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LONG-TERM INVESTMENT PLAN

IN-4-AHA Project – Innovation Networks for Scaling Active and Healthy Ageing

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More information about the project can be found on the IN-4-AHA webpage and social media pages: <u>https://innovation4ageing.eu/</u> <u>https://www.facebook.com/IN4AHA</u>

https://twitter.com/EIP_AHA https://www.linkedin.com/groups/8912125/

More information about the EIP on AHA community and FUTURIUM platform: <u>https://futurium.ec.europa.eu/en/active-and-healthy-living-digital-world</u> <u>https://digital-strategy.ec.europa.eu/en/policies/eip-aha</u>

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Abbreviations

AHA – Active and Healthy Aging B2B – Business-to-Business B2B2C - Business-to-Business-to Consumer CEA - Cost-effectiveness analysis CIMIT - Consortia for Improving Medicine with Innovation & Technology CUA - Cost-utility analysis D2C - Direct-to-Customer ENoLL - European Network of Living Labs FFF – Family, Friends and Fools HTA - Health Technology Assessments **IP** – Intellectual Property IPO – Initial Public Offering IVDR - In Vitro Diagnostic Medical Device Regulation MDR – Medical Device Regulation NGO - Non-governmental organization PCC – Person-centred care PMCF - Post-market clinical follow-up QALY - Quality-adjusted-life year SMEs – Small and medium-sized enterprises TRL – Technology Readiness Level VC – Venture Capital

Glossary

Digital health products - health applications, which consist of certain essential elements such as wireless devices, hardware and software sensors, microprocessors and integrated circuits, the internet, social networking mobile and body area networks, health IT, genomics, and personal genetic information.

Elderly-focused and elderly-inclusive digital health products – any digital health product aiming to improve the health and lives of elderly. Elderly-focused products are designed with the elderly population as the main target segment. Elderly-inclusive products are designed for a wider target segment that also includes elderly (e.g. all adults).

In Vitro Diagnostic Medical Device Regulation - (EU IVDR; 2017/746) tackles in vitro diagnostic medical devices only.

Medical Device Regulation - (EU MDR; 2017/745) tackles all medical devices for human use manufactured or sold into the EU.

Person-centredness - in the context of this project, it is meant human-centeredness, person-centred, personal centred and patient-centredness.

Solution – any innovation to make users' lives better / more comfortable.



Executive Summary

Many significant gaps in investment readiness in the market for digital health solutions aimed at the aging population are related to the **complexity of the digital health market** in general. The market structure and business development are unintuitive and complex even for those innovators and investors already experienced in the consumer tech market. The broad objective of the current report, **aimed primarily to innovators**, is to provide clarity about options for attracting investments and financing through having a solid understanding of the market structure and business development. Clarity is provided to innovators about relevant **rules**, **behaviours and processes** in the market, not only for them to know which type of investor to approach in a certain development stage, but also be prepared and competitive business-wise for raising funds by being competitive and demonstrating **cost-efficiency** of their product both for investors (increased risk-adjusted return of their funds) as well as societies (scoring high at both cost-effectiveness analysis and cost-utility analysis for insurers to be interested).

The high-level differences between digital health and consumer technology market are firstly established. Broadly, it has been claimed that the **iterative innovation approach used in the latter market is not suitable for the former**. While developing digital health solutions, a need-driven risk-averse innovation approach is better suited because making continuous iterative changes to the product is much more difficult.

Furthermore, the digital health market itself must be divided into two. On the one hand, there are the **solutions not classified as medical devices** in the eyes of the law. Such a solution could for example be an application developed for people with neurogenerative diseases that aims to slow their cognitive function deterioration through digital gamified activities. Such solutions manage to follow a more classical technology product development model, largely unencumbered by significant clinical and regulatory costs. However, such solutions would also remain in the periphery of the healthcare sector, without generally being authorized for use in clinical setting. On the other hand, there are digital health solutions **classified as medical devices**. An example of that is software monitoring the clinical state of a patient, where the outputs are used for clinical inputs. For such solutions, the development path is more complex and specific but their potential impact in enabling active and healthy ageing is also much higher as they can stand in the middle of the healthcare ecosystem.

The report explains the development paths and related financing implications (innovator **investment strategy**) for both categories. However, the focus and detail are put on the medical device categorised digital health solutions as this is the more complex and misunderstood market in which many innovators lose time and money by not anticipating the regulatory, clinical and reimbursement hurdles ahead. Firstly, a **Competence Matrix** constituted by three competence streams (advisory, executive, technical) is introduced as an actionable tool for an innovator to plan their company development and reinforce investment readiness.

A **deep dive into the development model** of medical device digital health solutions is then presented. The structure of the model is borrowed from the Consortia for Improving Medicine with Innovation & Technology (CIMIT) model originally developed by various healthcare stakeholders to "find, fund, and facilitate" healthcare innovation. During the deep dive, a **particular focus is placed on the financing implications** relevant for each of the four phases (Ideation, Development, Market Entry, Adoption) of the model. For each phase, the focus will be on explaining leveraging and blending relevant financing sources



(Venture Capital, public grants, family offices, etc.) together with concrete examples of new partners for implementation - relevant financing bodies (specific funds, grant programs). The deep dive allows the innovator to delicately understand their positioning on the development curve as well as the prerequisites and insights of optimal product development (including insights specific for the aging population), business development as well as financing position. The deep dive is also complemented by an innovator **Cheat Sheet** condensing the most relevant insights.

Finally, **two case studies** are presented which have been referred to throughout the report. The first case study covers an **Estonian company TempID** which develops a reusable body temperature logger together with complementary smartphone application. TempID is close to getting CE-certified and has strategically so far chosen to be mainly self-financed. The second case study covers **Avecen solution from Spain** which is a software application aiming to improve the lives of people with dementia, their caregivers and family. Avecen is an interesting example both because they have opted not to apply for CE mark and because its development has followed a consortium model to which many companies and institutions are formally tied. Both case studies contain relevant practical insights for other innovators regarding product development for the ageing population segment as well as investment strategy.



Quick Navigation Guide

Useful for jumping to specific parts of the reports.

Reading this report likely provides value to everyone tied to the digital health ecosystem.	<u>Read more</u>
Digital health market is fundamentally different from markets such as consumer technology.	Read more Introduction to Digital Health Market and Possible Development Paths
Innovators within digital health market could face very different development paths.	<u>Read more</u>
Understanding regulation governing the digital health market is vital for every innovator, and medical device categorization is not as straightforward as it sounds.	<u>Read more</u>
Solutions not categorized as medical devices have a development path like consumer tech.	<u>Read more</u>
CIMIT model is a great framework to understand for innovators developing medical devices.	<u>Read more</u>
Living Labs could provide great value for digital health innovators.	Read more
A forward-looking competence stream approach could be valuable to all innovators trying to navigate and anticipate challenges in the complex waters of digital health sector.	<u>Read more</u>
Every digital health innovator and ecosystem member should grasp the four phases of company and product development, each with their own specific financing implications – Highly Recommended	<u>Read more</u>
Demonstrating cost-efficiency and understanding evaluation frameworks are vital for innovators monetizing via insurers.	<u>Read more</u>
Case studies of two digital health companies demonstrate different product categorizations, financing strategies and insights about AHA end-user testing.	<u>Read more</u>
Summary of general financing options and capital needs for each digital health company development phase.	See summary
Summary of relevant financing sources with examples of funds and other organisations	See summary
Summary of most relevant digital health innovator insights from report - Investor Cheat Sheet	See summary



1. Introduction

This report is compiled to contribute to the main objective of the IN-4-AHA project - to **develop a practical**, **validated innovation scale-up model to facilitate the scale-up of innovative solutions across EU in active and healthy ageing (AHA).** Among the 4 sub-objectives of the project, this report contributes both to changing the entrepreneurial ecosystem of active and healthy ageing for the better through actionable insights for innovators and investors, as well as to providing actionable insights for sector innovators to formulate their own development and investment strategy.

The current document is **primarily aimed at innovators to guide them towards the investor in the silver and the digital health market** in the EU, although investors pondering entry into the digital health space would also find value in the insights provided here. The name of the report is **Long Term Investment Plan**, which is to be understood as a plan for attracting investments (and other sources of financing) over the long-term development curve for companies developing solutions for the ageing population. Otherwise put, the report aims to fulfil the purpose of **actionable guidelines for a digital health innovator to better understand the market, evaluate their investment readiness, and therefore position themselves adequately in terms of attracting financing that in the long term would increase investments into the AHA sector**. Having a thriving digital health market aimed at AHA would greatly benefit the European societies through improving the wellbeing, quality of life, social connectivity, and cohesion of the ageing population as well as help bear the economic costs to healthcare systems. However, vitality in the market and cost-efficiency of innovative solutions can only be achieved at scale through **increasing the competitiveness of digital health companies** for them to compete with other sectors for funding and investor attention.

