KARYN MARTINELLI LOPES

**Análise dos fatores influenciadores no desenvolvimento de projetos de
soluções médicas em empresas empreendedoras**

São Paulo
2020

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in entrepreneurial companies**

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São Paulo to obtain the title of Doctor in Sciences.

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I dedicate this research to my mother (*in memoriam*) and my father.

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Knowing is not enough; we must apply.

Willing is not enough; we must do.

Johann Wolfgang von Goethe

RESUMO

LOPES, K. **Análise dos fatores influenciadores no desenvolvimento de projetos de soluções médicas em empresas empreendedoras.** 2020. 193 p. Tese (Doutorado em Engenharia de Produção) - Escola Politécnica da Universidade de São Paulo, São Paulo, 2020.

O objetivo desta pesquisa é identificar os fatores no desenvolvimento de projetos de soluções médicas que influenciam os resultados de performance de inovação. Tais fatores compreendem características de companhias empreendedoras de saúde, equipes e processos. O método de pesquisa *survey* foi realizado entre maio e outubro de 2019 em 79 companhias empreendedoras da área da saúde que receberam bolsa da Pesquisa Inovativa em Pequenas Empresas (PIPE), a partir da Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). A amostra incluiu companhias focadas nas áreas de saúde digital, equipamento médico, farmacêutica e biotecnológica. Os resultados indicam que a primeira venda resultante de um projeto de inovação, ou seja, o tempo de comercialização, é mais rápido quando a companhia possui mais sócios e fundadores nas áreas de saúde e *hard sciences*. Companhias com projetos mais orientados a serviço e projetos em fase de produção em escala e comercialização levam menos tempo para realizarem sua primeira venda após receberem o auxílio PIPE. Além disso, os resultados indicam que o total de projetos PIPE influencia o número total de publicações. Os resultados também apontam que há relação entre a solução do projeto mais voltada para *software* ou *hardware* e a área da companhia. Adicionalmente, os resultados descritivos fornecem esclarecimentos sobre o cenário da inovação médica. O estudo apresenta amplas descobertas que podem ser aplicadas para melhorar os rumos de pesquisas futuras sobre a tomada de decisões em inovação médica.

Palavras-chave: Inovação médica. Companhias empreendedoras. Performance de inovação.

ABSTRACT

LOPES, K. **Analysis of influencing factors under medical solutions projects development in entrepreneurial companies**. 2020. 193 p. Tese (Doutorado em Engenharia de Produção) - Escola Politécnica da Universidade de São Paulo, São Paulo, 2020.

This research aims to identify the factors under the medical solution project development that influence innovation performance outcomes. Such factors comprehend entrepreneurial health companies, teams, and process characteristics. A survey research method was carried out from May to October 2019 in 79 entrepreneurial health companies that received a research grant from the Innovative Research in Small Business Program (PIPE) from the São Paulo Research Foundation (FAPESP). The sample included companies focused on digital health, medical device, pharmaceutical, and biotechnology domains. The results indicate that the first sale resulting from an innovation project, i.e., the time to market, is faster when the company has more partners and founders in the health and hard sciences areas. Companies with more service-oriented projects and companies in scale production and commercialization project phase take less time to make their first sale after receiving a PIPE grant. Furthermore, the results indicate that the total of PIPE projects influences the number of publications. The results also point out a relationship between a more software or hardware project solution and the company domain. Additionally, the descriptive findings provide insights into the medical innovation setting. The study presents comprehensive results that may be applied to improve directions in upcoming research on medical innovation decision-making.

Keywords: Medical innovation. Entrepreneurial companies. Innovation performance.

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LIST OF ACRONYMS

ANVISA	National Health Surveillance Agency
CEO	Chief Executive Officer
CFO	Chief Financial Officer
CSIO	Chief Strategy and Innovation Officer
CTO	Chief Technology Officer
FAPESP	São Paulo Research Foundation
FDA	Food and Drug Administration
I-CORPS	National Science Foundation's Innovation Corps
IP	Intellectual Property
IPT	Institute for Technological Research
NSF	National Science Foundation
OECD	Organization for Economic Co-operation and Development
PAHO	Pan American Health Organization
PIPE	Innovative Research in Small Business program
R&D	Research and Development
RD&I	Research, Development and Innovation
SBIR	Small Business Innovation Research
SENAI	National Service of Industrial Training
SUS	Unique Health System
USP	University of São Paulo
WHO	World Health Organization
WOS	Web of Science

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1 INTRODUCTION

Staying healthy and getting proper healthcare is one of the most critical issues in our society (SPEKOWIUS; WENDLER, 2006). Discoveries and innovations continue to revolutionize medical research, resulting in advances that could not have been imagined a decade ago (FONTANAROSA; BAUCHNER, 2015). Throughout the years, the routes and advances in medical innovation have improved the way of treating diseases (MORLACCHI; NELSON, 2011; SOENKSEN; YAZDI, 2017).

Medical innovation comprehends a variety of combinations, for instance, new drugs, devices, technologies, and clinical practices, which are deployed in the provision of health (DJELLAL; GALLOUJ, 2005; PAMMOLLI et al. 2005; BAUCHNER; BERWICK; FONTANAROSA, 2016; CONSOLI et al., 2016). The medical innovation cycle is a long and complicated process (TERZIOVSKI; MORGAN, 2006). The differences in medical innovation, compared to other fields of activity, is that the human body is a complex structure, and designing solutions to humans' diseases involves chemical compounds or mechanical artifacts (CONSOLI et al., 2016).

Progress in molecular biology, genomic sciences, cellular and tissue engineering, regenerative medicine, bioengineering, bioimaging, and computational methods are among the many medical research advances. This scenario creates unique opportunities for bringing forward medical science and improvements in health outcomes (FONTANAROSA; BAUCHNER, 2015). Such progress is part of digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), and pharmaceutical and biotechnology (EVENS; KAITIN, 2015) entrepreneurial companies, also referred to as small businesses or startups.

Given the continually growing spread of technologies in the current setting, the medical sector has attracted attention. The rising improvements and progress in human health lead to new challenges, especially for those who develop, produce, and distribute. Thus, it is necessary to rethink tasks and strategies to hold future markets (DAIM; BREM, 2020).

1.1 Justification

Scientific and technological growth and the aging of the population represent potential medical innovation issues (MORLACCHI; NELSON, 2011; LOPES; ZANCUL, 2017; SOENKSEN; YAZDI, 2017). Life expectancy expanded by 5.5 years between 2000 and 2016, the fastest increase since the 1960s (WHO, 2018). In such circumstances, medical innovation has increased longevity and enhanced quality of life (LICHTENBERG, 2017).

Health in developing countries improved significantly over the past century and emerged into a booming sector with plentiful opportunities for growth (FATUNDE; BHATIA, 2012). Health systems in developing countries are more fragile than those in the developed world. In the context of large and diverse disease burdens, significant challenges include limited health infrastructure and highly constrained financing (BROOKS et al., 2012).

Brazil is facing an increased demand for medical technologies. There is a need for a higher number of cost-effective products and services designed specifically to address patients' needs with fewer resources (YOCK et al., 2015). Brazil has a significant market for health. While the market size is an essential advantage for developing new health technologies, it is also important to note that Brazil has appropriate scientific expertise in health-related domains (DUTTA; LANVIN; WUNSCH-VINCENT, 2019).

This situation creates an environment for new challenges and opportunities (CIURANA; ÖZEL; SERENÓ, 2017), discussed, for instance, in a recent Technological Forecasting and Social Change special issue on how to address the challenges and new research regarding emerging economies (AMANKWAH-AMOA et al., 2020). Besides, advances in design, materials, and technologies increased the potential to find better solutions for medical problems (CIURANA, 2014).

The issue of innovation is the basis for national economies, individual businesses, educational systems, and the health area (BAUCHNER; BERWICK; FONTANAROSA, 2016). Medical innovation is a complicated aspect that results from the interplay of science, technology, and medical procedures. It involves entrepreneurial companies, also named startups or small businesses (YOCK et al., 2015; HELLER et al., 2019; SZYCHER, 2019), teams (MORLACCHI; NELSON, 2011; YOCK et al., 2015;

GULBRANDSEN et al., 2016; MILLER; FRENCH, 2016), and specific processes (YOCK et al., 2015).

It is worth mentioning that universities play a crucial role in national and regional economic development for research generation, technology transfer, and knowledge dissemination to organizations (THURSBY; THURSBY, 2011; WU; WELCH; HUANG, 2015; GULBRANDSEN et al., 2016; ARCHIBUGI; FILIPPETTI, 2018; THOMPSON; ZIEDONIS; MOWERY, 2018). Besides, governments have been demanding collaboration between universities and organizations through enhancing innovation and frequently contributing to new technology and product developments (BARNES; PASHBY; GIBBONS, 2002; FAN; GARNSEY, 2014; BANERJEE; SIEBERT, 2017). Governments have initiated various regional and national research programs in the form of providing financial support and promoting Research and Development (R&D) cooperation (CALOGHIROU; TSAKANIKAS; VONORTAS, 2001; BANERJEE; SIEBERT, 2017; ANKRAH; AL-TABBAA, 2017). In this context, there is a wide array of funding agencies assisted by governments (VARGAS; CALLAWAY; ARISS, 2017), such as the São Paulo Research Foundation, referred to as FAPESP (GOVERNO DO ESTADO DE SÃO PAULO, 2000). Since 1997, FAPESP has been offering a considerable Innovative Research in Small Business program, titled PIPE (SOBRE O PIPE, 2020). From the moment of its inception, PIPE has awarded grants for more than 1,700 projects from over 1,100 companies (MARQUES, 2017). PIPE supports companies' innovation projects without industry sector constraints, including several projects and companies focusing on healthcare. Due to its 20 years path and considerable size, the PIPE companies sample offers an opportunity to investigate influencing factors under medical solutions projects development in entrepreneurial companies.

Among influencing factors for innovation, multidisciplinary teams are essential to permit knowledge sharing (WEISS; TILIN; MORGAN, 2018). Typical health innovation groups should encompass experts, such as physicians and engineers (YODA, 2016; SOENKSEN; YAZDIB, 2017). The integration between health and technology areas has received increasing attention intending to enable new treatments, reducing costs for patients, and providing new professional performance fields. In this sense, universities are setting up specific initiatives in the engineering-medicine interface, such as the University of São Paulo (USP) (ZANCUL et al., 2017; LOPES et al., 2018)

and Stanford University (BRINTON et al., 2013). Such institutions have contributed to accelerating the innovation of medical solutions.

In particular, USP has an optional elective undergraduate course (ZANCUL et al., 2017; LOPES et al., 2018) with multidisciplinary teams that follow Design Thinking (D.SCHOOL, 2018) and Biodesign (YOCK et al., 2015) process in partnership with health organizations. The course outcomes are projects that have contributed to medical innovation, such as the development of a hospital asset management solution, the improvement in the oxygen flow control (INPI, 2015), and improvements in the exam collection process (SILVA et al., 2019). Additionally, projects are developed for the prevention of primary infections in the bloodstream, prevention of accidents with surgical perforating-cutting materials (LOPES; ZANCUL, 2017), together with the development of a portable device for measuring blood test hemolyzed samples based on computer vision and neural network (LOPES; ZANCUL, 2017; LOPES et al., 2019; INPI, 2020).

Accordingly, an entrepreneurial health company starts up at the university, through an organization, government, or foundation grants, by employing discoveries and a pathway that is particularly interesting and appealing for disease intervention or treatment (MEHTA, 2004; HOTZ-HART; ROHNER, 2014). For instance, the previously mentioned project portable device for measuring blood test hemolyzed samples based on computer vision and neural network (LOPES; ZANCUL, 2017; LOPES et al., 2019) resulted in an entrepreneurial company that earned funding from the PIPE program (SOBRE O PIPE, 2020) for solution development.

Such entrepreneurship interactions may be measured by applying innovation performance indicators to set goals and track progress over time (OKWIR et al., 2018). For instance, Fleuren et al. (2014) measure the determinants of innovations in the health area. Elg, Broryd, and Kollberg (2013) contribute to how performance measurement drives health practice improvements.

Additionally, the relationship between university and entrepreneurship has also been discussed in special issues in *Technological Forecasting & Social Change* journal (FAYOLLE et al., 2017; LAMINE et al., 2017). The interface between technology and entrepreneurial companies has been addressed in a special issue in *Technovation*, together with the *Journal of Small Business Management* (LINTON; SOLOMON,

2017). Challenges and opportunities for innovation, entrepreneurship, and expertise have been recently the focus of a special issue in *Technological Forecasting and Social Change* (GUAITA; CASTILLO; GARCÍA, 2020). Furthermore, studies of innovation related to human health have emerged substantially (THUNE; MINA, 2016).

Besides, as previously mentioned, processes with multidisciplinary teams (YOCK et al., 2015; D.SCHOOL, 2018) have been applied in the health area. Notwithstanding, the focus is on product development activities. Consequently, Soenksen and Yazdib (2017) propose one of the first efforts to comprehend the process of supporting entrepreneurial health companies and prospective investors. Also, Shluzas and Leifer (2014) study the interactions between multidisciplinary health teams.

However, efforts have been based on case studies, and there is a lack of statistical, in conjunction with empirical shreds of evidence. There is limited research on innovation performance outcomes in the context of medical domains (SHLUZAS; LEIFER, 2014), such as digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), and pharmaceutical and biotechnology (EVENS; KAITIN, 2015) entrepreneurial companies. In sum, additional studies are mandatory to communize investment, intending to support health innovation, and comprehend the potential for economic growth and social benefit (SOENKSEN; YAZDIB, 2017).

1.2 Research objectives

The general objective of this research is to identify the factors under the medical solution project development that positively influence innovation performance outcomes. Such factors comprehend the characteristics of entrepreneurial health companies, teams, and processes.

This main objective is outspread into the following specific goals.

1. Identify the constructs related to medical innovation in the literature, including innovation performance, entrepreneurial health companies, teams, and process characteristics.
2. Evaluate the influence of entrepreneurial health companies, teams, and process characteristics in innovation performance outcomes.
3. Validate the hypothesized model.

Regarding the first specific objective, a literature review is necessary to identify and select the most appropriate constructs for the proposed goal. The second specific objective relates to the definition of the adequate hypothesized model. Lastly, the third specific objective regards the model assessment through empirical research with the utilization of a survey research method.

1.3 Thesis structure

The thesis is structured into five chapters. Figure 1 depicts the thesis structure overview.

Figure 1 - Thesis structure overview

Source: Prepared by the author.

As illustrated in Figure 1, Chapter 1, Introduction, comprises the medical innovation setting, together with the justification, research objectives, and the thesis structure overview. Chapter 2, Literature review, encompasses the theoretical background on medical innovation and entrepreneurship, including collaborative locations for entrepreneurial companies, such as incubators, accelerators, and technological parks, resources for entrepreneurial companies, including personal funds, angel investors, venture capital, hospitals, universities, organizations, government, Innovative Research in Small Business (PIPE), and the collaborative resource hurdles. Additionally, the chapter addresses the medical innovation process, coupled with regulatory agencies, particular features among medical devices, pharma/biotech, and digital health domains. Subsequently, the chapter depicts medical innovation teams and innovation performance outcomes. Lastly, the hypothesized model is generated from the existing findings in the literature review. Chapter 3, the Research method, describes the research instrument development, involving the survey research method and data collection. Chapter 4, Results and discussion, initially encompasses the descriptive analysis, including entrepreneurial companies, teams, and process characteristics, together with innovation performance outcomes. As a complement, the chapter comprehends a content analysis of the survey open-ended questions. Afterward, the chapter provides statistical data analysis, including regression models, correlations, and chi-square methods. Lastly, Chapter 5, Conclusions, involves the concluding remarks, theoretical and managerial implications, study limitations, and further research.

2 LITERATURE REVIEW

This chapter comprises the initial research and literature review on medical innovation and entrepreneurship, comprising collaborative locations and resources for entrepreneurial companies, including collaborative resource hurdles. Subsequently, the chapter addresses the medical innovation process, followed by regulatory agencies and particular features among digital health, medical device, and pharma/biotech domains. Afterward, the chapter encompasses medical innovation teams and innovation performance outcomes to further develop the constructs and the hypothesized model.

Initially, the research was conducted in April 2017, in the Web of Science (WoS), the world's dominant scientific database that has been employed in a large number of published academic studies throughout the years (LI; ROLLINS; YAN, 2018). Most of the medical research context has been published in journals related to health routines (e.g., surgeries, stem cells, and implants) with specific terms and little reference to innovation management. To unfold this issue, the research in WoS considered publications in leading innovation management journals (HALL, 2017).

The research was updated throughout the thesis development, and relevant papers were integrated into the study and employed in the analysis of results. The following strings were applied due to the integration of subjects referred to the thesis theme: "innovat*" OR "performance*" OR "*entrepreneur*" OR "process*" OR "approach*" OR "method*" OR "team*" OR "*disciplinar*" AND "*medic*" OR "health*". The research considered in "publication name" all the journals of Table 1, in conjunction with "all years", whose prior mentioned strings appeared in the fields "subject", "abstract" or "keywords". The results are presented in Table 1.

Table 1 - Research results in leading innovation management journals

Journal	Total of articles per journal
Technological Forecasting and Social Change	222
Research Policy	138
International Journal of Operations & Production Management	82
Technology Analysis & Strategic Management	68
Technovation	55
California Management Review	45
Strategic Management Journal	39
Journal of Technology Transfer	34
R&D Management	33
Journal of Product Innovation Management	27
Research-Technology Management	22
Journal of Strategy and Management	7
Total	772

Source: Prepared by the author.

As a result, it was applied a content analysis of 772 articles, and 58 significant publications were selected. In addition to the database research, the snowball technique, articles, and books were utilized to determine relevant literature (GREENHALGH; PEACOCK, 2005), in conjunction with official web pages (HUNSINGER, 2020), such as FAPESP, PIPE, ANVISA, and FDA, since encompassing plenty of opportunities and the gathering of perspectives to this study. Consequently, the following sections present the theoretical background.

2.1 Medical innovation and entrepreneurship

Competitiveness has required companies to increasingly look towards innovation, which has become one of the current priorities, including new technologies development. Innovation represents a significant role in shaping the survival of new companies (CEFIS; MARSILI, 2006; DAVEY et al., 2011; LIU; HODGKINSON; CHUANG, 2014; DEWANGAN; GODSE, 2014).

The definition of innovation may vary in the literature. It is essential to understand the meaning in the context of business and enterprises, as it is relevant to the perspective of this thesis. In this study, innovation is defined as invention plus exploitation. Invention implies considering and developing the idea into a possible application,

whereas exploitation entails the process of commercialization and obtaining the benefits (ROBERTS, 1998; DEWANGAN; GODSE, 2014). This definition includes the implementation of a new or significantly improved product, service, or process (OECD, 2018). Thus, innovation refers to both innovative ideas intended to be commercialized in the market and ideas that have already been successfully commercialized (DZIALLAS; BLIND, 2019).

