health information in a current clinical setting creates a significant challenge for medical digital twins given the wide variation in data capture, quality standards, error rates, overall accuracy, missing data and inter- and intra-organizational variations. |
| **7** | **Generally Wrong Information -** There is a lot of information used in training foundation models and Large Language Models (LLMs) that is, unfortunately, wrong. *Quality of data* used to develop and support these efforts needs to be emphasized over *quantity of data*. |

| | |
|---|---|
| **8** | **Data Gaps –** Real-world data around patient treatment tends to have gaps which limits its use in assessing risk. Data are generally available at the beginning of treatment and near the end of life when more intense attention is focused on the patient. Unfortunately, there is little longitudinal information acquired between these points. To reduce these data gaps, regular physical exams remain an important part of the post treatment process. |
| **9** | **Trustworthy Data -** In the short- and mid-term, a resource is needed that would curate data and information to reduce the amount of extraneous information and noise, and to harmonize data. Longer term, to make use of continually growing volumes of data and bring value, an investment is needed in the way we generate and flow data in healthcare. Healthcare data must be organized and coordinated across systems to ensure appropriate use with clear understanding of the context for the data . This will also ensure interoperability and reusability. |
| **10** | **Clinical and Research Data Integration -** Integrating clinical and research data will be an important step forward. Research, clinical and academic information are commonly kept separate, and it would be helpful to integrate this information with appropriate annotation. It would also be helpful to have a single version of the data, curated with authority copies for reference. |
| **11** | **Data Volume -** There will be enormous amounts of data, in the near future (well beyond petabyte scale), and the scale of data will continue to increase – perhaps beyond what is imaginable today. |

### 5.6 Guidance for Clinical Efforts in Medical Digital Twins

**TABLE 5-3. Guidance for Clinical Efforts with Medical Digital Twins**

| | |
|---|---|
| **1** | **Radiation Oncology Starting Point -** Radiation oncology is well-positioned as a starting point for digital twins. From a computational standpoint, radiation oncology has employed simulations and machine learning methods for many years. |
| **2** | **Critical Illness Starting Point -** The concept for the Critical Illness Digital Twin is a potential exemplar to focus on. |
| **3** | **Clinical Education -** Clinicians need further education about machine learning and mechanistic model-driven methods. It is important that newly introduced technologies help and aid clinicians and do so without additional administrative effort and without a steep learning curve. |
| **4** | **Defined Clinical Problems -** Digital twin efforts should commence with knowledge of what the digital twin will be used for, insights the digital twin would provide, and the decisions it would support. This includes understanding what is being addressed and what degree of uncertainty is acceptable. Furthermore, efforts should start with defining the clinical need to establish the goal for the development of a medical digital twin. |
| **5** | **Broadened Decision Criteria** - The *best treatment* not only includes the best survival and acceptable biologic toxicity, but also should address time and financial barriers to the patient. |
| **6** | **Data Transparency -** Data should be made transparent and FAIR (findable, accessible, interoperable, and reusable) and in the future be generated in a FAIR manner to reduce the burden to convert data into FAIR standards. |
| **7** | **Challenge Results -** Results from predictions should not be accepted without challenge. Results should be used in conjunction with other predictions for the similar case. |
| **8** | **Learn from All Patients** - Develop capabilities to learn from every cancer patient and their data. |
| **9** | **VA and DoD Starting Point** - A promising path forward is offered by the longitudinal cohort from the Department of Defense (DoD), Veterans Affairs (VA), and NCI collaborative Applied Proteogenomics OrganizationaL Learning and Outcomes (APOLLO) network.[5] APOLLO also serves as the foundation for the PROject for Military Exposures and Toxin History Evaluation in US serve members (PROMETHEUS) program in which APOLLO patients will be approached to request access to his/her Individual Longitudinal Exposure Record (ILER) and his/her samples from the DoD Serum Repository. Since inception in 1989, the repository has grown to contain more than 74 million vials of serum collected longitudinally from more than 12 million active duty members.[6] |

[5] https://ascpt.onlinelibrary.wiley.com/doi/10.1002/cpt.1425

[6] https://www.health.mil/Military-Health-Topics/Health-Readiness/AFHSD/Functional-Information-Technology-Support/Department-of-Defense-Serum-Repository

| | |
|---|---|
| **10** | **Start Early -** A strong consensus point was to not only take a practical approach to develop medical digital twins, but to simply get started now. |
| **11** | **Integrated Approach -** The Virtual Human should incorporate clinical trial and real-world experience, develop approaches to ameliorate time and financial barriers for the patient, and prompt patients, oncologists, and treatment teams to ask and answer these and other questions in a timely and useful way. |
| **12** | **Healthcare System Leadership/Healthcare Systems and Medical Digital Twins**. Healthcare systems should be leaders for digital twin innovations. While no one doctor has the necessary resources, the healthcare system collectively has the range of resources necessary when working collaboratively with other healthcare systems. It is a big risk to the individual healthcare organization but has an incredible amount of potential reward across health systems collectively. |

## Section 6. Supporting Biomedical Digital Twin Development

### 6.1 Introduction

Summit Session D provided insights to and discussion around past, present and potential future support for biomedical digital twin efforts, with an initial focus on governmental efforts in the US, EU and extending to other potential sources.

- Government interest in enlisting the National Academies to study the digital twins in medicine was at least partially motivated by a recognition that digital twins are a rapidly developing approach in other domains and that biomedical applications should be included. A second objective for creating the NASEM report was to provide guidance on both starting points and directions that would advance the use of digital twins in medicine.

- As an interdisciplinary perspective study, the NASEM study approach involved first connecting across disciplines and forming workshops to connect with the communities in each area. The NASEM report has attempted to address the inconsistencies with a definition approved across the contributors to the report from all disciplines.

### 6.2 Perspectives on the 2023 National Academies Report on Digital Twins

*Note: As specified previously, the perspectives of Summit attendees on the 2023 NASEM digital twin report were introduced following the Summit and public release of the NASEM report in December 2023. Perspectives among Summit attendees were shared during discussion in a session held in January 2024 involving more than half of the attendees of the October 2023 Virtual Human Global Summit.*

The NASEM report on digital twins primarily focused on research gaps and opportunities to advance digital twins across multiple sectors, engineering, climate and biomedical. Many of these opportunities and gaps paralleled insights from the VHGS Summit. The sections that follow summarize areas of alignment between the Summit and the NASEM report as well as additional insights brought forward during the Summit.

The following were areas of consistent concurrence of Summit insights and the NASEM report.