The current guidelines have been preceded by a deliverable 6.1 Investment readiness assessment **(Task 6.1)** which can be seen as complementary insofar as it presented, through a more holistic and high-level view, many investment gaps that exist today in the elderly-focused digital health solution market in the EU. The current guidelines will represent the first efforts towards closing some of those gaps, notably those related to the general complexity of the market and lack of market understanding. It does that by **extracting, condensing, and structuring** all the relevant, and too often misunderstood or overlooked, information about the digital health market (gathered through secondary research and expert interviews) into actionable guidelines the innovators could find value in.

After having read the report, an innovator of an elderly-focused or -inclusive digital health solution will:

- be **better prepared** by having a clearer, practical understanding of the digital health market, including its main differences compared to a consumer technology market
- **save time and money** by anticipating the existence (or not) of the regulatory and clinical requirements for their solution
- be better positioned for investment-readiness due to:
 - o understanding financing implications of different stages in the product development
 - \circ grasping relevant financing sources for their unique situation
 - o anticipating the rationale and stakes behind different sources of financing
- **discover actionable insights and tips from companies** developing elderly-focused or elderlyinclusive digital health products



2. Introduction to Digital Health Market and Possible Development Paths

While developing digital health solutions aimed specifically or partly at the ageing population, start-ups, and SMEs (hereafter together referred to as "innovators") must have a **delicate understanding of the functioning of the broader digital health market, its stakeholders as well as regulation**. That is because developing a health-oriented technology company comes with its specific challenges as opposed to, for example, consumer technology. Figure 1 shows the main points of comparison between the two.



Health technology innovator, and professor of medicine and bioengineering Dr. Paul Yock has suggested that many digital health companies fail because they apply the **"move fast and break things"** strategy, known to work in consumer technology, without realizing that digital health is an entirely different industry with its own set of rules.¹

The risk-prone "move fast and break things" approach of consumer technology aims to get the product on the market as fast as possible and then make iterative changes while validating and searching for product-market-fit. On the other hand, the right approach in the digital health sector could carry the principle of **"do no harm"**. It is risk-averse and market entry could generally be attained only after a timeconsuming validation of the safety and efficacy of the product. It also means that the validation of the product-market-fit happens more slowly, one iteration round is usually more costly, and significant iterations are to be avoided as changing the product could also mean going back to the regulatory drawing board and having to prove the solution's safety and efficacy all over again.



Figure 1. Comparison of Digital Health and Consumer Tech Development Strategies

Source: Compiled by authors

¹ https://www.fastcompany.com/90251795/why-do-digital-health-startups-keep-failing



2.1 Digital Health Product Development Paths

When talking about the digital health market and envisioning the steps an innovator must take to successfully develop its product, attract financing, achieve market launch, and scale up the userbase, it is crucial to understand that there are broadly two fundamentally different paths of development. The right path is determined by the nature of the product, i.e., whether it classifies as a medical device or not. The paths and their corresponding strategic categories are shown in Error! Reference source not found.. S trategic categories are to be understood as the focus areas that the innovator must get right for the business to be successful. Broadly, the first path, in which an innovator is developing a solution that does not qualify as a "medical product" in the regulatory sense, is simpler and more akin to the development of a consumer tech product. In this path, the innovator must develop a product that works well technically and that the market wants while having a company with a strong enough business plan that the venture would be profitable and satisfy shareholders (both investors, founders, and option-holding employees). This path of development is quicker and more iterative, but the digital health solution is likely to exist on the periphery of the healthcare world as it generally cannot be used in a clinical setting. Examples of such solutions are apps in the wellbeing category such as Avecen app² developed for the ageing population with neurogenerative diseases, it performs a continuous evaluation of the users through activities or games based on gamification techniques (see also Case Study 2 in Chapter 3).

Figure 2. Digital Health Market Development Paths



Source: Compiled by authors

The second development path is more healthcare sector specific and applies to the solutions requiring medical device certification (including a CE mark in Europe). Such a solution is for example developed by TempID that builds disposable or reusable smart thermometers with specialized software (see Case Study 1 in Chapter 3). This path will be the general focus of this document as it is more complex and time-consuming.

Regulatory and clinical strategic categories are important in this path, but they are often not understood, seem startling for innovators that are not industry-insiders and act as entry barriers to the digital health

² https://avecen.com/en/home-en/

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sector. Those two additional categories do not only lengthen the product development phase but also fundamentally reshape many aspects of it, such as end-user testing, common monetization channels as well as financing strategy due to modified risk profile for investors resulting in higher capital cost in the early stages of development. On the other hand, the complex and unintuitive development path has a reason – the medical device companies aiming to succeed in the digital health market have the ambition to make a significant impact to the health and wellbeing of the patients, are used in a clinical setting in which margins of error are slim, and fundamentally add healthy life years for the society. For such ambition, the risks are also higher and that is why additional hurdles must be crossed. In any case, due to the fundamental differences between the two development paths,



the innovator must be rigorous in the early stage and understand what it wants to offer, who will be the stakeholders involved and what implications it has on the categorisation of the digital health solution.

Failing to do so is rather common, for example the experience of Temp ID (Case Study 1) demonstrates practically how a team of engineers could have a useful idea, start building the product and then only later discover the regulatory and clinical categories to consider. Even though it did not become an existential obstacle in their case, anticipating regulatory and clinical requirements would still have saved the company time and probably also money. Below, concise instructions are presented that could guide the innovator to the right track regarding product categorisation.



DETERMINING WHETHER A DIGITAL HEALTH SOLUTION IS A MEDICAL DEVICE

There are two regulations on the EU level that determine categorization of a health solution as a medical device:

- Medical Device Regulation (EU MDR; 2017/745) that tackles all medical devices for human use manufactured or sold into the EU.
- In Vitro Diagnostic Medical Device Regulation (EU IVDR; 2017/746) that tackles in vitro diagnostic medical devices only.

The definition of a medical device is given in MDR art. 2(1)³ and it is broad. Most importantly to digital health solutions, **the definition also includes software** that is intended by the manufacturer to be used, alone or in combination, for human beings for diagnosis, prevention, monitoring, the prognosis of a disease, or for diagnosis, monitoring, treatment, alleviation of an injury or disability, etc. It is also separately underlined that devices for the control or support of conception fall under the medical device definition. Therefore, even devices such as wellness apps might be argued to fall under the definition. **European Commission has developed instructions** aiming to help identify whether a given software can be categorised as a medical device and these could be helpful for the innovator.⁴

MDR and IVDR also have different data reporting needs. An aspiring innovator must be especially considerate of pre-market data reporting which must be attached to CE technical files. This is important as CE marking is required to sell or distribute medical devices in Europe. Post-market data reporting is relevant for continuous oversight of the product on the market:

³ https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745&from=EN

⁴ https://ec.europa.eu/health/system/files/2021-03/md_mdcg_2021_mdsw_en_0.pdf

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- MDR: clinical evaluation report for pre-market and ongoing post-market clinical follow-up activities.
- **IVDR**: performance evaluation and performance studies for pre-market and post-market surveillance and vigilance.

Finally, in terms of regulatory cost that medical device producers or providers must account for, it is important to know that **self-assessment is generally not sufficient to get CE-certified** and an **approval of Notified Body** is required.⁵ As of 08.04.2022, there are 28 Notified Bodies designated under MDR located in 12 different European countries. There have been suggestions that the number is not enough to handle the certifications given that conformity assessment takes months to complete.⁶ Also, there is little transparency around the total cost of MDR certification as Notified Bodies report only hourly rates (in the region of 300 EUR).⁷ However, 72% of the 110 participant companies in a 2020 survey noted "increased resource costs" as a challenge to MDR implementation.⁸ Hence, the **regulatory cost of certification** is definitely a **factor companies must take into consideration** in development.

Furthermore, a thorough understanding of the market and related implications are relevant for streamlining the development of many digital health companies in other aspects, such as business-plan-related monetization channels.



RockHealth has found in 2017 that 61% of the 85 digital health companies they surveyed in the U.S. started out as B2C but converted to B2B or B2B2C.⁹

The main purpose of this document is to **help innovators anticipate such problems** and hopefully avoid the trouble of significant business plan change. Finally, before delving into the development paths more thoroughly, there are two things to emphasise:

- Current guidelines will briefly explain the development path of the solutions not categorized as medical devices but then **focuses on the world of medical devices**. Still, innovators in the digital health market belonging to the first category will have a lot to learn from the more complex development path, for instance in terms of the market structure and financing implications.
- Even though the development models and methodologies used in this report take a **start-up-centric approach**, they are **also valid for other types of digital health solution companies** with slight modifications to be made according to the situation. For example, a spin-off from a pharmaceutical company might already have the required research and funding available due to corporate resources so it can fast-track these stages. An SME adding digital health solutions to its product offering might already have the marketing channels set up to engage first users. Alternatively, an SME already engaged in digital health that wants to modify its solution to be elderly-inclusive or -focused might mainly concentrate on the end-user testing stage to validate a need in a new customer segment, etc. While companies, their starting points, and available resources differ, the sequence of stages in the development path tends to be the same.