In the same context, health innovation identifies new or improved products, services, and technologies, and delivery methods that improve people's health and wellbeing, along with a response to unmet health requirements by generating new ways of thinking and working with an emphasis on individual's needs (WHO, 2020). The issue of innovation in the health area is where the biological structures of human beings are examined and tracked, and there is an unusual and steady request for novel treatments that bring improved, harmless, and inexpensive medical innovations (STYHRE, 2015). Health innovation consists of complex bundles of new medical technologies and future developments, which significantly contribute to improving the currently accepted health trajectories (DAVEY et al., 2011; MORLACCHI; NELSON, 2011; SOENKSEN; YAZDI, 2017).

Innovation is the basis on which an entrepreneurial business is created through the provision of competitive advantage (SZYCHER, 2019). Entrepreneurship and innovation have a significant relationship (HULT; HURLEY; KNIGHT, 2004). Entrepreneurship is a primary factor of change across companies and is essential for both developing and developed economies. It encompasses the discovery, creation, and exploitation of opportunities as well as involves the design, launch, and manage a new business, which usually begins as a startup, to create value based on the introduction of new products or services (BLANCO, 2007; YETISEN et al., 2015).

Startups, also referred to as entrepreneurial companies, are small businesses with rapid growth that remain fragile and dependent on human, legal, tax, and financial factors. Startups appear to be the future of entrepreneurship and offer benefits for entrepreneurs and investors, as well as for innovation in a broader sense (HELLER et al., 2019). The size of an entrepreneurial company may be classified as (SEBRAE, 2016): microenterprise (until nine employees), small enterprise (10 to 49 employees), medium-sized enterprise (50 to 99 employees), and large-sized enterprise (100 or more employees).

Despite its importance, as a research area, entrepreneurship is still a relatively young scholarly field and is recently emerging in the health setting (WILDEN et al., 2018). Usually, the health domain comprises a high number of small and specific businesses, which perform a range of highly specialized and interdependent roles within a complex and potentially global industry. In addition to considerable challenges toward their survival and growth, health innovations have significantly affected the industry (MITTRA; WILLIAMS, 2007; JONES; WHEELER; DIMITRATOS, 2011; STYHRE; REMNELAND-WIKHAMN, 2016). For instance, products and services that are related to health, but not traditional offerings such as drugs, hospitals, and medical applications, may be perceived in the many collaborations emerging between established organizations and startups, as well as companies from other industries developing in the health sector (WILDEN et al., 2018).

As more entrepreneurial companies access the novel and expanding markets nationally and abroad, challenges come up, such as the threat of competition from emergent entrants into their national businesses, frequently competing harshly on price (SZYCHER, 2019). The health sector is characterized by intense competition, such as large organizations, which have control over price or amount supplied in the market, including competitive market price (HINE; KAPELERIS, 2006; MITTRA; WILLIAMS, 2007), where advance towards innovation are along with the boundaries of a regulated industry. Resources for development may be in limited supply or difficult to access. Thus, health entrepreneurs need to be resourceful, innovative, and prepared for opportunities to encourage successful operations in a global industry (JONES; WHEELER; DIMITRATOS, 2011; STYHRE; REMNELAND-WIKHAMN, 2016).

Most countries have been facing the same set of challenges, in conjunction with high health costs and increased life expectancy (PEINE; MOORS, 2015; YOCK et al., 2015; LOPES; ZANCUL, 2017; WHO, 2018), in addition to a rapid increase in lifestyle-related and chronic diseases, including a demand for new medical treatments and technologies, and also a shortage in the number of available clinicians, nurses, and other health providers (BARDRAM; MIHAILIDIS; WAN, 2007). Generally, innovation research has been concentrated on industrialized countries. However, emerging economies, such as Brazil, have initiated innovation opportunities for companies (MCMAHON; THORSTEINSDÓTTIR, 2013; FREITAS; MARQUES; SILVA, 2013; VAALAND; ISHENGOMA, 2016). From this perspective, the rate of medical innovation

progress has been remarkable, and significant advances and achievements have been made in medical technology (BEAULIEU; LEHOUX, 2018). Such growth is part of digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), in addition to pharmaceutical and biotechnology (EVENS; KAITIN, 2015) entrepreneurial companies.

Digital health technologies have the potential to accelerate, streamline, and optimize clinical research operations while reducing costs (SHARMA et al., 2018). The digital health area comprehends how technologies that provide digital data accessible to caregivers and patients lead to a physician-patient relationship with shared decision-making and improvements in health delivery (MESKÓ et al., 2017; SHARMA et al., 2018). The medical device area is an increasingly central role in clinical practice and home care, bringing health and quality of life benefits (SORENSEN; KANAVOS, 2011). The medical device may be used alone or in the combination of diagnosis, prevention, monitoring, treatment, or alleviation of diseases and injuries (IMDRF, 2005). Devices may also assist health care providers in making more accurate and timely diagnoses, enhancing not only the outcome of medicine but also its practice (SORENSEN; KANAVOS, 2011). Pharmaceutical and biotechnology areas have established a sector called biopharma (EVENS; KAITIN, 2015) or pharma biotech (THE LIFE..., 2016). Pharmaceutical and biotechnology companies conduct research, development, and product sales of molecule (biologic) drugs based on or engineered from biological tissue (EVENS; KAITIN, 2015).

As previously mentioned, entrepreneurship, especially in the health setting, is emerging these days as a significant innovation driver across companies in both developing and developed countries (WILDEN et al., 2018). Typically, an entrepreneurial health company starts up from a motivating discovery at the university, through an organization, government, or foundation grants. Subsequently, the entrepreneur inscribes a small business innovation research grant to fund the startup activities and rounds up some collaborators to launch the entrepreneurial company (MEHTA, 2004; HOTZ-HART; ROHNER, 2014). In such circumstances, the most common collaborative locations for entrepreneurial companies are incubators, accelerators, and technological parks (HELLER, 2019; SZYCHER, 2019), stated as follows.

2.1.1 Collaborative locations for entrepreneurial companies

Entrepreneurs usually reside in the first few months in an incubator that provides premises and services in trade for a small percentage of the new entrepreneurial company (MARCOLONGO, 2017; HELLER et al., 2019; MAZZAROL; REBOUD, 2019). Other likely subsequent locations include accelerators (MARCOLONGO, 2017; HELLER et al., 2019) and technological parks (PRODAN, 2007; SZYCHER, 2019), described hereafter.

2.1.1.1 Incubators, accelerators, and technological parks

The incubators' role is to contribute to entrepreneurial companies in preparing for the market, establishing projects, and requesting resources. Incubators have evolved over the years. Firstly, incubators offered space and shared facilities to entrepreneurial companies, together with a reactive support. Subsequently, incubators provided proactive support and advisory services to create growth-potential entrepreneurial companies. Afterward, incubators established more access to funding, mentoring, and technological labs, looking outwards to economic opportunities. Currently, incubators offer more than just business support services, such as International Business Incubator in Silicon Valley, which provides services to entrepreneurial companies from other countries to develop their businesses in the US market (LALKAKA, 2006; SAFFAR, 2012; KHALID; GILBERT; HUQ, 2014). Accordingly, incubators provide services, training and facilities, advice, and networking opportunities, including access to equipment and technology support (MARCOLONGO, 2017; MAZZAROL; REBOUD, 2019; HELLER, 2019).

Accelerators generally admit high-growth potential and profitable entrepreneurial companies. There is a highly selective process that usually includes business plan evaluation, startup presentations to the board of advisors, and follow-up interviews with the startup management. The accelerator seeks a significant market potential concept and a management team capable of launching a successful company (MARCOLONGO, 2017). Additionally, accelerators provide training for business and sector experts, in addition to financing solutions. Starting in an accelerator does not preclude a startup from later using an incubator. Nonetheless, accelerators and

incubators are pathways to transition from the lab to become an independent company (MARCOLONGO, 2017; HELLER, 2019).

Technological parks are often a combination of research and business interests. Government, districts, cities, major companies, and universities contribute to their formation (PRODAN, 2007; SZYCHER, 2019). Technological parks establish innovative companies connecting science with industrial usage and other fields through retaining and incorporating expert workers. Technological parks are an incredibly effective strategy for universities to diversify the connection with the entrepreneurial world (PRODAN, 2007). In such a scenario, research outcomes progress to viable commercial products (SZYCHER, 2019).

In addition to collaborative locations, collaborative resources for the survival of entrepreneurial companies, stated as follows, are also significant.

2.1.2 Collaborative resources for entrepreneurial companies

In a continuous effort, investments optimize medical innovation, together with the quality and efficiency of health (SPEKOWIUS; WENDLER, 2006). Entrepreneurial companies face significant financing needs to support their development and growth, and turning to external funders is a necessary step (HELLER, 2019). Many entrepreneurs attempt to find capital to start a new business, and it is essential to apply from a wide variety of funding sources and consider the whole financing options (SZYCHER, 2019). In the medical innovation area, if the entrepreneur decides to pursue the commercialization of the discovery actively, the most common funding may come from personal funds, angel investors, venture capital, hospitals, universities, organizations, and government, worded as follows (MEHTA, 2004; BAUCHNER; BERWICK; FONTANAROSA; 2016; LEHOUX; MILLER; DAUDELIN, 2016; MILLER; FRENCH, 2016; SZYCHER, 2019).

2.1.2.1 Personal funds, angel investors, and venture capital

Most entrepreneurs finance their startups with their funds combined with the provision of loans, but eventually, external funding will be required to expand the operations (MAZZAROL; REBOUD, 2019; SZYCHER, 2019). The leading source of capital for a

new business is the entrepreneur's own money due to ease of use, quick access, and no payback terms (SZYCHER, 2019).

Angel investors are commonly successful entrepreneurs and advisers who have the capital and usually provide the first round of independent external investment. They typically invest in situations where the founding team has exhausted their savings. Angels expect to be directly involved in management decisions and thereby do not compete with venture capitalists due to offering a source of funding for young, innovative, and high growth businesses (SUH; SOHN, 2016; MAZZAROL; REBOUD, 2019; SZYCHER, 2019).

Venture capital is a source of funding to invest in new and rapidly growing entrepreneurial companies that are likely to expand. Venture capitalists allocate financial resources for a specific duration to entrepreneurial companies with few tangible assets and that scarcely generate revenues along with their initial R&D activities (LEHOUX; MILLER; DAUDELIN, 2016). Notwithstanding, it is common for venture capital providers to pursue influence on the company business. Most venture capital and corporate investment feats inventions that have already been converted into new products and services with clear market opportunities (TYKVOVÁÁ, 2018; MAZZAROL; REBOUD, 2019, SZYCHER, 2019).

2.1.2.2 Hospitals

Entrepreneurship has also been adopted by hospitals, which are organizations that perform essential roles in medical innovation. Hospitals contribute to the production and diffusion of knowledge, linking of practice with science and technology, use of and feedback on prototypes and concepts, in addition to the implementation of new medical procedures (GULBRANDSEN et al., 2016; MILLER; FRENCH, 2016). A hospital seeks to constitute infrastructure and connect researchers to solve specific problems (FRENCH; MILLER, 2012).

Health providers, such as hospitals, may serve as suitable empirical sites for improved understanding of the multifaceted role of the state in innovation (GULBRANDSEN et al., 2016) and are adopters and users of new technologies, along with potential developments. Hospitals contribute to new idea generation via experimental learning in clinical practice and research by diagnosing problems and possible solutions

(THUNE; MINA, 2016). Some research results are extended to form innovative entrepreneurial companies or are licensed to existing organizations (THUNE; MINA, 2016; FRENCH; MILLER, 2012).

Hospitals are concerned as partners of industrial development and the commercialization of science. Besides, hospitals are part of the principles and goals of research between clinical innovators and industry (LEHOUX; MILLER; DAUDELIN, 2016) and may complement innovation activities carried out by external organizations, such as collect evidence on experimentation with new drugs and devices (THUNE; MINA, 2016).

2.1.2.3 Universities, organizations, and government

Universities are institutions that contribute to educating large proportions of the population and generating knowledge (PERKMANN et al., 2013) and a significant source of inventions that may result in relevant technological, commercial outcomes (CHESBROUGH, 2003).

The concept of entrepreneurship in academia has grown significantly and may be considered a growing scholarly field. Entrepreneurship has been taught at universities throughout the world (LANDSTROM; HARIRCHI, 2018), and considerable attention is given to entrepreneurs who form new, high-technology firms (LUCAS et al., 2009). In this sense, students need to have their interest stimulated in entrepreneurial topics (SCHULTE, 2006; DAVEY; HANNON; PENALUNA, 2016).

In this context, USP has contributed to medical solution innovation through multidisciplinary teams and partnerships with organizations (ZANCUL et al., 2017; LOPES et al., 2018). As a consequence, numerous projects are developed to improve and assist health requirements, such as the development of a hospital asset management solution, the improvement in the oxygen flow control (INPI, 2015), and improvements in the exam collection process (SILVA et al., 2019). Additionally, projects are developed for the prevention of primary infections in the bloodstream, prevention of accidents with surgical perforating-cutting materials (LOPES; ZANCUL, 2017), together with the development of a portable device for measuring blood test hemolyzed samples based on computer vision and neural network (LOPES; ZANCUL, 2017; LOPES et al., 2019; INPI, 2020).

Universities pursue development and commercialization activities in the form of interaction with corporate and government sources (VARGAS; CALLAWAY; ARISS, 2017). Programs and alliances are emerging, through which universities, governments, and organizations maintain relationships for knowledge exchange (TOSCANO; MAINARDES; LASSO, 2017). External organization funding promotes interest in research, production of R&D outputs, and demand for Intellectual Property (IP) protection (AGRAWAL; HENDERSON, 2002; FRIEDMAN; SILBERMAN, 2003; SIEGEL; WALDMAN; LINK, 2003; WU; WELCH; HUANG, 2015). Researchers who receive external organization funding are usually required to conduct research with higher applicability (WU; WELCH; HUANG, 2015). University research, which produces results relating to practice, may develop research projects with a more significant application potential (SLAUGHTER, 2004; WU; WELCH; HUANG, 2015).

From the university perspective, Hotz-Hart and Rohner (2014) state the following advantages of collaboration with external organizations: access to personal and business knowledge, stimulating new issues and refer ideas; procurement of funds from private partners; access to R&D facilities. From the perspective of partner organizations, the advantages are the access to research results of the universities and the optimization of resource use in organizations by outsourcing costly research projects at universities. In sum, collaboration may provide technology advances at a lower cost to organizations.

Governments are interested in enhanced levels of institutional and entrepreneurial activities and have encouraged universities to prepare students for innovation careers (LUCAS et al., 2009). In this context, governments have assisted universities and enabled students to develop expertise for innovative applications in new entrepreneurial companies (HARTSHORN; HANNON, 2005; LUCAS et al., 2009). The government frequently intervenes to promote collaboration between universities and organizations through enhancing innovation (BARNES; PASHBY; GIBBONS, 2002; FAN; GARNSEY, 2014; BANERJEE; SIEBERT, 2017).

Typically, an entrepreneurial health company emerges from the university through initial research grants (MEHTA, 2004). For instance, the previously mentioned project that leads to a portable device for measuring blood test hemolyzed samples based on computer vision and neural network (LOPES; ZANCUL, 2017; LOPES et al., 2019) emerged from an elective undergraduate course at USP in partnership with a health

organization. The project resulted in a patent with rights granted for the invention. Afterward, the project earned funding from PIPE for continuity, and, consequently, a new entrepreneurial company was instituted.

Occasionally, health organizations are unlikely to form partnerships with entrepreneurial companies at an early stage due to the unpredictable nature of health research product outcomes. In these circumstances, an entrepreneurial company needs to obtain research grants or angel investor funding to improve the trustworthiness and the benefits of getting access to expertise. Creating a partnership with an organization is a complex process due to inexperience in the process, especially on the side of the new entrepreneurial company (HINE; KAPELERIS, 2006; MALSHÉ; BIEMANS, 2014; MAZZAROL; REBOUD, 2019).

However, over recent years, organization efforts have produced a variety of practices to cooperate with entrepreneurial companies through established models, such as corporate venture capital (WEIBLEN; CHESBROUGH, 2015). For instance, General Electric StartUp Health has themed initiatives in which applying startups may receive funding and the chance to collaborate with the organization (CHESBROUGH, 2012). Strategic alliances and partnerships may be a considerably valuable procedure for companies of all sizes, especially entrepreneurial companies, to secure access to resources and expertise, which may take a long time to be individually developed (MAZZAROL; REBOUD, 2019).

Additionally, many national and regional governments offer programs to encourage small and medium-sized businesses (SZYCHER, 2019). Research grants are generally funded by public and not-for-profit public sources (GLÄSER; VELARDE, 2018). There are considerable amounts of funding agencies assisted by the government that comprehend an interest in technological and scientific research. Funding agencies support innovative research and are in charge of the budget, along with specific programs dedicated to R&D (NEDEVA, 2013; LLOPIS; D'ESTE, 2016; LEHOUX; MILLER; DAUDELIN, 2016). In Brazil, it is noteworthy to mention PIPE (SMALL BUSINESS RESEARCH, 2020), addressed as follows.

2.1.2.4 Innovative Research in Small Business (PIPE)

The PIPE was created in 1997 and is part of FAPESP, a public foundation linked to São Paulo State Government Economic Development Secretary (GOVERNO DO ESTADO DE SÃO PAULO, 2000) with the mission to foster research, scientific, and technological development in Brazil, specifically in the state of São Paulo (SOBRE O PIPE, 2020).

PIPE program invests in innovation for economic growth. It influences the creation of new careers by representing a substantial funding source for entrepreneurial companies to develop new technologies and subsequently reach the commercialization phase. PIPE is essential for science advances and encompasses a broad range of knowledge areas, such as health, engineering, among others. Although the PIPE program operates exclusively in São Paulo state, it is the leading funding source of innovation support in Brazil (FALEIROS, 2018; BALANÇO FAPESP, 2020).

PIPE supports the execution of scientific or technological research in entrepreneurial companies (SOBRE O PIPE, 2020), which should have a research unit in the State of São Paulo that provides adequate infrastructure conditions and qualified personnel to carry out the research. The research projects selected for the PIPE grant should be developed by researchers who have an established work relationship with the company and reside in the state of São Paulo (NORMAS PIPE, 2020).

The origin of PIPE was motivated by the Small Business Innovation Research (SBIR) from the National Science Foundation (NSF) - a program to support technological innovation in small businesses created by the United States Congress in the early 1980s (VASCONCELOS, 2017). Such a program promotes scientific excellence and technological innovation by investing federal resources in suitable projects (LINK; SCOTT, 2013). Whereas SBIR is federal and supported by several agencies with national coverage, PIPE is an initiative of a single and state institution (VASCONCELOS, 2017).

PIPE supports research as an instrument to promote technological innovation and business development. It increases competitiveness and enables companies to associate with researchers from the academic environment in research projects; contribute to the formation and development of technological development centers and

the placement of researchers in the corporate market (NORMAS PIPE, 2020). PIPE projects are carried out under the responsibility of a principal investigator who has an employment contract with an entrepreneurial company or is associated with it for research development. The project selection is through a peer-reviewing system (SMALL BUSINESS RESEARCH, 2020).

