Digital innovation in cardiovascular medicine: a multi-stakeholder business

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The rise of digital tools in healthcare

The healthcare sector is currently experiencing a digital transformation at every level, and cardiovascular medicine is no exception. With the increasing use of digital methods to study diseases, treat patients and create new therapies, the field of in silico medicine, or the use of computer-based tools to predict biomedical and clinical outcomes, has emerged. The term in silico refers to the silica in our computers’ chips.

Those in silico methods are highly innovative. Scientists agree on their potential to solve numerous challenges facing cardiovascular therapies, such as the personalisation of treatments, reduction of R&D cost, the inclusion of under-represented sub-populations in clinical trials and regulatory complexity. Nevertheless, they can also disrupt traditional practices. Therefore, it is of utmost importance to involve all relevant stakeholders in the process of their development, including patients, medical practitioners, regulators etc. (Figure 1).

How can in silico approaches help with cardiac health?

In silico technologies are increasingly being used at every step of the cardiac therapy life-cycle. Indeed, there are numerous applications from the stage of medical product design and development to regulatory approval (FDA, 2021a), but also in the clinical practice (Lesage et al., 2022) and for improving patient experience.

SimCardioTest use cases

The SimCardioTest is a Research and Innovation Action funded by the European Commission (2020–2024) to develop new digital tools for cardiovascular therapies. It focuses on developing a cloud-based platform for the virtual testing of cardiac medical devices and drugs. The aim is to lower the need for animal models, increase the number of tested scenarios or refine later phases of trials, etc. Computational models are built and validated for the platform for device manufacturers and pharmaceutical companies to run virtual clinical trials and test parameters such as the long-term mechanical resistance of devices and the safety and efficacy of therapies, among others. Examples of applications covering some of the most relevant heart problems are developed with three use cases:

1. Pacing devices used in cardiac arrhythmias associated with heart failure
2. Left atrial appendage occluders used to reduce the risk of stroke
3. Drugs evaluated to ensure safety, efficacy and limit cardiotoxicity.

For more details, see our article: What computational sciences can do for your heart (Barbier et al., 2021).

Multiple stakeholder engagement

Involving the public and patients

The primary objective of computational medicine is to improve patients’ health and safety. Hence, it is crucial that members of the public and patients are involved in the technology development process. A common misconception by scientists is to see patient outreach and engagement solely as a way to communicate their research to a large audience in layman’s terms towards the end of the research and development phase. Yet, informing the public is a valuable task, strongly encouraged by the European Commission, which emphasises the importance of responsible research and innovation (ERA Learn, no date).
as a way to engage and involve various stakeholders to steer innovation in a direction that is meaningful and useful for the society at large.

Patient organisations, such as the European Patient Forum, or more specific ones, such as SAFE (Stoke Alliance for Europe) and the Global Heart Hub, raise Therapeutic products (with cardiovascular diseases) and open the dialogue on the digital transformation in healthcare (European Patients’ Form, no date). This underlines the importance of not letting technology development and patient dialogue happen in separate ways.

Following that strategy, SimCardioTest organises discussion groups involving patients and medical practitioners about their expectations, needs and concerns related to the in silico technologies being developed in the project. During these discussion groups, amongst others, fictitious scenarios describing the context in which the technology would be used are explained and illustrated to trigger discussions (Figure 2).

The resulting discussions raise awareness about the developed technologies and are fed back to researchers for future guidance. Additionally, they may provide useful recommendations to inform policymakers when appropriate.

Guidelines and standards exist to assist scientists with engaging patients in the development of health technologies. However, there is currently a lack of guidance or standards for involving patients in particular. The engagement tools and material produced as part of the SimCardioTest engagement activities are also intended to benefit the broader computational modelling community.

Raising awareness and building trust among medical practitioners

The use of in silico technologies in clinical practice is envisioned and can be used for understanding cardiac pathophysiology, planning interventions, informing the patient, improving diagnosis, or as a collaborative tool for true patient-centric and team-based care (Dassault Systemes, no date). One point on which most stakeholders agree is that opinions vary between different medical practitioners and countries. The level of familiarity with computational technologies is low, and trust and distrust in the technology is not always rightly placed.

However, medical practitioners are often the end-users of the in silico tools or the prescriber of the medical products whose development was based on modelling and simulations. Hence, the necessity of growing visibility, raising awareness and building trust among that community. This endeavour may take various forms and go through assessing actual situations in the field, consulting, involving clinicians in technological co-creation processes as well as training, and disseminating relevant information and success stories.

For example, SimCardioTest invites cardiovascular interventionists, surgeons and cardiologists to the discussion groups for patients (see ‘Involving the public and patients’). The aim is to evaluate their expectations and back expectations and concerns with respect to the project’s use cases. The reporting of this information will guide the researchers and help inform policymakers as well as the broader in silico medicine community.

On a larger scale, the VPHI and its partners conduct surveys targeting the clinical community to generate actionable public data about the current perception and use of computer modelling and simulation in clinical practice and identify potential barriers and opportunities.

It is important to note that full uptake of in silico technologies for cardiovascular therapy development may also imply targeting other types of clinical acture. Indeed, clinical opinion leaders and trial experts in regulatory bodies also strongly impact that matter.

Dialogue and collaboration with regulators

Opening the dialogue with health regulators is relevant when it comes to getting computer-based tools approved for medical use. Tools based on predictive modelling and the simulations themselves should be approved as software as a medical device (SaMD) for use in medical practice. Besides that, in silico methods are employed for supporting the safety and efficacy of medical products in market approval dossiers provide what is commonly called ‘digital evidence’. So, an in silico tool may itself be ‘qualified’ as a methodology for medical product development regulatory agencies such as FDA or EMA.

In practice, things are not straightforward. Many recent digital innovations, such as in silico technologies, do not fit neatly into the traditional market landscape as recognised by existing regulatory bodies. There is a need for knowledge-sharing and collaboration between frontier innovators and regulators to establish how those in silico tools can be validated and accepted as part of regulatory submissions. This is key to achieving the potential of in silico approaches while maintaining high patient-safety standards.

Regulatory stakeholders are currently collaborating with academia and industry to set guidelines and standards on which everyone could rely. For example, regulatory sandboxes are being proposed by the European regulator (European Commission, 2023a), and regulators are calling for public feedback on draft guidelines for modelling and simulation in healthcare (FDA, 2022b). International guidance may also arise from expanding and harmonising existing standards (e.g. ASME-V&V40). In addition, ongoing collaborative efforts to establish good simulation practice (Viceneti, 2021) for quality insurance.

Because use cases and success stories are key to fuelling that dialogue, the vocation of the SimCardioTest use cases is also to provide proof of principle, exemplifying how computer-based technologies may be used and validated.

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