⁵ https://advisera.com/13485academy/blog/2021/04/06/ivdr-vs-mdr-comparison/

⁶ https://www.medtechdive.com/news/mdr-is-live-here-are-5-things-to-know-on-where-the-rule-stands/600733/ ⁷shorturl.at/rzE04

⁸ shorturl.at/bgyzX

⁹ https://rockhealth.com/insights/streamlining-enterprise-sales-in-digital-health/



3. Development Path for Solutions Not Categorised as Medical Devices

The development path for solutions not categorised as medical devices broadly follows a classical consumer tech growth roadmap shown in **Error! Reference source not found.**. Below the figure, the d evelopment phases and financing implications are briefly elaborated upon with emphasis on aspects relevant for AHA digital health non-medical device innovator.



Figure 3. Roadmap and Product Development Stages for a Typical Technology Company



IDEATION | The founders come together around a novel idea and do as much research as possible about the market to have an initial validation of market need and the viability of their idea. The goal is to **understand whether the idea works on paper** and then formulate first strategic documents detailing how they see it working. The following things are important to consider:

- The founders must **trust each other** enough to share the significant burden that starting a company usually represents.
- Apart from desk research (e.g., reading industry reports), **networking in the community** is vital to establish informal pools of industry expertise to draw from.
- For a digital health company focused on the ageing population, gathering **feedback from the target segment** is imperative. This is especially so if the founders themselves are younger.

The following **financing-related implications** are noteworthy for the phase:

- The founders are expected to do research for free. Limited costs can arise (e.g., paid market reports, travel costs to ecosystem events) but these should be financed by founders.
- It is possible in this phase to raise money via the famous three Fs "family, friends and fools". The three F's make sense as a concept because at this point, there is no product nor even a clear business plan, so the risk is extremely high. On the other side, even if any external financier would be prepared to invest for equity, the conditions would be relatively unfavourable for founders to compensate the investor for the risk.
- Hackathons could help with idea generation and incubators as well as living labs (see more in next chapter) could be joined to access know-how and connections.



DEVELOPMENT | The founders become committed and develop a minimum viable product (MVP) that undergoes rounds of initial testing and feedback and is then launched in the market. Then, **traction is sought** as first paying users could show if the theoretical need (validated previously) translates into actual willingness to pay for the product. The company also hires its first employees, works on engagement and monetisation channels, and defines business KPIs. The following things are important to consider:

- Having a product end-users need is only a part of the puzzle. This is especially true for the elderlyfocused market as first **users might not be effectively found through social media** advertising. Representative organisations could be one channel to engage early users and gain valuable feedback.
- Even if the business model is direct-to-consumer (D2C), it could be the case that the payer is a family member more at ease with digital solutions instead of the end-user. **End user feedback is vital for founders** to explore which models work. Country-specific factors could make a big difference here (digital literacy rates, social exclusion, deposable income among the ageing population, etc.).
- In this phase, the company must **concentrate on increasing its traction** as more users translates into more feedback which then translates into closer alignment to market needs and product-market-fit. Traction, and related KPIs, are also essential for investors.

The following **financing-related implications** are noteworthy for the phase:

- **Considerable costs** can arise related to product development and marketing. To cover these costs, founders would likely explore external financing opportunities. However, as the product and business are still in the early stages, financing is expensive due to the risks involved.
- From **private funding**, pre-seed and seed financing rounds are suitable in this phase, for which **business angels** and **Venture Capital** (VC) funds are the most suitable channels. **Accelerators** could also provide some financing in addition to other benefits (business coaching, network, office space, etc.).
- Exploring **public grants** for product development could also be an option. Available public programs are worth mapping, but the innovator must understand that most of the grants require founder co-financing and could come with a **considerable administrative burden** (both for writing the application and reporting after being awarded with money) which is time not spent on product development.

MARKET ENTRY | The phase begins once significant traction is achieved and product-market-fit found. This phase is all about **improving your solution and processes focusing on customer experience**. Based on the valuable feedback from core group of loyal paying customers, the company focuses on improving aspects such as product design, pricing, features, and customer service with the goal of broadening the customer base from the early adaptors. The following things are important to consider:

- As the company focuses on attracting traction, it **constantly iterates on** (changes) its product to serve the objective. For example, customer retention is focused on improving the overall design and pricing structure, new customers are attracted via additional features, etc.
- During the market entry, the company **slowly starts to reorient itself** from start-up to a solid functioning business. For this, processes need to be reworked for the "controlled chaos" of the start-up to be streamlined into better-defined processes.



The following **financing-related implications** are noteworthy for the phase:

- If the company demonstrates tangible improvements in its product as well as strong growth in
 user base, it has a good chance to raise more money in further rounds of private financing. Around would be used for gaining further traction and honing product-market-fit. VC remains the
 most likely financing source even though new, later-stage financing options also emerge, such as
 corporate funds, family offices, and investment firms (see next chapter for further information).
- **Public grants** also remain an option, notably those focused on later-stage product development (Technology Readiness Level (TRL) 7-9). However, innovator should note that public money is likely to remain a marginal source of funds in the Market Entry phase.
- Ideally, by the end of the phase, the company is **already generating operating revenue** to finance a part of its development.

ADOPTION In this phase, the product-market-fit is already firmly established, and the company is now **concentrated on growth**, **margin optimisation** and **transformation into a mature business**. As organic growth in key markets slows down, it must take strategic decisions of expansion and partnerships. Adoption phase will last until the product (or company itself) constitutes a profitable, self-standing business. The following things are important to consider:

- By the beginning of this phase, many employees have usually been recruited and the **company structure becomes more specialised**, i.e., the founders offload small tasks and concentrate on high-level strategic business growth.
- **New strategic dimensions** include for example poaching customers from competitors or enlarging the potential customer base through strategic partnerships.
- As it matures, the company will stop growing fast in the core markets as it has captured the optimal market share and further **customer acquisition becomes much more expensive**. New customers must be strategically sought from new markets or segments.
- As the requirements for running a business differ between one with fast investment-led growth and another with moderate organic growth, the **strategy might need to be** reworked and new competencies brought in. Strategic decisions regarding growth remain, but these will be made around acquisitions of other companies and expansions to difficult markets.

The following **financing-related implications** are noteworthy for the phase:

- If the business is now functioning well in its core niche and could theoretically **support moderate growth from its own operations**, the further financing rounds pose the founders a strategic decision. On the one hand, further financing could fuel rapid further growth, increasing the value of the business. On the other hand, raising financing always comes with an implication of the founders decreasing their share of the business as they give away equity, i.e., shares of ownership.
- To fuel non-organic growth, the company could raise larger investment rounds (**B-round**, sometimes **C-round**). Apart from VC, all **private funding sources** underlined in the previous phase remain adequate. The importance of public money decreases as growth and marketing activities are not generally funded by grants.
- Once we are already talking about a profitable business with moderate growth, the most common financing channels become **debt-financing** or **equity-financing through going public**. The first becomes possible as the company now has a strong cashflow to service its debt year-by-year. Debt-financing channel is not available earlier as the company's cashflows are irregular and the



cash available needs to be invested back into growth and product development. However, note that for mature businesses, debt financing done in moderation is usually cheaper than equity-financing. Still, innovators should also note that debt often comes with collateral requirements which could be difficult to attain for non-capital-intensive (e.g. software) businesses.

• Equity-financing through going public means conducting an **initial public offering (IPO)** and floating a part of the company's shares in the public stock market. This provides a benefit of providing liquidity to stock owners, i.e., the founders and early employees (who have stock options) so that they can decide sell their stake (or part of it) in the business. However, going public comes with high regulatory costs and requirements for transparency. Finally, equity-financing without going public is also possible at this stage through **private equity** funds as investors.

A reader surely notes that in the previous description of the phases, **not many sector-specific considerations were brought out**. That is because while there certainly are differences (such as engagement channels, target segment digital literacy, disposable income, etc.) between a digital health company focusing on the ageing population and for example a digital consumer technology company focusing on children, **the development path and financing implications of these companies are fundamentally very similar**, as sketched below.

- **1.** Define an unmet need or inefficiency.
- 2. Sketch out an idea to solve the need or inefficiency.
- **3.** Gather as much information and feedback as possible related to the market and customers to validate the idea.
- **4.** Commit and build a prototype of a solution after which this solution is launched in the hopes of finding traction.
- 5. This traction brings valuable feedback and validation whether the solution is attractive enough for the market. If it is, then the money is spent on tweaking the solution and finding as many people as possible interested in using, and paying for, the solution.
- **6.** If that is done successfully, the idea has become a growing business and if the growth is sustainable then at some point it has established itself as a mature business.

If a company manages to successfully progress along these stages while showing promise, then investors who have money to deploy will consider investing in the hopes of making returns later. However, this fundamental similarity of development requirements **does not hold once we start talking about digital health solutions categorised as medical devices**. That's what justifies exploring this development roadmap more in-depth going forward.



4. Development Path for Digital Health Solutions Categorised as Medical Devices

As explained earlier, the **development path is more complex for medical device category digital health solutions**. Because of that, a different and more specialized model should be used to illustrate the development phases of innovation in the digital health context. **Error! Reference source not found.**. i Illustrates such an adapted model.