Based on the SBIR program, research proposals submitted to PIPE are organized into Phase 1, Phase 2, and Phase 3. Phase 1 encompasses technical-scientific feasibility analysis, Phase 2 is the development of the research proposal, and Phase 3 is the application of the results aiming at the commercialization of the product or process that was the object of the innovation created from the research supported in Phase 1 or Phase 2 (NORMAS PIPE, 2020).

More specifically, Phase 1 has an expected duration of nine months, intended to research the technical viability of the proposed study. The maximum financing amount is R\$ 200,000 for each project. At the end of 9 months, the responsible researcher should submit a final scientific report and the accountability of the resources invested by FAPESP. If there is an interest in sending the Phase 2 proposal, a scientific progress report should be provided at the end of the 6th month of Phase 1, simultaneously with the Phase 2 proposal submission. Such a scientific progress report is added to the final scientific information of Phase 1, which should be presented in the 9th month. The quality of the results presented is decisive for the qualification for Phase 2 of the PIPE Program (PROGRAMA FAPESP, 2015; NORMAS PIPE, 2020).

During Phase 1, FAPESP offers a high-tech entrepreneurship training program called Entrepreneurial PIPE, launched in 2016 and based on the National Science Foundation's Innovation Corps (I-Corps) program. Such a program aims to enhance business model proposals and allow researchers to reduce the time to translate a promising idea to the marketplace (PIPE EMPREENDEDOR, 2020; NATIONAL SCIENCE FOUNDATION, 2020).

FAPESP offers the Entrepreneurial PIPE four times a year. In each time, approximately 20 companies that demonstrate interest and commitment to innovation are selected. The training allows these companies to evaluate their business model, increasing the chances of being approved in Phase 2 and later offering an innovative product to the

market. In some cases, Phase 2 projects in the initial months of their execution may also participate (PIPE EMPREENDEDOR, 2020).

Phase 2 has an expected duration of up to 24 months, intended for the development of the research proposal itself. The maximum financing amount is up to R\$ 1,000,000 for each project. During the 24 months of Phase 2, the company should develop and demonstrate to FAPESP the efforts for product development, commercialization, and financing in the scientific reports, essentials for Phase 3 (NORMAS PIPE, 2020).

There are situations in which a project is directed to Phase 2 without having a previous Phase 1 grant. However, a detailed justification for skipping the Phase 1 grant must be presented, with a description of prior research results related to the proposal, clearly demonstrating that Phase 1 related activities have already been carried out through the small company by other means (NORMAS PIPE, 2020).

In Phase 3, the company is expected to carry out commercial and industrial product development, based on the results of Phase 1 and 2. Funding for Phase 3 should be obtained by the company from the market, from other company financing agencies or FAPESP, whereas there is a specific call for proposals. The presentation of concrete perspectives for the Phase 3 financing is considered a decisive element in evaluating proposals for Phase 1 and Phase 2. Research proposals for Phase 1 or Phase 2 are assessed in batches, four times a year, every three months, generally beginning in January and ending in October (NORMAS PIPE, 2020).

It is worth mentioning that FAPESP analyzes proposals from companies that have not yet been established. In case of approval, the applicant should formally open the company before signing the grant term and receiving the funding. FAPESP requires a royalty agreement for the IP resulting from the financed project. In all PIPE projects, the research must be developed in the company. Eventually, some specific research activities may be subcontracted from universities or consultants as long as they are justified and do not constitute the central part of the research (PIPE FAQ, 2020).

The common term expected for proposal analysis, such as due diligence or return without advisory issues, is approximately 150 days. However, there may be more extended time, depending on the area. Although FAPESP, on average, complies with the 150 days deadline, there is no commitment due to the quality of the analyses and

the proposal selection process. FAPESP cannot entirely control the evaluation process since they are sent to ad hoc advisors to issue an opinion (NORMAS PIPE, 2020).

In sum, it is noteworthy that the PIPE program supports the innovative drive of small business projects that rely on funding to advance and actively pursue commercialization (FALEIROS, 2018). However, particularly in the health area, collaborative resource hurdles may occur with entrepreneurial health companies in the following sequence.

2.1.3 Collaborative resource hurdles

The main hurdles associated with research grants are related to ensuring sufficient applications and contributions, along with the provision of funding where there is a shortfall as most funding agencies do not award the full research costs and publishing findings regularly. Public institutions are frequently the primary source of health entrepreneurs (HINE; KAPELERIS, 2006).

Organizations attempt to safeguard the research continuation and face growing complexity in their funding environments, while small business partners and founders are confronted with more promising and research activities than they may maintain (GLÄSER; VELARDE, 2018). Investments tend to derive from large organizations or public and private investors (HINE; KAPELERIS, 2006), and ensuring the profitability of health investments has been a relevant issue over the years (SOENKSEN; YAZDI, 2017).

Despite medical innovation contributions usually leads to a variety of product concepts, there exist limited funding for ongoing developments and commercialization. A key hurdle for the health area is that due to high capital costs for R&D, innovation dissemination is sluggishly deprived of significant levels of investment. In many cases, health technologies take several years to advance from concept to commercialization due to project development complexities and regulations (HINE; KAPELERIS, 2006; DAVEY et al., 2011; CAO et al., 2013).

In this context, partners and founders should have access to methods to structure their entrepreneurial companies (WEIBLEN; CHESBROUGH, 2015). In the following section, the main approaches and health regulatory processes are addressed.

2.2 Medical innovation process

Medical innovation is a long and rigorous process with an extensive development cycle and substantial financial investments required, in conjunction with the careful integration of diverse disciplines, regulatory requirements, and administrative project controls (TERZIOVSKI; MORGAN, 2006; FRIES, 2013). Most entrepreneurial health companies face significant technical and clinical challenges that should be identified and prioritized concerning difficulties that impose a significant medical burden (YOCK et al., 2015). Potentially medical innovation challenges comprehend multiple stakeholders, such as universities, hospitals, government entities, and health organizations. Each stakeholder has individual needs, requirements, and interests, together with different product development roles, from concept to commercialization (VAN GEMERT-PIJNEN et al. 2011; YOCK et al., 2015; WIELD et al., 2017; VAGAL et al., 2020).

A variety of health products have emerged from hardware or software, along with their related services (YOCK et al., 2015) and embedded software to control particular operations of devices (LEE, 2002). Software and technologies contribute to the diagnosis, treatment options, and more capable clinical practice (FDA, 2018b). For instance, Tahir et al. (2020) designed a hardware/software fall detection system for appropriate medical assistance, which achieves 99.38% fall detection accuracy. Advances in technology are resulting in innovative services and shifting how customers are assisted before, during, and after the service provision (OSTROM et al., 2015). Investment in products and services results in further company differentiation over enhanced components, functionality, trustworthiness, and suitability to customer needs (GEBAUER; FRIEDLI, 2005).

In sum, there has been an interest among companies to improve competitiveness by adding services to product offerings. Services may assist and accelerate new market entrances and also be useful alternatives for products (CUSUMANO; KAHL; SUAREZ, 2015), in conjunction with market opportunities, company performance improvements, and higher profit results (MONT, 2002; STEINER et al., 2016; BENEDETTINI; SWINK; NEELY, 2017). For instance, consumer durables producers such as General Electric, Otis, Siemens, and Xerox are increasingly supported on services, and approximately 50% of their total revenue and profit arises from services offerings (OLIVA; GEBAUER;

BRANN, 2012). Some services complement products or are substituted with products. Services such as software as a service or device leasing with usage and maintenance contracts may be considered a different way of gaining access to the market (CUSUMANO; KAHL; SUAREZ, 2015).

In such a scenario, approaches are necessary to ensure functionality, economic, and competitive success for the producer under a reliable and affordable investment (TERZIOVSKI; MORGAN, 2006; FRIES, 2013). Medical innovation is different from other fields because the process initiates with an unmet clinical need, and only after that need is understood, medical technology is produced (MAKOWER, 2017). Due to the high regulation and multidisciplinary, the product development process is distinctive. Additionally, the main point of designing medical novelties is to consider safety aspects, including the repercussions of design flaws (FRIES, 2013).

Managing medical innovation requires considerable amounts of approaches to ensure the progress from idea to market as long as both business development and research outcomes advance (TERZIOVSKI; MORGAN, 2006). For instance, Design Thinking is a nonlinear and iterative approach that has been applied both in medical education and by health professionals to deal with complex medical decision making and improve clinical outcomes (DEITTE; OMARY, 2019; MCLAUGHLIN et al., 2019). Design Thinking has been applied in a diverse health setting, which may result in functional and reasonable interventions (ALTMAN; HUANG; BRELAND, 2018).

Typically, Design Thinking encloses a five-stage iterative process. The Empathize phase comprises the goal to shape the basis for ideas. The Define phase synthesizes the findings of empathy into needs and insights. The Ideate phase generates as many creative solutions as possible. In the Prototype phase, potential solutions become tangible. Lastly, the Test phase refines solutions and makes them better (D.SCHOOL, 2018).

Based on Design Thinking, Biodesign has emerged as an alternative, cyclical, and iterative approach for medical innovation with an emphasis on understanding clinical needs (YOCK et al., 2015). Biodesign has been highly applied in the academic area (BRINTON et al., 2013; YOCK et al., 2015; ZANCUL et al., 2017) and comprises the following phases: Identify, Invent, Implement, and Project Launch. The Identify phase entails Needs finding and Needs screening stages, and the purpose is to identify and

screen unmet medical needs through observation and formulate opportunities for the concept proposal. The Invent phase implies Concept generation and Concept screening stages to generate ideas and select the final concept. At last, the Implement phase refers to the Strategy development, along with IP registration, for instance, patents, copyrights, and trademarks. Additionally, Business planning is employed in conjunction with Marketing and sales strategy definition and Technical feasibility to finish the innovation process and prepare to project launch.

Pietzsch et al. (2009) apply the stage-gate process (COOPER, 2008) to develop an iterative approach based on best-practices analysis with medical specialists. Such a strategy encompasses Phase 1, where initiation, opportunity, and risk analysis occur. It is the beginning of the development process and is characterized by the early project evaluation aimed at tackling clinical needs. If the project is accepted, the development proceeds to Phase 2, where the concept formulation and feasibility assessment occur. After a concept has been formulated and several prototyping rounds have occurred to assess feasibility, the development proceeds into Phase 3, where design, development, verification, and validation occurs. During this phase, a matrix for the verification and validation test is created. Phase 4 encompasses the final validation and product launch preparation, along with the creation of formal design prints, sales launch preparation, and regulatory approval. Lastly, Phase 5 comprises Product launch and commercialization, in addition to Postlaunch assessment.

Following medical innovation approaches, El-Haik and Mekki (2008) specify the Design for Six Sigma (DFSS) approach. It comprises the Identify phase for idea creation, the voice of the customer, and business understanding; Characterize to concept development and preliminary design; Optimize to design optimization; Verify for verification and validation along with launch readiness. Subsequently, Scale production and commercialization, Consumption, and Disposal phases. During the Scale production and commercialization phase, the product will be produced and distributed to the market, and suppliers might provide some parts. In the Consumption phase, products are consumed by customers. Such a stage is the most important to consumers, who will form opinions of design and brand name. In the Disposal phase, all products and services become obsolete, replaced by either new technologies or new methods.

There are other specific medical approaches, such as van Gemert-Pijnen et al. (2011), which points out a holistic and cyclic process for the development of eHealth technologies. Such an approach might also be employed to general medical progress and encompasses the Contextual inquiry phase, which entails information gathering from the intended users and the environment in which the technology will be implemented. Subsequently, Value specification, which most good solutions emerge along with user and organizational requirements. The best solution will be most beneficial to key stakeholders. The next phase is Design, which refers to building prototypes that fit with the values and user requirements. Afterward, the Operationalization phase concerns the introduction, adoption, and employment of the technology in practice. Lastly, the Summative evaluation phase refers to the actual uptake of technology and the assessment of the impact of technologies in terms of clinical, organizational, and behavioral conditions.

In the same direction, Santos et al. (2012) developed an approach with the following phases: Idea creation; Identification of the customer; The voice of the customer; Concept generation; Concept selection; Preliminary design; Design optimization; Clinical and non-clinical studies; Approval processes; Launch; Post-market surveillance. The identification of the customer is essential to understand the product selection and arguments used to make a decision. The voice of the customer is the step in which the needs are gathered. In the concept selection phase, the design team is committed to a concept whose modification implies delays and additional costs. After the product design, the next steps are the clinical and non-clinical studies, along with the approval process until product launch and post-market surveillance.

Additionally, agile approaches have been applied to shorten the time from idea to implementation (WYSOCKI, 2019; PIPE EMPREENDEDOR, 2020), such as Customer Development (BLANK, 2020) and Scrum (PRIES; QUIGLEY, 2011). For instance, Customer Development has been provided by Entrepreneurial PIPE to assist startups during the initial months of execution of Phase 1 or Phase 2. The training allows startups to evaluate their business model and propose an innovative product to the market (PIPE EMPREENDEDOR, 2020). Customer Development conducts a startup search for an extendable business model and establishes a successful company (BLANK; DORF, 2012). Likewise, Scrum focuses on business needs in conjunction with a commercial and feasible product to the customer (PRIES; QUIGLEY, 2011).

Customer Development is an iterative model that encompasses the customer-related activities of an early-stage company. The first two steps aim to search for the business model. Stages three and four execute the developed and tested business model. The first step is Customer discovery, which seizes the founders' vision and transforms it into business model hypotheses. Subsequently, a plan is developed to test customer responses and convert them into evidence. Customer validation phase tests if the established business model is customizable, and Customer creation is the beginning of business execution. Lastly, Company-building focuses on implementing a validated model (BLANK; DORF, 2012; BLANK, 2020).

Scrum originated from agile software development and has lately been implemented in a wide diversity of projects (PRIES; QUIGLEY, 2011). Scrum is also an iterative approach with enhanced customer involvement and enfolded five significant phases. The Initiate phase encompasses the beginning processes, such as create a project vision, identify scrum master and stakeholders, and prepare the team. Estimate aims to plan and estimate responsibilities, together with creating user stories. Implement aims to execute the tasks and activities to establish a product and deliverables. Review and retrospect aim to revise and improve the deliverables. Lastly, Release focuses on delivering the customer approved deliverables and documenting the insights (SCRUM STUDY, 2017).

It is noteworthy that the Business Model Canvas has been employed as a visual business guide to entrepreneurial companies and compels nine boxes to fill in, described hereafter. In sum, a business model consists of the critical elements of a startup (OSTERWALDER; PIGNEUR, 2010; BLANK, 2020).

1. Value proposition comprises the benefits given by the company;
2. Customer segments encompass groups with similar characteristics;
3. Distribution channels connect manufacturers and customers with unique selling points;
4. Customer relationships involve demands to improve the customer experience;
5. Revenue streams encompass unique selling points;
6. Resources are essential to enable the business model;
7. Activities are critical to performing the business model;

8. Partners are the people who take part in the business;
9. Cost structure includes the costs and expenses acquired from the business model.

Table 2 depicts a high-level representation of relevant phases of the previously mentioned approaches applied to generate optimized medical innovation.

Table 2 - High-level representation of relevant phases of approaches applied to generate optimized medical innovation

Design Thinking (D.SCHOOL, 2018)	Biodesign (YOCK et al., 2015)	Stage-gate (PIETZSCH et al.; 2009)	DFSS (EL-HAIK; MEKKI, 2008)	VAN GEMERT- PIJNEN et al., 2011	SANTOS et al., 2012	Customer Development (BLANK, 2020)	Scrum (SCRUM STUDY, 2017)
Empathize Define	Identify Needs finding Needs screening	Initiation, opportunity, and risk analysis	Identify Idea creation Voice of the customer and business	Contextual inquiry	Idea creation Identification of the customer The voice of the customer	Customer discovery	Initiate Estimate
Ideate	Invent Concept generation Concept screening	Formulation, concept, and feasibility	Characterize Concept development	Value specification	Concept generation Concept selection	Customer validation	Implement
Prototype	Implement Strategy development IP registration Business planning Marketing and sales strategy definition Technical feasibility	Design and development Verification and validation	Preliminary design Optimize Design optimization Verify/Validate	Design	Preliminary design Design optimization	Customer creation	Review and retrospect
Test	Project launch	Final validation and project launch preparation	Verification and validation	Operationalization Summative evaluation	Clinical and non-clinical studies Approval processes	Company- building	Release
-	-	Product launch and commercialization Postlaunch assessment	Scale production and commercialization Consumption Disposal	-	Product launch Post-market surveillance	-	-

Source: Prepared by the author.

The phases presented in Table 2 usually go from the creation of the concept to the retreat and involve practices such as design, production management, and post-marketing surveillance. Due to the complexity of medical products, it is necessary to develop the prototype, preclinical, and clinical analyses to test, improve, retest, validate, optimize, and finalize before product launch, as well as consider the verification and validation of control process and government regulations (FERRER et al., 2017). The focus encompasses processes involved in transforming a concept or idea into a commercialized product (PIETZSCH et al., 2009; SHLUZAS; LEIFER, 2014; YOCK et al., 2015).

In product development approaches, the project is decomposed into phases, and the conceptual discussion begins with the customer need. Once the customer's need is identified, the product is developed and subsequently commercialized. In contrast, Scrum and other agile approaches, such as Customer Development, propose that the product adapts to the demands of customers over time, and various process repetition allows for changes that arise during product development (PRIES; QUIGLEY, 2011).

Approaches may vary according to the location and size of the company, including the product development phase. Usually, entrepreneurial companies start with the idea that requires an assessment during the early stage to verify if it is worth commercializing (HINE; KAPELERIS, 2006). Entrepreneurial companies have applied approaches to managing their processes, leading to an emphasis on execution instead of learning and discovery, along with the lack of significant sales, marketing, and business development milestones (BLANK, 2020).

Additionally, design-based approaches are time and resource-intensive, and more research is needed to demonstrate the long-term success and sustainability of innovative strategies. Both design-based and agile methods rely heavily on collaborative and iterative development (ALTMAN; HUANG; BRELAND, 2018; VAGAL et al., 2020). Furthermore, there is a lack of directions to perform activities of early-stage proposal evaluation. Medical innovation approaches pertain primarily to product development activities and do not provide adequate guidance to prospective investors. To attempt to unfold this issue, a method to comprehend the investment process in entrepreneurship medical innovation has been proposed in stages by Soenksen and Yazdib (2017). In such an approach, Phase 1 embraces investment strategy definition; Phase 2 combines venture search, screening, and rapid pre-evaluation; Phase 3

encompasses negotiation of terms and Phase 4 portfolio management, evaluation, and conclusion of the investment cycle.

Likewise, according to WHO (2010), there are many medical solutions on the market but not the most appropriate ones. The situation is critical due to such solutions that have been acquired unnecessarily, not being used safely and effectively for their proposed purposes, or not been adequately assessed for precise health outcomes. Despite the application of approaches and the global growth of medical innovation, solutions have been presented but not mature enough for real demand on the market (BARTELMES et al., 2009; CIURANA, 2014; MARESOVA et al., 2015).

