

LIFE SCIENCES & HEALTHCARE

VIRTUAL TWIN EXPERIENCES IN HEALTHCARE: NEXT GENERATION PRECISION MEDICINE



PREFACE

At the cusp of a new era, where the boundaries between the physical and digital worlds are blurring, Dassault Systèmes envisions a future driven by the seamless convergence of the virtual and real. Our "From Things to Life" manifesto articulated this paradigm shift - from decades of designing inert products to a sustainable future that harmonizes product, nature, and life experiences through the virtual world.

Healthcare stands at the forefront of this transformation. The imperative to provide precision care tailored to each patient's unique biology necessitates a new approach that transcends conventional practices. Virtual twin experiences of humans represent the next frontier, enabling us to comprehend, explore, and optimize the depths of human physiology and healthcare systems with unprecedented fidelity.

This white paper outlines our vision for next-generation precision medicine powered by virtual twin experiences spanning individual patients to entire healthcare systems. It outlines how integrating multi-scale modeling,

simulation, and real-world data can revolutionize clinical decisions, therapeutic design, care delivery, and public health management.

From virtual cardiac twins that amalgamate genomic and imaging data to guide personalized treatments, to hospital twins optimizing resources through predictive analytics, to system-wide twins informing pandemic response strategies - we open new pathways to navigate the complexity of human health and disease. This paradigm shift empowers patients as partners, enhances provider efficiency, reduces costs, and unlocks innovation to address unmet medical needs.

We provide the foundational architectures to realize this vision by bridging the virtual realm of data-driven, model-based simulations with the physical world of healthcare delivery. Collaborating with our rich ecosystem of partners and tapping into the collective imagination of the global healthcare community, we can co-create a future where virtual twins become catalysts for hyper-personalized, sustainable healthcare for all.

This paper marks not just an aspiration, but a call to action to collectively experience the fusion of products, nature, and life through virtual twins. A pivotal moment to reimagine healthcare in the image of the human for all humans.



Figure 1. 3 types of virtual twin experiences are needed to achieve medical practice excellence and value-based care: virtual twin experience of individual patients or populations, virtual twin experiences of a hospital or care center, virtual twins of entire healthcare systems.

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EXECUTIVE SUMMARY

The global healthcare industry has reached a tipping point. Overwhelmed by the complexities of diverse regulations, aging populations, and increasing demands for more precise and personalized treatments, it has become financially unsustainable. Unlike others that offer band-aid AI solutions that simply mask the problems, this white paper outlines a systematic transformation from today's massively fragmented, data-driven systems to scalable, knowledge based virtual twin experiences as the optimal way to meet these challenges.

KEY POINTS:

1. Virtual twins help navigate massive data complexity by integrating science with machine learning and AI to analyze vast data sets, identify key relationships, and automate routine tasks. This enhances decision-making, reduces human error, and improves patient outcomes.
2. Use of Virtual Twins should be built upon three key pillars:
 - I. Patient experiences that offer a detailed, dynamic representation of the human body and individual health conditions. By integrating data from biosciences, material sciences, and information sciences, virtual twins provide a comprehensive understanding of human anatomy and physiology, enabling precise diagnostics and patient-centric, personalized treatment planning.
 - II. Hospital structure and operations can be optimized by simulating design, layout, operating conditions as well as staff and patient workflows. Improvements to the entire patient journey can be envisioned and changes to overall operational efficiency can be safely evaluated.

III. Entire healthcare systems can be represented at a functional level, aiding policymakers in critical processes such as resource allocation, public health strategy optimization, and evidence-based policymaking.

3. The **3DEXPERIENCE®** and Medidata platforms provide secure foundations for healthcare solutions powered by virtual twin experiences. Real-world data can be used to simulate patient populations, systemic treatment effects and long term outcomes. Researchers can perform complete in silico clinical trials or construct synthetic control arms that not only accelerate the development of new innovations, they also reduce the uncertainty and scale of physical trials, improve success rates, and lower overall costs..

FUTURE OUTLOOK:

Virtual Twin experiences will redefine healthcare practices as they have in all other industries that have successfully navigated digital transformations.. Patient-centric, multidisciplinary care is enabled, while enhanced diagnostic and treatment accuracy translates to operational efficiency gains. Generative machine learning methods combine proven multiscale/multiphysics simulation of complex systems with curated databases of patient experience to create trustworthy medical processes that are scalable and efficient, ensuring better patient journeys and outcomes. Healthcare becomes more predictive, preventive, and patient-enabled.



INTRODUCTION

In today's globally diverse healthcare landscape, the industry finds itself at a crucial crossroads. At the frontlines are patients demanding greater participation in their healthcare, while often making choices driven by economics or lifestyle without the ability to understand the medical implications. It is a time of unprecedented complexity, with increasing and diverse global regulations leading to unsustainably escalating costs. All of this in the context of public pressure for more personalized and effective treatments - while the number of medical professionals cannot keep up with demand. As we define healthcare for the 21st century, for the first time in history we must prioritize sustainability in terms of resources; natural, human and financial. As all other industries have done, the history of trial-and-error medicine must be just that... history.

Throughout the modern era, industries from transportation or mining to high-tech and consumer goods have reckoned with similar, conflicting and overwhelming demands. In the face of overpowering complexity, they turned toward the development of virtual twin experiences. This has allowed them to experience the design, manufacturing and use of their product or service, optimizing the tradeoffs of cost, performance, safety, aesthetics etc., before committing to physical production costs. This "get-it-right-the-first-time" approach has resulted in precision and efficiency in the most complex of product development processes. Today we see a complete transformation of these industries, who are now reaping the benefits of using virtual twin experiences across the lifecycle of new products. We all witness the pace and breadth of innovation it has enabled in the products we buy.

Healthcare, with the stakes higher and the need even greater, has no other option than to embrace this sustainable mindset. Fortunately, technology is now capable of providing what had been missing; medically relevant virtual twin experiences for the human body. That opens the door to a transformation that is not limited to what happens inside the body, it can include the full patient journey. Virtual twin experiences can enable healthcare systems leaders to imagine a new generation of care centers, designed to work in tandem with today's mobile lifestyle to optimize the efficiency and quality of diagnostic and treatment environments, allowing patient-centric medicine to become a reality.

To make this work while reducing the overall cost of care, new models for the administration of these patient care systems will need to be constructed. Ones with better alignment between the financial goals of the caregivers and payers, so each benefit when the public is healthier. These systems must reflect a

greater empowerment of the public to engage in preventative care and provide incentives for caregivers that create both the time and rewards for precision. While it may be impossible to imagine modern healthcare achieving an "engineering level" of accuracy in diagnosis and treatment, a commitment to its principles, where inefficiencies are systematically erased and the only acceptable errors are those predetermined to have negligible impact on outcomes are a worthy goal.

Our vision for the future incorporates the six core factors driving change:

1. From passive care recipients to empowered patients
2. From "one-size fits all" to personalized therapies
3. From fee-for-service to value based care
4. From overloaded to augmented physicians
5. From siloed care to coordinated patient journeys
6. From treatment to prevention

This white paper advocates a transformational approach to realizing this vision, while creating collaborative virtual twin experiences emerge as pivotal processes for reconciling these paradoxes.

This is not a wholly new idea, but it is one whose time has come. The virtual twin of a patient has emerged from more than a decade of fundamental science, demonstrating that virtual twin experiences of the human body are now feasible and are poised to become essential to the future of healthcare. They enable a novel, truth-based approach to healthcare. An approach that is human-centric, collaborative, integrative, and grows increasingly precise and more cost effective over time, positioning itself to be the cornerstone of modern medical care.