Figure 4. Development Roadmap for a Medical Device Digital Health Product



Source: Compiled by authors based on CIMIT model

The model is a slight modification of a model developed by CIMIT, a broad coalition of healthcare ecosystem participants from mainly the US but also Europe. National Health Service (NHS) from the UK is one example of a European-affiliated organization. The CIMIT model was developed to "find, fund and facilitate" collaborations that drive solutions to patient care, with emphasis put on the importance of starting with an intimate understanding of an unmet medical need ("clinical pull") and then identifying collaborators to work on developing and advancing solutions to the problem, thereby improving the standard of care.¹⁰

The CIMIT model is divided into four phases – **Ideation**, **Development**, **Market Entry** and **Adoption**. In turn, each phase encompasses stages that the innovator should traverse. It must also be noted that even though the model depicts the development roadmap in a simplified and linear way, the planning and anticipation of many later stages should start from the Ideation phase.

LIVING LABS AS USEFUL TESTING GROUND FOR DIGITAL HEALTH COMPANIES

A promising opportunity for innovators (including those without medical device categorisation) would be to **join a living lab specialized in person-centred care** (PCC). Living Labs are open innovation ecosystems in real-life environments using iterative feedback processes throughout a lifecycle approach of an innovation to create sustainable impact. In Europe, the **European Network of Living Labs** (ENoLL) is an international, non-profit, independent association of benchmarked Living Labs which facilitates knowledge exchange, joint actions, and project partnerships between its 480+ members in Europe and worldwide.

ENoLL website¹¹ is a good source for innovators to discover whether suitable living lab programs exist, notably as "Health and Wellbeing" is one of their major thematic work streams.¹² Under the work stream,

¹⁰ shorturl.at/gJNTY

¹¹ https://enoll.org/

¹² https://enoll.org/about-us/what-are-living-labs/



living labs have for example enabled worked with innovators on **user-driven innovation and evidencebased research** in the AHA domain, enabled **collaboration with nursing homes**, **daily care centres**, **elderly homes** as well as facilitated channels for **active user validation of wearables** on the health domain.

A collaboration with the right PCC-focused living lab could provide innovators with broad-based value, including channels to engage with **specialist advisors**, **validation of the market need**, **alignment of the product to the end-user requirements** through end-user testing as well as potentially **supporting the company with clinical validation and regulatory filings**. For example, both companies introduced in case studies (see Chapter 5. Case Studies.) participated in living labs under IN-4-AHA project and discovered valuable insights related to ageing population end-users.¹³

4.1 Competence Streams Required for Digital Health Medical Device Development

Before delving into the nuances and financing implications of each phase and stage in the digital health sector targeted at the ageing population, it is also important for an aspiring innovator to have a framework in mind regarding the **competencies needed to successfully traverse the stages**. In parallel, following this framework also serves to boost investor confidence as it emphasizes the company's capability to find the right talent and competences to achieve success. **Error! Reference source not found.**. provides such a f ramework constituted by three competence streams – **advisory work**, **executive work**, and **technical work**.



Figure 5. Competence Matrix for Digital Health Medical Device Innovators

Source: input from expert interviews, graph prepared by authors

ADVISORY WORK STREAM should be constituted by **people with specialist competencies and experience** required for the business. These people would not be hands-on in the business development but **engaged periodically** by giving the founders advice and helping them anticipate the hurdles on the road. Advisory work stream members could have various profiles:

¹³ Read more about living labs organised under IN-4-AHA in D4.1 Living Lab testing and innovation scale-up playbook



- In the early stages, well-intentioned and experienced ecosystem members could be found to give initial advice for free. These could for example be **people having already succeeded** with founding a digital health business or **friends** with healthcare industry experience.
- Specialists and mentors engaged via **separate programs** such as hackathons, incubators, accelerators or living labs could serve as advisors under the framework of the program.
- Further down the road, **investors** constitute the most important part of advisory work. Specialist investors could formally join the advisory board of the company.
- Advice could also be gathered from the representatives of partner or client organisations (e.g., hospitals), representatives of the end-users (e.g., companies developing a digital solution aimed at increasing the well-being of people with Alzheimer's disease, NGOs focusing on Alzheimer patients could be willing to help) as well as representatives of the payors (e.g., national health insurance) to anticipate the solution having maximal chances of being reimbursed.

EXECUTIVE WORK STREAM composes of **founders** and hired executive-level employees in the later stages. This stream constitutes mainly **tactical and strategic work** based on ideation and analysis.

- The founders need to always have a **6–18-month perspective.** Within this timeframe, they should have a clear idea regarding where the company is going, and which are the directions that require the development resources the most.
- Starting from the later stages of the Development phase, it would also be an option to bring in external, experienced executive-level employees to reinforce the group of company founders.

TECHNICAL WORK STREAM consists of **actual work on the product** (programming, experiments, trials, applications, etc.) and is very **operational**.

- Substantial technical work starts from the Development phase and therefore these competences should not be prioritised over market research in the Ideation phase.
- Technical work is carried out by employees with corresponding capabilities. Still, founders are usually also very engaged in the technical work stream during most of the development curve and market entry phases. This is especially the case if **founders are technologists** in nature as we for example see in the Case Study 1.

Conceptually, the company should always have this matrix in front of them helping them understand **which specific expertise is needed** for each level for each stage and **how deep should the expertise be**. Correspondingly, each box should be filled with **2-3 names** who are available upon need to take responsibility for the work in each stage. To achieve this, the **motivational package** for each person should also be thought through. This is crucial for optimizing the company's development path and anticipating its needs. Furthermore, using the matrix should also **reinforce the company's investment readiness** by being always on top of the business and product development.

For example, let's take the **Initial Clinical Trial stage as an example**. The founders should prepare for it during the Development phase by figuring out (or starting processes for acquiring externally, if necessary) the competences:

- Helping the company as advisors. Ideally, these people should have deep experience with clinical trials.
- Technical experts of carrying out the operational work for clinical trials, including continuous reporting and documentation, data management, trial planning and oversight activities.



• The founders should also decide who among them (or a wider executive team) will be heading the tactical development of the stage.

4.2 Digital Health Development Model Deep Dive and Financing Implications

Below, the development phases and stages for a digital health solution classified as a medical device are described more thoroughly. Capitalizing on the insights from expert interviews conducted as well as work published by the digital healthcare market stakeholders, this part aims to walk an innovator through the main aspects of digital health sector company and product development for the elderly target segment. Focus is put on the **aspects especially relevant for financing implications**. Further useful information for non-financing-relevant aspects could for example be found from the Digital Health Milestones Framework by EIT Health¹⁴. **Error! Reference source not found.**. provides a handy general overview of the model.



Figure 6. Overview of CIMIT Development Model

¹⁴https://eithealth.eu/wp-content/uploads/2021/09/EIT-Health_DigitalHealth_Milestones-Framework_VFlog.pdf



Ideation Phase

NEED | The Ideation phase consists of two stages. The **Need** stage is focused on **identifying the existing clinical need** in the market and figuring out what solutions are currently out there to **answer the need**, with a special focus put on **state-of-the-art** solutions. Note that starting the business-development from

the need is the manifestation of the need-driven nature of digital health innovation.

IDEA | The second stage of Ideation is **Idea**. There, the innovator hones out their idea for the novel solution to the need and **formulates the initial value proposition** of the solution. This also includes a thorough mapping of the competitive landscape as well as the **potential stakeholders** involved (who could be my end-users, partners,



STATE-OF-THE-ART

State-of-the-art care can be loosely defined as innovative, cutting-edge, and often beyond "the norm" of traditional treatment. It can be thought of as the ceiling of current medical care for a given disease. State-of-the-art care can be applied to technology, practices, and physicians.¹⁵

payers, financing channels). Innovators developing elderly-focused or age-inclusive solutions should also consider market opportunities **specifically for that target segment**. For example, if a solution to a universal clinical need exists, but is not elderly-focused or age-inclusive then the market could have room for a more specialized solution. In general, it is very important that the innovator familiarizes themselves with the market structure in general by the end of the Ideation phase. They need to have a clear idea whether their solution would **classify as a medical device**, a good overview of the **regulatory regime** in their core market, as well as an understanding of the **potential reimbursement channels** in that market.

The Ideation phase **does not require deep competencies in the technical work**. The founders in the executive work stream do not even need to do a lot of operational-tactical work (it is not yet so important having a clear plan for the next 6-18 months). Rather, the most important is that the founders work on the strategic matters of putting the idea into the context of the market opportunity. Secondly, it is vital they find the possibilities to **talk with various healthcare ecosystem members**, some of whom could act as mentors or coaches either informally or formally under programs such as incubators and living labs. Feedback from at least 5 clinical stakeholders would be required to validate the idea.

Source: own resources, FFF

Typical cost points: business travel and meetings, market research

Financing need: 50k – 70k EUR

Generally, the money used in the Ideation phase must come from the **team's own resources** or **FFFs** ("family, fools, and friends"). The question is not so much about spending on capital investments or talent but rather the team must **dedicate a lot of intellectual resources**, i.e., work hours. Some cost categories could be travelling, networking events, acquiring market reports on relevant topics. But the focus is on work hours dedicated to gathering, systematising, and analysing information.