- *The definition of the digital twin as shared in the NASEM report was viewed as a needed contribution to the advancement of digital twins in medicine*. With this definition becoming the foundational definition, increasing precision and clarity are expected to follow in ensuing medical digital twin discussions.

- *The focus on validation, verification, and uncertainty quantification (VVUQ) were significant points of interest and discussion*.

- The VHGS attendees also *identified the importance to manage the hype and set expectations appropriately, clearly delineating the current state of medical digital twin development from the aspirational aims* and long term vision for digital twins in medicine.

- *Cancer was an exemplar in both the NASEM report and with the VHGS attendees.*

- *The VHGS attendees also shared that AI methods, while contributing to the success of digital twins, had substantial limitations*. AI will have a role in the development of medical digital twins (feature extraction, surrogate models, generation of hypotheses, etc.) but will be limited in its predictive accuracy for the complexities of human biology.

- *The importance of delivering results in a timely manner for the given decision was of high significance in both reports*.

- *The importance of collaborations across organizations, disciplines and agencies was also of high importance in both reports*.

The VHGS Summit complemented or extended the insights provided in the NASEM report in the following ways:

- The NASEM report provides a primary focus on identifying the research challenges and gaps for advancing digital twins, comparing digital twin efforts across three domains. These fundamental insights are extended by the VHGS Summit which considered the full cycle of medical digital twins from research to first and sustained operational use.

- With the focus on medical digital twins, the VHGS Summit appropriately emphasized the role of the individual (as patient or non-patient) and identifying opportunities and challenges in the context of successfully bringing patient-centric digital twin and virtual human models into clinical use. This further involved focused discussion on management of the digital twin implementation, as well as ownership, rights and management of data associated with the individual.

- Ethical implications of developing and utilizing medical digital twins, both near and long-term implications, were part of the discussion at the VHGS Summit.

- The importance of the individual longitudinal health record was increasingly emphasized in the VHGS Summit as an essential element.

## Section 7. Community Adoption and Path Forward for Medical Digital Twins

### 7.1 Introduction

Summit Session E explored topics related to fostering community adoption and identifying potential next steps to move ahead with medical digital twins. These topics include education, workforce development, physical infrastructure, commercialization, regulatory requirements, public-private partnerships, international efforts, and collaborations.

### 7.2 Community Adoption Challenges

**TABLE 7-1. Community Adoption and Path Forward Challenge Areas**

| | |
|---|---|
| **1** | **Build Community Awareness -** Fostering engagement and discussion to integrate the views of a large and diverse ecosystem of stakeholders ranging from technology experts to patients and clinicians and from members of the public to policymakers and regulators to encourage and support uptake of the technology |
| **2** | **Workforce Education** - Educating the current and future generations of biomedical researchers and health care workers in DT-informed healthcare delivery via mechanisms ranging from university education through continuing professional development courses. |
| **3** | **Bridging Technology to Clinic -** Ensuring that human digital twin models can be developed for and deployed on the latest technologies including exascale and quantum machines whilst providing a mechanism for access and use by medical practitioners in a clinical setting. |
| **4** | **HPC Education -** Medical education and training are essential elements of buy-in. Computational education has been underway at University College London for several years. The experience of training medical students in the uses of HPC has both established an interest in and understanding of the role of HPC in medicine. HPC education has also established the foundation for future discussions and training in the use of personalized medical digital twins. |
| **5** | **Individual Patient Involvement -** Patient engagement and participation will also be important for the development of digital twin models and datasets. As has already been seen in companies such as ELEM Biotech, participation of individuals in the development of these models results in commitment and buy-in. An added benefit of patient involvement in the development of digital twin models is insight into the communication approaches that are effective in conveying insights from the digital twin with the patient. This creates a specific challenge in the area of human subject research which is inherent in patient medical digital twin development and will need to be addressed. |
| **6** | **Equitable Patient Compensation** - Patients' rights to derivative value of their medical digital twin. A first dimension is the rights of individuals contributing personal data to the development of successful digital twin models that become broadly used across the medical and research community. There is a priority to avoid recreating a situation analogous to what happened in the Henrietta Lacks cancer case in which her cells were used unknown to her as the basis for an industry in cancer research. While technically challenging to keep each patient involved in the development of medical digital twin models, efforts should be made to |

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| | maintain connection with patients and foster awareness of the role of a patient's data in the development of medical digital twin approaches. |
| **7** | **Patient Digital Twin Rights** - Patients' rights to access medical digital twin capabilities. A second dimension of rights management is individual access to digital twin technologies as they are developed. While challenging in health systems that have not yet achieved parity among patients within and across systems, a conscious effort should be undertaken to forestall creating a medical digital twin divide, in which health systems and patients are not equally able to access medical digital twin capabilities. Optimistically, medical digital twin technologies also hold promise to address healthcare disparities, first by bringing visibility to existing disparities and a means to address them with improved predictive models for underrepresented communities. Secondly, by employing medical digital twins to help bridge the gap in access to specialized medical insights in which patient and physician have reduced or no access to specialists. |

### 7.3 Guidance for Community Adoption of Medical Digital Twins

Getting started with medical digital twin efforts includes multiple points for recommendation and guidance.

**TABLE 7-2. Guidance for Community Adoption and Path Forward for Medical Digital Twins**

| | |
|---|---|
| **1** | **Public Communication** - Start communicating with the public on personal medical digital twins as soon as possible and start crowdsourcing efforts to expand participation. |
| **2** | **Expectations Management** – Choose targeted applications to demonstrate success and the current state of the art of what is possible while avoiding lifting expectations too high in the early stages. |
| **3** | **Global Community -** Build a global community among the attendees of the Virtual Human Global Summit and increase participation with other international communities. |
| **4** | **Exemplar Projects -** Identify problems in the clinic which can be addressed with medical digital twin approaches and engage research communities and stakeholders for a sustainable, deployable solution to address these problems. |
| **5** | **Patient Engagement -** Engage with patients and patient advocate groups on the potential and value for medical digital twins, and specific application in targeted disease domains. |
| **6** | **Individual Medical Baseline -** Create a framework from which to develop patient baseline information that is expected to be integral to future digital twin solutions. This includes incorporating and integrating individual patient medical records. |
| **7** | **Model and Dataset Management -** Many elements are already in place such as mechanistic models, AI models and datasets. An organizational structure to enable these to move ahead collectively is needed. |
| **8** | **Integrated Training -** Bring patients, advocates, and the medical community together and start engaging them in the topic of medical digital twins. Start with education and awareness, creating training opportunities for those that seek to learn more. |
| **9** | **Build Basis for Trust -** Begin the process of building trust in the technology and the benefits for medical digital twins. Start addressing the patient medical education gap. |
| **10** | **Aggregate Data** - Aggregate datasets and assess value of aggregated data for use in the development of different classes of medical digital twins. As value is established, identify approaches for sustainable and equitable access to datasets for use in medical digital twin development. |
| **11** | **Positive Workflow Impact -** Avoid efforts that would encumber clinicians and clinical operations to steer clear of potential negative reputation such as resulted from the introduction of electronic medical records. |

| | |
|---|---|
| **12** | **Wellness and Health** - The foundation for development of medical digital twins should encompass the full health and wellness journey of the individual. |

## Section 8. Industry and Commercial Perspectives on Medical Digital Twins

Standardization and precedents were shared as preferred aspects for securing investment in digital twin technologies. In terms of scaling impact of the investment, the questions of globalization and standardization are important as well as returning medical insights to the individual and to the local community.