Even though previous processes are not entirely effective in addressing challenges in health settings, it is possible to share a variety of core principles. Approaches may be applied together, combining the most appropriate process in each specific case (ALTMAN; HUANG; BRELAND, 2018; VAGAL et al., 2020).

2.2.1 Regulatory agencies

The other component of the medical innovation process is regulation, which is concerned with safety and efficacy, and assessment of all significant intended as well as unintended consequences of technology use (WHO, 2011). Typically, the major phases of a regulatory process comprise Submission preparation, which clinical data are necessary to support a submission and the development of essential documents—subsequently, the Pre-market evaluation submission phase, with classification, safety, and performance principles. At last, Regulatory agency approval and Post-marketing surveillance phases with notifications and reports after the commercial approval (YOCK et al., 2015).

In most countries, regulations are intended to keep products under control, considering quality and safety aspects. For instance, in the United States, the Food and Drug Administration (FDA) is an agency of the Ministry of Health and Human Services. In Brazil, the National Health Surveillance Agency (ANVISA) belongs to the Ministry of Health. Only companies in Brazil may apply for ANVISA registration (YOCK et al., 2015).

Medical devices under ANVISA include medical, dental, laboratory, or physiotherapy, directly or indirectly, for the diagnosis, therapy, rehabilitation, or monitoring of human beings. Medical devices are classified into four risk classes, according to the risk associated with their use: Class I – low risk; Class II – medium risk; Class III – high risk, and Class IV – maximum risk (ANVISA, 2020a). In addition to the risk classification, the device is classified as non-invasive, invasive, active products and special rules, such as medical products that incorporate as an integral part a substance, which, if used separately, may be considered a medicine (ANVISA, 2001).

Medical devices under FDA comprise an apparatus including any component, part, or accessory for employment in the diagnosis of disease (FDA, 2020a). FDA classifies medical devices Class I to III. Class I includes the ones with the lowest risk and Class III, the ones with the highest risk, such as mechanical heart valves and implantable infusion pumps (FDA, 2017). Class I devices present minimal potential harm to the person. Class II devices are often non-invasive but tend to be more complicated in design than Class I devices, e.g., X-ray machines and surgical needles. Class III devices are high-risk and typically implantable, therapeutic, or life-sustaining devices, e.g., replacement heart valves and implantable pacemakers (YOCK et al., 2015). Class I devices with low risk of harm are merely under general controls, and most are exempt from pre-market notification requirements, such as elastic bandages and surgical gloves (FDA, 2017; FDA, 2020b).

Concerning the pharmaceutical area, ANVISA prescribes that a drug is any product, technically obtained or elaborated, for prophylactic, curative, palliative, or diagnostic purposes. Thus, any product, regardless of nature (vegetable, animal, mineral, or synthetic) with therapeutic claims, must be considered a drug and needs registration to be manufactured and marketed (ANVISA, 2016). Additionally, biological medicines, such as vaccines, blood products, and biomedicines, are also submitted for ANVISA analysis and registration (MINISTÉRIO DA SAÚDE, 2010). There are no biological products exempt from registration, given the therapeutic specificities of this medication type (ANVISA, 2018).

Drugs under the FDA, including biologics licensing applications (FDA, 2018a), encompass the use in the diagnosis or prevention of disease and are envisioned to the body structure (FDA, 2020a). FDA approval of a drug is based on benefits that overcome its recognized and possible risks for the population (FDA, 2019). New

medicines and certain biologics, such as therapeutic proteins, vaccines, cellular therapies, blood, and blood products, should be confirmed safe and effective to FDA before commercializing (FDA, 2017).

Some products are exempt from registration. For instance, ANVISA (2015) exempts glassware and general laboratory instruments, gas generators, and anaerobic indicators, reagents sold as inputs for the manufacture of products for in vitro diagnosis and developments in the intermediate stage of production. Additionally, FDA Class I devices with low risk of harm are merely under general controls, and most are exempt from pre-market notification requirements, such as elastic bandages and surgical gloves. A much smaller number of Class II devices are exempt due to a minor safety risk. No Class III devices qualify for the exemption. However, if a device is determined to be exempt, it still must comply with a minimum set of FDA general control requirements, which oblige the company to register their facility or establishment with the FDA (YOCK et al., 2015; FDA 2017; FDA, 2020b).

Concerning digital health technologies, which allow consumers to support decisions and afford possibilities for simplifying prevention and early diagnosis of diseases (FDA, 2018b), there is limited evidence on the effectiveness of most digital health technologies. Regulators need evidence on safety and efficacy when technology is employed to diagnose or treat a condition (SHARMA et al., 2018). Although ANVISA and FDA regulations are evolving, several ANVISA rules do not apply to the software. For instance, health information or instructions for use that should be on the labels are not present in mobile applications or software distributed over the Internet (ANVISA, 2020b). Additionally, software as medical devices and various medical devices with the software are not certifiable. Brazil does not have a regulatory certification process of software as a medical device (ANVISA, 2019). However, both ANVISA and FDA recognize the necessity of regulating digital health products and adapt their processes (ANVISA, 2019; FDA, 2020c).

Regulatory approval is one of the most critical business achievements of entrepreneurial companies. Once a product is approved, slight modifications may be applied in the design and manufacturing process (LEHOUX et al., 2017).

2.2.2 Particular features among medical devices, pharma/biotech, and digital health domains

There are considerable individual factors among pharmaceutical and biotechnology, medical devices, and also digital health domains, described as follows.

The most significant regulatory issues affecting pharmaceutical and biotechnology companies are those relating to drug testing and approval. Such a process is lengthy with requirements for the extensive clinical trial in animals and humans, in conjunction with an appropriate and specialized expertise to overcome severe regulatory difficulties before commercialization (HINE; KAPELERIS, 2006; SHIMASAKI, 2014). Biotechnology and pharmaceutical areas have a greater focus on research, and major pharmaceutical companies may proceed as complements and support to science (LAURELL, 2013; STYHRE; REMNELAND-WIKHAMN, 2016).

Medical devices are often mechanical, electrical, or materials engineering-based and often with shorter product development cycles and continuously evolving, with incremental modification. Concurrently, drugs are chemical-based over longer life cycles with a stable compound. Clinical evaluation of drugs is usually more formalized and extensive (CRAVEN, 2007; LAURELL, 2013). Furthermore, due to different regulatory and coverage requirements of medical devices, the evidence on added value at market launch is less robust than drugs (ORIANA et al., 2016).

The advances of digital health technologies enable rapid creation, iteration, and distribution, with shorter design development times and minimum verification and validation activities to meet user needs. Despite digital health technologies are being applied much more broadly in medicine, including diagnosis, treatment, clinical decision support, care management, and care delivery, there is a scarcity of digital solutions evidence for benefits and harms. There is a need for an accurate evaluation of digital health products to provide greater transparency to the digital health business (MATHEWS et al., 2019; JANDOO, 2020).

Besides the particular factors aforementioned and the application of approaches, to ensure the evolution from idea to market and business development, medical innovation also requires teams with specific expertise and management skills,

including partners and founders (WEIBLEN; CHESBROUGH, 2015). In the following section, the main factors of a medical innovation team are addressed.

2.3 Medical innovation teams

Medical innovation is a complex combination of a varied range of knowledge and specific companies involved in different stages of research, development, and commercialization (JONES; WHEELER; DIMITRATOS, 2011). One of the most critical issues of an entrepreneurial company is the development of a reliable operational team (MAZZAROL; REBOUD, 2019). From this perspective, medical innovation requires teamwork and multidisciplinary to provide great potential for technological progress, and the characteristics of individuals have significant consequences in business operations (SZYCHER, 2019). To form productive and efficient teams, it is necessary a knowledge base with members prepared to be collaborative and productive (WEISS; TILIN; MORGAN, 2018).

Usually, the entrepreneur is a researcher with extensive skills and technical knowledge who perceives the research successes into practice through commercialization (HINE; KAPELERIS, 2006). The size of successful entrepreneurs' teams varies from three to six individuals, each one with the capacity to become the Chief Executive Officer (CEO) if required (MAZZAROL; REBOUD, 2019; SZYCHER, 2019). Bachelor students also play a significant role as the CEO or founder at the beginning of an entrepreneurial company (BOH; DE-HANN; STROM, 2016; HAYTER; LUBYNSKY; MAROULIS, 2016).

As entrepreneurial companies may operate in a continuously changing environment, the challenges of such companies are higher, together with innovative, entrepreneurial, and managerial skills that are limited to perform successfully in a competitive setting. There are constant changes in customers' needs, market expectations, and technological advances (SZYCHER, 2019). Towards this end, technical skills with an understanding of customers and markets are essential to allow future innovative products to evolve according to customer needs. Thus, the existence of different but complementary varieties of experience may have a positive effect on innovation (PROTOGEROU; CALOGHIROU; VONORTAS, 2017; SZYCHER, 2019).

In this context, an entrepreneurial company should clearly define the partners' and founders' expertise, and members should be committed to ensuring success (SZYCHER, 2019). The main concerns are the knowledge and skills of the founders. A competitive entrepreneurial company advantage relies on what the founders may do better than others (TERZIOVSKI; MORGAN, 2006). Founders are responsible for concrete action to set up a commercial business in conjunction with collaborative teams that utilize and empower the skills and knowledge of individuals (TERZIOVSKI; MORGAN, 2006; BLANCO, 2007). Typically, partners and founders are the group key personnel and advisers that establish the entrepreneurial company, and their characteristics have significant consequences on the business operation (SZYCHER, 2019).

Financial resources may be scarce in entrepreneurial companies to hire the most qualified member resulting in an inadequately structured team (MAZZAROL; REBOUD, 2019; SZYCHER, 2019). In the same direction, entrepreneurial companies may have restricted access to an array of funding. However, multidisciplinary and experience provide expertise in practicing entrepreneurial activities. Founders, including partners and members with a diversified professional background, may have a higher probability of producing innovation along with the increase of expertise and the enhancement of opportunities. Thus, different backgrounds and experiences imply that an entrepreneurial company may have access to a broader range of practices (PROTOGEROU; CALOGHIROU; VONORTAS, 2017).

It is worth mentioning that in the area of medical innovation, several new training initiatives are being developed and deployed (YOCK; BRINTON; ZENIOS, 2011). Even though universities generate specialists, there is an absence of skills necessary to create and develop a commercially viable health solution in graduate programs (YAZDI; ACHARYA, 2013). Additionally, although there are faculty members at many universities who are experienced entrepreneurs, such experts to the number of faculty inventing medical technologies are not high (YOCK; BRINTON; ZENIOS, 2011).

Several incubators and investment groups usually operate under the assumption that medical innovation investment requires unique kinds of expertise to be conducted successfully, at least compared to other less regulated industries (SOENKSEN; YAZDIB, 2017). Medical innovation demands expertise at each stage of commercial product development. Besides, entrepreneurial companies cope with limited access to

qualified expertise in regulatory affairs and commercialization. Eligible scientific, regulatory, e.g., ANVISA and FDA, and commercial know-how are valuable to entrepreneurial health companies (STYHRE; REMNELAND-WIKHAMN, 2016). In this context, experience in health organizations, prior business entrepreneurial, and IP are the major drivers to engage in entrepreneurial activity, in conjunction with previous experience with regulatory agencies. Individuals with such characteristics may be more prepared for business opportunities and may be more likely to assess if solutions are suitable for commercialization (KRABEL; MUELLER, 2009; YOCK et al., 2015; SOENKSEN; YAZDIB, 2017).

Additionally, a set of skills is necessary, which are rarely encountered in a single person (HOYOS-IRUARRIZAGA; MENDIALDUA; SANTOS, 2015). No sole individual is able to effectively produce, develop, and implement an effective solution (YAZDI; ACHARYA, 2013). The expertise and skills of teams have been considered valuable in performance outcomes (TAJVIDI; KARAMI, 2015). Concerning the know-how of team members, skills, and other competencies, such as professionalism, communication, collaboration, and teamwork, are required (HARRIS, 2016). Investors tend to prefer entrepreneurs who appear to have a broader range of skills. The kind of experienced entrepreneurs has before embarking on an entrepreneurial company process influence the set of skills prior mentioned, which contributes to expertise (RÉDIS; SAHUT, 2015). Career experience is a strong predictor in engaging entrepreneurial activity (KRABEL; MUELLER, 2009).

From this standpoint, a typical recommended medical innovation team may encompass the undermentioned experts (PURDY et al., 2012; YAZDI; ACHARYA, 2013; NECK; GREENE; BRUSH, 2014; WIEMAN, 2014; DENIS, 2015; YOCK et al., 2015; SOENKSEN; YAZDIB, 2017).

- Physicians with medical specialties, for instance, cardiology and dermatology;
- Health professionals (non-physicians), as nurses, pharmacists, biologists, and dentists. In this study, a biologist is considered a health professional due to the forefront of genetic engineering and health transformation. The application of biology is noticeable in medicine and pharmacy (WASSWA; MUGARURA; NDIWA, 2017);
- Engineers, such as mechanical, electrical, software, chemical, and biomedical;
- Technology professionals (non-engineers), such as computer scientists;

- Other areas professionals, such as administrators and lawyers;
- Hard sciences professionals, as physicists, medical physicists, statisticians, mathematicians, and chemists.

Additionally, the team degree may comprise Postdoc, Ph.D., Master, Bachelor, Undergraduate, and Technician (YOCK et al., 2015; WALL et al., 2017). Access to such teams may be facilitated through collaboration with academic institutions, incubators, and medical centers with established programs to train entrepreneurs in medical technology development and commercialization (SOENKSEN; YAZDIB, 2017).

Consequently, the composition of teams matters for successful medical innovation (ALI; GITTELMAN, 2016), with multidisciplinary involving different professions working together and playing an increasingly important role in the health setting (MITCHELL et al., 2010). For every successful new medical solution, insights from many areas of science, medicine, engineering, humanities, business, and law are necessary, together with a deep comprehension of medical needs (YAZDI, ACHARYA, 2013). The most successful and productive health teams are those in which all members, regardless of status, are confident and committed to assuming leadership and responsibility for the continually evolving (WEISS; TILIN; MORGAN, 2018).

Medical research remains an important innovation engine because researchers have unique possibilities for experiences that emerge from established proceedings (ALI; GITTELMAN, 2016). In this context, physicians are both the primary customers and innovators and an essential source of ideas for firms and new contributors (CHATTERJI, 2009). Consecutively, physicians perceive unmet clinical needs and provide the most feasible solutions (CHATTERJI et al., 2008).

Prior research focuses on the collaboration of physicians in teamwork and their influence on innovation performance outcomes. For instance, an expanded body of knowledge regarding the role of the physician in medical device development, and the mapping of design and development practices to outcomes, has implications for both the health business and the broader fields of product development (SHLUZAS; LEIFER, 2014). However, the relationships between physicians and engineers are still scarce, although developing medical solutions involves the cooperation of physicians

and engineers. Product acceptance and use depend heavily on a product's ability to enhance physician experience (YODA, 2015; SHLUZAS; LEIFER, 2014).

Besides, as stated by the World Health Organization (WHO, 2010), the drive to improve health is dominant among many physicians and engineers beyond their interest in discovering new theories and solutions that advance scientific knowledge. Notwithstanding, the absence of cooperation and exchange of ideas between medical and engineering teams put off new solutions development (BERGSLAND; ELLE; FOSSE, 2014). Scientists and physicians skilled in their scientific fields often know little about business and its management (LI; HALAL, 2002). The issue of inexperience, along with science but an inadequate business background, have an impact on the business outcome (HINE; KAPELERIS, 2006).

Thus, experienced staff is necessary to bring about the knowledge of past successful and unsuccessful outcomes, in conjunction with the appropriate plans and motivation for the implicated team (HINE; KAPELERIS, 2006). Researchers are intrinsically motivated by their commercial aims, which appear to satisfy the desire to act righteously socially (LAM, 2011), and motivation has a positive relationship with innovation outcomes (SHIMASAKI, 2014).

The ability to attract and engage advanced research is critical to business success. It is essential to create a stimulating environment that attracts innovative researchers to motivate the development of products in a competitive market (LI; HALAL, 2002). Therefore, appropriate expertise is needed to overcome stringent regulatory hurdles before a product reaches the market. Entrepreneurs are the primary source of motivation with technology and business skills. Without a capable team, most companies do not achieve their potential (SHIMASAKI, 2014).

In sum, innovation is teamwork in which entrepreneurial companies should measure and manage their innovation process to provide potential and profitable outcomes (TERZIOVSKI; MORGAN, 2006). The next section focuses on significant innovation performance outcomes.

2.4 Innovation performance outcomes

Innovations intend to improve company performance in acquiring a competitive benefit by launching and enhancing new products and services (OECD/EUROSTAT, 2005). As prior mentioned, typically, an entrepreneurial company begins from a project in conjunction with a subscription to a research grant program, such as PIPE, to subsidize the company operations (MEHTA, 2004; NORMAS PIPE, 2020). Projects contribute to company success and effectiveness (SHENHAR; DVIR, 2007). Each project requires measurements related to its success criteria, and how a company defines and measures success is critical to innovation (MCLAUGHLIN; RICHINS, 2015).

Projects should be evaluated based on their contribution to a broader business result (DAVILA; EPSTEIN; SHELTON, 2006; SHENHAR; DVIR, 2007), and the interest in measuring innovation is due to its relation to the performance of companies (OECD/EUROSTAT, 2005). In this context, innovation performance is the process of creating and developing new products or services (TERZIOVSKI; MORGAN, 2006), and innovation performance indicators allow the monitoring of the company's progress regularly. However, numerous entrepreneurial companies rely merely on annual financial statements to determine their business performance (MAZZAROL; REBOUD, 2019).

Thus, it is noteworthy to include accurate indicators to evaluate the proposals of different innovation projects, and improving the evaluation process of innovations may also assist investors in new entrepreneurial companies (DZIALLAS; BLIND, 2019). The use of indicators leads to more transparent, traceable, and reliable innovation decisions and avoid misallocation of resources (DZIALLAS, 2020).

Existing studies demonstrate that innovation performance outcomes play a central role in driving progress in companies. Particularly in the health area, Fleuren et al. (2014) measure the factors that may affect the stage of innovation implementation. Elg, Broryd, and Kollberg (2013) provide how performance measurement leads to advances in health practice.

Despite innovation indicators have been analyzed, additional alternatives are needed to evaluate the commercial potential of innovations (DZIALLAS; BLIND, 2019). There is limited research on performance outcomes in the context of medical domains

(SHLUZAS; LEIFER, 2014), such as digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), and pharmaceutical and biotechnology (EVENS; KAITIN, 2015) entrepreneurial companies. A more thorough understanding should assist in focusing on the most promising innovations and in supporting them (DZIALLAS; BLIND, 2019). In this context, specifically in the medical realm, the following indicators are suggested to measure project innovation performance outcomes, which impact the overall company business results.

Time to market is an indicator for assessing the interval from developing a product until the final product launch (DZIALLAS; BLIND, 2019) and may be critical to a company's current competitive position. Focus on the shortest time to market is essential because delays may cause loss sales to faster competitors (SHENHAR; DVIR, 2007).