The innovators could also consider joining an **incubator** or a **living lab**. At this stage, the argument would not be attracting financing (some incubators do not provide financing at all, others do so for

¹⁵ https://www.huffpost.com/entry/stateoftheart-medical-tre_1_b_4283319



around 30k EUR) but rather developing fundamental entrepreneurship skills in business development, funding, and marketing. While digital health innovators would surely also benefit from a generalist incubator, digital health, health-tech, or deep tech focused ones would be ideal as they could provide specialized market knowledge and connections to potential partners and investors. One example is <u>Terkko Health Hub</u> from Finland – a pre-incubator for health tech and life science teams offering a 6-week online program with 13 expert-led workshops. An EU-led initiative <u>EIT Health Bootcamp</u> with varying locations is another example.

On average, the financing need in the "Ideation" should remain in the region of **50k – 70k EUR**.

Development Phase

PROOF OF CONCEPT | The **Development** phase consists of three stages. The **Proof-of-Concept** stage is all about validating the key components of the solution and **testing the value proposition**. The company starts building its solution, establishes preliminary system and software architecture as well as gets its first demonstration results, indicating that the solution mechanism broadly works. In parallel, the company should conduct their preliminary regulatory classification and put down on paper the **preliminary regulatory pathway**. From the business side, the value proposition of the solution will be further specified and it's very important in this phase to come up with a **preliminary path-to-payment plan**. Finally, it is important to **continue looking for constant feedback** as the product develops. Feedback should come from both the target end-user segment (the ageing population) as well as from clinical stakeholders in different settings (hospitals, care homes, nurses visiting the end-users in their homes, etc.) to understand where the use-case shows promise and what are the obstacles.

PROOF OF FEASIBILITY | The **Proof of Feasibility** stage focuses on demonstrating the feasibility of the solution both technically (**in models**) but also regarding stakeholder use-cases. The first **"works like"** prototype should be born in this phase as well as regulatory preparation advanced, such as drafting product claims and defining a **clear regulatory submission pathway**, i.e., steps and practicalities needed to get the paperwork submitted for eventually getting CE-certified. The company should also update its need statements and clearly **define the use case scenarios** as well as draft a **preliminary business plan** in anticipation of raising external investment. Finally, feedback is still very important in this phase. Users need to be involved and engaged and their **feedback gathered in many different settings**. Also, the company should start more clearly thinking about monetization channels and gather **feedback from potential economic buyers**. In this stage, formally composing an advisory board would also be reasonable. It would be plausible looking for raising a **pre-seed investment round** in this stage.

PROOF OF VALUE | The **Proof of Value** stage focuses on **tying together all the validation** gathered at previous stages and determining the solution **works**, and **is valuable and interesting**, for all stakeholders. It is a very important stage in which the company seriously commits to the solution. As the technical team works on creating a **"works like, looks like"** prototypes of the solution, the regulatory push intensifies as **clinical investigation approvals** are needed to conduct the first clinical pilot(s) in this phase. It is also incredibly important in this stage that the **core team becomes committed**. 2-3 people at the company should be dedicating at least 50-75% of their work hours to the company both to meet the increasingly intensifying operational requirements of business development but also as a **prerequisite for attracting funding**.



Indeed, this is the first stage in which larger external (seed) funding could be attracted. For that, the

company should have developed an investor-ready business plan. Furthermore, in this stage clinical pilots begin, therefore the company should have relevant expertise (possibly in the form of a medical advisory board) as well formalized as key relationships and partnerships with clinical establishments engaged in carrying out the pilots. The best way to establish contact and partnerships with these establishments is through the network and advisors. Finally, the throughout stage, feedback is still very important, and its scale should be expanded, ideally gathering insights from 100+ users and 20+ economic buyers.

By the end of the "Development" phase, the company would need to have proven their product-marketfit and team-market-fit (the

A challenge in the medical device digital health market is **testing your solution in its intended use** and this challenge is especially relevant in the Development phase before clinical trials have started. Usually, the value-added by digital health solutions is centred around software, with some companies (see Case Study 1) also producing physical products feeding data into the software. In any case, **digital health companies need data to work with** while developing the software and they need the data to reflect the real use-case. One opportunity would be to **work with living labs** which could enable controlled testing on 100+ end users with different profiles.

However, if such an arrangement is not possible and innovators cannot gather relevant data before the clinical trials directly from endusers/patients, they need to **work with model data** to calibrate their software (participating in **living labs** would also be an option¹⁶). One way to get this data is licence it in anonymized form from dedicated service providers but this could prove too costly for early-stage innovators. Another, and potentially more suitable option would be to **obtain the data from clinical stakeholders** such as hospitals **in exchange for involving the stakeholder as an investor** (giving them equity). Also, sometimes the required data has been developed in a university and exists in the form of intellectual property belonging to the university. For these cases, some universities have investment bodies specialized in this sort of IP-for-equity investments, one examples of which are <u>Cambridge Entreprise</u> from the UK and <u>UniTartu</u> <u>Ventures</u> from the University of Tartu in Estonia.

team understands the market specifics). This is where the focus should be on. As one of the industry experts interviewed put it: "By the midpoint of the market entry phase, you should already have some clients, a business model, some partnerships formed and **all you need to do is to hit the gas pedal**. To hit the gas pedal, you'd need money and for you to get the money, you need a product-market fit and teammarket-fit."

¹⁶ Read more about living labs at report D4.1 Living Lab testing and innovation scale-up playbook, chapter 1- Living Lab Testing



Source: Angel Investors, Venture Capital, Grants, Innovation Procurement, In-Kind Investments from Clients

Typical cost points: product development, feedback gathering, regulatory and clinical preparations

Financing need: 0.8M – 2M EUR

In the Development phase, there are many different potential sources of financing but also larger expenses in product development, regulatory work, organising pilot trials etc. Firstly, the innovator should look at **accelerators**, many of which offer seed financing, business development services as well as valuable access to industry insiders and clinical partners. There are many different Healthtech-focused Accelerators in the EU and many different models of operation. For example, Bayer Pharma in Germany has a digital health-focused accelerator <u>G4A</u> providing mentorship from industry experts as well as financing up to 100 000 EUR in convertible loans (debt that converts into equity under specified conditions). In Italy, <u>Open Accelerator</u> fast-track accelerator program dedicated to life sciences and digital health offers services valued at 25 000 EUR as well as seed investment up to 100 000 EUR. In Denmark, <u>Accelerace</u> has a 5-month equity-free program for Danish Medtech and Healthcare companies with a possible investment. Finally, if the solution in question is not developed by a start-up but for example an existing industry player or a consortium of enterprises (such as the consortium behind the Avecen app covered in Case Study 2), specialized Accelerator options exist that should be considered. For example, <u>i&l Prague</u> from the Czech Republic is open to invest in a spin-off company with project-focused structure.

To raise a seed-round, **angel investors** and **venture capital (VC)** funds are an option. The former category is more fragmented (usually wealthy start-up founders themselves) and could be approached via regional industry events and broader ecosystem connections. VC fund contact information can generally be found online. Many of the EU VC funds are open to making healthcare-focused investments, such as <u>Credo Ventures</u> from the Czech Republic, <u>iBioNext</u> from France and <u>EarlyBird</u> from Germany. IN-4-AHA Deliverable 6.1 Investment readiness assessment has composed useful guidelines for VC due diligence process worth exploring.

The Development phase is also the most abundant for **public grants**. Many countries and regions have grant programs for supporting innovation which the innovator should explore in their home market. Furthermore, there are many prospective programmes on the EU-level, such as <u>EIC Pathfinder</u> for early-stage products (TRL 1-3), <u>EIC Accelerator</u> for SMEs, start-ups and spinout companies to develop and scale up game-changing innovations. As a different example, EIT Health <u>Investor Network programme</u> offers matchmaking services for attracting equity investments. It must be noted that even though public money might seem particularly attractive as the innovators don't generally have to give away equity, it still comes with administrative requirements and costs to be mindful of. Finally, it could also be worth exploring **innovation procurement**¹⁷ programs available in the innovator's home market in which a public buyer describes its digital health related need. European network of competence centres for innovation procurement can be found <u>here</u>.

¹⁷https://single-market-economy.ec.europa.eu/single-market/public-procurement/strategicprocurement/innovation-procurement_en

IN-4-AHA project - Horizon 2020 programme, Grant Agreement No. 101017603



The final type of investment that is relevant for the "Development" phase is **in-kind** investment from partners. As explained earlier, access to relevant data could be obtained through in-kind data-for-equity transaction with an institutional partner (such as a university). Another opportunity would be engaging the clinical partners as a strategic investor in a model where they would cover the costs of the clinical pilot in exchange for equity.

On average, the financing need in the "Development" phase consists of a pre-seed round of **0.3M** – **0.5M EUR** and **a seed round of 0.5M** – **1.5 MEUR**, for a total financing need of **0.8M** – **2 MEUR**.