Dassault Systèmes, a leader in virtual twin experiences, has been at the forefront of this movement, dedicating decades to research, strategic partnerships and showcase studies. The company's **3DEXPERIENCE** platform, with its deep-rooted understanding of physics, biology, and chemistry, has led to significant advancements in creating organ twin experiences and system models, virtual clinical cohorts as well as complex hospital environments. Further, from its outset, the MEDIDATA platform has continually redefined clinical trial management, data analytics and patient engagement in the modern era, with scalability only possible through virtualization. At their foundations, both platforms facilitate medical research collaboration globally while maintaining high level security measures to assure the protection of medical data.



VIRTUAL TWIN EXPERIENCES: THE CORNERSTONE OF MODERN HEALTHCARE

THE UNIVERSAL CONCEPT OF THE VIRTUAL TWIN EXPERIENCE

Experiences are uniquely human and are about utilizing art, science and technology to imagine and create a better world for all. In the complex, interconnected modern world, they are essential to allow us to create a sustainable future. Virtual twin experiences have transformed major industries such as aerospace and automotive, emerging as the ideal way to create what you can imagine. Virtual twin experiences let you visualize, model and simulate the behavior of the most complex system, to understand them, explore novel approaches and ultimately deliver exactly what you need.

Because they are virtual, they are boundless and facilitate sustainable innovation across the full product lifecycle. Their utility doesn't end when a product or process is created. They allow for synchronization between data from the real-world and the twin to mirror its experience, revealing information that would otherwise be lost or predict when maintenance is needed. Because they are built on physical laws and validated scientific principles, they are not limited by past experience. They can use these principles to simulate future behavior, providing experiences that have yet to happen, delivering insights that allow for proactive decision-making. Distributed teams can gain a full understanding of the current state, or run "What if" scenarios sharing the same experience maximizing the use of their collective expertise.

Today, virtual twin experiences are poised to bring a similar transformation to healthcare. How is this possible? Much like the success of a new commercial jet relies on virtual twin experiences of that jet as the single-source-of-truth, whether it is for design, manufacture or operation, healthcare must become efficient at creating virtual twin experiences of the human as its foundation. Virtual human twin experiences on the **3DEXPERIENCE** platform integrate modeling, simulation,

information intelligence and collaboration. They bring together biosciences, material sciences and information sciences to create a complete virtual living model. By centralizing human understanding, they provide an enhanced understating of the human body's complexity – from DNA to tissues, organs and the organism as a whole.

They can be used to imagine and test new treatments using a human environment from the start. To experience the care journey from healthy to sick and back again. To design healthcare treatment experiences with not just the structures and machines in mind, but the people as well. It can redefine the regulatory pathway or help practitioners prepare for, and execute new surgical techniques combining the science of the human body with best-in-class experience. And, just as modern aircraft transmit data from sensors on their engines to anticipate maintenance before a problem arises, MEDIDATA Patient Cloud can aggregate relevant patient information to enable a preventative care system.

Today, we see in the literature many examples of virtual twin experiences of a patient's anatomy, many created within the Living Heart and Living Brain projects. More recently, we are also seeing virtual twin experiences that go beyond the individual patient and encompasses a physical treatment area or even the entire healthcare facility to create more patient-centric care journey. We have even seen entire healthcare systems designed using virtual twin experiences, tracking all of the uncertainties and interdependencies into a manageable system model. These are becoming important components of new virtual healthcare paradigms that are driving the new medical policies that will be necessary for sustainable healthcare in the future.



NAVIGATING COMPLEXITY AND BRINGING CLARITY

Today we sit at the dawn of the complete digitalization of healthcare. We recognize this will result in a tsunami of medical data that will overwhelm a system not designed to handle it. Machine learning algorithms are well suited to digesting this data yet the inherent limitations in quality and completeness render them unreliable. It is natural for the industry, facing exponentially growing data repositories, to look to these tools to bring clarity to the intricate workings of healthcare systems. Unfortunately, they will not.

Virtual twin experiences, however, can seamlessly include generative AI methods along with modeling and simulation to unlock significant synergies and benefits, bridging the gap between predictive analytics and trustworthy personalized healthcare. AI's advanced data processing capabilities can analyze vast data sets from genetic information, medical imaging, and electronic health records to speed the construction of virtual twin experiences with unprecedented accuracy. This integration enhances the field of possibilities, enabling healthcare professionals to simulate various treatment outcomes, identify potential risks, and tailor interventions to the individual needs of patients with greater precision. Moreover, the continuous learning aspect of information intelligence ensures that virtual twin experiences evolve based on new health data, improving experience reliability and effectiveness over time. This synergy paves the way for a new era of precision medicine, where treatments are not only personalized but also continuously optimized, leading to better patient outcomes, reduced healthcare costs, and more efficient medical research processes.

APPLICATIONS ARE ACROSS ALL SCALES AND TIME HORIZONS

Why are virtual twin experiences essential? Modern healthcare represents the largest industry on the planet. One built on a fragmented, house-of-cards of understanding, leading to unprecedented complexity and what it is now clear, unsustainability. Virtual twin experiences can span all scales of healthcare, providing a rational way to decompose this complexity down to a practical level, yet still maintain the full context for each component. In this paper, we will consider three unique scales, 1) patient level, 2) hospital or care center level and 3) healthcare system level:

- The virtual twin experience of the patient, as a way to understand the disease, test different treatment options and predict outcomes. The value for the physician is to gather and share best practices, and achieve the best possible outcome for the patient. The value for the patient is to better understand their own health status and make informed decisions.
- The virtual twin experience of the hospital or the local point of care, as a way to understand the context in which the care will be provided. The value for the physician is to work in an optimized setting. The value for the patient is to experience an enhanced care journey.
- The virtual twin experience of the healthcare system itself, as a way to understand the incentives, the money flow, and to ensure affordable and accessible care at the population level.

Moreover, because virtual twin experiences draw from fundamental science and natural laws rather than pure observed data, they offer the unique ability to have a holistic understanding in space and in time. This helps to explain the past, replicate present and predict future effects of various medical treatments and health scenarios across multiple disciplines.





VIRTUAL TWIN EXPERIENCES: MODELS, SIMULATION PLUS DATA

BRIDGING HUMAN INSIGHT AND MACHINE INTELLIGENCE THROUGH VIRTUALIZATION

Virtual twin experiences can be conceptualized as a functional extension of human creativity. This perspective emerges from the understanding that people, when faced with complex problems, engage in a mental simulation process where potential solutions are visualized in our minds, albeit without the ability for empirical testing. Virtual twin experiences mirror this process by encapsulating the fundamental characteristics of the systems they represent, enhancing both the accuracy and applicability of these virtual models of real-world applications, and now with the means to test all possible solutions. Viewed in this way, modern computing technology can be considered an extension of individual or collective cognitive processes. It empowers medical professionals to augment their expert decision-making with computational modeling and machine intelligence, not as a substitute for human expertise. This integration is pivotal to advancing medical treatment accuracy and efficiency, incorporating human experience and observation, while enabling the processing of information at speeds and scales that are beyond human capability.

It is important to recognize that when Generative AI methodologies are employed without the contextual foundation provided by virtual twin experiences, they operate as independent entities, detached from human collaboration. It is important to note that when Generative AI is used without the context provided by virtual twin experiences, it is not only subject to unchecked errors, it lacks human input. This weakens the synergy between real and artificial intelligence needed to build reliable medical framework that enhances human expertise, not replaces it.