Successful commercialization of innovations may be concretized into sales and increased sales, typical for-profit business measures (ASTEBRO; MICHAELA, 2005; OECD/EUROSTAT, 2005; SCHMOCH; RAMMER; LEGLER, 2006; TERZIOVSKI; MORGAN, 2006; SHENHAR; DVIR, 2007; ARVANITIS; SYDOW; WOERTER, 2008; CHIESA et al., 2009; CAIRD; HALLETT; POTTER, 2013; MCLAUGHLIN; RICHINS, 2015; DZIALLAS; BLIND, 2019; LEIGNEL; MÉNAGER; YABLONSKI, 2019). Other indicators, such as exports and increased exports may also be applied (OECD/EUROSTAT, 2005; SCHMOCH; RAMMER; LEGLER, 2006; CAIRD; HALLETT; POTTER, 2013; CAVDAR; AYDIN, 2015; DE FUENTES et al., 2015; KAMASAK, 2015; PEKOVIC; LOJPUR; PEJIC-BACH, 2015; DZIALLAS; BLIND, 2019; LEIGNEL; MÉNAGER; YABLONSKI, 2019).

Regulatory indicators, such as ANVISA and FDA registers, may also be implemented in health businesses before commercialization. The set of regulations, bureaucracy, and lengthy procedures are the main obstacles for medical innovation sales and exports (OECD/EUROSTAT, 2005; SCHMOCH; RAMMER; LEGLER, 2006; TERZIOVSKI; MORGAN, 2006; YOCK et al., 2015).

The number of publications and IPs may even indicate evidence of performance outcomes in the health area. Papers are relevant medical innovation indicators (OECD/EUROSTAT, 2005; HINE; KAPELERIS, 2006; SCHMOCH; RAMMER; LEGLER, 2006; TERZIOVSKI; MORGAN, 2006; YOCK et al., 2015; THOMPSON;

ZIEDONIS; MOWERY, 2018). Supporting agencies, such as FAPESP in Brazil, have contributed to promoting researches and scientific productions (ZAGO, 2012).

To remain competitive, companies should protect and enforce their IP, which creates barriers to entry for potential competitors in the market (KALCHEVA; MCLEMORE; PANT, 2018). IP is a critical component of medical innovation since it is an area that is not only highly dynamic but, at the same time, requires significant investments for developing new technologies and products. IP rights are intended as instruments to provide incentives for financing and innovation (OECD/EUROSTAT, 2005; TERZIOVSKI; MORGAN, 2006; HORNER, 2014; WOO; JANG; KIM, 2015; YOCK et al., 2015; GRAF; ZECH, 2017; KIM; BAE, 2017; LEIGNEL; DZIALLAS; BLIND, 2019; LEIGNEL; MÉNAGER; YABLONSKI, 2019).

Another indicator may be the introduction of new products, i.e., the number of products launched, which may be further a source of market advantage. The development of new products increases innovation performance outcomes (OECD/EUROSTAT, 2005; TERZIOVSKI; MORGAN, 2006; SHENHAR; DVIR, 2007; LUZ; FRANCISCO; PIEKARSKI, 2015; TAJVIDI; KARAMI, 2015; DZIALLAS; BLIND, 2019).

In sum, innovation performance measurement is acknowledged to determine how to understand company settings by measuring outcomes, which should be part of business activities as a continuing practice to conduct improvement efforts and encourage awareness of specific company factors (ELG; BRORYD; KOLLBERG, 2013).

2.5 Hypothesized model

Based on the theoretical background, Table 3 depicts a synthesis of constructs and the main factors considered in the development of a medical solution.

Table 3 - Constructs and main factors considered in the development of a medical solution

Constructs	Factors	References
Entrepreneurial company characteristics	Company profile	Sharma, 2018; Beaulieu; Lehoux, 2018; Evens; Kaitin, 2015
	Company size	SEBRAE, 2016
	Company existed before the first PIPE	Normas PIPE, 2020
	Quantity of PIPE projects the company had support in each phase	Normas PIPE, 2020
	First PIPE date	Normas PIPE, 2020
	Collaborative company resources Total of collaborative company resources	Agrawal; Henderson, 2002; Barnes; Pashby; Gibbons, 2002; Chesbrough, 2003; Friedman; Silberman, 2003; Siegel; Waldman; Link, 2003; Nedeva, 2013; Mehta, 2004; Slaughter, 2004; Hartshorn; Hannon, 2005; Hine; Kapeleris, 2006; Schulte, 2006; Lucas et al., 2009; Chesbrough, 2012; French, Miller, 2012; Perkmann et al., 2013; Fan, Garnsey, 2014; Hotz-Hart; Rohner, 2014; Malshe; Biemans, 2014; Weiblen; Chesbrough, 2015; Wu, Welch, Huang, 2015; Davey, Hannon, Penaluna, 2016; Gulbrandsen et al., 2016; Lehoux; Miller; Daudelin, 2016; Llopis, D'este; 2016; Miller, French, 2016; Suh; Sohn, 2016; Thune, Mina, 2016; Banerjee; Siebert, 2017; Toscano; Mainardes; Lasso, 2017; Vargas; Callaway; Ariss, 2017; Zancul et al., 2017; Gläser, Velarde, 2018; Landstrom; Harirchi, 2018; Lopes et al., 2018; Tykvová, 2018; Mazzarol; Reboud, 2019; Szycher, 2019; Small Business Research, 2020
	Collaborative company locations Total of collaborative company locations	Prodan, 2007; Marcolongo, 2017; Heller et al., 2019; Mazzarol; Reboud, 2019; Szycher, 2019
	Company growth	Hine; Kapeleris, 2006; Davey et al., 2011; Cao et al., 2013
Team characteristics	Total of physicians	Chatterji et al., 2008; Chatterji, 2009; Mitchell et al., 2010; Purdy et al., 2012; Yazdi; Acharya, 2013; Neck; Greene; Brush, 2014; Shluzas, Leifer, 2014; Wieman, 2014; Denis, 2015; Yock et al., 2015; Yoda, 2015; Ali; Gittelman, 2016; Soenksen; Yazdib, 2017; Weiss; Tilin; Morgan, 2018
	Physicians partners and founders Physicians members <i>Idem for health professionals (non-physicians), engineers, technology professionals (non-engineers), and other areas professionals, including hard sciences professionals</i>	

continue

continuation

Constructs	Factors	References
Team characteristics	Postdoc partners and founders physicians	Chatterji et al., 2008; Chatterji, 2009; Mitchell et al., 2010; Purdy et al., 2012; Yazdi; Acharya, 2013; Neck; Greene; Brush, 2014; Shluzas, Leifer, 2014; Wieman, 2014; Denis, 2015; Yock et al., 2015; Yoda, 2015; Ali; Gittelman, 2016; Soenksen; Yazdib, 2017; Wall et al., 2017; Weiss; Tilin; Morgan, 2018
	Ph.D. partners and founders physicians	
	Master partners and founders physicians	
	Bachelor partners and founders physicians	
	Undergraduate or Technician partners and founders physicians	
	Postdoc members physicians	
	Ph.D. members physicians	
	Master members physicians	
	Bachelor members physicians	
	Undergraduate or Technician members physicians	
	<i>Idem for health professionals (non-physicians), engineers, technology professionals (non-engineers), and other areas professionals, including hard sciences professionals.</i>	
	ANVISA participation	Hine; Kapeleris, 2006;
Process characteristics	FDA participation	Terziovski; Morgan, 2006;
	IP participation	Krabel; Mueller, 2009; Yazdi, Acharya, 2013; Hoyos-Iruarizaga; Mendialdua; Santos, 2015; Tajvidi; Karami, 2015; Rédis; Sahut, 2015; Yock et al., 2015; Harris, 2016; Styhre; Remneland-Wikhamn, 2016; Protogerou; Caloghirou; Vonortas, 2017; Soenksen; Yazdib, 2017; Szycher, 2019
	Business experience	
	Health organization experience	
	Motivation	Li; Halal, 2002; Lam, 2011;
	Structure	Shimasaki, 2014
	ANVISA medical device classification	ANVISA, 2015; ANVISA, 2019; ANVISA, 2020a
	FDA medical device classification	Yock et al., 2015; FDA 2017; FDA, 2020b; FDA, 2020c
	Regulation phase	Yock et al., 2015
	Embedded software medical solution	Lee, 2002; Yock et al., 2015
	Software/hardware medical solution	FDA, 2018b; Tahir et al., 2020
	Service/product medical solution	Mont, 2002; Gebauer; Friedli, 2005; Oliva; Gebauer; Brann, 2012; Cusumano, Kahl, Suarez, 2015; Ostrom et al., 2015; Steiner et al., 2016; Benedettini; Swink; Neely, 2017

continue

continuation

Constructs	Factors	References
Process characteristics	Approaches Total of approaches	Cooper, 2008; El-Haik; Mekki, 2008; Pietzsch et al.; 2009; Pries; Quigley, 2011; Van Gemert-Pijnen et al., 2011; Blank, Dorf, 2012; Santos et al., 2012; Yock et al., 2015; Scrum Study, 2017; Altman; Huang; Breland, 2018; D.School, 2018; Deitte; Omary, 2019; Mclaughlin et al., 2019; Blank, 2020; PIPE Empreendedor, 2020
	Stakeholders Total of stakeholders	Van Gemert-Pijnen et al. 2011; Yock et al., 2015; Wield et al., 2017; Vagal et al. 2020
	Project phases	El-Haik; Mekki, 2008; Pietzsch et al.; 2009; Van Gemert-Pijnen et al., 2011; Santos et al., 2012; Yock et al., 2015; Scrum Study, 2017; D.School, 2018; Blank, 2020
	Clinical challenge	Yock et al., 2015
	Technical challenge	
	PIPE experiences	Normas PIPE, 2020
	PIPE improvements	
	Competitive advantage	Cefis; Marsili, 2006; Davey et al., 2011; Liu; Hodgkinson; Chuang, 2014; Dewangan; Godse, 2014
	Supplies	Dimitratos, 2011; Styhre; Remneland-Wikhamn, 2016
	Competitors	Hine; Kapeleris, 2006; Mittra; Williams, 2007
Innovation performance outcomes	Distribution channels	Osterwalder; Pigneur, 2010; Blank, 2020
	First sale date Time to market (<i>first sale date - PIPE date</i>) Increased sales	Astebro; Michaela, 2005; OECD/EUROSTAT, 2005; Schmoch; Rammer; Legler, 2006; Terziovski; Morgan, 2006; Shenhar; Dvir, 2007; Arvanitis; Sydow; Woerter, 2008; Chiesa et al., 2009; Caird; Hallett; Potter, 2013; Mclaughlin; Richins, 2015; Dziallas; Blind, 2019; Leignel; Ménager; Yablonski, 2019
	First export date Increased exports	OECD/EUROSTAT, 2005; Schmoch; Rammer; Legler, 2006; Caird; Hallett; Potter, 2013; Cavdar; Aydin, 2015; De Fuentes et al., 2015; Kamasak, 2015; Pekovic; Lojpur; Pejic-Bach, 2015; Dziallas; Blind, 2019; Leignel; Ménager; Yablonski, 2019

continue

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Constructs	Factors	References
Innovation performance outcomes	Total of ANVISA registers First ANVISA date Total of FDA registers First FDA date	OECD/EUROSTAT, 2005; Schmoch; Rammer; Legler, 2006; Terziovski; Morgan, 2006; Yock et al., 2015
	Total of intellectual properties	OECD/EUROSTAT, 2005; Terziovski; Morgan, 2006; Horner, 2014; Woo; Jang; Kim, 2015; Yock et al., 2015; Graf; Zech, 2017; Kim; Bae, 2017; Kalcheva; Mclemore; Pant, 2018; Leignel; Dziallas; Blind, 2019; Leignel; Ménager; Yablonski, 2019
	Total of publications	OECD/EUROSTAT, 2005; Hine; Kapeleris, 2006; Schmoch; Rammer; Legler, 2006; Terziovski; Morgan, 2006; Zago, 2012; Yock et al., 2015; Thompson; Ziedonis; Mowery, 2018
	Total of products launched	OECD/EUROSTAT, 2005; Terziovski; Morgan, 2006; Shenhar; Dvir, 2007; Luz; Francisco; Piekarski, 2015; Tajvidi; Karami, 2015; Dziallas; Blind, 2019

Source: Prepared by the author.

Given the findings in the existing literature together with Table 3, as prior mentioned, there is a lack of statistical and empirical shreds of evidence, along with limited research on performance outcomes in the context of medical domains (SHLUZAS; LEIFER, 2014). Additional studies are mandatory to communize investment, intending to support health innovation (SOENKSEN, YAZDIB; 2017). To address such gaps and to gain further insights regarding medical innovation, this research concentrates on identifying the factors under the medical solution project development that positively influence innovation performance outcomes. Consequently, the hypothesized model is presented in Figure 2.

Figure 2 - Hypothesized model

Source: Prepared by the author.

As established in the hypothesized model (see Figure 2), the development of a medical solution is complex (CONSOLI et al., 2016). It involves particular factors of entrepreneurial companies (YOCK et al., 2015; HELLER et al., 2019; SZYCHER, 2019), teams, including partners, founders, and members (MORLACCHI; NELSON, 2011; YOCK et al., 2015; GULBRANDSEN et al., 2016; MILLER; FRENCH, 2016), in conjunction with process characteristics (YOCK et al., 2015) to ensure successful innovation performance outcomes (ELG; BRORYD; KOLLBERG, 2013). The hypotheses resulting from the model are described hereafter.

- Hypothesis 1 (H1): Entrepreneurial company characteristics positively influence innovation performance outcomes.
- Hypothesis 2 (H2): Team characteristics positively influence innovation performance outcomes.
- Hypothesis 3 (H3): Process characteristics positively influence innovation performance outcomes.

Additionally, due to the individual factors among medical devices, pharma/biotech, and digital health domains (HINE; KAPELERIS, 2006; SHIMASAKI, 2014; EVENS; KAITIN, 2015; ORIANA et al., 2016; BEAULIEU; LEHOUX, 2018; SHARMA, 2018; JANDOO, 2020), the following claims on the entrepreneurial company profile are considered: clinical and technical challenges (YOCK et al., 2015), more service or product solution

(CUSUMANO; KAHL; SUAREZ, 2015), more software or hardware solution (TAHIR et al., 2020), and the application of approaches (YOCK et al., 2015), as follows.

- Claim 1: there is a relationship between the clinical challenge and the company profile.
- Claim 2: there is a relationship between the technical challenge and the company profile.
- Claim 3: there is a relationship between a more service or product solution and the company profile.
- Claim 4: there is a relationship between a more software or hardware solution and the company profile.
- Claim 5: there is a relationship between the application of approaches and the company profile.

3 RESEARCH METHOD

As presented in chapter 2, the study initiated with a literature review, reaching the constructs and the hypothesized model. Once such a phase was completed, there was a need for field research, including the instrument research development and data collection, further detailed.

3.1 Instrument research development

As discussed in the Introduction, there is a need for statistical shreds of evidence on innovation performance outcomes to boost innovation of entrepreneurial health companies (SHLUZAS; LEIFER, 2014; SOENKSEN, YAZDIB; 2017). Additionally, human health has been an important aspect to be considered in innovation researches (THUNE; MINA, 2016), including digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), and pharmaceutical and biotechnology settings (EVENS; KAITIN, 2015).

Brazil is facing increased demand for medical technologies (YOCK et al., 2015), and typically an entrepreneurial company initiates from a project in conjunction with a subscription to a research grant program, such as PIPE, to subsidize the company operations (MEHTA, 2004; NORMAS PIPE, 2020). Projects contribute to company success and effectiveness (SHENHAR; DVIR, 2007), and the PIPE program represents a substantial funding source for entrepreneurial companies to develop new technologies and subsequently reach commercialization. Although the PIPE program operates exclusively in São Paulo state, it is characterized as the leading funding source of innovation support in Brazil (FALEIROS, 2018; BALANÇO FAPESP, 2020).

In the context of this research, whose purpose is to identify the factors under the medical solution project development that positively influence innovation performance outcomes, ongoing or completed entrepreneurial human health company projects that obtained support from PIPE should be explored.

Consequently, a survey research method was employed to provide statistics on the characteristics of the target population by describing a sample. The answers to survey questions are operated to express the experiences accurately, opinions, and other aspects of respondents (FOWLER, Jr., 2014).

After determining the constructs and the main aspects based on the theoretical background, including the hypothesized model, a survey questionnaire was developed to investigate the interest constructs. The survey questionnaire was reviewed by innovation specialists, including Professors of the Production Engineering Department at the Polytechnic School of the University of São Paulo; a health specialist Professor at the Faculty of Medicine at the University of São Paulo; a statistician specialist Professor of the Production Engineering Department at the Polytechnic School of the University of São Paulo; entrepreneurial health company specialists of the Polytechnic School of the University of São Paulo, comprising a Production engineer, Mechatronics engineer, Mechanical engineer, and an Electrical engineer. After nine versions of incorporating the suggested adjustments, the survey was piloted among the entrepreneurial health company specialists to estimate the time and review the flow of interaction and content coherence.

The questionnaire encompassed four sections: (1) company characteristics, (2) team characteristics, (3) development process of the first (oldest) PIPE project by the company, (4) the oldest PIPE project results. It was highlighted in the questionnaire that the most past PIPE project referred to the first PIPE project that the company carried out and the possible sequence of additional phases of the same project. The most past PIPE project might possibly be recent and under development. The survey questionnaire was developed through the Survey Monkey cloud-based tool (SURVEY MONKEY, 2019).

Besides, additional open-ended questions were compiled based on the existing theoretical background presented in chapter 2 in conjunction with the relevant questions developed by Harroch and Kane (2019) about what venture capitalists ask before investing in an entrepreneurial company. Appendix 1 lists the survey questions and the corresponding constructs.

3.2 Data collection

To the data collection, the target population included researchers of entrepreneurial human health companies with PIPE projects. From this standpoint, research of ongoing and completed projects in the publicly available PIPE Research Grants database (BIBLIOTECA VIRTUAL DA FAPESP, 2019) was applied in April 2019, following the criteria Health Sciences knowledge area, such as Physiotherapy and Occupational Therapy, Speech Therapy, Medicine, Dentistry, and Collective Health, together with Engineers knowledge area, particularly Biomedical Engineering, resulting in 159 companies. However, the PIPE Research Grants database did not provide the contact information of respondents, such as telephones and e-mails. In this regard, numerous researches on the web were necessary to find out the missing data.

The survey interviews were conducted from May 2019 to October 2019, via telephone or face-to-face, to ensure the accuracy of responses (TOURANGEAU, 2018). The duration of interviews varied from 40 to 50 minutes, with notes made directly on the Survey Monkey database questionnaire, with no recorded audio files.