Market Entry Phase

INITIAL CLINICAL TRIAL | The **Market Entry** phase consists of three stages. The **Initial Clinical Trial** stage centres around **pivotal clinical investigation** executed together with clinical partners. Before the trial, the solution is modified technically respective to the outcomes of the pilots conducted in the previous stage. Essentially, the clinical investigation conducted aims to validate the solution's ability to achieve its intended purpose, thereby leading to a **clinical benefit**. Clinical benefit is understood as the positive impact of the device on the health of an individual, expressed in terms of a meaningful, measurable, patient-relevant clinical outcome(s). Put simply, the aim is to prove that the device is both safe to use and useful for the intended purposes.



UNDERSTANDING CLINICAL INVESTIGATIONS (TRIALS)

EU regulation (MDR) defines clinical investigation (commonly known as a **clinical trial**) as any systematic investigation involving one or more human subjects, undertaken to assess the safety or performance of a device.

A pilot clinical investigation is typically an **early-stage clinical investigation** designed to enrol a limited number of subjects to assess a device early in its development phase regarding **clinical safety and performance** (e.g., device functionality). The outcomes of an early-stage clinical investigation can often support further development and iterative changes to the device. The data generated in pilot stage clinical investigations are in general insufficient to obtain the CE mark for the device.

In the "Initial Clinical Trial" stage, we are talking about **more comprehensive and stricter trials** (called **"pivotal clinical investigations"** in MDR sense) conducted to prove the **intended performance**, the **clinical benefits**, as well as **clinical safety** of an investigational device. Pivotal clinical trials require authorization by both, Member State(s) and validation from an ethics committee.

MDR also defines post-market clinical follow-up (PMCF) clinical investigations potentially happening after the solution is CE-marked. Read more about the subject <u>here</u>.

The specific regulatory pathway of a company depends on **how innovative the solution** is. If the solution does not have a **predicate** (similar product/service in the market), the regulators might demand a lot of long-term and comprehensive clinical data from you. For instance, if you are developing a solution for which the regulatory authority requires clinical data over two years on 10 000 patients, then you really must **start planning for the Initial Clinical Trial stage in the Ideation phase** to understand when the patients are the be found and when you must start collecting the info. If you have a simple technological solution classifying as a Class I device (self-evaluation-based and do not require conducting a pivotal clinical investigation) then for that you maybe need to start data gathering 3 months prior to submission



in the Validation of Solution stage. Furthermore, to ease the administrative burden, some **living labs** could support innovators with data gathering, regulatory file composition as well as streamlining submission. In any case, the current stage is **resource-intensive** and most digital health companies should **raise their first bigger investment round here** (A-round).

VALIDATION OF SOLUTION | If the last stage focused of showing (hopefully satisfactory) clinical effect, then the Validation of Solution stage focuses on showing that everything works more holistically, including business-wise. As explained in the very beginning of this document, what makes this market difficult is the number of stakeholders and the non-intuitive (especially payment-related) dynamics between them. One model of monetization in the sector is selling the solution to the clinical user (a doctor or a hospital or care establishment more broadly) who deploys it for the benefit of the end-user/patient (an elderly person) while the cost is reimbursed for the clinical user by the medical insurance establishment. In this case, it is possible that the clinical user is happy to deploy the solution, the elderly patient is happy with the effects it provides but the insurer is not happy paying for it. One of the major end goals of this stage is to have all the stakeholders aligned so that the company had purchasing intent from different buyers. For that, the innovator must prove that the solution has a value proposition suitable for all stakeholders. Furthermore, this stage also includes a significant regulatory milestone in the submission of the Technical file to the regulatory body for CE-certification.

요가 ELEMENTS OF COST EFFICIENCY, I.E. WHAT ARE INSURERS REIMBURSING?

For an insurer (both state healthcare and private) to pay for your solution, they need to be convinced it provides **value-for-money** (including other characteristics such as clinical efficiency and effectiveness, innovative characteristics, equity considerations, etc). To determine that, insurers conduct **Health Technology Assessments** (HTAs) in the reimbursement or insurance coverage schemes.

A successful HTA is vital for a company wanting their solution to be reimbursed. HTA is a multidisciplinary process that summarizes information about the medical, social, economic, and ethical issues related to the use of health technology. It is conducted via sophisticated models by HTA-bodies, each of which have slightly different methodologies. AdHopHTA has compiled a <u>list of HTA-bodies</u> as a good starting point for an innovator to find the relevant ones for their markets.

EU-wide HTA provider network EUNetHTA has composed <u>guidelines</u> for methods for health economic evaluations. Important terms for an innovator to understand are **cost-effectiveness analysis (CEA)** and **cost-utility analysis (CUA).** More commonly, these are to be understood as **methodologies for assessing cost-efficiency.** The first compares the costs and effects of at least two alternative technologies, determining information on the "greatest effect for a given cost" or alternatively achievement of "given effect at minimum cost". CUA uses health-state-value scores as a measure of outcome, allowing the measurement and comparison of different outcomes with the same metric (e.g. quality-adjusted-life year (QALY)). For further information on how to find metrics for person-centred care, see Deliverable 5.1. Overview of evaluation toolkits, Deliverable 5.2. AHA innovation assessment framework, and Deliverable 4.2. Mapping of Accessibility and Adoption of Services and Products.

It is important the innovator understands the methodologies for economic evaluation of the solution and **plans their pilot and pivotal clinical investigations in a way that relevant input for HTA is gathered**. Insurers work under budget constraints and business objectives of their own and demonstrating economic value to them is imperative.



Finally, note that some countries are explicitly incentivizing the embedding of digital health into the healthcare landscape. One of the examples of that is Germany which has adopted **DiGA fast-track process** to reimbursement of digital health applications. Two years into DiGA, 28 applications had been approved ¹⁸ for reimbursement, many of which age inclusive.

APPROVAL AND LAUNCH | The **Approval and Launch** stage focuses on **formalizing the regulatory requirements** and **officially launching the sales**. After institutional and regulatory approval has been received resulting from the clinical investigations, Technical file submission and HTAs, the company must complete its registration and listing processes and work on establishing clinical training materials and support for the clinical users of the solution. From the business perspective, the company **finalizes its initial sales** (based on the purchasing intent acquired in the previous stage) and **starts normal business operations**. A lot of focus will be put on widening the client base and marketing. It is a milestone stage for the company as the solution is finally launched on the market. Sometimes, in anticipation of formal market entry post-CE mark, the companies will raise the **second round of institutional investment** (B-round) to prepare themselves for market entry. However, B-round might also be considered to fall to the beginning of the next, Adoption phase.

FINANCING IMPLICATIONS

Source: Venture Capital, Various Private Funds and Investment Firms, Grants, Innovation Procurement, In-Kind Investments

Typical cost points: clinical investigations, product development, networking for stakeholder alignment, regulatory submission costs

Financing need: 2M – 3M EUR (significantly more if B-round is considered)

In the Market Entry phase, the financing sources remain broadly the same as in the Development phase. The innovators should still consider **accelerators**, but now the choice of the accelerator should be heavily targeted on the expertise and network it provides, rather than the financing implications as accelerator-provided financing amounts are marginal relative to financing needs in this phase. It is also possible that the accelerator partners worked with previously expand the cooperation, have themselves a willingness to become an investor in the further rounds or help with finding investors for the company. Furthermore, some accelerators, such as <u>G4A</u> ran by Bayer Pharma, have more advanced tracks the company could transition to and offer more dedicated expertise and partnering opportunities.

As the financing need of the Market Entry stage is already significant with at least the A-round necessary, **private sector funds** should be relied on the most. **VC funds** remain an option, with some of them being multi-stage, i.e., willing to invest from the seed round up to B-round and further. One such example would be UK-based <u>Atomico</u>. Then you have **specialized funds** engaged mainly in earlier rounds and standing somewhere between VC and growth capital, for example, Belgium-based <u>Capricorn Partners</u>. Furthermore, many **big corporates** have their own investment funds, such as the French multinational telecommunications corporation Orange, with their fund <u>Orange Ventures</u>. Then

¹⁸ https://www.meddeviceonline.com/doc/years-after-germany-s-regulation-for-digital-health-apps-what-can-we-learn-0001

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you also have **family offices** through which wealthy families invest their money. A good digital-healthfocused example is <u>MAJYCC</u> from France. Finally, **larger**, and non-start-up-focused **investment firms** could be turned to, especially for the B-round. For example, in the beginning of 2022, a Berlin-based digital health company <u>Ada Health</u> closed its B-round at over 105 million euros with US-based investment firm <u>Farallon Capital</u> and Europe and US-located <u>Red River West</u> among the investors.

The Market Entry phase could also partly rely on **public financing**, with the main focus on large-scale EU funding programs. <u>Horizon Europe</u>, focusing on research and innovation programme stands out as one option. Furthermore, the <u>EIC Transition</u> programme, aimed at maturing a novel technology and developing a business case to bring it to market, offers grants of up to 2.5 million euros and could be an attractive option. Finally, EIT Health <u>Investor Network programme</u> offering matchmaking services connecting digital health companies with equity investors remains relevant in this phase. Furthermore, **innovation procurement** opportunities, if available, still remain relevant.