**TABLE 8-1. Industry Perspectives on Medical Digital Twins**

| | |
|---|---|
| **1** | **Proprietary Technology -** Many challenges exist in standardizing technology foster greater integration and efficient scaling. Internal design, operational, and proprietary secrets for devices impede the desired transparency. |
| **2** | **Data Format Standards -** To address proprietary and company-specific variability, data format standards are important for effective globalization and achieving interoperability. The DICOM[7] standard serves as a reference example for industry standardization of file formats in medical applications. |
| **3** | **Measurement Context -** The context for the data values in the dataset are frequently the most meaningful to provide a basis for interpreting the standardized representations. Unfortunately, the metadata needed to inform the context of standardized representations are frequently not shared or available. A particularly illustrative example of this need is in the measurement of blood pressure, a value known to widely vary for each individual. While each measurement is reported consistently, the context for the measurement is imperative to the correct interpretation of that value. For example, many factors are known to impact blood pressure, yet these are rarely captured in association with the measurement, |
| **4** | **Device Interoperability Standards -** Standards will aid industry participation. Medical device interoperability has been a challenge for many years. Discussions have even taken place with the British Parliament on the topic of standards which have provided guidance that stakeholders of the standards are best suited for developing the standards. A suggested priority for the VHGS community is to facilitate the interoperability among medical devices. |
| **5** | **Manufacturer Data Limitations -** Medical device interoperability and advances are curtailed at the manufacturer with only approximately 10 percent of real world data from devices are ever accessible for analysis. The data available are generally not provided for use for product improvement and do not represent the diversity of applications and populations using the device. This makes it a challenge to analyze the data to make improvements or assure appropriate use across populations and applications. |
| **6** | **Model Interoperability -** Interoperability in biomedical digital twin models will require addressing the challenge of cross-scale measurements coherence. Some advances are occurring in the active AI space which may prove helpful in advancing interoperability within the space of medical digital twins. As standards are developed, it is expected that global standards will be the most effective to support translation of digital twin insights across |

[7] DICOM® is the international standard to transmit, store, retrieve, print, process, and display medical imaging information. https://www.dicomstandard.org/

| | |
|---|---|
| | stakeholders at all levels globally. Effective communication across global stakeholders will be essential to the development of such global standards. |
| **7** | **Data Quality -** The quality of data employed during development and deployment is essential in the successful deployment of biomedical digital twins. Quality data are important for the development of successful medical digital twin models to establish confidence and validity in the model even prior to deployment. Following deployment, data quality is essential during the personalization of virtual models when employed with patients, during twinning, and in the decision support process. |
| **8** | **Data Integrity -** Data integrity will be a fundamental aspect of data in the domain of personal medical digital twins. Without high-quality data integrity, the utility of models to provide insight and decision support will be limited by the uncertainty around the data itself. |
| **9** | **Operational Flexibility -** Flexibility will also be essential in the ongoing collection of data for medical digital twins. Flexibility will be needed to add context around previously acquired data, incorporate new types of data, and to address inaccuracies in previously collected data. |

## Section 9. Virtual Human Models, Biomedical and Medical Digital Twin Examples

Throughout the Summit, many references were made to existing and anticipated virtual human models, medical, and biomedical digital twins. While many more examples exist than are shared below, the list is provided to provide a contextual basis for discussions during the Summit.

***AML cancer digital twins*** – *International collaborative* efforts are underway to develop a virtual human model of AML cancer with support from the National Cancer Institute. Large datasets of information are being analyzed and used to develop a knowledge graph to relate the cumulative information. Machine learning models are used together with the knowledge graph to predict which drug will be effective. The effort is in its early stages, and as the predictive basis is developed, it will be possible to personalize to reflect each patient and to implement digital twins for AML cancer.

***Mechanistic models of cancer-immune interactions in pulmonary micrometastasis*** - A mechanistic model of cancer-immune interactions in pulmonary micrometastasis was shared. The model has been shown to express a wide range of patient trajectories, from complete tumor elimination to uncontrollable growth. Using high-throughput computing platforms, the study analyzed 100,000 virtual patient trajectories by exploring the parameter space of this model. Investigation revealed that the same patient could have completely different trajectories, making it challenging to categorize patients. The mechanistic model employed in the study provided insights showing that early or non-interactions between macrophages and invading tumor cells were responsible. The study highlighted the need for digital twins that are patient-specific, dynamical, and continuously updated with new patient data instead of one-time calibration.

***Cardiovascular and pulmonary digital twins*** – Computational models for cardiovascular and pulmonary systems were presented during the Summit. The power of supercomputing and HPC was highlighted as a key technology to boost the Virtual Human Twin (VHT), fostering translation from research to reaching the patient. ELEM Biotech (established 2018), a startup company of the Barcelona Supercomputing Center (Spain), is one of the world-class research centers in the field. In 2005, the team started to develop Alya, a supercomputer-based multi-scale / multi-physics modelling code, developed from scratch to be efficient in large-scale computing facilities. The Alya environment provides the means to create virtual populations of human systems for cardiac, cardiovascular, and respiratory systems. The flexibility of the developed computational methods makes it possible to extend the computational models to other systems including muscle systems, notably the uterus.

***Personalization and assessing cardiological impacts and toxicities with digital twins*** - Virtual human heart models currently exist. To be transformed to a digital twin for an individual patient, models need to be tailored for each case. To move ahead, we need a better understanding of what makes individuals different, why some individuals respond negatively to select drugs and why others develop specific diseases. In cardio models, there is a clear difference between male and female hearts and there will need to be respective differences in male and female digital twins. The heart models developed at BSC have been used to observe and predict the cardiac impact of important toxicities and issues with the heart that have been seen in the clinic. For example, the effects of hydroxychloroquine and azithromycin were observed in the model. A final point is that core modeling technologies, in this case muscle models for cardiac modeling, and modeling other muscles is made possible. A model has been developed for the virtual uterus to study pregnancies, starting with the muscle model capabilities developed.