As a result, 79 companies participated, including eight digital health, 35 medical device, and 36 pharma/biotech profiles, comprising 25 face-to-face interviews and 54 telephone interviews, involving companies located in a wide range of cities in the state of São Paulo. The participation rate was around 50%, which corresponds to a representative sample of entrepreneurial health companies (BARTLETT; KOTRLIK; HIGGINS, 2001). The size of the companies encompassed 52 micros, 23 small, one medium-sized, and three large enterprises, according to SEBRAE (2016) classification¹. The respondents comprised the founders, CEOs, or other related management positions. Table 4 demonstrates the characteristics of respondents.

¹ The size of an entrepreneurial company may be classified as (SEBRAE, 2016): microenterprise (until nine employees), small enterprise (10 to 49 employees), medium-sized enterprise (50 to 99 employees), and large-sized enterprise (100 or more employees).

Table 4 - Characteristics of respondents

Company	Company profile	Position	Type of interview
C1	Medical device	CEO	Face-to-face
C2	Pharma/biotech	Research Coordinator	Face-to-face
C3	Medical device	Scientific Director	Telephone
C4	Medical device	Business Manager	Telephone
C5	Medical device	Chief Financial Officer (CFO)	Face-to-face
C6	Medical device	Director	Face-to-face
C7	Medical device	Founder	Telephone
C8	Medical device	Director	Telephone
C9	Pharma/biotech	CEO	Face-to-face
C10	Pharma/biotech	R&D Analyst	Face-to-face
C11	Pharma/biotech	CEO	Face-to-face
C12	Pharma/biotech	Director	Face-to-face
C13	Medical device	Associate Professor	Face-to-face
C14	Medical device	Associate Professor	Face-to-face
C15	Medical device	Founding Partner	Face-to-face
C16	Pharma/biotech	Business Director	Face-to-face
C17	Medical device	Owner	Face-to-face
C18	Medical device	Scientific Chief	Face-to-face
C19	Medical device	Chief Technology Officer (CTO)	Telephone
C20	Digital health	Associate Professor	Telephone
C21	Pharma/biotech	New Pharmaceuticals Rational Planning Coordinator	Face-to-face
C22	Pharma/biotech	Research Director	Telephone
C23	Medical device	CTO	Face-to-face
C24	Medical device	Partner and Coordinator	Face-to-face
C25	Medical device	Founding Partner	Face-to-face
C26	Pharma/biotech	Founder	Telephone
C27	Medical device	CEO	Face-to-face

continue

continuation

Company	Company profile	Position	Type of interview
C28	Digital health	Responsible Researcher	Telephone
C29	Medical device	Founding Partner	Face-to-face
C30	Medical device	Managing Partner	Telephone
C31	Medical device	Principal Researcher and Founder	Telephone
C32	Medical device	CEO	Telephone
C33	Medical device	CEO	Telephone
C34	Digital health	Founder	Telephone
C35	Pharma/biotech	Founder	Telephone
C36	Pharma/biotech	Managing Director	Telephone
C37	Pharma/biotech	Founding partner	Telephone
C38	Pharma/biotech	R&D Manager	Telephone
C39	Medical device	Researcher	Telephone
C40	Pharma/biotech	R&D Manager	Telephone
C41	Digital health	Director	Telephone
C42	Medical device	Chief Strategy and Innovation Officer (CSIO)	Telephone
C43	Pharma/biotech	Commercial Director	Telephone
C44	Digital health	CEO	Face-to-face
C45	Pharma/biotech	CEO	Telephone
C46	Digital health	CEO	Telephone
C47	Medical device	Co-founder	Face-to-face
C48	Pharma/biotech	Researcher	Telephone
C49	Pharma/biotech	Principal Researcher and Founder	Face-to-face
C50	Pharma/biotech	Founding partner	Face-to-face
C51	Pharma/biotech	Founder	Telephone
C52	Pharma/biotech	Founder	Telephone
C53	Pharma/biotech	Scientific Director	Telephone
C54	Pharma/biotech	Financial Management Coordinator	Face-to-face
C55	Pharma/biotech	CEO	Telephone

continue

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Company	Company profile	Position	Type of interview
C56	Pharma/biotech	Project Director	Telephone
C57	Pharma/biotech	Founder and researcher	Telephone
C58	Pharma/biotech	Responsible for the project	Telephone
C59	Digital health	CEO	Telephone
C60	Medical device	Research Coordinator	Telephone
C61	Pharma/biotech	Partner	Telephone
C62	Medical device	CEO	Telephone
C63	Medical device	Responsible for the scientific part in the chemical area	Telephone
C64	Medical device	Founder	Telephone
C65	Medical device	Founder	Telephone
C66	Pharma/biotech	Founding Partner	Telephone
C67	Medical device	Managing Director	Telephone
C68	Pharma/biotech	Partner	Telephone
C69	Pharma/biotech	Founder	Telephone
C70	Digital health	Responsible Researcher and Founder	Telephone
C71	Medical device	CEO	Telephone
C72	Medical device	CEO	Telephone
C73	Pharma/biotech	Founder and scientific technician	Telephone
C74	Pharma/biotech	Research, Development, and Innovation (RD&I) Manager and Technical Responsible	Telephone
C75	Pharma/biotech	Partner	Telephone
C76	Pharma/biotech	Partner and CEO	Telephone
C77	Medical device	Founding Partner	Telephone
C78	Pharma/biotech	Founding Partner	Telephone
C79	Medical device	Responsible Researcher	Telephone

Source: Prepared by the author.

As demonstrated in Table 4, the company names and data were maintained anonymously in the analysis and conclusions of the study, and groups of companies aggregated the analyzes. In this context, data confidentiality was guaranteed, which ensured a trusting relationship with the respondents (HEGGEN; GUILLEMIN, 2012). The following chapter presents the results and discussion.

4 RESULTS AND DISCUSSION

This chapter presents the results and discussion comprising the descriptive analysis of entrepreneurial companies, teams, and processes, including innovation performance outcomes. Additionally, as a complement, a content analysis of the survey open-ended questions is considered. Subsequently, the statistical data analysis involves the regression models, correlations, and chi-square methods.

4.1 Descriptive analysis

This section provides the first insights into the medical innovation setting, which is part of digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), and pharma/biotech (EVENS; KAITIN, 2015) profiles. Such a scenario was considered in the following sections concerning entrepreneurial companies, teams, and process characteristics. The descriptive statistics were undertaken in Minitab software (MINITAB, 2020). As a complement, a content analysis of open-ended questions is also presented.

4.1.1 Entrepreneurial companies' characteristics

Regarding entrepreneurial companies' characteristics, Figure 3 and Table 5 present the companies' cities interviewed by digital health, medical device, and pharma/biotech profiles.

Figure 3 - Companies' cities interviewed by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 5 - Companies' cities interviewed by the company profile

Company Profile	City	Quantity
Digital health (n=8)	Araraquara	2 (25%)
	Ribeirão Preto	2 (25%)
	Santo André	1 (13%)
	São Paulo	3 (38%)
Medical device (n=35)	Araraquara	1 (3%)
	Campinas	1 (3%)
	Ribeirão Preto	3 (9%)
	São Bernardo do Campo	1 (3%)
	São Carlos	2 (6%)
	São José do Rio Preto	3 (9%)
	São José dos Campos	1 (3%)
	São Paulo	23 (66%)
Pharma/biotech (n=36)	Araraquara	1 (3%)
	Campinas	1 (3%)
	Ribeirão Preto	10 (28%)
	Santos	1 (3%)
	São Caetano do Sul	1 (3%)
	São Carlos	4 (11%)
	São José do Rio Preto	1 (3%)
	São Paulo	17 (47%)

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 3 and Table 5, most of the digital health, medical device, and pharma/biotech companies interviewed were located in the city of São Paulo, and Ribeirão Preto city had a considerable concentration of pharma/biotech companies interviewed. Figure 4 and Table 6 present the companies' sizes interviewed by the company profile.

Figure 4 - Companies' sizes interviewed by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 6 - Companies' sizes interviewed by the company profile

Company profile	Company size	Quantity
Digital health (n=8)	Microenterprises	5 (63%)
	Small enterprises	3 (38%)
Medical device (n=35)	Microenterprises	20 (57%)
	Small enterprises	13 (37%)
	Large enterprises	2 (6%)
Pharma/biotech (n=36)	Microenterprises	27 (75%)
	Small enterprises	7 (19%)
	Medium-sized enterprises	1 (3%)
	Large enterprises	1 (3%)

Source: Prepared by the author under the validation of the statistical specialist.

According to SEBRAE (2016), the size of an entrepreneurial company may be classified as micro (until nine members), small (10 to 49 members), medium-sized (50 to 99 members), and large-sized enterprises (100 or more members). As indicated in Figure 4 and Table 6, most companies interviewed were microenterprises, followed by small enterprises. There were no medium enterprises for digital health and medical device profiles. Concerning large enterprises, there were two for medical device and one for pharma/biotech profiles due to a special call for proposals. Table 7 demonstrates if the companies interviewed already existed before the first PIPE project or not, by the company profile.

Table 7 - Existed or not existed companies before the first PIPE project

Company profile	Companies existed before PIPE	Companies did not exist before PIPE	Total companies
Digital health	7 (88%)	1 (13%)	8
Medical device	17 (49%)	18 (51%)	35
Pharma/biotech	21 (58%)	15 (42%)	36

Source: Prepared by the author under the validation of the statistical specialist.

As shown in Table 7, most companies already existed before the first PIPE project. Regarding the total quantity of PIPE projects, the companies had support, including Phase 1, Phase 2, Phase 3, Straight to Phase 2, and Straight to Phase 3. Figure 5 and Table 8 present the results of the company profile.

Figure 5 - Total of PIPE projects by phase and company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 8 - Total of PIPE projects by phase and company profile

Company profile	Phase 1	Phase 2	Phase 3	Straight to Phase 2	Straight to Phase 3	Total PIPE Projects
Digital health	10 (63%)	4 (25%)	1 (6%)	1 (6%)	0 (0%)	16
Medical device	36 (45%)	27 (34%)	9 (11%)	6 (8%)	2 (3%)	80
Pharma/biotech	58 (69%)	23 (27%)	1 (1%)	1 (1%)	1 (1%)	84

Source: Prepared by the author under the validation of the statistical specialist.

As demonstrated in Figure 5 and Table 8, most of the companies had Phase 1 projects. Phase 2 also had a considerable amount. Few companies went straight to Phase 2 and Phase 3. It is worth mentioning that medical device companies had more Phase 3, Straight to Phase 2, and Phase 3 than the other profiles. Figure 6 presents a histogram concerning the interval from the first PIPE Phase 1 to the first PIPE Phase 2 by the company profile.

Figure 6 - Interval from the first PIPE Phase 1 to the first PIPE Phase 2 by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 6, for the companies that had the first PIPE Phase 1 and the first PIPE Phase 2, two digital health companies took to go to Phase 2 between 15 and 25 months, one between 25 and 35 months, and one between 75 and 85 months. Regarding the medical device companies, four took between 5 and 15 months, four between 15 and 25 months, and four between 25 and 35 months. Lastly, three pharma/biotech companies took between 5 and 15 months, six between 15 and 25 months, four between 25 and 35 months, and two between 45 and 55 months. Figure 7 presents a histogram concerning the interval from the first PIPE Phase 2 to the first PIPE Phase 3 by the company profile.

Figure 7 - Interval from the first PIPE Phase 2 to the first PIPE Phase 3 by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 7, for the companies that had the first PIPE Phase 2 and the first PIPE Phase 3, one digital health company took to go to Phase 3 between 25 and 35 months. Regarding the medical device companies, two took between 25 and 35 months, three between 35 and 45 months, and one between 55 and 65 months. Lastly, one pharma/biotech company took between 65 and 75 months.

The findings in Figures 6-7 indicate that the interval among PIPE phases in entrepreneurial health companies may be longer. Such results contemplate medical innovation, which is a long and complicated process with multiple development cycles and the involvement with diverse fields of study and regulatory hurdles (TERZIOVSKI; MORGAN, 2006; FRIES, 2013; CONSOLI et al., 2016).

Collaborative resources further PIPE contributes to medical innovation and the quality and efficiency of health (SPEKOWIUS; WENDLER, 2006). Figure 8 and Tables 9-10 present the percentage of companies' collaboratives resources additional to PIPE by the company profile.

Figure 8 - Companies' collaborative resources further PIPE by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 9 - Companies' collaborative resources further PIPE by the company profile (Part 1)

Company profile	Personal funds	Angel investors	Other funding agencies	Universities	Hospitals
Digital health	8 (29%)	3 (11%)	4 (14%)	2 (7%)	3 (11%)
Medical device	28 (29%)	7 (7%)	11 (11%)	15 (15%)	9 (9%)
Pharma/biotech	31 (30%)	5 (5%)	10 (10%)	14 (13%)	8 (8%)

Source: Prepared by the author under the validation of the statistical specialist.

Table 10 - Companies' collaborative resources further PIPE by the company profile (Part 2)

Company profile	External organizations	Accelerator / Incubator	Venture capital	Other	Total
Digital health	3 (11%)	3 (11%)	1 (4%)	1 (4%)	28
Medical device	7 (7%)	9 (9%)	6 (6%)	5 (5%)	97
Pharma/biotech	11 (11%)	16 (15%)	3 (3%)	6 (6%)	104

Source: Prepared by the author under the validation of the statistical specialist.

In agreement with Mazzarol; Reboud (2019), and Szycher (2019), Figure 8 and Tables 9-10 presents the percentage of responses by the company profile. Such responses indicate that the leading collaborative resource further PIPE was personal funds. Other

funding agencies further PIPE were also relevant and assist in innovative research (NEDEVA, 2013; LLOPIS; D'ESTE, 2016; LEHOUX; MILLER; DAUDELIN, 2016). It is worth mentioning that universities were cited for contributing to medical innovation (MEHTA, 2004; ZANCUL et al., 2017; LOPES et al., 2018), together with external organizations (AGRAWAL; HENDERSON, 2002; FRIEDMAN; SILBERMAN, 2003; SIEGEL; WALDMAN; LINK, 2003; WU; WELCH; HUANG, 2015). Accelerator and incubator resources were mentioned since providing training, facilities, advice, and networking opportunities (MARCOLONGO, 2017; MAZZAROL; REBOUD, 2019; HELLER, 2019). Hospitals were also considered collaborative resources of research and clinical practice (GULBRANDSEN et al., 2016; MILLER; FRENCH, 2016; THUNE; MINA, 2016). The other collaborative resources responses comprised the company revenues.

As stated by Lehoux and Miller, and Daudelin (2016), venture capital invests in rapidly and likely to expand entrepreneurial companies. Notwithstanding, the findings presented that venture capital was limited among companies. Figure 9 and Table 11 illustrate the companies' locations by the company profile.

Figure 9 - Companies' locations by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 11 - Companies' locations by the company profile

Company profile	Technological parks	Incubators	Accelerators	Other	Total
Digital health	3 (23%)	5 (38%)	2 (15%)	3 (23%)	13
Medical device	7 (16%)	17 (39%)	5 (11%)	15 (34%)	44
Pharma/biotech	13 (25%)	26 (49%)	3 (6%)	11 (21%)	53

Source: Prepared by the author under the validation of the statistical specialist.

In consonance with Marcolongo (2017), Heller et al. (2019), and Mazzarol and Reboud, 2019, most entrepreneurial companies reside in incubators, as depicted in Figure 9 and Table 11. Technological parks were also mentioned in research and business interests (PRODAN, 2007; SZYCHER, 2019). Despite accelerators and incubators are the main trajectories from the laboratory to an independent company, few accelerators were mentioned. Additionally, the other companies' locations comprised supporting institutions, such as the Nuclear and Energy Research Institute (IPEN), hospitals, universities, institutions abroad, and the founder's and partners' own properties.

4.1.2 Teams' characteristics

Concerning the team's characteristics, some initial highlights are presented. There were 18 teams with non-physicians and non-health professionals. Besides, there were 61 teams with physicians or health professionals, including 52 of them with Postdoc or Ph.D. degrees. Six companies encompassed only physicians or health professionals, and six companies comprehended only hard sciences professionals. Lastly, three companies comprised only physicians and engineers. The subsequent descriptions present the findings related to the academic background in medical, health (non-medical), engineering, technology (non-engineering), hard sciences, and other branches. Figure 10 presents the medical specialties of partners, founders, and members. It is noteworthy to mention that in this study, partners and founders are considered current operational controllers, and members are considered team components (non-partners and non-founders).

Figure 10 - Medical specialties of partners, founders, and members

Source: Prepared by the author under the validation of the statistical specialist.

Figure 11 presents health (non-medical) branches of partners, founders, and members.

Figure 11 - Health (non-medical) branches of partners, founders, and members

Source: Prepared by the author under the validation of the statistical specialist.

Table 12 presents the quantity and percentage of medical specialties and health (non-medical) branches of partners, founders, and members.

Table 12 - Medical specialties and health (non-medical) branches of partners, founders, and members

Medical specialties	Quantity	Health (non-medical) branches	Quantity
Gynecology	20 (28%)	Biology	86 (32,1%)
Medical Clinic	11 (15%)	Biomedicine	47 (17,5%)
Pulmonology	7 (10%)	Pharmacy	46 (17,2%)
Cardiology	5 (7%)	Dentistry	39 (14,6%)
Radiology	4 (6%)	Nursing	10 (3,7%)
Neurology	3 (4%)	Physiotherapy	10 (3,7%)
Oncology	3 (4%)	Veterinary	8 (3,0%)
Allergy and Immunology	2 (3%)	Nutrition	6 (2,2%)
Hematology	2 (3%)	Nursing Technician	4 (1,5%)
Pathology	2 (3%)	Psychology	4 (1,5%)
Urology	2 (3%)	Biotechnology	2 (0,7%)
Vascular Surgery	2 (3%)	Molecular Sciences	2 (0,7%)
Anesthesiology	1 (1%)	Fundamental Sciences for Health	1 (0,4%)
Angiology	1 (1%)	Genetics	1 (0,4%)

continue

conclusion

Medical specialties	Quantity	Health (non-medical) branches	Quantity
Cardiovascular Surgery	1 (1%)	Medical Technique	1 (0,4%)
Endocrinology	1 (1%)	Physical Education	1 (0,4%)
Gastroenterology	1 (1%)		
Infectology	1 (1%)		
Intensive Medicine	1 (1%)		
Ophthalmology	1 (1%)		
Traumatology	1 (1%)		
Total Medical	72	Total Health	268

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 10 and Table 12, the leading medical specialties were Gynecology, Medical Clinic, and Pulmonology. It is noteworthy to mention that Gynecology was on the top list due to a reputable in vitro fertilization clinic. According to Figure 11 and Table 12, the leading health (non-medical) branches were Biology, Biomedicine, Pharmacy, and Dentistry. As aforementioned, in this study, Biology is considered a health domain (WASSWA; MUGARURA; NDIWA, 2017). Figure 12 presents the engineering branches of partners, founders, and members.

Figure 12 - Engineering branches of partners, founders, and members

Source: Prepared by the author under the validation of the statistical specialist.

Figure 13 presents the technology (non-engineering) branches of partners, founders, and members.