INTEGRATING DATA-DRIVEN MODELING INTO VIRTUAL TWIN EXPERIENCES

An important component of virtual twins are their ability to seamlessly integrate pathophysiological models (real and virtual) and data-driven models into combined experiences, despite their different foundations, history and training sets. One could describe them as bottom-up and top-down respectively. By combining these two approaches, virtual twin experiences yield a more comprehensive understanding of medical conditions, taking into account both the underlying biochemical and physiological mechanisms, while incorporating the observed experience from patient interactions to fine tune it to the individual situation. Similar to how a GPS system utilizes its comprehensive understanding of the road network to monitor an individual's travel history, noting preferences in speed and chosen paths, and subsequently offering guidance based on both personal behavior and real-time traffic information. This fusion of data enables a more comprehensive perspective on patient health. Consequently, such integration facilitates enhanced diagnostic accuracy and the formulation of more effective treatment plans.

VIRTUAL TWIN EXPERIENCE OF THE PATIENT

As described, the virtual twin experience of the patient stands at the forefront of a healthcare revolution, poised to transform the landscape of medical care. This section delves into how the virtual twin experience of the patient is redefining healthcare through improved diagnosis and treatment, enhanced patient experience, informed data-driven decision-making, and the integration of real-time monitoring with predictive analytics. By simulating the patient condition, a more complete picture is revealed, allowing a more robust diagnosis that may include secondary concerns or even primary causes of observed symptoms. Further, the virtual twin allows for a more collaborative decision-making process, so clinicians with multiple specializations can evaluate to ensure nothing is overlooked. With this in hand, different medical scenarios and therapeutic strategies can be explored in a risk-free environment, enhancing the likelihood of choosing the right treatment, the first time.

VIRTUAL TWINS FOR MEDICAL PRACTICE EXCELLENCE

Informed Diagnosis and Team Based Treatment Planning

The virtual twin of a patient offers a groundbreaking approach to diagnosis and treatment planning. Moving past the limitations of 1D monitoring and 2D imaging, clinicians can use detailed, 3D functioning replicas of an individual patient's anatomy as their next generation medical record. It not only provides a valuable visual representation, but can also add a functional diagnosis and patient history, and increasingly be updated by real-time patient biometrics for a more complete picture. The virtual world offers limitless possibilities for data collection, processing and communication, enabling healthcare providers to understand a patient's complex medical conditions with greater clarity and context.

One pertinent example emerging from the Living Brain project, is the application of virtual twin experiences to improve surgical accuracy in deep brain stimulation procedures for patients with Epilepsy. Through the generation of a virtual twin of the patient's brain utilizing functional MRI data, physicians are afforded the ability to visualize intricate details, including the electrical impulses responsible for seizures. This enhanced visual representation facilitates a greater level of precision during the conduction of invasive treatments, as well as exploration of various treatment options. Further, the virtual twin experience of patient can then be used by the entire surgical team to foster optimal communication and preparation necessary for the precision execution that is required in such intricate medical interventions.

Patient-Specific Precision Medicine

Much has been said about a future state of healthcare based on patient specific precision medicine. Doctors are quick to point out that today, healthcare is patient specific, but only to the extent they understand the patient. As for precision, it all depends on what measurement is used for precision. Virtual twin experiences allow us to imagine a new reference bar for each. While the healthcare journey needs to be patient-centric, the goal of each step in medical care is treatment specificity, delivering the right treatment, at the right time, to an informed patient. The virtual twin enables the entire care team, including the patient to include everything that is known about the patient at that time, whether it is genotype or phenotype or other social determinants of health and other humans that are similar. Moreover, by centralizing healthcare around the development of virtual twin experiences, the accuracy of that picture grows more robust and accurate over time as more is learned. This is a sustainable approach that ensures that treatments will maximize the effectiveness over time without change in the process.

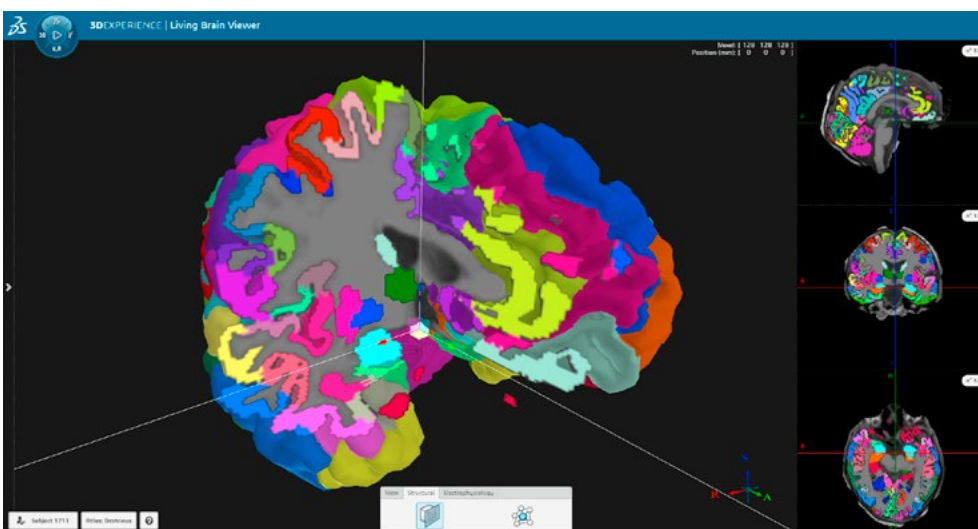


Figure 2. Snapshot of Living Brain Project patient dashboard showing 3D reconstruction along with traditional 2D slices

Surgical Design Guided by Virtual Twin Experiences

Virtual twin experiences represent a paradigm shift towards informed, data-centric decision-making in healthcare and allow us to enter into a new phase of treatment design. By integrating and analyzing vast amounts of personalized health data, including genetics, lifestyle, and environmental factors, virtual twin experiences offer deep insights into individual health risks and responses to various treatments. This methodology empowers healthcare practitioners to formulate decisions that are meticulously customized to the distinct requirements and health conditions of each patient and the tools they have available at the time, leading to more effective and efficient healthcare delivery.

These virtual twin models begin with generalized human physiology and incorporate a patient's medical history and health status to establish the current state. They can utilize details from individual cases or draw from vast amounts of clinical records to predict potential future health scenarios as appropriate for the individual and condition. For example, by reconstructing a virtual twin of a patient's heart, doctors can virtually test invasive measures such as a valve replacement, to ensure the right size, shape and placement is selected that

will restore their hemodynamics to that patient's normal state. More profoundly, a virtual heart twin can be used to design complete reconstructions of mal-formed cardiovascular systems, such as an aortic arch reconstruction for a patient that has never known normal. By considering the patient's entire cardiovascular system and predicting the impact of each interventional option, a procedure can be designed that could provide a lifetime of health. These insights help guide even the most experienced surgeon to the right treatment, lowering re-hospitalization rates and unforeseen complications.

This is not a future vision, but a reality that is possible today. Driven by the belief that their patients deserve every chance at a full, normal life, today doctors at Boston Children's Hospital are creating virtual twin experiences to take the guesswork out of complex cardiac reconstructions, or in their words, "Moving from 'Figuring it out in the OR, to a Virtual Cardiac Twin'". In one example, a child with several holes of varying sizes between their mitral valve and pulmonary valve, would need patches to enlarge the aorta and close the holes. The patches would need to be strong and flexible enough to stretch against the pressure of blood flow.