***Multiscale modeling of fundamental biology in RAS related cancer*** - In the multiscale molecular discovery effort around RAS, AI is used to create a latent space for exploration of candidate options. Structural, affinity, time series measurements, and drug discovery data are all incorporated. Despite the confounding nature of RAS oncogenes being implicated in many cancers and part of fundamental cellular processes, recently approved drugs for RAS inhibition are becoming available. It is anticipated that mono-drug treatments will not be sufficient over the long-term, and multi-target approaches will be needed.

***Sepsis and critical illness virtual human models*** – The critical illness digital twin incorporates a mechanism-based simulation model of the cellular/molecular processes. This model drives sepsis while utilizing a novel machine learning parameterization method that harnesses the Maximal Entropy Principle. This method addresses the perpetual epistemic uncertainty. regarding any mechanism-based "*biosimulation"* model and captures the heterogeneity of human biology (representing any individual means being able to represent every individual). Lastly, the model employs deep reinforcement learning to train artificial intelligence to discover novel multimodal and adaptive therapeutic strategies that can account for the interindividual and temporal heterogeneity of sepsis.

***Radiation Oncology Digital Twins*** – Radiation oncology is a promising medical application for digital twin approaches that could be implemented in the not too distant future. Key factors include the current use of well-established computational models of the radiation physical dose for treatment planning, longitudinal monitoring with imaging, and use of multiple treatments over time in the context of a medical system linked to other clinical testing and specialists.

As with all digital twins, the digital twins in radiation oncology would be developed to support patient-specific treatment decisions such as creating tumor treatment response models involving radiation or involving selection and deployment timing of chemotherapy agents. Digital twins may also be employed to minimize and monitor radiation treatment toxicity at the disease site and for the whole patient.

Finally, digital twins could be employed to provide critical insight that is not readily available at present due to challenges in following patients treated with radiation therapy effectively or timely. Digital twins could be used to help both patients and clinicians decide when patients need to be seen, when patients can see a local physician rather than the radiation oncologist which may involve travel burden for rural patients, and when patients may require interventions to prevent side effects.

Because digital twins will excel in assimilation and analysis of multidimensional data and in helping make clinically relevant decisions, medical digital twins will impact discovery science and hypothesis testing in the field. In addition, digital twins offer promise for the field of radiation oncology by developing an expanded, personalized "biological" dose. This will involve optimizing the physical dose to the patient's biology, both tumor biology and normal tissue biology. This is a long term goal that is sorely needed in radiation oncology, and across medicine, and something likely impossible to do without using digital twins.

## Section 10. Summary of Key Summit Perspectives

### 10.1 Introduction

The Summit attendees, program, and discussion provided a wealth of insight into the future roles and contributions that will be important to a successful future for virtual human models and medical digital twins. The following perspectives were selected to summarize and highlight key areas central to the success of medical digital twins.

### 10.2 Consolidated Perspectives

**Definition.** There are potentially multiple definitions for digital twins that will inhibit harmonization and introduce ambiguity in the use of medical digital twins. An agreed upon definition and maturity model would be potentially useful to the community.[8]

**Healthy.** A personal baseline of "healthy" state is needed to effectively deploy individual medical digital twins to achieve the full potential benefit. Currently, standardized normal clinical ranges, while providing valuable guidance, are likely not always optimal or appropriate for a given individual. Several suggestions were offered as ways to establish a baseline and subsequently update that baseline. These potential avenues include:

- Sequence newly born babies to then be able to observe disease risk and with ongoing monitoring discern between disease progression and non-progression.
- Utilize databases of countries that have collected healthy patient data and consider collecting health patient data in the US so there is a baseline of data where disease is not knowingly present.
- Consider having a full body ultrasound as part of an annual checkup.
- Incorporate studies of human development to provide a stronger background for the healthy baseline for individuals, even in the context of chronic disease.

**Data**. Data remains a central element in the success of virtual human models and fit for purpose medical digital twins. The topic of data was prevalent in all sessions of the Summit. With specific observations presented previously within the sessions discussed, the discussions at the Virtual Human Global Summit revolved around the following key aspects:

- *Data availability* – the necessary observations were completed, and data captured
- *Data accessibility* – the data exist and are available for use
- *Data interoperability* – the data can be aligned syntactically and semantically into a coherent and accurate longitudinal representation sufficient for use with the medical digital twin of interest
- *Data quality* – the data are of sufficient quality for use with the digital twin of interest to inform the desired insights

[8] This challenge has been addressed with the release of the December 2023 NASEM Digital Twin report which occurred following the October 2023 Virtual Human Global Summit. The definition provided by the NASEM report has been utilized for this VHGS report.

### 10.3 The Central Role of the Patient in Virtual Human Models and Medical Digital Twins

The Summit placed a high emphasis on the patient as the central focus and primary beneficiary of deploying medical digital twin approaches. Realizing that individual patient-focused medical digital twins will be developed to support insights into specific questions, a broad range of virtual human models will be developed and refined in the process. Education will be essential for the patient to achieve full patient participation. With the patient experience at the center, two key perspectives were shared and highlighted.

- Output from digital twin predictive modeling must be understandable by patients and their families and caregivers and be accessible to users with variable reading levels and medical literacy. The output format should be usability tested prior to widespread use.

- Output from medical digital twin modeling must be easily integrated into the physician and medical team workflow, require minimal physician input, and be tested for usability before adoption.

### 10.4 Research into Virtual Human Models and Medical Digital Twins

Multiple workshops, meetings, and reports regarding Digital Twins research can be reviewed on the HHS Interagency Modeling and Analysis Group (IMAG) Digital Twins wiki site (https://www.imagwiki.nibib.nih.gov/working-groups/digital-twins).
The earlier work was noted to have dated back to the group's 2019 multiscale modeling meeting (https://www.imagwiki.nibib.nih.gov/imag-events/integrating-machine-learning-multiscale-modeling-biomedical-biological-and-behavioral). At the IMAG meeting the promise of virtual twins as noted in the radiation oncology section above was noted but no specifics were discussed because programs were not yet released to the public at the time of the Virtual Human Global Summit. The fact that medicine was doing digital twins in small areas was noted.