Figure 13 - Technology (non-engineering) branches of partners, founders, and members

Source: Prepared by the author under the validation of the statistical specialist.

Table 13 presents the quantity and percentage of engineering and technology (non-engineering) branches of partners, founders, and members.

Table 13 - Engineering and technology (non-engineering) branches of partners, founders, and members

Engineering branches	Quantity	Technology (non-engineering) branches	Quantity
Electrical	53 (31%)	Computer Science	23 (33%)
Mechanical	23 (13%)	Biomedical Informatics	13 (19%)
Computer	19 (11%)	Systems Analysis	7 (10%)
Production	17 (10%)	Information Technology	5 (7%)
Civil	13 (8%)	Electronics Technician	4 (6%)
Materials	11 (6%)	Game Design	4 (6%)
Mechatronics	11 (6%)	Mechanical Technician	4 (6%)

continue

conclusion

Engineering branches	Quantity	Technology (non-engineering) branches	Quantity
Chemical	7 (4%)	Information Systems	3 (4%)
Agronomic	4 (2%)	Biomedical Technology	2 (3%)
Control and Automation	4 (2%)	Industrial Automation	2 (3%)
Biochemical	3 (2%)	Science and Technology	2 (3%)
Environmental	2 (1%)	Digital Game Technology	1 (1%)
Aeronautical	1 (1%)		
Forest	1 (1%)		
Telecommunications	1 (1%)		
Teleinformatics	1 (1%)		
Total Engineering	171	Total Technology	70

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 12 and Table 13, the leading engineer branches were Electrical, Mechanical, Computer, and Production. According to Figure 13 and Table 13, the leading technology branches (non-engineering) were Computer Science, Biomedical Informatics, and Systems Analysis. Figure 14 presents the hard sciences branches of partners, founders, and members.

Figure 14 - Hard sciences branches of partners, founders, and members

Source: Prepared by the author under the validation of the statistical specialist.

Figure 15 presents the other branches of partners, founders, and members.

Figure 15 - Other branches of partners, founders, and members

Source: Prepared by the author under the validation of the statistical specialist.

Table 14 presents the quantity and percentage of hard sciences and other branches of partners, founders, and members.

Table 14 - Hard sciences and other branches of partners, founders, and members

Hard sciences	Quantity	Other branches	Quantity
Physics	50 (47%)	Administration	28 (38%)
Chemistry	43 (41%)	Assistant	11 (15%)
Mathematics	5 (5%)	Clothing Technician	7 (9%)
Medical Physics	5 (5%)	Advertising and Marketing	5 (7%)
Chemistry Technician	2 (2%)	Law	5 (7%)
Statistics	1 (1%)	Accounting Sciences	4 (5%)
		Design	3 (4%)
		Economy	3 (4%)
		Logistics	2 (3%)
		Social Communication	2 (3%)
		Aviation	1 (1%)
		Communication and Art	1 (1%)
		Human Resources Management	1 (1%)
		Languages	1 (1%)
Total Hard sciences	106	Total Other	74

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 14 and Table 14, the leading hard sciences branches were Physics and Chemistry. According to Figure 15 and Table 14, Administration was the top branch related to other areas. Figure 16 and Table 15 present the background areas of partners, founders, and members by the company profile.

Figure 16 - Background areas of partners, founders, and members by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 15 - Background areas of partners, founders, and members by the company profile

Company profile	Physicians	Health	Engineers	Technology	Hard sciences	Other	Total
Digital health	7 (12%)	8 (14%)	11 (19%)	24 (41%)	8 (14%)	0 (0%)	58
Medical device	30 (8%)	65 (18%)	131 (37%)	37 (10%)	85 (24%)	10 (3%)	358
Pharma/biotech	35 (10%)	199 (57%)	29 (8%)	9 (3%)	47 (13%)	32 (9%)	351

Source: Prepared by the author under the validation of the statistical specialist.

Figure 16 and Table 15 compares the background areas of partners, founders, and members by the company profile. The technology area was dominant in the digital health profile. Concurrently, engineers and hard sciences were the leading areas in the medical device profile. Lastly, the health area was the most relevant in the

pharma/biotech profile. Figure 17 and Table 16 present the background areas of partners and founders by the company profile.

Figure 17 - Background areas of partners and founders by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 16 - Background areas of partners and founders by the company profile

Company profile	Physicians	Health	Engineers	Technology	Hard sciences	Other	Total
Digital health	2 (13%)	4 (27%)	3 (20%)	4 (27%)	2 (13%)	0 (0%)	15
Medical device	15 (16%)	9 (10%)	43 (46%)	1 (1%)	25 (27%)	1 (1%)	94
Pharma/biotech	8 (10%)	40 (51%)	10 (13%)	1 (1%)	14 (18%)	6 (8%)	79

Source: Prepared by the author under the validation of the statistical specialist.

Figure 17 and Table 16 compares the background areas of partners and founders by the company profile. The health and technology areas were dominant in the digital health profile. Concurrently, engineers and hard sciences were the leading areas in the medical device profile. Lastly, health and hard sciences were the central areas in the pharma/biotech profile. Figure 18 and Table 17 present the background areas of members by the company profile.

Figure 18 - Background areas of members by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 17 - Background areas of members by the company profile

Company profile	Physicians	Health	Engineers	Technology	Hard sciences	Other	Total
Digital health	5 (12%)	4 (9%)	8 (19%)	20 (47%)	6 (14%)	0 (0%)	43
Medical device	15 (6%)	56 (21%)	88 (33%)	36 (14%)	60 (23%)	9 (3%)	264
Pharma/biotech	27 (10%)	159 (58%)	19 (7%)	8 (3%)	33 (12%)	26 (10%)	272

Source: Prepared by the author under the validation of the statistical specialist.

Figure 18 and Table 17 compares the background areas of members by the company profile. The technology area was dominant in the digital health profile. Concurrently, health, engineers, and hard sciences were the leading areas in the medical device profile. Lastly, the main pharma/biotech profile area was health. Figure 19 and Table 18 present the educational attainment of partners, founders, and members by the company profile.

Figure 19 - Educational attainment of partners, founders, and members by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 18 - Educational attainment of partners, founders, and members by the company profile

Company profile	Postdoc	Ph.D.	Master	Bachelor	Undergraduate or Technician	Total
Digital health	3 (5%)	13 (22%)	7 (12%)	33 (57%)	2 (3%)	58
Medical device	47 (13%)	62 (17%)	40 (11%)	180 (50%)	29 (8%)	358
Pharma/biotech	49 (14%)	62 (18%)	38 (11%)	164 (47%)	38 (11%)	351

Source: Prepared by the author under the validation of the statistical specialist.

Figure 19 and Table 18 compares the educational attainment of partners, founders, and members by the company profile. The Bachelor was dominant in all profiles, followed by Ph.D. Figure 20 and Table 19 present the educational attainment of partners and founders by the company profile.

Figure 20 - Educational attainment of partners and founders by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 19 - Educational attainment of partners and founders by the company profile

Company profile	Postdoc	Ph.D.	Master	Bachelor	Undergraduate or Technician	Total
Digital health	1 (7%)	5 (33%)	3 (20%)	6 (40%)	0 (0%)	15
Medical device	27 (29%)	29 (31%)	14 (15%)	23 (24%)	1 (1%)	94
Pharma/biotech	29 (37%)	22 (28%)	12 (15%)	15 (19%)	1 (1%)	79

Source: Prepared by the author under the validation of the statistical specialist.

Figure 20 and Table 19 compares the educational attainment of partners and founders by the company profile. Ph.D. and Bachelor were dominant in the digital health profile. Concurrently, Ph.D., Postdoc, and Bachelor were more relevant in the medical device profile. Lastly, Postdoc, Ph.D., and Bachelor were in greater prominence in the pharma/biotech profile. Figure 21 and Table 20 present the educational attainment of members by the company profile.

Figure 21 - Educational attainment of members by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 20 - Educational attainment of members by the company profile

Company profile	Postdoc	Ph.D.	Master	Bachelor	Undergraduate or Technician	Total
Digital health	2 (5%)	8 (19%)	4 (9%)	27 (63%)	2 (5%)	43
Medical device	20 (8%)	33 (13%)	26 (10%)	157 (59%)	28 (11%)	264
Pharma/biotech	20 (7%)	40 (15%)	26 (10%)	149 (55%)	37 (14%)	272

Source: Prepared by the author under the validation of the statistical specialist.

Figure 21 and Table 20 compare the educational attainment of members by the company profile. The Ph.D. degree was dominant in all profiles. Figure 22 and Table 21 present the team expertise by the company profile.

Figure 22 - Teams' expertise by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 21 - Teams' expertise by the company profile

Company profile	ANVISA participation	FDA participation	IP participation	Business experience	Health organization experience	Total
Digital health	2 (14%)	1 (7%)	2 (14%)	5 (36%)	4 (29%)	14
Medical device	14 (14%)	6 (6%)	29 (29%)	26 (26%)	26 (26%)	101
Pharma/biotech	13 (14%)	3 (3%)	24 (26%)	21 (23%)	31 (34%)	92

Source: Prepared by the author under the validation of the statistical specialist.

Figure 22 and Table 21 compare the teams' expertise by the company profile. Business experience followed by health organization experience, IP participation, and ANVISA participation were dominant in the digital health profile. Concurrently, IP participation, followed by business experience, health organization experience, and ANVISA participation, were more relevant in the medical device profile. Lastly, health organization experience, IP participation, business experience, and ANVISA participation were in greater prominence in the pharma/biotech profile.

The findings demonstrated that multidisciplinary involved different areas in the health setting, as stated by Mitchell et al. (2010), Ali and Gittelman (2016), Yazdi and Acharya (2013). A typical recommended medical innovation team may encompass physicians,

health professionals, engineers, technology professionals, hard sciences professionals, and other areas professionals, such as lawyers (PURDY et al., 2012; YAZDI; ACHARYA, 2013; NECK; GREENE; BRUSH, 2014; WIEMAN, 2014; DENIS, 2015; YOCK et al., 2015; SOENKSEN; YAZDIB, 2017). However, although previous research focuses on physicians' collaboration in teamwork (SHLUZAS; LEIFER, 2014; YODA, 2015), results show the prominence of health professionals (non-physicians), especially in medical device and pharma/biotech companies. Additionally, even though entrepreneurial companies may have limited access to qualified teams' expertise, as stated by Styhre and Remneland-Wikhamn (2016), the results demonstrated that most teams had advanced degree professionals and might be prepared for entrepreneurial activities.

4.1.3 Processes' characteristics

Concerning the process characteristics, initially, Table 22 presents ANVISA and FDA classification of the medical device solution.

Table 22 - ANVISA and FDA classification of the medical device solution

ANVISA medical device classification	Quantity (%)
Class II - medium risk	7 (20%)
Class III - high risk	1 (3%)
Not applicable	27 (77%)
Total	35
FDA medical device classification	Quantity (%)
Class I - low to moderate risk	1 (3%)
Class II - moderate to high risk	2 (6%)
Not applicable	32 (91%)
Total	35

Source: Prepared by the author under the validation of the statistical specialist.

According to Table 22, few medical device solutions had ANVISA and FDA registers, and the majority were not applicable due to no requisition or no need to register. Figure 23 and Table 23 presents the regulation phase of the medical solution by the company profile.

Figure 23 - Regulation phase of the medical solution by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 23 - Regulation phase of the medical solution by the company profile

Company profile	Submission preparation	Pre-market evaluation	Regulatory agency approval	Post-marketing surveillance	No phase	Total
Digital health	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (100%)	8
Medical device	12 (34%)	1 (3%)	1 (3%)	2 (6%)	19 (54%)	35
Pharma/biotech	8 (22%)	2 (6%)	0 (0%)	1 (3%)	25 (69%)	36

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 23 and Table 23, Digital health companies were not pursuing regulatory approval due to no current ANVISA and FDA regulations of digital products. However, both ANVISA and FDA recognize the necessity of regulating digital health products and adapt their processes (ANVISA, 2019; FDA, 2020c). Regarding the medical device profile, most companies have not yet started the regulatory process, followed by companies in the submission preparation phase. Lastly, a similar situation was encountered at pharma/biotech companies. Figure 24 and Table 24 presents the existence of embedded software in the medical solution by the company profile.

Figure 24 - Existence of embedded software in the medical solution by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 24 - Existence of embedded software in the medical solution by the company profile

Company profile	Yes	No	Total
Digital health	8 (100%)	0 (0%)	8
Medical device	25 (71%)	10 (29%)	35
Pharma/biotech	8 (22%)	28 (78%)	36

Source: Prepared by the author under the validation of the statistical specialist.

Following Figure 24 and Table 24, the existence of embedded software in digital health medical solutions was dominant, together with the medical device profile. On the contrary, most pharma/biotech did not have embedded software. Such results are in line with the expected product types in each studied company profile. Figure 25 and Table 25 present the ranging from predominantly software or hardware medical solution, i.e., more software or more hardware medical solution by the company profile.

Figure 25 - More software or more hardware medical solution by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 25 - More software or more hardware medical solution by the company profile

Company profile	More software (from 0 to 39)	Software and Hardware (from 40 to 59)	More hardware (from 60 to 100)	Not applicable	Total
Digital health	7 (88%)	1 (13%)	0 (0%)	0 (0%)	8
Medical device	5 (14%)	10 (29%)	20 (57%)	0 (0%)	35
Pharma/biotech	7 (19%)	0 (0%)	7 (19%)	22 (61%)	36

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 25 and Table 25, following a continuous scale from 0 to 100, where 0 is more software-oriented and 100 more hardware-oriented, digital health profiles presented more software solutions. In contrast, medical device profiles showed solutions based predominantly on hardware. Lastly, in most pharma/biotech solutions, there was no existence of hardware and software. Figure 26 and Table 26 presents the positioning between pure service and pure product medical solution, i.e., more service or more product medical solution by the company profile.

Figure 26 - More service or more product medical solution by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 26 - More service or more product medical solution by the company profile

Company profile	More service (from 0 to 39)	Service and Product (from 40 to 59)	More product (from 60 to 100)	Total
Digital health	3 (38%)	3 (38%)	2 (25%)	8
Medical device	9 (26%)	9 (26%)	17 (49%)	35
Pharma/biotech	10 (28%)	4 (11%)	22 (61%)	36

Source: Prepared by the author under the validation of the statistical specialist.

In regard to Figure 26 and Table 26, following a continuous scale from 0 to 100, where 0 is more service-oriented and 100 more product-oriented, digital health companies predominantly presented service and service coupled with product solutions. In contrast, medical device and pharma/biotech profiles indicated mostly product solutions. Interestingly, the results demonstrate that approximately one-fourth of the medical device companies are focusing on services. Figure 27 and Tables 27-28 present the application of development approaches by the company profile.

Figure 27 - Application of development approaches by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 27 - Application of development approaches by the company profile (Part 1)

Company profile	Biodesign	Design Thinking	Stage-gate	Design for Six Sigma	Scrum	Customer development
Digital health	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (50%)	0 (0%)
Medical device	3 (7%)	9 (20%)	0 (0%)	1 (2%)	7 (15%)	3 (7%)
Pharma/biotech	0 (0%)	7 (16%)	1 (2%)	0 (0%)	7 (16%)	0 (0%)

Source: Prepared by the author under the validation of the statistical specialist.

Table 28 - Application of development approaches by the company profile (Part 2)

Company profile	None	Others	Total
Digital health	4 (50%)	0 (0%)	8
Medical device	19 (41%)	4 (9%)	46
Pharma/biotech	21 (48%)	8 (18%)	44

Source: Prepared by the author under the validation of the statistical specialist.

Although approaches are necessary to ensure functionality, economic, and competitive success (TERZIOVSKI; MORGAN, 2006; FRIES, 2013), according to Figure 27, Tables 27-28, most of the companies, independent of their profile, did not apply approaches. Despite a variety of processes, such as Design Thinking (D.SCHOOL,

2018), Biodesign (YOCK et al., 2015), Stage-gate (PIETZSCH et al.; 2009), DFSS (EL-HAIK; MEKKI, 2008), Customer Development (BLANK, 2020), and Scrum (SCRUM STUDY, 2017), there was no relevant application in all company profiles. The mere exception is the application of Scrum for digital health companies. Additionally, other methods encompassed Canvas, Design of Experiments (DOE), Good Manufacturing Practice (GMP), and SMART (Specific, Measurable, Attainable, Relevant, Time-bound).

Among Digital Health companies, Scrum is applied by only half of the companies in the sample, despite Scrum's wide application to support software development in startups in the industry. The Stage-gate process, which aims to set development phases and pace, is not adopted by almost any medical device company. Finally, customer development, which would be relevant for typical entrepreneurial companies' initial stage, is also only adopted in few cases. Figure 28 and Table 29 present the stakeholders involved in the project development by the company profile.

Figure 28 - Stakeholders involved in the project development by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 29 - Stakeholders involved in the project development by the company profile

Company profile	Universities	Hospitals	Government entities	Health organizations	Others	Total
Digital health	4 (21%)	5 (26%)	6 (32%)	3 (16%)	1 (5%)	19
Medical device	31 (32%)	24 (24%)	20 (20%)	18 (18%)	5 (5%)	98
Pharma/biotech	30 (34%)	16 (18%)	19 (21%)	20 (22%)	4 (4%)	89

Source: Prepared by the author under the validation of the statistical specialist.

Figure 28 and Table 29 comprehend the involvement of multiple stakeholders during the project development, as stated by Van Gemert-Pijnen et al. (2011), Yock et al. (2015), Wield et al. (2017), and Vagal et al. (2020). Digital health profiles presented more government entities, hospitals, and universities. Medical device and pharma/biotech profiles demonstrated more universities as stakeholders, which have contributed to entrepreneurship (MEHTA, 2004; YOCK et al., 2015). Some projects receive assistance from other supporting institutions, such as the Lemann Foundation, Pan American Health Organization (PAHO/WHO), National Service of Industrial Training (SENAI), and the Institute for Technological Research (IPT). Figure 29 and Tables 30-31 present the completed project phases of the medical solution development process during PIPE by the company profile.

Figure 29 - Completed project phases of the medical solution development process by the company profile during PIPE

Source: Prepared by the author under the validation of the statistical specialist.

Table 30 - Completed project phases of the medical solution development process by the company profile during PIPE (Part 1)

Company profile	Concept generation	Prototyping	Technical feasibility	Clinical feasibility	Intellectual property registration
Digital health	8 (20%)	6 (15%)	6 (15%)	3 (8%)	2 (5%)
Medical device	35 (19%)	30 (16%)	25 (13%)	13 (7%)	11 (6%)
Pharma/biotech	36 (20%)	34 (19%)	30 (17%)	12 (7%)	7 (4%)

Source: Prepared by the author under the validation of the statistical specialist.

Table 31 - Completed project phases of the medical solution development process by the company profile during PIPE (Part 2)

Company profile	Regulation	Business model definition	Marketing and sales strategy definition	Scale production/Commercialization	Total
Digital health	0 (0%)	7 (18%)	5 (13%)	3 (8%)	40
Medical device	6 (3%)	31 (17%)	22 (12%)	11 (6%)	187
Pharma/biotech	1 (1%)	30 (17%)	18 (10%)	10 (6%)	179

Source: Prepared by the author under the validation of the statistical specialist.