Dr David Hoganson explained: "The challenge is, when you operate inside the heart, or reconstruct the aorta or pulmonary artery, everything is zero pressure: flaccid. It is not the size and shape you are targeting." Dassault Systèmes' simulation solutions were used to ensure that the patch material, which starts out flat, would fold into the correct shape to meet the patient's unique needs. "In **3DEXPERIENCE** there is a phenomenal algorithm built for the aerospace industry that we're using in cardiac surgery to flatten those patches and incorporate the mechanical properties of those patches. Until now, we didn't have any information the surgeon would need about how it flexes and how much it flexes. I can tell you it is absolutely phenomenal to go in with a perfect plan as opposed to making it up as you go, which is what we've done for decades," Hoganson said. "I owe it to my patients to perform the best surgery possible, and now that I know what is possible, I have no other choice."

Real-Time Sensor Monitoring and Predictive Analytics

The integration of real-time monitoring and predictive analytics is an emerging but transformational use of virtual twin experiences to understand patient response, anticipate treatment and improve outcomes. The technology to take real-time sensor data from operating machines and feed it into a virtual twin to monitor the real machines' maintenance requirements and perform remote diagnosis is highly utilized in the aerospace and automotive industries. It allows for continuous or on-demand monitoring of performance and system markers. Similarly, sensor technologies capable of delivering critical human biomarkers have emerged over the past decade and are rapidly becoming a standard tool for certain disease conditions.

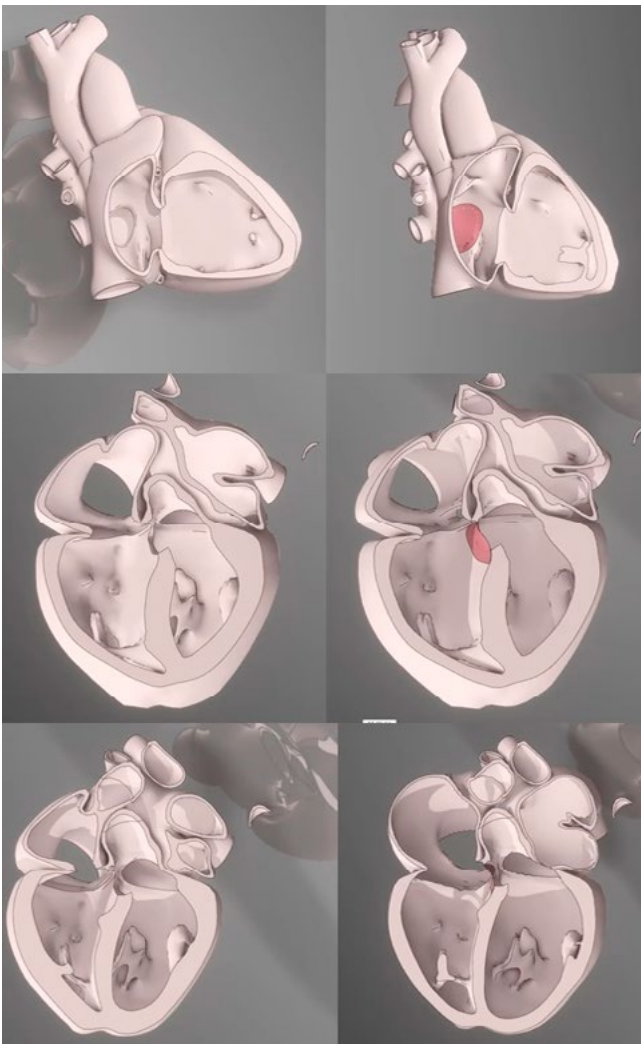


Figure 3. Pre and Post-surgical Virtual Human Twins of Congenital Heart Diseases (atrial septal defect, ventricular septal defect, tetralogy of Fallot)



Patient Engagement and Education

One of the primary benefits of virtual twin experiences is their ability to visually convey complex anatomical and physiological details. Traditional methods of explaining medical conditions often rely on verbal descriptions and 2D images, which can be difficult for patients to fully grasp. A virtual twin, however, presents these details in an intuitive 3D format. As a further benefit learned in the previous example of virtual twin based surgeries at Boston Children's Hospital, the virtual twin allows for a unique doctor-patient, or in this case patient-family relationship. Doctors recall many instances where the virtual twin of a child's complex heart anatomy was shown to a mother or father, and for the first time they were able to understand their child's condition, bringing tears of relief and clarity. This level of understanding is crucial for making informed decisions about medical care.

As a pivotal tool in creating patient-centric healthcare, virtual twin experiences offer many facets of patient education and engagement. These are:

- Enhancing Understanding Through Visualization
- Facilitating Informed and Engaged Decision-Making
- Reducing Anxiety and Building Trust
- Enhancing Communication within the Patient Family/ Care Team

Through our MEDIDATA brand, we have introduced a medical grade cloud platform (Sensor Cloud) specifically designed to collect, integrate and evaluate sensor data from a target population. Using these human mounted wearable sensors, a patient's health status can be monitored, providing real-time data that can be fed into their virtual twin to diagnose, predict and even prevent potential health issues. This technology became essential during the COVID-19 pandemic, when it was unsafe and at times, nearly impossible to collect patient data in a hospital setting. Sensor Cloud was used to eliminate the need for participants in clinical trials to record their medical data at a hospital or any physical care center. Sensor Cloud allowed patients to participate in trials without frequent trips to the hospital, improving patient participation and enabling more continuous monitoring of health, in a realistic environment consistent with their daily lives. This decentralization or virtualization, allowed clinical trials to continue and in fact become more effective as patient recruiting, adherence and data quality all increased.

Virtualizing into a common model enables creation of a data driven virtual twin by aggregating data with time synchronization. Thus, predictive analytics can be applied to provide early indications of concerns, forecast the progression of diseases, the likelihood of complications, and the patient's response to treatments. This proactive approach in healthcare not only helps in early intervention and prevention of serious health issues but also aids in optimizing ongoing treatments and improving long-term health outcomes. Virtual twins used in these programs can provide the patient's medical experience back to the clinician, or in the case of a trial to the sponsoring company to understand their treatment in great detail and serve as a virtual test environment for future treatment development.

Virtual twins empower patients and their families to become active participants in the decision-making process. By visualizing complex anatomy and potential surgical outcomes, patients can better comprehend the benefits and risks associated with different treatment options. This collaborative and transparent approach demystifies the medical process, reducing anxiety and building trust between patients and healthcare providers. In preoperative counseling sessions, having access to a virtual model in virtual reality or even smartphone, allows families to see and understand the surgical plan, fostering a sense of involvement and confidence in the chosen medical procedures.

In the example, we highlight the critical importance in engaging pediatric patients and their families as they ultimately have primary responsibility for care. However, this poses particular challenges as children with unique conditions require communicating complex medical information in an understandable way. Virtual twins are particularly beneficial in this context, as they offer a straightforward and engaging method for explaining medical conditions and treatments to children and their parents. The ability to show, rather than just tell, helps bridge the communication gap, ensuring that even young patients and their non-medically trained family members can comprehend what is happening within their bodies. As described by Dr. Hoganson, "It's totally changed the tension and anxiety of the family as they're trying to understand the complexity of what we're doing. It allows them to be a real part of the decision making process when you have these complex scenarios."

As this technology continues to evolve and become more widely adopted, it will undoubtedly play a crucial role in enhancing patient-centered care.

