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eHealth ENTREPRENEURSHIP

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Heidrun Flaadt Cervini • Jörg Dogwiler

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ENTREPRENEURSHIP

How to start and grow a digital health startup

We dedicate this book to our students and Case BioMed alumni: the courage, perseverance and enthusiasm of these talents was a constant motivation for us to further develop our entrepreneurship training programs.

IMPRESSUM

Heidrun Flaadt Cervini, Jörg Dogwiler (Eds.)
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How to start and grow a digital health startup

I'm convinced that about half of what separates the successful entrepreneurs from the non-successful ones is pure perseverance. Being an entrepreneur is challenging, and it's easy to give up and move on to something else. But the biggest part of being successful is having the stamina to stick through the hard times without quitting.

Steve Jobs

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Dear Reader,

While you hold this book quietly in your hands, our earth is rotating up to 465 meters per second (!) and our world is changing at an incredible speed.
We live in a dynamic universal society and the surge of global megatrends leads to groundbreaking advances in technology, but also in medicine.
For any society (and organization) to persist and to succeed in such a vital environment, one of the key factors is innovation.

The life sciences industry is one of the strongest industrial sectors in Switzerland and it is driven by its innovative strength. In fact, the life sciences community – which includes bio- and medical technology as well as healthcare service providers – has helped people to live longer and enjoy a better quality of life.
Despite this increasing progress in medical science, however, many unmet medical needs subsist and a large number of diseases cannot be sufficiently treated or cured.

Research results and inventions generated by universities can make a major contribution to the progress in medicine if they are transferred into a corporate environment and developed into marketable products and services.
In particular, the establishment of new companies, spin-offs or start-ups, ensures that the results of research are turned into innovative medical products and treatments.
Normally, these companies are founded by the scientists and researchers who have generated the research results and inventions. For such scientists, a professional transition is necessary from "researcher to entrepreneur" or from "scientist to CEO". While such transition offers the possibility of a third career path, namely "academic entrepreneurship", the academic entrepreneurs must possess a rare blend of skills, competences and entrepreneurial know-how that are usually not provided by the life sciences curricula offered at Swiss and European universities.

To fill this gap in academic life sciences entrepreneurship training, we from the Center of Advanced Studies on Entrepreneurship in BioMedicine (CASE BioMed) at Università della Svizzera italiana (USI) developed and implemented a series of three unique advanced entrepreneurship programs: BioBusiness, MedTech Business and eHealth Business.
The portfolio of these life science entrepreneurship programs was completed by the publication of an accompanying book to the BioBusiness and MedTech Business programs in 2018.

Due to disruptive innovations in the digital eco-system in recent years, digital health technologies are rapidly changing the practice of medicine and the doctor–patient relationship.
Digital health entrepreneurs have the ambition to create customized value through the development and launch of innovative digital health products, services and platforms.
While the digital health market is booming, a high percentage of eHealth start-ups are not successful in the mid or long term.
To help emerging eHealth companies understand and develop the keys to success, we at CASE BioMed have created a one-week comprehensive program on eHealth Business.
This advanced training on eHealth Entrepreneurship launched in 2021 and provides young and future entrepreneurs with the knowledge and skills with which to tackle the critical issues vital for their companies to establish a strong position in the market, preparing the basis for future growth.
Participants are trained on how to start, finance and grow an eHealth business. The teaching program also includes topics on health information technology, national strategies in eHealth, technology platforms, regulatory affairs, intellectual property rights and reimbursement.
The lectures and seminars are taught by world-class instructors from the eHealth industry, academia and venture capital.

In times full of change and global opportunities, we decided to publish this book in order to support emerging business ideas in the field of eHealth and to allow our students better preparation and a review of the eHealth Business program week.
The compilation can either be read as a whole or individual chapters can be selected.
However, the book is not intended to replace the eHealth Business week, attendance at which is essential in order to take full advantage of the theoretical and project-based knowledge needed to develop, fund and market innovation, as well as to share related ideas and experience with other participants. This book should be mainly considered as a useful tool to prepare oneself to follow the program with the highest possible benefit.