Research in medical Digital Twins has, in some ways, been ongoing for a long time in small pockets of medicine, The synergies and collaborative science brought forward by the Summit will greatly benefit these and other areas of medicine. One example that was shared is radiation treatment planning. For example, integrating the concept of relative biological effect visualization (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862688/) in these plans, initiates multidimensional approaches. To date, these efforts have had limited impact because they are employed in very small areas of radiation oncology research focused on hadron therapy and did not reach mainstream thought until recently when the idea of biological dose became recognized as a critical goal for the field.

Computational neuroscience is another example of medical research that was discussed at the Summit. For decades, computational neuroscience has used what amounts to digital twins, by employing multiscale modeling to study of brain electrical activity. Current areas of research in computational neuroscience include epilepsy, traumatic brain injury, ischemic (brain) disease, neurorehabilitation, drug addiction, schizophrenia, and neurostimulation.

A third example of digital twin research being present in a nascent form is in infectious disease and the study of how infections spread, such as the worldwide COVID-19 pandemic. A common perspective in discussions at the Summit was that likely all aspects of what is now called precision medicine will benefit from digital twins, particularly if focused on adding timescales.

### 10.5 Artificial Intelligence and the Future of Virtual Human Models and Medical Digital Twins

By integrating AI techniques such as machine learning and deep learning into computational human models, virtual human representations can evolve beyond static simulations to dynamic, adaptive entities that continuously learn and improve from data. Furthermore, AI surrogate models will enable rapid adaptations and predictions when detailed biological models are either unavailable or computationally expensive to derive.

### 10.6 The Role of Computing and the Future for Virtual Human Models and Medical Digital Twins

High Performance Computing (HPC) and co-design are pivotal for advancing virtual human models and medical digital twins. HPC provides the computational muscle necessary for intricate, multi-scale simulations, while co-design principles optimize the synergy between software algorithms and hardware architectures, enhancing computational efficiency and modeling performance. This approach also fosters interdisciplinary collaboration, bridging the gap between computational scientists, biomedical researchers, and hardware architects. Furthermore, the interleaving of modeling and simulation with artificial intelligence required to advance human digital twins pushes the boundaries of supercomputing by driving innovation in hardware design, algorithmic development, and scalability.

Due to the computational complexity of the challenge, supercomputer-based implementation of ad-hoc algorithms should become a substrate on which the virtual human twin will be rooted. New computer architectures, new programming models and languages, and new mathematical methods should be involved in co-design strategies. This is a successful paradigm which is not at all new, it has already been observed in applied science (notably in the cases of the mature AI and the nascent quantum computing, in which architectures and algorithms are co-developed).

It is worth mentioning that a supercomputer today will be a workstation in 10 years and a laptop in 20 years. Developing for current supercomputers is both timely and future-oriented, when virtual human models and medical digital twins will contribute to the standard of care.

### 10.7 Building Trust through Stakeholder Engagement

Incorporating diverse stakeholder engagement in the development of digital twins is crucial for ensuring fairness and equity in these advanced tools. Transparent collaboration across patients, healthcare providers, policymakers, and technologists are necessary to address varied perspectives and needs effectively. This inclusive approach guarantees that digital twins reflect diverse health dynamics and social determinants accurately. Transparency throughout the digital twin lifecycle—from design to deployment—enhances trust and facilitates equitable access to these technologies. By openly sharing updates, methodologies, and impacts, stakeholders can collectively ensure that digital twins serve as fair, unbiased, and universally beneficial healthcare solutions.

### 10.8 Community Involvement and Engagement

Using virtual human models to inform healthcare will require engagement with and understanding of the needs of a broad community of stakeholders with very diverse backgrounds. For patients, people with lived experience and clinicians, it will be critical to understand their perception of DT technology and to surface and address their concerns around data ownership and financial cost, so that others in the DT ecosystem are able to shape the technology to meet these needs. At the same time, a deeper public and clinical understanding of the potential benefits for using personalized digital twins for healthcare and treatment strategies will be needed to enhance the uptake of the technology in regular clinical usage and to instill public confidence in its use. It will also be necessary to advocate for beneficiaries of the technology to influence policymaking within the healthcare and broader public sectors. The concerted effort required to deliver each of these key aspects builds on the philosophy of co-design that has been adopted in the development of human digital twin technology, to date. By recognizing this and broadening the community engaged in the co-design of virtual human models, we will be able to accelerate the pace at which digital twins are able to be used to as a healthcare solution to inform clinical decision-making.

### 10.9 Community Health Systems

The community health systems will be central to the future success and impact of medical digital twin approaches providing the connection to the broader patient base and healthcare professional cohort. Though interested in improving patient outcomes, operational constraints (e.g. financial, fully assigned personnel, adherence to standard of care) create a challenging environment for initial adoption of medical digital twins. Early medical digital twin approaches will need to improve operational or care decisions without negatively impact the clinical workflow to establish a favorable long-term environment for future medical digital twin innovations.

### 10.10 International Collaborations

International collaborations provide unique opportunities to advance virtual human models and the development of medical digital twins. The global community already collaborates internationally in disease specific areas (e.g. Global Alliance for Genomics and Health) and technical standards (IEEE), providing examples and potential avenues for international collaboration in other domains supporting virtual human models and medical digital twins. Multinational efforts are also prevalent such as CompBioMed and EDITH, both European efforts to advance digital twins for health, also serving as both exemplars and communities to engage in the broader development of virtual human models and medical digital twins.

International collaborations hold potential to advance virtual human models and medical digital twins through cooperative development and sharing of technology even as the movement of data among countries is restricted. Technical approaches hold potential for evaluation and cross-validation across international boundaries where medical systems may be more receptive to early adopters of medical digital twin approaches.

## Section 11. Acknowledgments

The organizers of the Virtual Human Global Summit wish to first acknowledge the Summit attendees who shared their expert insights and experiences Summit to foster the global improvement of wellness and health outcomes through collaboration and future applications of medical digital twins.

The organizers also wish to acknowledge the many presenters and panelists who provided outstanding contributions serving as a basis for key discussions in the Summit.

The organizers also wish to acknowledge sponsors contributing to the collaborative environment of the Summit including Brookhaven National Laboratory, NY Data Science Initiative, Catawba-Mohawk Accelerated Intelligence, Eviden, Frederick National Laboratory for Cancer Research, Datavault Holdings, JLL, and University College London.