VIRTUAL TWIN FOR ACCELERATED THERAPEUTIC INNOVATION

ACCELERATING CLINICAL TRIALS WITH SYNTHETIC CONTROL ARMS

A key capability of a virtual twin in the medical product development setting is the ability to provide better estimates of efficacy and safety associated with an innovator product earlier in the product development cycle so that the most advantageous decisions about which products are promising can be made early. This allows continued resourcing where it is warranted and removing it for products with less potential and thereby delivering promising new products to patients more efficiently. Typically, estimates of the relative differences between an innovator product and the current standard-of-care treatments on efficacy and safety measures are learned only after many years of development in so-called phase 2 and 3 trials. However, by reusing patient-level data from historical clinical trials and employing sophisticated statistical methods to create a fair comparison with earlier phase single arm trials, such estimates can be predicted years sooner. As a premier provider of electronic data capture services for the clinical trials industry, MEDIDATA hosts a unique cross-sponsor data insights program. With this data, MEDIDATA has pioneered approaches for the creation of Synthetic Control Arm® (SCA) that is a virtual twin representation of a traditional randomized control. The role of the SCA is to capture the behavior of a cohort in the absence of treatment or with standard of care, so that differences in outcomes in the innovator group can be reliably understood enabling many economic and ethical benefits, a win for all stakeholders. For example, MEDIDATA created such an SCA aligning to a phase 1 trial in ovarian cancer and accurately predicted efficacy findings that eventually were confirmed after the conduct of a gold standard design, a randomized controlled phase 2 trial more than two years later. The earlier knowledge enabled better resource decision-making and better, more efficient design of that gold standard trial.

Importantly, SCA is also used in later phase development to substantiate regulatory decisions about whether to approve marketing of the medical product. In this setting, the FDA has already accepted SCA as an augmentation for control groups in certain indications, where the disease under study is exceedingly rare or is very severe and current standard-of-care or control treatments are ineffective. This enables efficient trial conduct with a more patient centric design that offers more hope to clinical trial patients since assignment to the new therapy is more likely with the use of the SCA than would have been so in a traditional clinical trial, all while maintaining the ability to draw high quality scientific conclusions from the trial.

In addition to SCA, MEDIDATA has developed a unique technology called Simulants that aggregates prior clinical trial data in a way that these patients have no traceability back to the original population. Patient level data from these simulated populations can be safely shared and mined.

IN SILICO CLINICAL TRIALS

An important, advanced use of virtual patient twins is for *in silico* clinical trials, or a complete clinical trial conducted computationally using virtual twin experiences, in preparation for experimentation on real patients. In a breakthrough example, the FDA has co-sponsored the ENRICHMENT project, using the Living Heart virtual twin model to simulate the experience of a known trial, to define the process of replacing real patient experience with virtual twin experience. The result of the project is a detailed playbook on the use of *in silico* clinical trials in the regulatory process, published in *Frontiers in Medicine* journal: [“Toward trustworthy medical device in silico clinical trials: a hierarchical framework for establishing credibility and strategies for overcoming key challenges”](#), Aycock et al. (2024)

In-Silico Clinical Trial

Workflow for AI Designed Virtual Twin Trial Population

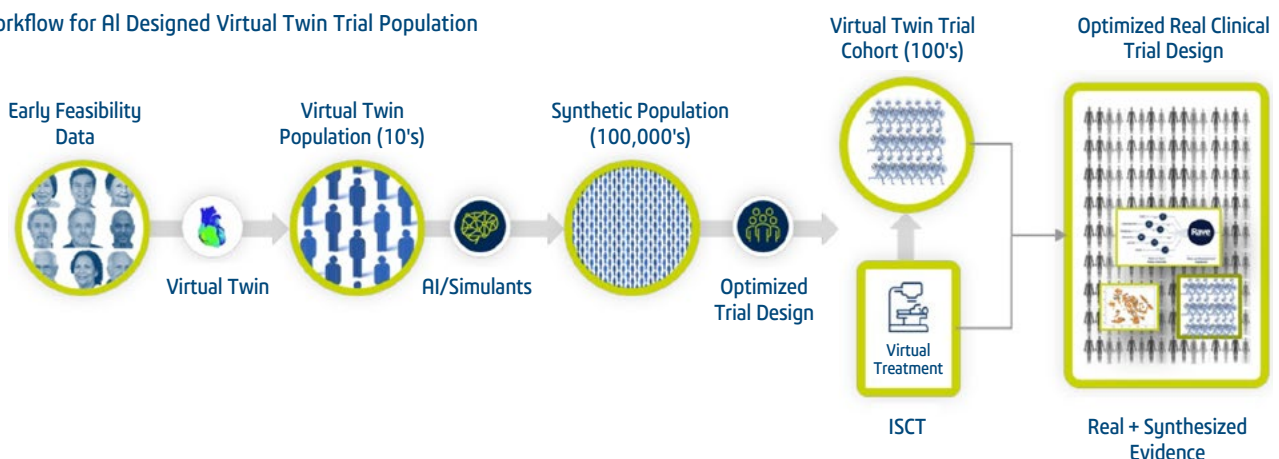


Figure 4. High level workflow of an *in silico* clinical trial. Virtual twins combine sparse amounts of patient data into functional models of disease and treatment, using AI methods to design enriched physical clinical trials with higher likelihood of success.

In this project, a small number of diseased patients were selected to serve as the training set. The data set included pre-operation physiology with biomarkers, details of their procedure and clinical outcomes.

Using this rich training set, generative AI could create a virtual population of diseased patients. With this, inclusion criteria could be applied, resulting in an experimental design containing the minimum set of patients necessary to represent the real population, who were subsequently treated virtually to evaluate efficacy and indicators for safety. The *in silico* clinical trial methodology, allows rehearsal of the trial in advance, enabling researchers to design an optimized trial, provide guidance for treatment protocols and ultimately facilitate a smaller, lower risk trial.

COMPLETELY RETHINKING THE CLINICAL TRIAL EXPERIENCE

While the trial-and-error approach to clinical trials has served for nearly a century, massive advances in science and technology have not translated into improvements in trial success. These have plateaued at 10-15% for new drugs and 40-50% for devices for decades. To break through this barrier, virtual twins uniquely offer the possibility of rigorous and transparent clinical validation, if implemented properly from early in the discovery/development process and maintained throughout.

As evidenced by the past decade of FDA regulatory science research, *in silico* clinical trials represent the next plateau in evidence based medicine for regulatory processes. Patient data is still critical, playing a vital role in validating the virtual twin experiences as reliable evidence. By using both clinical trial and real-world data, virtual twin experiences can be tuned to appropriate populations and even further tuned to reflect individual patient conditions and their known responses. This

validation process is then essential for ensuring the reliability of the virtual twin experiences and the transparency needed to establish trust in their use. Once this is established, virtual twin experiences offer the potential for medical professionals to understand the complex causation behind individual health conditions and explore the likely progression of various treatment options, offering deeper insights than what raw data alone can provide.

From this, a new model for pre-clinical research emerges. We can think of today's development process as a continuum of testing that begins with only model data (laboratory or animal) which is then slowly augmented with human testing, first for safety and then efficacy on increasingly large groups. This process can take more than a decade, even for the most effective treatments.

However, this can be re-imagined as beginning with human virtual twin experiences at the outset of the development cycle, insuring a human-like test environment from the start. This way, target patients can offer their virtual twin to participate in *in silico* clinical trials many years before it could be possible to consider as real patients. Once the virtual testing is successful, a fuller understanding of the risks and population dependencies is available and can be shared across a wide range of experts to be validated using targeted physical testing. With reduced reliance on other pre-clinical models, there is now direct translation of pre-clinical experience it the real trial. The result is reduced uncertainty and patients with a high likelihood of safely responding will already be identified. Over time, virtual twin populations will become increasingly predictive, lowering cost and risks and eventually be used directly as regulatory evidence. This paradigm-shift in trial conception leads to the minimum amount of human testing, with maximum population coverage, the opposite of the current direction.