Finally, I'd like to wish further success to our alumni across the globe and encourage them to continue their entrepreneurial path by using the words of Prof. Dr. Ruggero Fariello, the founder of Newron, who stated:
Bringing new treatments to fruition for the benefit of suffering human fellows is one of the most rewarding experiences deriving from a professional activity entailing the vision of a leader, the multidisciplinary efforts of many and the combined force of a team.

I hope you enjoy reading this book and that it contributes to preparing you and our global society for a hopefully promising tomorrow.

Dr. Heidrun Flaadt Cervini
Founder and Director, Center of Advanced Studies on Entrepreneurship in BioMedicine (CASE BioMed), Università della Svizzera italiana

The eHealth Business program at Università della Svizzera italiana – a unique experience

Once again in 2023 the Comprehensive Advance Program on eHealth Business at the Center of Advanced Studies on Entrepreneurship in BioMedicine (CASE BioMed) brought together a highly professional group of participants with experience in developing or running eHealth companies in the audience and an astounding group of international experts presenting a set of lectures and use cases around setting up companies, developing interoperative products, understanding the legal framework, paving the way for financing, and finally getting products into the market. This astounding course, embedded in the fascinating landscape and atmosphere of the Ticino, is a unique experience indeed. The program is specifically designed to meet the needs of entrepreneurs in the field, to enhance their capabilities and enable an exchange on high level. It is not so much of a teacher and student relation – it is more of a dialogue on interoperability carried out on a platform where long-term experiences meet with new ideas and recent learnings from research and development in eHealth.

The topics and use cases as described in this book are offering solutions for the intricate challenges that entrepreneurs in the field are facing in an environment that is highly dynamic and influenced by medical research, innovative developments like artificial intelligence and an ever-changing regulatory framework. And it is for these reasons that entrepreneurs starting a business in eHealth must cover an enormous amount of "homework" before they become operative. They need to deliver a sovereign and comprehensive insight into the subject matter before developing a product, need to acquire a deep understanding of the competitive situation and take into account all aspects of this complex market's framework.

As eHealth like no other concept in the healthcare market bears the potential to disseminate into other markets of the European Union and Switzerland, the amount of preparation for understanding the market and shaping the product accordingly is multiplied even though there might be similarities and regulations that are very similar throughout this marketplace. Some of the recent legislative developments have actually triggered not only the possibility of growing into many of these markets but have also incinerated ideas for new products and services that would not have been thought of a decade ago. Data Act, Data Governance Act and the upcoming European Health Data Space, just to name a few, produce opportunities, create new marketplaces and introduce possibilities to close gaps in life sciences and healthcare. We do live in a very exciting time!

The core of eHealth is around data. This is not really completely new as medicine already in ancient times was dependent on information collected from the patient or his surroundings. However, with today's approach towards a multiplied source for gathering data not only from the patient but also from huge databases enabling in-silico research, this is the era of data usage for the improvement of quality and care. We have understood that it is no longer sufficient to collect data and keep it sealed in silos. The essence of modern medicine is making optimum use of data available and allow research to blend in with treatment for real time improvement in prediction, prevention, diagnostics and care. But mind you, this does not necessarily imply a reduction of the rights of self-determination. Unlike some of the Data Protection Authorities might want to make us believe, this is not the end of the occident, it is the beginning of a new era.

There now is a consciousness arising that research with anonymous data is facing two severe problems: on the one hand, in times of artificial intelligence and big data anonymization cannot be guaranteed as securely as before. To keep up the promise, data sets would need to be reduced in a way that makes them less and less useful for research purposes. On the other hand, anonymized data does not allow cross period research, cannot avoid duplication of data sets and most importantly: it thwarts deploying good or positive results to the individual whose data contributed to the research in the first place. In our current understanding there should not only be a right to be forgotten, there should also be a "right to be found". Patients should be informed as part of the consent procedure that pseudonymization is preferential to anonymization as it allows the immediate application of results to the individual. The current development around the European Health Data Space and the national legislation to enable data use and data linkage are impressive landmarks illustrating this paradigm shift in healthcare data processing. And there is more to come!