A portion of activities related to this report have been funded in whole or in part with Federal funding by the NCI-DOE Collaboration established by the U.S. Department of Energy (DOE) and the National Cancer Institute (NCI) of the National Institutes of Health (NIH), Cancer Moonshot Task Order No. 75N91019F00134 and under Frederick National Laboratory for Cancer Research Contract 75N91019D00024. This work was performed under the auspices of the U.S. Department of Energy by Argonne National Laboratory under Contract DE-AC02-06-CH11357, Lawrence Livermore National Laboratory under Contract DE-AC52-07NA27344, and Oak Ridge National Laboratory under Contract DE-AC05-00OR22725.

## Appendix A. Virtual Human Global Summit Organizational Attendee List

*Amazon Web Services*

*Ansys*

*Argonne National Laboratory*

*Barcelona Supercomputing Center*

*Boston College*

**Brookhaven National Laboratory*

*Cancer Registry of Norway*

*Catawba Mohawk Accelerated Intelligence*

*Columbia University*

*Cornell University*

*Data Vault Holdings, Inc.*

*Digital Twin Consortium*

*Duke University*

*EcoLong LLC*

*ELEM Biotech*

*Ellison Institute of Technology*

**Eviden*

**Frederick National Laboratory for Cancer Research*

*Georgetown University*

*GreyBird Ventures*

*Healthcare IT Leaders*

*Healthero*

*Herne Law*

*Indiana University*

*Institute for Systems Biology*

*Institute of Nuclear Medicine*

*IPQ Analytics LLC*

*JLL*

*Johns Hopkins School of Medicine*

*Lawrence Livermore National Laboratory*

*Los Alamos National Laboratory*

*Marks DiPalermo Wilson PLLC*

*Microsoft*

*N-formatix, llc*

*National Cancer Institute*

*NIH-National Institute for Biomedical Imaging and Bioengineering*

*Northwell Health*

*Oak Ridge National Laboratory*

*Open Health Systems Laboratory Inc.*

*P-Chip Corporation*

*Robert Morris University*

*Simons Foundation*

*Stanford University*

*Tewathahonni Corporation / Saint Regis Mohawk Tribe*

*Twinome Health*

**University College London*

*University of Maryland at Baltimore County*

*University of Texas MD Anderson Cancer Center*

*University of Vermont*

*Viome Life Sciences Inc.*

*Weil Cornell*

*Westchester County*

*Yale University*

**Organizing Committee*

## Appendix B. Virtual Human Global Summit Individual Attendees

| *Attendee* | *Institution* |
|---|---|
| *Acker, Rachael* | *Healthero* |
| *Aguado Sierra, Jazmin, PhD* | *Barcelona Supercomputing Center* |
| *Alexander, Francis, PhD* | *Argonne National Laboratory* |
| *An, Gary, MD, FACS* | *University of Vermont* |
| *Atif, Mohammad, PhD* | *Brookhaven National Laboratory* |
| *Banavar, Guruduth* | *Viome Life Sciences Inc.* |
| *Black, Sean T.* | *Frederick National Laboratory for Cancer Research* |
| *Bell, Jason* | *JLL* |
| *Blayney, Douglas, MD* | *Stanford University School of Medicine* |
| *Borkon, Lynn* | *Frederick National Laboratory for Cancer Research* |
| *Bubeck, Robert (Bob)* | *Data Vault Holdings, Inc.* |
| *Buchsbaum, Jeffrey, MD, PhD, AM* | *National Cancer Institute* |
| *Cahill, John* | *JLL* |
| *Carbone, Matthew* | *Brookhaven National Laboratory* |
| *Chatterjee, Ansu, PhD* | *University of Maryland at Baltimore County* |
| *Chung, Caroline, MD, MSc. FRCPC, CIP* | *University of Texas MD Anderson Cancer Center* |
| *Coughlin, Robert* | *JLL* |
| *Coveney, Peter, PhD* | *University College London* |
| *Cushing, Edward (Eddie)* | *Data Vault Holdings, Inc.* |
| *Del Valle, Sara, PhD* | *Los Alamos National Laboratory* |
| *DiPalermo, Christian* | *Marks DiPalermo Wilson PLLC* |
| *Elemento, Olivier, PhD* | *Weil Cornell* |
| *Glascoe, William* | *Robert Morris University* |
| *Govang, Patrick* | *Cornell University* |
| *Greenspan, Emily, PhD* | *National Cancer Institute* |
| *Hadjisavas, Michael* | *P-Chip Corporation* |
| *Harvey, Richard (Bill)* | *JLL* |

| | |
|---|---|
| *Hendriks, Bart* | *Twinome Health* |
| *Hernandez-Boussard, Tina, PhD, MPH, MS* | *Stanford University* |
| *Herne, Owen* | *Herne Law* |
| *Hudson, Florence, BSE* | *Columbia University* |
| *Isaacs, Dan* | *Digital Twin Consortium* |
| *Isenberg, Natalie, PhD* | *Brookhaven National Laboratory* |
| *Jantre, Sanket Rajendra, PhD* | *Brookhaven National Laboratory* |
| *Jenkins, Ken* | *Westchester County* |
| *Jha, Shantenu, PhD* | *Brookhaven National Laboratory* |
| *Kapadia, Anuj, PhD* | *Oak Ridge National Laboratory* |
| *Kelly, Sean M.* | *n-Formatix* |
| *Kibbe, Warren, PhD* | *Duke University* |
| *Kleese van Dam, Kerstin, PhD* | *Brookhaven National Laboratory* |
| *Koster, James (Jay)* | *JLL* |
| *L Rocha, Heber, PhD* | *Indiana University* |
| *Lee, Jerry, PhD* | *Ellison Institute of Technology* |
| *Liebman, Michael, PhD* | *IPQ Analytics LLC* |
| *Lin, Meifeng, PhD* | *Brookhaven National Laboratory* |
| *Litster, Steve, PhD* | *Amazon Web Services* |
| *Lopez-Marrero, Vanessa, PhD* | *Brookhaven National Laboratory* |
| *Lubben, James, PhD* | *Boston College* |
| *McCoy, Matthew, PhD* | *Georgetown University* |
| *McDaniel, John* | *Healthcare IT Leaders* |
| *McGibbon, Graham* | *Healthero* |
| *Miller, Tom* | *GreyBird Ventures* |
| *Min, Judy* | *EcoLong LLC* |
| *Min, Nancy* | *EcoLong LLC* |
| *Mitchell, Allyson* | *Catawba Mohawk Accelerated Intelligence* |
| *Nandi, Tarak, PhD* | *Argonne National Laboratory* |