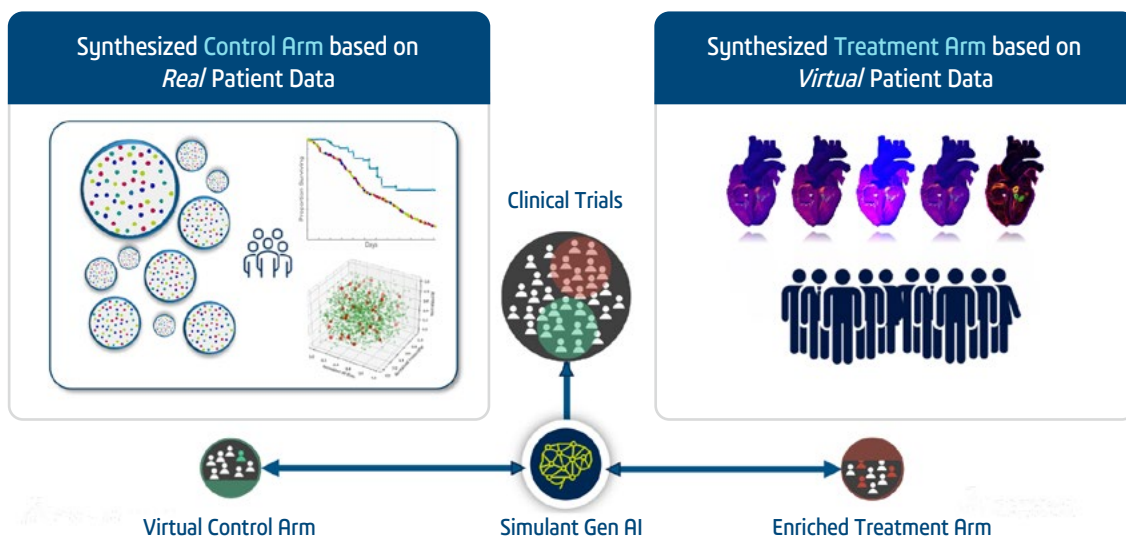


Figure 5. Illustration of the spectrum of virtual patient populations. On the left are data-driven populations constructed from previous human testing, limited to control arms as treatment cannot be predicted. On the right, science based virtual twin populations that allow prediction of treatment outcomes. Over the lifetime of a treatment, *in silico* clinical trials can use data from both populations as appropriate.

VIRTUAL TWIN EXPERIENCE OF A HOSPITAL

The concept of a virtual twin experience of a hospital or care center offers a new standard that is both patient-centric and optimized for hospital efficiency. The value for the physician is to work in an optimized setting. The value for the patient is to experience an enhanced care journey.

This section of the white paper discusses the imperatives driving the use of virtual twin experiences in the design and operation of physical care centers. As the care center remains the centerpiece for any healthcare system, is increasingly becoming blended with virtual care centers into a hybrid virtual + real system. Just as the retail industry has learned to harmonize the benefits of virtual + real consumer interactions, so must the healthcare industry. But, there are many fundamental differences in complexity, needs and risks that have held back healthcare from successfully making this transition. Virtual twin is the key.

PATIENT-CENTRIC, OPTIMIZED HOSPITAL OPERATIONS

The escalating pressures confronting the modern healthcare center presents a formidable challenge for hospital leaders - striking a balance between delivering an exceptional patient experience, quality outcomes and controlling operational costs, all while supporting a workforce that is often overstretched. In this intricate environment, virtual twin experiences that replicate part or all of a hospital's functions offer a powerful guidance system toward a patient-centric and operationally optimized model. By creating a virtual counterpart of the physical hospital premises, administrators gain the ability to conduct simulations that explore diverse scenarios related to design, spatial layout of rooms and equipment, and workflow optimization. These experiences empower strategic resource allocation, minimization of patient wait times, and the refinement of care pathways tailored to individual patient needs, while also accommodating future growth and technological advancements. The resultant optimization transcends mere improvements in care quality, encompassing a comprehensive enhancement of the hospital's operational efficiency across every stage of the patient journey - from admission to discharge.

ENHANCING PATIENT EXPERIENCE

The implementation of a virtual twin significantly enhances the patient experience during their hospital journey. Immersive learning experiences representing real-life care scenarios in the virtual world, enable interactive patient-centric education and engagement, thus improving the quality of care.

By providing a more personalized approach to healthcare, patients feel more understood and cared for. Virtual twins allow for clearer communication between healthcare providers and patients, as they can visually explain complex medical conditions and treatment plans using the patient's own

virtual model. This not only improves patient understanding and engagement in their own care but also helps in building trust and confidence in the treatment process, which is known to deliver better outcomes.

A simple example of the potential for virtual twin experiences to enhance the patient experience while also enhancing the accuracy of the treatment is the VORTHEX project. Through



Figure 6. The VORTHEX project creates virtual twins of entire treatment facility, allowing patients as well as technicians to fully experience the treatment in advance.

Dassault Systèmes' **3DEXPERIENCE** Lab, a collaboration with the H. HARTMANN Institute and the Rafaël Institute, has created the world's first entirely 3D-simulated radiotherapy room. This innovative project, situated at the H. HARTMANN Institute in Levallois-Perret, France, is designed to enhance patient comfort and understanding of radiotherapy, a complex procedure endured by 50% of patients treated for cancer. By leveraging Virtual Reality, patients can experience their treatment in a highly-realistic simulated environment, before undergoing the actual procedure. The key component of the experience is the fully automated virtual twin of the radiotherapy robot, Accuray's innovative Cyberknife. This virtual experience is now part of the patient's treatment plan and is guided by healthcare professionals.

This virtual twin experience aims to alleviate the anxiety and stress often associated with the radiotherapy treatment, making the process less daunting for patients. Unequivocal testimonials from patients and healthcare practitioners highlight the project's success in enhancing patient understanding and reducing apprehension. Clinical studies aimed at measuring the educational and operational effectiveness of this immersive experience within the patient journey will be conducted this year, in order to foster the integration of innovative technologies into patient care.



USE IN INFECTION PREVENTION AND CONTROL

Another very interesting application of hospital virtual twin experiences is infection prevention and control, critical both for routine care and pandemic conditions. Airborne hospital acquired infections are a major concern for hospitals worldwide, and were particularly in the limelight during the COVID-19 pandemic.

Virtual twin technology coupled with numerical simulation is used to better understand airborne contamination pathways and imagine mitigation measures to prevent them. The architectural layout, ventilation parameters and patient characteristics are used to create a realistic representation of a hospital room or department. Their modelling through 3D computer fluid dynamics (CFD) simulation provides information relating to the spread of infectious diseases within the facility.



Figure 7. Airflow within a hospital room can be evaluated for transmission potential of airborne pathogens. Redesign to minimize possible transmission can be performed rapidly and safely. [Hôpital Saint-Louis](#) airflow simulation illustrate such case.

With these insights, healthcare providers can better understand airborne transmission risks and adapt their behavior in consequence, as well as improve collaboration with the facilities department to put in place mitigation measures. In the end, this use of the virtual twin helps minimize airborne cross contamination risks for patients during their hospital stay. This innovative approach can also be used with even more impact during the design phase of a new hospital, as evidenced by its use during the conception of Wuhan's new Leishenshan modular hospital, which was built in days at the very start of the COVID-19 pandemic to accommodate the surge of new patients infected with SARS-CoV-2. Using 3D CFD simulation provided by Dassault Systèmes, the engineers and architects were able to design and test different ventilation configurations for the new isolation rooms under construction. This enabled them to choose the optimal one to build in terms of minimizing exposure risks.