The **in-kind** investment model introduced under the Development phase remains also relevant for the given phase for engaging the clinical partners as a strategic investor. The in-kind investments partly cover the costs of pivotal clinical investigations, and it could also be possible to negotiate prepayment from the buyers with purchasing intent.

Overall, the financing need in the Market Entry phase still varies a lot between digital tech companies depending on the nature of the solution. On average, A-round should remain in 2M - 3M EUR range, and the B-round in 10M - 15M EUR range. Note that the experts interviewed disagreed whether the B-round should be considered necessary at the end of the Market Entry phase or the beginning of the next, Adoption phase (where most of it will be deployed for growth). Therefore, the average combined financing need for the given phase remains between 2M - 3M EUR, or 12.5M - 19.5M EUR (also considering B-round).



Adoption Phase

The **Adoption** phase consists of two stages. In general, now that the solution is **certified for use**, and **launched to the market**, the most important sector-specific market barriers have been overcome and the

business development aligns itself more closely to the classical model of growing a business with a product validated in the market.

CLINICAL USE | The Clinical Use stage encompasses the business development to achieve profitability in the home market as well as launch the product in new markets. Entering other EU markets with the prescription-based digital product will remain a challenge. It would bring further work understanding the stakeholder and healthcare market structure in the new market, going through the HTAs of that market etc. However, this challenge is minor compared to the initial regulatory challenges now that the company is experienced in

INTENDED USE/PURPOSE

One term the company must understand is "intended use" ("intended purpose" in MDR), defined in Article 2 (12) as "the means the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use or in promotional or sales materials or statements and as specified by the manufacturer in the clinical evaluation". Intended use also determines the composition of clinical investigations.

Therefore, if the intended use of the product changes after CEcertification, the company must account for the possibility of requiring new clinical investigations composed for the new intended use. For example, if the solution is intended to be used on the ageing population in the context of care homes, and the company wants to also start selling it for hospital use, new investigations could be required. Therefore, determining the intended use early on is particularly important to avoid unexpected regulatory and time costs.

the processes. For example, TempID (see Case Study 1) envisions that market expansion will be **relatively easy in Europe** after the company has received a CE mark and even the regulatory regimes in further markets such as India and Japan are relatively aligned to Europe. However, the regulatory burden could once again increase if the company now decided to make substantial changes to its product that **cause deviations from its original intended use**. Still, overall, the company must focus on establishing a market presence in this stage that primarily involves heavy **marketing- and sales-related efforts**. If the company produces hardware as a part of its elderly-focused digital health solution, then it must also grapple with the challenges of scaling production.

STANDARD OF CARE | The **Standard of Care** stage signifies reaching the coveted goal for any digital health company of **having their solution as the "standard of care"**. While the precise definition of the term is often debated¹⁹ in its medical and legal implications, it is commonly understood as the dominant and the best solution for a given disease or clinical situation. This would be the solution a competent doctor or clinical stakeholder would turn to first in case of the specific need. From the business perspective, having a solution as the standard of care would mean having a **dominant market share** in your niche and supposedly also **highly profitable operations**. The goals of a company having a standard of care solution would be **expanding its product scope** (for instance expanding its intended use) as well as **expanding to new markets**. All of this continues to require financing but a part of it would come from the profits the

¹⁹ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3088386/

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company generates from its operations. Also, as the company is now mature and therefore its **financing avenues are changed**.

Source: Later-Stage Private Funds and Investment Firms, IPO, Debt-Financing

Typical cost points: scaling production, customer experience development, marketing and sales, expansion and scaling to foreign markets

Financing need: 10M - 15M EUR +

In the Adoption phase, the company grows into an established, mature business and its financing options change accordingly. It is notable that for mature companies, financing is no longer sought for the development of a company not yet producing a cashflow but for strategic decisions of business development and ownership change.

Private sector funds and investment firms (including already mentioned family offices and corporate funds) remain relevant with funds providing growth capital in focus. For example, in 2021 an American investment firm <u>Tiger Global Management</u> led a 200 M USD Series D round for the US. digital health company <u>Dispatch Health</u>. Furthermore, **Private Equity** (PE) funds will now become relevant in financing deals of different structures, including M&A activity. For example, in 2021 <u>Five Arrows</u> and <u>TA Associates</u>-backed global healthcare software company <u>RLDatix acquired</u> the UK-based <u>Allocate</u> <u>Software</u>, a leading provider of human capital management solutions that help healthcare organisations. For such late-stage equity-financing deals, investors generally believe their involvement can create additional value for the company and often they require significant say over company's strategic decisions such as restructuring, management team, etc.

A new option of financing in this stage is **going public**, i.e., conducting an **Initial Public Offering (IPO)** on a stock market. In doing this, the company will increase its regulatory reporting burden and required transparency as public companies are highly regulated. On the other hand, it broadens the company's capital access as investors from retail to institutional can now finance the company through the stock exchange. It also offers the founders and early employees with stock options an opportunity to monetize the success of their company by selling shares on the free market. In 2021, a UK-based digital-first health service provider <u>Babylon</u> was the first digital health company in Europe to <u>go public</u> in a deal worth 4.2 billion USD. Both institutional (big funds) and retail (individuals) investors could participate in the IPO, i.e., become the financer and shareholder.

Finally, a mature company with strong cashflow can also consider **debt-financing**. In this case, the company is not giving away ownership (equity) but takes on debt, which it must pay back over a longer term. Capital from debt financing is usually considered cheaper for existing shareholders than that from equity-financing but it requires the company to be financially strong enough to pay the debt back (and raise the debt at reasonable interest rates). In general terms, debt-financing can happen either through public markets (issuing corporate debt enabled by investment banks) or private markets (taking a business loan through commercial banks or other private-sector financers). However, a collateral



requirement could complicate debt-financing for software-based digital health AHA company which is capital-light.

If the B-round is conducted in the beginning of the Adoption phase, then it remains on average in the **10M – 15M EUR** range. The overall indicative financing need for the Adoption phase cannot be given as it is specific to the nature of the company and its long-term development strategy. A strong company that has no great ambitions to expand far from its home markets has significantly lower financing needs than the one aiming to expand everywhere in the world. Likewise, a digital health company also producing hardware has higher capital investment needs for scaling the production than the one focusing on developing a highly scalable software solution.

In conclusion, this chapter should give an innovator in the digital health sector, whose solution classifies as a medical device, a good understanding of the company's development needs with a focus on financing implications.



Figure 7. Overview of Medical Device Classification Digital Health Company's Financing Implications

*The financing needs presented were concluded based on publicly available materials and expert interviews. They are highly indicative as each digital health company is different.

Source: Compiled by authors

Error! Reference source not found.. gives a concise overview of the various financing options in different d evelopment phases as well as indicative financing needs while Table 1. summarizes available financing sources together with relevant examples.



Table 1. Summary of Financing Sources

	NATURE		DEVELOPMENT PHASE					
FINANCING	Public	Private	Ideation	Develop ment	Market Entry	Adoption	EXAMPLES	
Own capital		\checkmark	\checkmark	\checkmark			-	
FFF		\checkmark	\checkmark				-	
Incubators	\checkmark	\checkmark	\checkmark				<u>Terkko Health Hub, EIT Health</u> <u>Bootcamp</u>	
Accelerators	\checkmark	\checkmark		~	~		<u>G4A; Open Accelerator,</u> <u>Accelerace, i&I Prague, EIC</u> <u>Accelerator</u>	
Angel Investors		\checkmark		\checkmark			-	
Venture Capital		\checkmark		~	~		Credo Ventures, iBioNext, EarlyBird, Atomico	
Public Grants/ Programs	~			~	~		EIC Pathfinder, Horizon Europe, EIC Transition, Investor Network programme, Innovation Procurement	
In-kind investors	\checkmark	~		~	~		<u>Cambridge Entreprise</u> , <u>UniTartu Ventures</u> , clinical partners	
Specialized funds		\checkmark			\checkmark	\checkmark	Capricorn Partners	
Corporate funds		\checkmark			\checkmark	\checkmark	Orange Ventures	
Family offices		\checkmark			\checkmark	\checkmark	MAJYCC	
Investment firms		\checkmark			~	~	Farallon Capital, Red River West, Tiger Global Management	
Private Equity		\checkmark				 ✓ 	Five Arrows, TA Associates	
IPO		\checkmark				\checkmark	Conducted via investment banks	
Debt issuance		\checkmark				\checkmark	Conducted via investment banks or commercial banks	

The development roadmap is quite complicated for a digital health medical device but there are **many different channels of financing available to make it happen**. Figure 8. below condenses the most important insights covered into an **"Innovator Cheat Sheet"**. In general, it can be claimed that the innovator will find their way to investments if they are:

- **1.** Solving a problem that is severe enough.
- **2.** Committed to development.
- Relentless in their pursuit of feedback from various stakeholders, including the elderly customer segment.
- 4. Strategic in their monetisation channels and intended product use.
- 5. Attentive to the regulatory and clinical needs of their development.