| | |
|---|---|
| *Niecikowski, Andrew* | *Yale University* |
| *Nissley, Dwight, PhD* | *Frederick National Laboratory for Cancer Research* |
| *Nygård, Jan, PhD* | *Cancer Registry of Norway* |
| *Palmer, Mark* | *Ansys* |
| *Paradis, Marc, PhD* | *Northwell Health* |
| *Peng, Grace C.Y, PhD* | *National Institutes of Health (NIH)-National Institute of Biomedical Imaging and Bioengineering (NIBIB)* |
| *Phillips, Marvin* | *Catawba Mohawk Accelerated Intelligence* |
| *Pilch, Rich, PhD* | *Lawrence Livermore National Laboratory* |
| *Pouchard, Line, PhD* | *Brookhaven National Laboratory* |
| *Quinn, James* | *JLL* |
| *Rasheed, Adam, PhD* | *Amazon Web Services* |
| *Saboury, Babak* | *Institute of Nuclear Medicine* |
| *Sauerwald, Natalie* | *Simons Foundation* |
| *Shmulevich, Ilya, PhD* | *Institute for Systems Biology* |
| *Shrum, Christopher, PhD* | *Catawba-Mohawk Accelerated Intelligence* |
| *Smedira, Carrie* | *Microsoft* |
| *Spencer, Michals* | *Data Vault Holdings, Inc.* |
| *Srivastava, Anil* | *Open Health Systems Laboratory Inc.* |
| *Stahlberg, Eric A., PhD* | *Frederick National Laboratory for Cancer Research* |
| *Stubbs, John* | *Eviden* |
| *Terrance, Nicole* | *Tewathahonni Corporation / Saint Regis Mohawk Tribe* |
| *Thompson, Brandon* | *Microsoft* |
| *Tourassi, Georgia, PhD* | *Oak Ridge National Laboratory* |
| *Townsend-Nicholson, Andrea, PhD* | *University College London* |
| *Trulson, Derek* | *JLL* |
| *Urban, Nathan, PhD* | *Brookhaven National Laboratory* |
| *Vazquez, Mariano, PhD* | *ELEM Biotech* |
| *Yoo, Shinjae, PhD* | *Brookhaven National Laboratory* |
| *Yusufaly, Tahir, PhD* | *Johns Hopkins School of Medicine* |

## Appendix C. Virtual Human Global Summit Program

### Virtual Human Global Summit Program

*Making Connections to Advance Human Digital Twins in Medicine*
*(All sessions will be held in the SUNY Global Center Global Classroom*)

**Day 1 – Foundations for Virtual Human Models and Medical Digital Twins**

**7:00 am – 8:00 am – Continental Breakfast**
*On-site at SUNY Global Center, New York City*

**8:00 – 8:50 am Virtual Human Global Summit Welcome and Opening Remarks**

- Peter Coveney, University College London
- Kerstin Kleese Van Dam, Brookhaven National Laboratory
- Eric A. Stahlberg, Frederick National Laboratory for Cancer Research

**9:00 am – 11:45 am Session A – Virtual Human Models and Biomedical Digital Twins in Research**

***Session Moderator: Kerstin Kleese van Dam, Brookhaven National Laboratory***
*Each talk will be 10 minutes, plus 5 minutes for questions and answers.*

This session will cover topics that are research efforts and preclinical applications in human digital twins covering molecular, cellular, and multiscale models, AI and mechanistic models, physiological models, disease-specific models and other predictive approaches to human biology and physiology.

**9:00 am – 10:00 am – Talk session A-1**

- Peter Coveney (University College London)
  *Digital Twins: The Virtual Future of Medicine*
- Heber Lima da Rocha (Indiana University)
  *Multiscale Modeling and Data Assimilation: A Path to Personalized Medicine*
- Dwight V. Nissley (Frederick National Laboratory for Cancer Research)
  *The NCI-DOE ADMIRRAL Consortium – Predictive Computational Biology for Modeling Cancer Mechanisms*
- Ilya Shmulevich (Institute for Systems Biology)
  *Acute Myeloid Leukemia Digital Twin*

**10:00 am – 10:15 am – Break**

**10:15 am – 11:15 am – Talk session A-2**

- Mariano Vasquez (ELEM Biotech)

*Supercomputer-based Virtual Humans: The Future of Medicine NOW*

- Jazmin Aguado-Sierra (Barcelona Supercomputing Center)
  *In Silico Clinical Trials*
- Daniel R. Isaacs (Digital Twin Consortium)
  *Accelerating the Adoption of Digital Twins*
- Matthew McCoy (Georgetown University)
  *Parameterizing and Interpreting Biomedical Digital Twins*

**11:15 am – 11:30 am – Break**

**11:30 am – 12:15 pm – Moderated Panel Discussion A**

Topic: "Challenges, Needs, and Opportunities for Research and Pre-clinical Biomedical Digital Twins"
*Panelists:*

- Ilya Shmulevich (Institute for Systems Biology)
- Jazmin Aguado-Sierra (Barcelona Supercomputing Center)
- Heber Lima da Rocha (Indiana University)
- Mariano Vasquez (ELEM Biotech)

**12:15 pm – 1:30 pm – Day 1 Networking Lunch**
*Lunch will be onsite at SUNY Global Center. Participants are encouraged to network and meet with other attendees.*

**1:30 pm – 4:15 pm Session B – Infrastructure for Digital Twins in Biomedicine**

This session will cover computing, data science and computational science related to digital twins, including cloud, exascale, data and model sharing, digital twin operations, privacy, data sources, future data streams, frameworks, and FAIR approaches.

***Session Moderator: Eric Stahlberg, Frederick National Laboratory for Cancer Research***
*Each talk will be 10 minutes, plus 5 minutes for questions and answers.*

**1:30 pm – 2:15 pm – Talk session B-1**

- Francis (Frank) Joseph Alexander (Argonne National Laboratory)
  *On the Mathematical and Computational Challenges for Digital Twins of Complex Systems*
- Daniel R. Isaacs (Digital Twin Consortium)
  *Transforming Healthcare and Life Science with Digital Twins*
- Vanessa Lopez-Marrero (Brookhaven National Laboratory)
  *Predictive Digital Twin Framework Supported by Measure Transport Techniques*

**2:15 pm – 2:30 pm – Break**

**2:30 pm – 3:15 pm – Talk session B-2**

- Line C. Pouchard (Brookhaven National Laboratory)
  *Perspectives on Reproducibility of Data-driven Modeling Experiments Towards Responsible AI for Digital Twins*
- Anuj J. Kapadia (Oak Ridge National Laboratory)
  *From Individual Cells to Human Populations: A Multiscale Virtual Human approach to Radiation Dosimetry*
- Florence Hudson (Columbia University)
  *TIPPSS for Clinical IoT Privacy and Security*