Many other simulation studies were performed on the virtual twin of dozens of public and private hospitals in France, UK, US and Canada subsequently. The technology was so successful that it was also re-used to model and simulate numerous public venues such as concert halls, parliaments, and restaurants.

Overall, hospitals can create virtual twin experiences that allow them to predict the spread of infectious diseases within the facility, plan for patient surges, and manage resource allocation during routine care and crisis alike. This not only ensures a more effective response to epidemics and pandemics but also enhances the hospital's capacity to maintain operations under challenging conditions.



VIRTUAL TWIN OF A HEALTHCARE SYSTEM

The concept of creating virtual twin experiences of an entire healthcare system stands as a transformative approach that can catalyze comprehensive improvements across the healthcare sector, through understanding of the incentives and money flows. This powerful technology holds immense potential for optimizing public health strategies, enhancing resource allocation decisions, aligning incentives with outcomes and informing evidence-based governance. This section delves into the significant impact of this technology on public health strategy optimization, resource allocation, and policy-making.

TREATING HEALTHCARE AS A SYSTEM OF SYSTEMS

Most modern healthcare systems have developed organically, not by design but incrementally in response to a pressing need for one component. The result is a collection of independent systems, with overlaps and inconsistencies that reflect this lack of design. A virtual twin of the complex healthcare ecosystem can be constructed, as shown in Figure 8, mapping various sources of supply and demand, with governing policies and the economic implications. Policy-makers gain an unprecedented ability to understand these connections, model various scenarios, and test interventions in a risk-free environment forecasting their impacts across multiple dimensions to identify the best one. Through simulations, we can evaluate the ripple effects of policy changes on healthcare accessibility, quality metrics, cost trajectories, and population health outcomes. This data-driven approach allows for the proactive identification of potential bottlenecks, resource constraints, and unintended consequences, facilitating course corrections before policy implementation.

Moreover, the virtual twin technology empowers a collaborative approach by providing a shared platform for diverse stakeholders, including healthcare providers, payers, patients, and relevant government agencies. This fosters a synergistic environment where the perspectives of leaders in each of the component systems can be aligned, best practices disseminated, and innovative solutions co-created to tackle the most pressing public health challenges.

Ultimately, the adoption of virtual twin capabilities can revolutionize the entire process, ensuring that decisions are grounded in robust evidence, aligned with population needs, and optimized for delivering the highest value to taxpayers through efficient resource stewardship and improved health outcomes.

OVERARCHING SYSTEM IMPROVEMENTS

Creating virtual twin experiences of entire healthcare systems that involve a number of organizations, each with varying operational models is the ideal way to unravel the complex interdependencies. Extremes of conditions can be varied, so different operations can be assessed as beneficial and therefore reinforced or detrimental and to be deconstructed. Further, through realistic experience scenarios, entirely new system designs that incorporate the modern virtual health paradigms can be conceived and introduced. This allows for the identification and analysis of systemic inefficiencies, gaps in care delivery, resource bottlenecks, and general opportunities for improvement. These experiences can allow policy administrators to understand the effects of proposed changes, which would otherwise be impossible within such a massively complex system. It provides them with the knowledge to define operational efficiency targets, direct funding that will improve the patient journey, and enable innovative healthcare practices.

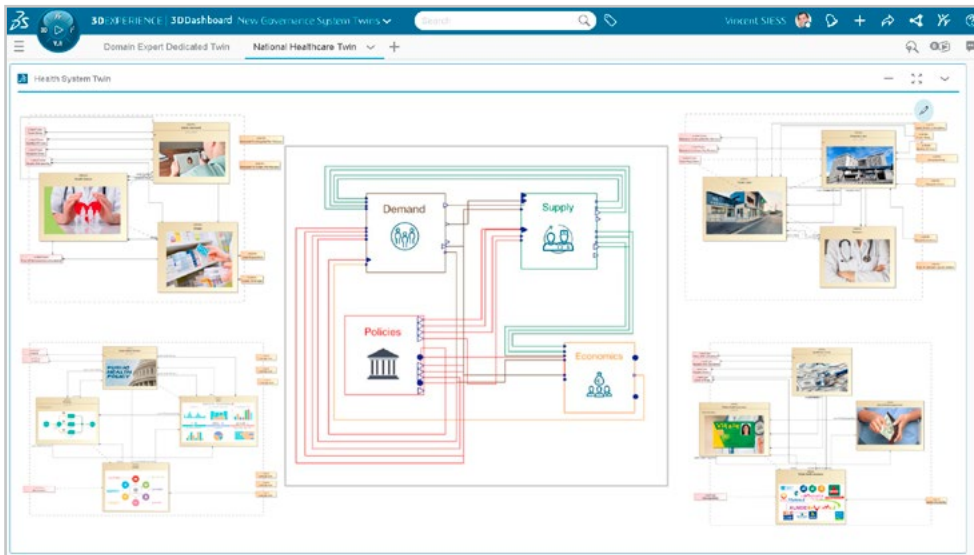


Figure 8. High level diagram of Economic model of the 4 pillars and interconnections of a healthcare system. The hierarchical model allows for drill down and adjustment of parameters within each pillar, allowing a prediction of its impact on the others.

Resource Allocation and Policymaking

PUBLIC HEALTH STRATEGY OPTIMIZATION

The virtual twin serves as a powerful tool for strategy development and optimization, enables health leaders and policy-makers to simulate and analyze the impact of various public health initiatives and interventions, such as vaccination programs, disease prevention strategies, and responses to health crises. The ability to model and predict the outcomes of these strategies in a virtual environment before implementation in the real world helps in fine-tuning public health policies, ensuring they are both effective and efficient.

Using the virtual twin of the healthcare system, different scenarios can be imagined and tested for the demand for finite healthcare resources, such as hospital beds, medical staff, and equipment, under various conditions. This predictive capacity is crucial in setting appropriate targets for resources in planning, and updated in real-time when abnormal conditions arise. By considering the impact on the whole system, reallocation of resources can reflect where they are most needed, leading to a more equitable and responsive healthcare system. Additionally, the insights gained from these simulations support evidence-based policy-making, helping to shape policies that are more aligned with the actual needs and dynamics of the healthcare system. Over time, the system is maintained in a holistic way that embraces growth.

SUPPORT TIME SCALE REALITY

Many healthcare decisions are necessary to address immediate concerns, while others require very long lead times. For instance, managing seasonal flu requires annual planning that reflects the current viral conditions, while changes in medical education programs might take a decade to show clinical impact. The virtual twin of a healthcare system must therefore be designed to consider this wide range of timeframes to provide effective simulation experiences..

GEOGRAPHICAL MODEL ADAPTATION

As challenges vary from the audience targeted, it is important to enable a twin to reflect the healthcare system at the size of a country. Therefore, it will support global decisions through policy support. Being able to address the reality at the regional level enables to connect the twin closer to the operations and their local specificities.

GOVERNMENT RESPONSE TO A PANDEMIC

An illustrative example of leveraging digital twins to inform healthcare policy-making during pandemics is the network epidemiology model developed by Linka et al.X (2020). Created during the early phases of the COVID-19 pandemic, this model combines a global mobility network based on real air travel statistics combined with a local epidemiological model (SEIR) to simulate the outbreak dynamics of COVID-19 across Europe. By integrating real-world data on population mobility with mathematical models of disease transmission, a virtual replica or "virtual twin" of the pandemic was created.

This virtual twin enabled experiences that could quantify the impact of travel restrictions that were implemented in March 2020, intended to contain the spread of COVID-19. Simulations contrasting scenarios with and without constrained mobility clearly demonstrated that unconstrained travel would have significantly accelerated the outbreak, especially in central European countries like Germany, as well as Spain and France. The modeling results provide essential evidence supporting the necessity of the drastic but controversial decision to restrict non-essential travel and close borders across the European Union.