This is no longer the time in which the entrepreneur will start developing a product based on a nice (or may be even brilliant) idea, bring some nerds and venture capital on board and present the innovation to an astounding world that will gladly purchase everything. This will not work anymore. We need to understand that suc-

cessful products in eHealth need to be part of a Digital Transformation. And sound Digital Transformation requires an analysis of the current process, restructuring it, followed by a digitalization of the newly designed processes. Without this digitalization is merely turning bad processes into bad digital processes. Today, the business plan must encompass the idea, consider IP rights, initiate clinical or in-silico research, understand the market, regulatory requirements, product design and the reimbursement process. And it is because of this, that the eHealth Business Program in Lugano is an essential base for success in this field. It is the great merit of Heidrun Flaadt and Jörg Dogwiler to have initiated this program and carried it through the years. I've never met somebody who was not enthused by this experience. We hope that this course will endure and be successful throughout our mutual eHealth future!

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Dr. Heidrun Flaadt Cervini *studied Biology at the University of Constance where she also completed her PhD. After her postdoctoral studies at Ecole Normale Supérieure in Paris, she attended Management Education in Zurich. She then served as COO of Diagene, a spin-off company at University of Basel. During that time, the company completed the first capital round. Driven by her interest for technology transfer she took over a position at the Office of Technology Transfer (OTT) at the University of Basel. In 2005, she started to build up a new OTT at EMPA in Dübendorf that she headed until end of 2007. In 2008, she moved to Ticino to join her husband and received a mandate from the Università della Svizzera italiana in Lugano to create new Executive Programs in the field of bio- and medtech entrepreneurship. Among others, she developed and implemented the BioBusiness, MedTech Business and eHealth Business program. Heidrun Flaadt Cervini is now the director of CASE BioMed, Center of Advanced Studies on Entrepreneurship in Biomedicine at USI.*

Heidrun Flaadt is also one of 16 Women in Healthcare Innovation 2021. The award was presented to her by the Innovation Office of the University of Basel (in collaboration with Impact Hub Basel, Healthcare Businesswomen Association, WomenMatters and WEHub) for her work as director of the Center of Advanced Studies on Entrepreneurship in BioMedicine (CASE BioMed) at the Faculty of Biomedical Sciences, Università della Svizzera italiana and her significant contribution to innovation.

She has been on the advisory board of Swiss Healthcare Startups since 2024.

After graduating as Master of Engineering in electronics from ETH Zurich, ***Jörg Dogwiler*** *joined ABB Power Systems as a system engineer in 1994 and later became group leader in systems engineering for combined cycle power plants. In 2000, he moved to Zühlke Engineering where he was project manager responsible for the development of various industrial products, including those for medical devices. During this period, he successfully filed for several patents to protect inventions in the field of infusion pumps.*

In 2006, he joined Confinis AG as partner, and spent 10 years playing an active role in the successful development of the medical device consultancy company. During this period, he acted as senior consultant and senior project manager on various customer projects specialized in the field of medical devices working, amongst others, on the implementation of quality management systems, global product registrations and operative quality support.

Since 2016, as founder and CEO of Congenius AG, he is in charge of the consultancy company that specializes in the field of medical devices, pharmaceuticals, diagnostics and biotechnology in Switzerland and abroad. In total, Jörg combines more than 20 years of experience in development and regulatory affairs of medical devices. He has supported several start-up companies, from a regulatory point of view, that are successfully marketing their medical devices.