**3:15 pm – 3:30 pm Break**

**3:30 pm – 4:15 pm – Moderated Panel Discussion B**
Topic: "The Global Learning Ecosystem for Biomedical Digital Twins from Research to Patient"
*Panelists:*

- Warren A. Kibbe (Duke University)
- Stephen Litster (Amazon Web Services)
- Kerstin Kleese Van Dam (Brookhaven National Laboratory)
- Georgia (Gina) Tourassi (Oak Ridge National Laboratory)

**4:15 pm – 4:30 pm – Day 1 Concluding Remarks**

**4:30 pm – 4:45 pm – Reception Sponsor Remarks**

**4:45 pm – 6:00 pm – Networking Reception**

**Location: SUNY Global Center, Terrace**

*Note to attendees: The Virtual Human Global Summit plans no evening events, allowing flexibility for attendees to network and connect with other attendees in accordance with their interests and preferences. Contact information for attendees will be provided to participants.*

**End of Day 1**

## Day 2 – Virtual Human and Medical Digital Twins Transforming Medicine

**7:00 am – 8:00 am – Continental Breakfast**
*On-site at SUNY Global Center*

**8:00 am – 8:15 am – Day 2 Welcome**
- Peter Coveney, University College London
- Kerstin Kleese Van Dam, Brookhaven National Laboratory
- Eric A. Stahlberg, Frederick National Laboratory for Cancer Research

**8:15 am – 9:00 am – Opening Presentation**
- Jerry Lee, Chief Science and Innovation Officer, Ellison Institute of Technology

  *Building Patient Journey Trajectories: Lessons Learned and Future Opportunities*

**9:00 am – 11:45 am Session C – Biomedical Digital Twins in Practice**

This session covers experiences and anticipated clinical use of medical digital twins – pediatrics, cancer, infectious disease, ICU care, telemedicine, etc. The session topics may also explore the potential for new data sources and personal use of medical digital twins.

***Session Moderator: Peter Coveney, University College London***
*Each talk will be 10 minutes, plus 5 minutes for questions and answers.*

**9:00 am – 9:45 am – Talk Session C-1**
- Caroline Chung (The University of Texas MD Anderson Cancer Center)

  *Practical Digital Twins for Personalized Oncology*
- Gary An (University of Vermont)

  *Critical Illness Digital Twins: Integrating Mechanistic Simulation Models with Artificial Intelligence for Personalized Precision Prediction and Control for Sepsis*
- Marc Paradis (Northwell Health)

  *Merlin's Mirror: A Vision for Digital Twins in Healthcare*

**9:45 am – 10:00 am – Break**

**10:00 – 10:45 am – Talk Session C-2**

- Douglas W. Blayney (Stanford Medicine (emeritus), Stanford University School of Medicine)

  *What Questions do Cancer Patients Have, and How Can Digital Twins Help?*

- Olivier Elemento (Weil Cornell Medical Center)

  *From Cancer Models to Digital Avatars - Building Virtual Models of Cancer*

- Guruduth (Guru) Banavar (Viome Life Sciences)

  *Human-microbiome Gene Expression Models for Biomedical Digital Twin Applications*

**10:45 am – 11:00 am – Break**

**11:00 am – 12:00 pm – Moderated Panel Discussion C**

Topic: "Challenges and Opportunities for Biomedical Digital Twins in Practice"
*Panelists:*

- John P. McDaniel (Healthcare IT Leaders)
- Jeffrey (Jeff) Buchsbaum (National Cancer Institute)
- Jan F. Nygard (Norwegian Cancer Registry)
- Marc Paradis (Northwell Health)

**12:00 pm – 1:00pm – Day 2 Networking Lunch**
*Lunch will be onsite at SUNY Global Center. Participants are encouraged to network and meet with other attendees.*

**1:00 pm - 1:30 pm Lightning Talks Session**

*This session will consist of brief talks (5 minutes).*

***Session Moderator: John Stubbs, Eviden***

**1:30 pm – 2:15 pm Session D – Supporting Biomedical Digital Twin Efforts**

This session will bring insights to and discussion around past, present and potential future support for biomedical digital twin efforts, with an initial focus on governmental efforts in the US, EU and extending to other potential sources.

***Session Moderator: Eric A. Stahlberg, Frederick National Laboratory for Cancer Research***

**1:30 pm – 2:15 pm – Moderated panel discussion D**
Topic: "Government-supported Biomedical Digital Twin Efforts"
*Panelists:*

- Caroline Chung (The University of Texas MD Anderson Cancer Center)
- Peter Coveney (University College London)
- Emily Greenspan (National Cancer Institute)
- Grace Peng (National Institutes of Health)

**2:15 pm – 2:30 pm – Break**

**2:30 pm – 4:30 pm – Session E – Community Adoption and Path Forward for Medical Digital Twins**

This session covers topics related to fostering community adoption and identifying potential next steps to move ahead with medical digital twins including, education, workforce development, physical infrastructure, commercialization, regulatory, public-private partnerships, international efforts, and collaborations.

***Session Co-Moderators: John Stubbs, Eviden; Eric A. Stahlberg, Frederick National Laboratory for Cancer Research***
*Each talk will be 10 minutes, plus 5 minutes for questions and answers.*

**2:30 pm – 3:15 pm – Talk Session E**

- Tina Hernandez-Boussard (Stanford University)
  *Building Trust and Momentum: The Future of Medical Digital Twins*
- Andrea Townsend-Nicholson (University College London)
  *Community Engagement: Shaping the future for Virtual Humans*
- Michael N. Liebman (IPQ Analytics)
  *Digital Twins: Fraternal or Identical?*

**3:15 pm – 3:30 pm – Break**

**3:30 pm – 4:30 pm – Moderated Panel Discussion E**
Topic: "Laying the Course for the Future of Medical Digital Twins and Virtual Human Modeling"

- Tina Hernandez-Boussard (Stanford University)
- Andrea Townsend-Nicholson (University College London)
- Michael N. Liebman (IPQ Analytics)
- Robert Coughlin (JLL)

**4:30 pm – 5:00 pm – Virtual Human Global Summit Closing Remarks**

- Peter Coveney, University College London
- Kerstin Kleese Van Dam, Brookhaven National Laboratory
- Eric A. Stahlberg, Frederick National Laboratory for Cancer Research

**5:00 pm Summit Concludes**