Moreover, the virtual twin experiences provided a virtual environment to systematically analyze various exit strategies from the imposed lockdowns and travel constraints. Policy-makers could explore gradual relaxations of restrictions between specific communities or countries and forecast their effects on outbreak trajectories. This capability to model diverse hypothetical scenarios allowed identifying safe strategies to ease controls while keeping new infection rates manageable within healthcare system capacities.

By mapping the outputs of the virtual twin to enacted policies across Europe, the effectiveness of interventions like travel bans, school closures and other containment measures could be quantified. This provided an evidence-based approach for optimizing resource allocation and tailoring the public health response proportionately across regions.

This example demonstrates the power of virtual twin experiences to create a bridge between previously disparate domains of mobility data and disease modeling to create a robust quantitative framework for evaluating outbreak mitigation policies. This exemplifies the potential of virtual twins experiences to enhance preparedness and more importantly, quantify the potential impact of routine policy decisions, guiding strategic decision-making for sustainable healthcare systems.

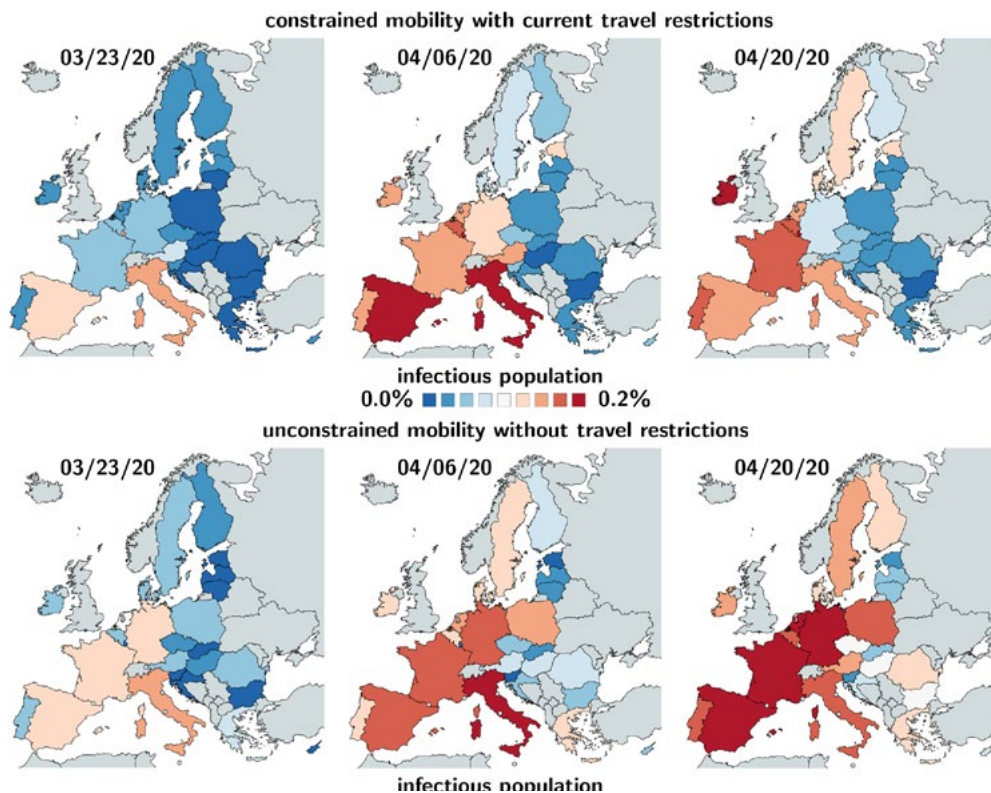


Figure 9. Outbreak dynamics of COVID-19 in Europe and the effect of travel restrictions Comput Methods Biomech Biomed Engin. 2020 August; 23(11): 710–717.

CONCLUSION

As we conclude this white paper, we reflect on the key takeaways of the transformative potential of virtual twin experience in healthcare.

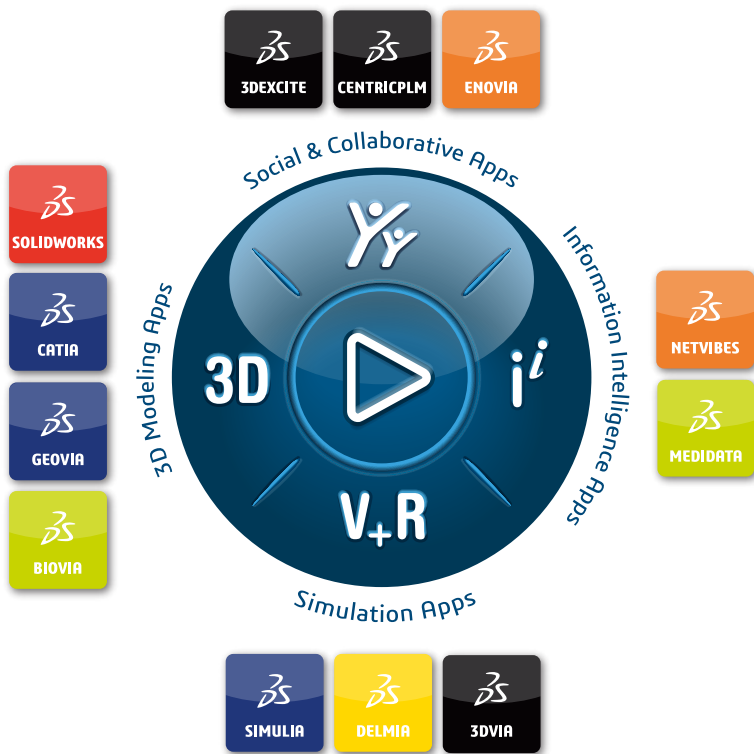
- **A Pivotal Moment in Healthcare** The industry currently stands at a pivotal crossroads, facing the dual challenges of increasing complexities and the pressing need for personalized, effective treatments. This scenario underscores the urgency for innovation and precision, which are essential in shaping 21st-century healthcare.
- **Precision is the Goal for 21st-Century Healthcare** Precision in healthcare is not just an aspiration but a necessity. The goal to achieve engineering precision in all aspects of healthcare, from the development of treatments to the delivery of patient care is high, but we should strive for nothing less.
- **Role of Virtual Twin Experiences** The virtual twin emerges as a unifying concept in this context, offering the means to make this precision a tangible reality. With applications that extend across research and development, patient care, hospital administration, and healthcare system management, virtual twin experiences enhance everything from medical discovery and diagnosis, to precision medicine and policy-making. They represent a bridge between

what we know scientifically and what we observe in real-life healthcare scenarios. Advances in Machine Learning deeply combined with the power of modeling and simulation brings a new level of efficiency, accelerating the ability to identify key relationships and dependencies, and provide healthcare, operational and medical for better care and overall patient health.

- **Dassault Systèmes' Unique Position** Dassault Systèmes holds a unique position in this transformative journey, with decades-long investment in virtual twin technology, healthcare and the **3DEXPERIENCE** platform. This platform is not just a technology capacity, but also the foundation of a scientific ecosystem that fosters global medical research collaboration, ensuring data security and facilitating the integration of diverse medical knowledge. Dassault Systèmes' commitment to this technology has been instrumental in advancing the frontiers of healthcare, making it a leader in the push towards a more precise, personalized, and effective healthcare systems.

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Our 3DEXPERIENCE® platform powers our brand applications, serving 12 industries, and provides a rich portfolio of industry solution experiences.

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