Model	Description	Pros	Cons
Digital therapeutics	Physicians prescribe a course of treatment that is paid for by the patient's health insurance.	Pharma-like reimbursement	Pharma-like development
Direct to consumer	The solution is sold directly to consumers who pay out of pocket.	Large customer base	Reluctance to pay
Employer as customer	The employer typically pays a set fee per month for each employee on the program.	Recurring revenue	Long sales cycle
Payer as customer	Payers offer the solution to policyholders, paying a set monthly fee to the solution provider for each member that uses it.	Recurring revenue	(Co-)promotion costs
HCP or pharma as customer	A free service to patients that is monetized either by a healthcare or pharmaceutical company paying for insights generated by the patient data.	Significant reach by customer	Ongoing development / sales costs
	A service that improves patient engagement or adherence.	High demand / interest	Difficult to measure

Tab. 1: Example digital health business models

It is common for digital health startups to mistakenly work on their business model last due to a focus on their product or service. No one of these models is the "best" one for a digital health startup. A key factor is having a deep understanding of your customer's unmet need, how your product or service fulfills that need, and the value chain into which your product or service will be delivered.

Strategically, you may also start with one model (e.g., DTC) and evolve to another (e.g., pharma), or you may need to change models as the market evolves. As an example, during the COVID-19 global pandemic, many of the successful digital health models were focused on remote monitoring and remote care; while the payer and employer models benefitted from reduced costs of travel. By contrast, healthcare professional / clinic / hospital models were hit hard by access and distraction challenges.

In digital health startups, a common value proposition relies on providing a clinical benefit (e.g., with digital therapeutics, value-based care models, etc.). Startups based on these models can take significantly more time to verify and validate and, as a result, they require a longer duration of funding for the significant clinical development work.

For example, a digital therapeutic (patient-facing mobile app and HCP-facing clinical decision support) would require evidence of technical, clinical, and analytical (e.g., algorithm) verification and validation. If the software product is regulated as a medical device, there are more significant design and development costs. If the economic customer is a third-party payer, there would likely be clinical study costs to demonstrate the clinical benefit of the product. All of this might require multi-year investment prior to any funding for the commercialization of the product and service.

When a digital health startup's business model is based on pharma as the customer, there are two dominant business models:

- Internal development tools based on products and eClinical services that provide remote monitoring and / or digital endpoints / biomarkers / measures; and
- Digital tools for creating new value for the patient. These include products and services that address: patient engagement, adherence to therapy or self-management, and broad disease management services.

A key consideration for pharma companies is whether the digital health offering is viewed as an "inducement to prescribe" in some markets and, therefore, difficult or impossible to offer due to anti-kickback statutes. Another challenge for pharma companies is leveraging digital health platforms that might create a situation where the pharma company's branded products exist on a platform that also has their competitors' products. For the digital health startup, it is therefore critical to understand your customers' competitive environment and business needs.

A final consideration for any digital health startup is both the threats and opportunities posed by "Big Tech". For example, Amazon continues to build a strong presence in healthcare with its combination of acquisitions (e.g., PillPack made it a national pharmacy; Whole Foods provided neighborhood bricks-and-mortar presence; One Medical made it an HCP) and for all of this it is able to leverage its significant core competencies in supply chain and digital services. Microsoft seems mostly focused on infrastructure for eHealth services and, as a result, may be a potential platform partner. Alphabet is less clear given its recent dispersion of Google Health and the major pivot of Verily to (re-)insurance. Apple is maintaining its core competency of retailing and branding, and has been adding health, wellness, and medical device capabilities as part of their ecosystem.

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Venture capital (VC) is a form of private equity and a type of financing from investors, investment banks, and any other financial institution for startup companies and small businesses with long-term growth potential (Hayes, 2022).
After World War II, the venture capital industry began to take form when, in 1946, the father of venture capitalism, Georges Doriot, founded and became president of the first public venture capital firm: Boston-based American Research and Development Corporation (Ante, 2008).
Nowadays, venture capitalists essentially invest in companies that are managed by a strong team offering a product or service with a significant competitive advantage for a large potential market. The COVID-19 pandemic triggered innovation in the digital health sector boosting investments worldwide: in 2021, funding by investors in the digital health industry totaled 44 billion US dollars; this was double the preceding year and by far the largest amount since 2010 (Stewart, 2022).
A continuously updated overview of VC firms investing in digital health in Switzerland, The Swiss Digital Health VC Map, is provided by Health-Trends (Mettler et al., 2021).

The next chapter provides a baseline from which to think about pursuing a fundraise.

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