Figure 8. Innovator Cheat Sheet: Roadmap of Insights for Digital Health Innovator in the AHA Market





5. Case Studies

Both companies have participated in the living labs organized within the IN-4-AHA project. To read more about the living labs, see the Deliverable: 4.1 Living Lab testing and innovation scale-up playbook.

CASE STUDY 1. TempID From Estonia

THE SOLUTION | TempID develops a core product called Smart Patch which is a **disposable and reusable body temperature logger**. Temperature data is "swipe readable" with mobile device over NFC connectivity (Android and iOS). Activation of the device, fetching the measurements and analytics is done through the company's proprietary smartphone application.

HOW THEY STARTED | The company was founded by **four engineers and technologists**. It was born out of two practical observations:



Source: Image from company website (tempid.ee)

- Taking temperature from children is difficult as they are not prone to being still.
- Being able to monitor the changes in body temperature (e.g., during the night-time) would provide more value than the occasional current temperature checks.

Having not found a solution providing answers to these two observations, the founders decided to build it themselves. During the development phase, they entered a hackathon from which they won an opportunity to enter the best-known (televised) start-up competition/accelerator in Estonia called Ajujaht (Brain Hunt)²⁰. They ended up winning Ajujaht in 2017, gaining 30 000 euros of award money as well as coverage and reputation in Estonian society.

CURRENT SITUATION At the beginning of the summer 2022, the company is on the path of getting their medical-device-categorized solution CE-certified. Their product is finalised, but they have not yet entered the market due to CE mark missing. However, they have had the opportunity to pilot the solution under a humanitarian-aid related cooperation project in Kenya and Ghana with the Estonian public sector. Currently, they are cooperating with a hospital in Estonia for fulfilling their clinical evidence needs. Finally, regarding sales channels, they will initially **sell the patches B2C in pharmacies** while expanding the business to **healthcare sector clients** (hospitals, clinics). In the longer term, they see the temperature patch as an **enabler to sell software-based services** (data analysis, system integration) to institutional clients. Regarding geographical expansion prospects, the company currently has no concrete plans, but their research has shown that European expansion is relatively easy regulation-wise once you have the CE mark. Markets such as Japan and India are not too far off the EU regulation either, so minimal extra regulatory effort is needed. US is a bit more different but still generally accessible.

FINANCING STRATEGY | So far, the company has **relied on founder financing**, the prize money from Ajujaht as well as minimal grant financing from the Estonian innovation support programs. This has been

²⁰ https://ajujaht.ee/en/

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a **strategic choice** as they have been in communication with investors for years. Firstly, the victory at Ajujaht brought them interested investors, but the company did not want to raise money before understanding the go-to-market financing needs themselves. After the company, as well as investors, discovered the regulatory cost attached, the investor interest cooled a bit, even though some interest remained. Ultimately, the company decided against external investment due to the terms not being very favourable in early stages. Hence, the strategic decision was to **obtain the CE mark before attracting external investments** and establish a **better negotiating position** with it. Finally, the company has also applied for EU-sourced Horizon financing programs but ended up closely missing out. TempID emphasizes that while the application for public money comes with its own costs and challenges, it is in their eyes worth it as early-stage private sector investments are expensive from founders' point of view.

USEFUL INSIGHTS FOR OTHER INNOVATORS | There is a significant difference whether your solution is external to the healthcare sector (not a medical device) or internal to it. Initially, the company had **no overview or understanding of the regulatory hurdles** their product would need to cross and that has slowed them in development. On the other hand, they note that not knowing initially could also be seen as positive because heavy regulations could have been a demotivating aspect in the initial stages. TempID has managed to navigate the regulatory landscape due to **engaging friends and other healthcare ecosystem stakeholders** who have been happy to give them informal advice for free.

The second insight is related to the **ageing population customer segment**. Their product is universal and therefore age inclusive. However, they discovered while testing on the ageing population segment (conducted via the living lab tests IN-4-AHA project) that on the one hand, their software is designed easily enough for the elderly users to have no problems with it. On the other hand, they discovered that the **flexibility of elderly people might be limited** in some cases which meant they struggled with attaching the patch to their armpit. This, for the company, clearly highlighted the benefits for end-user testing as surprising conclusions for the product use case could be discovered.



CASE STUDY 2. Avecen From Spain

THE SOLUTION | Avecen aims to **improve the lives of people with dementia, their caregivers and family members**, helping to prevent and self-manage neurodegenerative diseases characterized by a progressive

deterioration of cognitive functions such as Parkinson's or Alzheimer's disease. The solution is a **software application** that performs a continuous evaluation of the users based on proposals of activities or games based on gamification techniques. All these activities include cognitive and motor aspects, adherence to clinical routines, to the prescribed treatment and, in general, to good disease management practices.

HOW THEY STARTED | The project started as an **open innovation initiative** based on the quadruple helix model, where four main axis interact: Science, Policy, Business and Society.



Source: Image from project website (https://avecen.com/en/home-en/)

Therefore, the solution was **developed by a consortium** of three companies, a research centre linked to a public hospital as well as a research group at a public university. For example, the consortium included IT consulting and services companies <u>Plexus Tech and Inforhouse²¹</u>, digital health company <u>Insati²²</u>, and a research centre for technologies called Citius²³.

Avecen was planned as a R&D project and received a grant from the government for the first stage of the project which covered 50%-70% of the project budget. It took the consortium 2 years to develop the application. **Help from specialists on neurodegenerative diseases** involved in the consortium was imperative as the companies developing the solution did not have experience on that matter.

CURRENT SITUATION | Currently, the Avecen application is alive and available but still in its beta, requiring improvements and bug fixes. Many fixes have been implemented based on end-user beta-testing approached through regional patients associations those deal with neurodegenerative diseases.

The solution **do not** have neither **need CE Marking for Medical Devices** because of it is conceived of as a wellbeing tool (hence continuous iterations are possible). The consortium explored CE-certification but determined it too burdensome for the development model. Still, they acknowledge that **not having CE mark limits some of their potential monetization channels**. Currently, the application has no paying customers, and the company explores monetization opportunities through target sector associations that have budgets for grants or IT solutions. Currently, as the grant-financed project has ended, the companies in the consortium have been **deploying the app against their own resources** but development has lagged.

²¹ https://www.plexus.es/en/

²² https://insati.com/web/en/home-2/

²³ https://citius.gal/

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They have signed an agreement with a regional hospital to perform a beta testing pilot with users from that hospital.

FINANCING STRATEGY | The case differs from TempID as the consortium of companies developing the solution have been able to cover a part of the financing need from their **own operating revenues** allocated to R&D activity. As external funding, the company has used a public grant that covered 50%-70% of the project budget for the first two years of development. Going forward, the financing strategy is at a **crossroads**. One option the consortium has considered is applying for a follow-up grant for ongoing development. However, this would imply waiting for the opening of new suitable funding rounds, deploying resources for the application elaboration and submit as well as waiting for the assessment decision. This would in total **incur significant delays** in the solution development and its time-to-market as well as uncertainty regarding the continuation of the project if the grant is not received.

Finally, the interest from private sector investors has been limited for the consortium for two main reasons:

- From the products side, the application does not yet have meaningful traction and productmarket-fit to attract the interest of the investors.
- From the corporate structure side, attracting external investment is very complicated as the solution is not developed under a focused, limited liability company but rather in cooperation with different organizations. This means the ownership and responsibilities related to the solution are not well-defined which makes investment implausible.

USEFUL INSIGHTS FOR OTHER INNOVATORS | The consortium model used for development of Avecen offers two interesting insights:

- The model where many different organizations are engaged is good for by default **engaging expertise**. For example, due to having public hospital and university-related consortium members, the access to clinical stakeholders as well as to clinical insights was guaranteed.
- However, the model also comes with a significant drawback which is ambiguity regarding the direction and composition of the development. As mentioned earlier, Avecen exists as a cooperation project and has no separated legal structure. This may cause problems regarding attracting investments but also misaligned incentives between consortium members. For example, if one company decides to deprioritize the project then its ownership and continued development will immediately be in question.



Annexes

Annex 1 – Interviewees

Interviewee category (investor, company, ecosystem facilitator)	Name	Represented organisation/project	Position	Date of the interview
Ecosystem facilitator	Merike Leego	/lerike Leego EIT Health		24.03.2022
Company	mpany Esther Jager PHAB, me moment Fou		Founder & CEO	26.04.2022
Investor	Dr. Johan Hedevåg	Una AB	Founder & CEO	27.04.2022
Company	Ivan Pozuelo	Insati Innovation	СТО	28.04.2022
Investor	Erki Mölder	Health Founders	Co-founder	29.04.2022
Ecosystem facilitator	Javier Ventosa Rial	Xunta de Galicia	Deputy General Director of Planning in Directorate of Comprehensive Social and Health Care	04.05.2022
Company Mihkel Tedremaa T		TemplD	Co-founder	02.06.2022