Figure 29 and Tables 30-31 present the completed project phases of the medical solution development process during PIPE by the company profile. The concept generation was the dominant phase in all profiles, followed by the business model definition, prototyping, and technical feasibility phases. The clinical feasibility, IP registration, and scale production commercialization phases, together with the regulation phase (except for digital health), were not relevant. Such a scenario is part of the long and complicated medical innovation process, as stated by Terziovski and Morgan (2006) and Fries (2013). Figure 30 and Table 32 present the clinical challenge of the medical solution by the company profile.

Figure 30 - Clinical challenge of the medical solution by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 32 - Clinical challenge of the medical solution by the company profile

Company profile	From none to low (from 0 to 39)	Medium (from 40 to 59)	From high to very high (from 60 to 100)	Total
Digital health	5 (63%)	0 (0%)	3 (38%)	8
Medical device	13 (37%)	5 (14%)	17 (49%)	35
Pharma/biotech	9 (25%)	3 (8%)	24 (67%)	36

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 30 and Table 32, the foremost clinical challenge for digital health solutions was from none to low. In contrast, the principal clinical challenge for medical device and digital health solutions were from high to very high. Figure 31 and Table 33 present the technical challenge of the medical solution by the company profile.

Figure 31 - Technical challenge of the medical solution by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 33 - Technical challenge of the medical solution by the company profile

Company profile	From none to low (from 0 to 39)	Medium (from 40 to 59)	From high to very high (from 60 to 100)	Total
Digital health	1 (13%)	1 (13%)	6 (75%)	8
Medical device	2 (6%)	4 (11%)	29 (83%)	35
Pharma/biotech	2 (6%)	3 (8%)	31 (86%)	36

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 31 and Table 33, the leading technical challenge for all company profile solutions was from high to very high. In sum, most entrepreneurial health companies face significant technical and clinical challenges (YOCK et al., 2015).

4.1.4 Innovation performance outcomes

To the calculation of time to market, i.e., time to scale production/commercialization in months, the difference between the first sale date and the first PIPE date was considered. From 79 companies, 21 made a first sale, including two digital health, 13 medical device, and six pharma/biotech.

In two cases, the difference between the first sale date and the first PIPE date resulted in negative values, i.e., the company started selling before the first PIPE project. Such values were not considered in the subsequent histograms. However, they are described as follows. One medical device company started selling four months before the first PIPE project started, and one pharma/biotech company started selling ten months before the first PIPE project. Thus, Figure 32 presents the total time to market for a medical solution in months, considering the 19 positive values, including digital health, medical device, and pharma/biotech company profiles.

Figure 32 - Histogram of total time to market in months

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 32, 8 companies took between 0 and 10 months to place their solutions to the market, i.e., to make their first sale, followed by two companies between 10 and 20 months, five companies between 20 and 30 months, one company between 30 and 40 months, two companies between 50 and 60 months, and one company between 70 and 80 months.

Regarding the digital health company profile, two digital health companies took 9 and 29 months, respectively, to place their solutions to the market. Concerning the medical device company profile, Figure 33 presents the time to market in months.

Figure 33 - Histogram of time to market by the medical device company profile

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 33, five medical device companies took between 0 and 10 months to place their solutions to the market, followed by two companies between 10 and 20 months, one company between 20 and 30 months, one company between 30 and 40 months, two companies between 50 and 60 months, and one company between 70 and 80 months. Concerning the pharma/biotech company profile, Figure 34 presents the time to market in months.

Figure 34 - Histogram of time to market by the pharma/biotech company profile

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 34, two pharma/biotech companies took between 0 and 10 months to place their solutions to the market, and three companies took between 20 and 30 months.

As prior mentioned, such scenarios presented in Figures 32-34 are part of the extensive and complex development cycle of medical innovations (TERZIOVSKI; MORGAN, 2006; FRIES, 2013). Regulatory drug testing and approval of pharma/biotech companies are lengthy, with severe regulatory difficulties before commercialization (HINE; KAPELERIS, 2006; SHIMASAKI, 2014). However, the findings may be in contrast with Oriana et al. (2016), which pointed out that medical devices have shorter product development cycles. Additionally, the results may be unlike to Mathews et al. (2019) and Jandoo (2020), which affirms that digital health also has rapid creation and shorter development cycles.

Figure 35 and Tables 34-35 present the years in which the PIPE project led to increased sales by the company profile.

Figure 35 - Years in which the PIPE project led to increased sales by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 34 - Years in which the PIPE project led to increased sales by the company profile (Part 1)

Company profile	1st Year	2nd Year	3rd Year	4th Year	5th Year
Digital health	2 (15%)	1 (8%)	1 (8%)	1 (8%)	1 (8%)
Medical device	7 (10%)	7 (10%)	7 (10%)	7 (10%)	7 (10%)
Pharma/biotech	5 (10%)	5 (10%)	4 (8%)	2 (4%)	2 (4%)

Source: Prepared by the author under the validation of the statistical specialist.

Table 35 - Years in which the PIPE project led to increased sales by the company profile (Part 2)

Company profile	Other Years	No increased sales	N/A (ongoing project)	Total
Digital health	1 (8%)	2 (15%)	4 (31%)	13
Medical device	6 (9%)	10 (14%)	18 (26%)	69
Pharma/biotech	2 (4%)	15 (29%)	16 (31%)	51

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 34 and Tables 34-35, most projects were ongoing, i.e., not applicable. It is noteworthy to mention that most completed projects did not contribute to increasing the company sales, and few projects increased the company sales in the

first five and other years. When the project positively impacts sales, this impact may be lasting in time. Table 36 presents the difference between the first export date and the first PIPE date in months by the company profile.

Table 36 - Difference between the first export date and first PIPE date in months by the company profile

Company Profile	Difference between the first export date and first PIPE date in months
Digital health	82
	4
	-1
Medical device	14
	23

Source: Prepared by the author under the validation of the statistical specialist.

According to Table 36, only three medical device and one digital health companies exported after the first PIPE. One medical device company started exporting one month before the first PIPE. Figure 36 and Tables 37-38 present the years in which the PIPE project led to increased exports by the company profile.

Figure 36 - Years in which the PIPE project led to increased exports by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 37 - Years in which the PIPE project led to increased exports by the company profile (Part 1)

Company profile	1st Year	2nd Year	3rd Year	4th Year	5th Year
Digital health	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Medical device	1 (2%)	4 (9%)	4 (9%)	2 (4%)	2 (4%)
Pharma/biotech	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Source: Prepared by the author under the validation of the statistical specialist.

Table 38 - Years in which the PIPE project led to increased exports by the company profile (Part 2)

Company profile	Other Years	No increased	N/A (Ongoing project)	Total
Digital health	0 (0%)	3 (38%)	4 (50%)	8
Medical device	2 (4%)	12 (27%)	18 (40%)	45
Pharma/biotech	0 (0%)	20 (56%)	16 (44%)	36

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 36 and Tables 37-38, the majority of ongoing and completed projects did not contribute to increasing the company exports, and few projects increased the company exports in the first five and other years. Table 39 demonstrates the difference between the first ANVISA and the first PIPE dates in months by the company profile.

Table 39 - Difference between the first ANVISA and first PIPE dates in months by the company profile

Company profile	Difference between the first ANVISA and first PIPE dates in months
Medical device	-3
	14
	35
	53
	61
	99
Pharma/biotech	8

Source: Prepared by the author under the validation of the statistical specialist.

According to Table 39, considering the difference between the first ANVISA date and the first PIPE date of projects that received regulatory approval, there was no digital health company with ANVISA, six medical device companies with approved ANVISA regulation, being one of them with ANVISA three months before starting PIPE. Lastly, there was one pharma/biotech company with ANVISA certification. Only two medical device companies had FDA approval, with a difference between the first FDA date and the first PIPE date of 33 and 41 months, respectively. Table 40 presents the total of ANVISA and FDA registers since the first regulatory approval by the company profile.

Table 40 - Total of ANVISA and FDA registers since the first regulatory approval by the company profile

Company profile	Total of ANVISA registers	Total of FDA registers	Total
Medical device	17 (89%)	2 (11%)	19
Pharma/biotech	2 (100%)	0 (0%)	2

Source: Prepared by the author under the validation of the statistical specialist.

Following Table 40, the number of ANVISA and FDA registers of medical device companies was 17 and two, respectively. The number of registers of pharma/biotech companies was only two. There were no ANVISA and FDA registers for digital health due to the no existence of a regulatory certification process, despite the requirement of regulating digital health products (ANVISA, 2019; FDA, 2020c). The findings of Tables 39-40 on regulatory approval are in accordance with Lehoux et al., 2017, and constitute one of the most critical issues of entrepreneurial companies. Lastly, Figure 37 and Table 41 present the IPs, publications, and products launched resulting from the medical solution developed in the PIPE project, by the company profile.

Figure 37 - IPs, publications, and products launched resulting from the medical solution developed in the PIPE project by the company profile

Source: Prepared by the author under the validation of the statistical specialist.

Table 41 - IPs, publications, and products launched resulting from the medical solution developed in the PIPE project by the company profile

Company profile	Number of IPs	Number of publications	Number of products launched	Total
Digital health	1 (4%)	17 (74%)	5 (22%)	23
Medical device	16 (5%)	205 (60%)	120 (35%)	341
Pharma/biotech	9 (7%)	111 (81%)	17 (12%)	137

Source: Prepared by the author under the validation of the statistical specialist.

According to Figure 37 and Table 41, the number of publications was the foremost mentioned in all company profiles, followed by products launched and IPs. It is worth pointing out that publications are relevant for medical innovation, as stated by several authors, such as OECD/Eurostat (2005), Hine and Kapeleris (2006), Schmoch, Rammer and Legler (2006), Terziovski and Morgan (2006), Yock et al. (2015), and Thompson, Ziedonis, and Mowery (2018). In contrast, the number of IPs was much lower than the amount of generated solutions and continues to be a critical component of medical innovation, requiring significant investments. Such findings are in agreement with a variety of authors such as Horner (2014), Woo, Jang, and Kim (2015), Yock et al. (2015), Graf, Zech (2017), Kim and Bae (2017), Leignel, Dziallas and Blind (2019), and Leignel, Ménager, and Yablonski (2019).

4.1.5 Content analysis of survey open-ended questions

In addition to the previous findings, the following content analysis concerns the open-ended questions. The content analysis was computer-aided by MAXQDA software (MAXQDA, 2020), including figures undertook in Minitab software (MINITAB, 2020). Table 42 demonstrates the main topics mentioned by the respondents and sample findings on the PIPE process.

Table 42 - Main topics mentioned by the respondents and sample findings on the PIPE process

Topics	Sample findings
Entrepreneurial PIPE	<p>"The Entrepreneurial PIPE has a high impact and enables everything in the idea, solidify the team, prototype, and production."</p> <p>"The Entrepreneurial PIPE was cool. The market for our solution is bigger than we imagined."</p> <p>"The Entrepreneurial PIPE contributes to the entrepreneur's personal development and generates business."</p> <p>"With the Entrepreneurial PIPE, it was possible to learn the relationship of our solution with the business."</p> <p>"The Entrepreneurial PIPE was the biggest surprise that directly impacted the product, which was modified. The Entrepreneurial PIPE enabled business training and changed the course of the company."</p> <p>"The Entrepreneurial PIPE helps you get more business insight, move from university to real business."</p>
Project development	<p>"PIPE was significant to the development of the device, which was the main objective of the project. We implemented our device and grew in its development until we reached the level for sterilization of surgical materials."</p> <p>"Research, development, and innovation project management. PIPE was essential to leverage our service in terms of funding."</p> <p>"It was learning project management because it was the first time I contacted large development projects. I had no previous experience in project management."</p> <p>"Overcome barriers, gain knowledge, and partnerships in project development."</p>
Business	<p>"Understand that the dynamics of academic research are different from commercial ones."</p> <p>"Have a business-oriented look rather than academics."</p> <p>"It was learning about business and entrepreneurship. The technical part we already have from the university."</p> <p>"Understand the scientific application in the health market. Convert knowledge into something usable."</p> <p>"It is 'take the research off the paper' and has a business character."</p> <p>"We lived in the academic world, and when we left and went to the real world (...). We could understand who our customers were, the key people, the channels, the type of business in Brazil. It was a break from the university world."</p> <p>"We are academic researchers and had no idea how it was to apply science and product development to a product. It was learning about entrepreneurship and how to reach the market."</p> <p>"It was understanding the universe of the entrepreneur and how the scientist becomes an entrepreneur. For those who come from academia is a drastic change."</p>
Support	<p>"PIPE provides mentoring."</p> <p>"The support staff is helpful and supportive."</p> <p>"Only positive experiences, every time I needed to contact FAPESP, there was a return."</p> <p>"(...) people were wide open to discuss. I requested several project modifications to FAPESP and accepted."</p>
Financial resources	<p>"PIPE is a source of funding that can make high-risk projects feasible that the industry does not want."</p> <p>"PIPE is significant funding when you are at the academy."</p> <p>"PIPE, as the first step to innovation, is essential. If you do not have this resource, things get harder and are expensive. The researcher has no way to develop something from personal funds."</p> <p>"To be able to come close to developing a product through scientific research in Brazil with funding."</p> <p>"The financial resource helps a lot."</p> <p>"PIPE fills the gap in Brazil's economy."</p> <p>"PIPE is a financial contribution to developing something for society."</p>

Source: Prepared by the author.

As exposed in Table 42, the themes mentioned by the respondents were separated into topics on Entrepreneurial PIPE, project development, business, support, and financial resources. The Entrepreneurial PIPE topic regards the respondents' experiences during the Entrepreneurial PIPE program, and project development considers the respondents' experiences during medical solution development. The business topic refers to the respondents' experiences in the transition from the academic world to the business world. Support regards the respondents' experiences when support was necessary. Lastly, financial resources consider the respondents' experiences in developing medical solutions due to PIPE grants.

PIPE seems to be of great importance to entrepreneurs in financing project development, together with Entrepreneurial PIPE, which contributes to a more market-focused solution. These findings are in agreement with Mehta (2004) since, typically, an entrepreneurial health company starts up at the university with foundation grants and discoveries. As stated by Szycher (2019), entrepreneurs usually try to find capital to start a new business with funding sources. Additionally, suggestions to improve PIPE were mentioned, as presented in table 43.

Table 43 - Main topics mentioned by the respondents and sample findings on PIPE improvement suggestions

Topics	Sample findings
Support	<p>"If the company that received Phase 1 and it cannot go to Phase 2, there needs to be a question: Why? There needs to be a follow-up."</p> <p>"Review the processes of health companies, where third party infrastructure and services are often longer."</p> <p>"PIPE is seen by large companies as something of the academy. It is necessary to change such vision."</p>
Analysis	<p>"The reduction of approval phases analysis time, the clarity of processes and deadlines, more interactive and step by step manuals."</p> <p>"Higher analysis speed, more practical training in the Entrepreneurial PIPE."</p> <p>"Phase 1 and 2 should have a faster evaluation link. Perhaps an increase in Phase 1 time. Leave at least one year or 1.5 years in Phase 1."</p> <p>"Leave a separate Phase 1 service team and speed up the responses within 15 days."</p> <p>"Less bureaucracy, budget flexibility, speed up of approvals, and response time."</p> <p>"Shorten the review time that advisors take to evaluate each project and anticipate the meeting to take to the committee. Hold the meeting more strategically. The processes could be online, with a specific platform to facilitate the process flow."</p> <p>"Establish a continuous flow to avoid deadlines and have a faster assessment."</p> <p>"The assessment may be technically, but they need to try to get a market professional to assess the projects."</p> <p>"Insert a closer project manager to validate some steps in the project."</p>

Source: Prepared by the author.

As demonstrated in Table 43, the improvement suggestions mentioned by the respondents were separated into topics on support and analysis. The support topic regards the improvement suggestions on the current PIPE program, and the analysis topic concerns the improvement suggestions on the existing PIPE analysis process. As pointed by (TERZIOVSKI; MORGAN, 2006; FRIES, 2013), the health area is a complicated and lengthy process. Due to such particularities, the procedures might be reviewed, such as the duration of PIPE phases. Another respondent's observation is to reduce the analysis response time. However, as pointed by PIPE rules (NORMAS PIPE, 2020), there may be a more extended time in analyses, depending on the area. FAPESP has been determined to improve such processes, and usually, the most expected average deadlines are respected. Table 44 demonstrates the main topics mentioned by the respondents and sample findings on company growth limitations.

Table 44 - Main topics mentioned by the respondents and sample findings on company growth limitations

Topics	Sample findings
Financial resources	"Lack of investment after the business is scalable." "Lack of angel investment or venture capital." "The investment is very high in the health area."
Human resources	"We have very technical people on the team, and we need a business team member." "Lack of business experience." "High cost in hiring professionals."
Regulatory process	"Delays in ANVISA's response time." "Changes in ANVISA's process."
Brazil's economic situation	"The stagnant economy (...) the market in Brazil is unprepared." "Brazil's economic crisis and the tax system."

Source: Prepared by the author.

As presented in Table 44, the main themes mentioned by the respondents on company growth limitations were separated into topics on financial resources, human resources, regulatory process (when applicable), and Brazil's economic situation. Financial resources consider the hurdles in investments, and human resources refer to the difficulties in establishing teamwork. The regulatory process contemplates the current ANVISA system in Brazil. Lastly, Brazil's economic situation reflects the complicated financial circumstances in the country.

The impediments in Table 44 regarding financial resources follow Heller (2019), while there is limited investment in entrepreneurial companies. The high capital costs for R&D and the extended time to advance the project due to regulations, in some cases, are critical hurdles in the health area (HINE; KAPELERIS, 2006; DAVEY et al., 2011; CAO et al., 2013). Multidisciplinarity and expert teams are essential for business opportunities (KRABEL; MUELLER, 2009; YOCK et al., 2015; SOENKSEN; YAZDIB, 2017). Nonetheless, the findings demonstrated limited human resources. Brazil's difficult economic situation was also mentioned, despite having initiated innovation opportunities for companies (MCMAHON; THORSTEINSDÓTTIR, 2013; FREITAS; MARQUES; SILVA, 2013; VAALAND; ISHENGOMA, 2016).

However, competitiveness has required companies to increasingly look towards innovation (CEFIS; MARSILI, 2006; DAVEY et al., 2011; LIU; HODGKINSON; CHUANG, 2014; DEWANGAN; GODSE, 2014), and Brazil has been able to perform competitive and advantageous medical solutions, as demonstrated in Table 45.

Table 45 - Main topics mentioned by the respondents and sample findings on medical solution competitive advantage

Topics	Sample findings
Solution benefits	"Be portable and cheap."
	"More sensors, memory, and upper battery."
	"It is a non-invasive solution, has mobility, price, less time, and accessibility to all."
	"Our exam is much simpler, allows comfort, and has a low cost."
	"Image quality, connectivity, usability. Our product is technically better than competing products."
	"Our solution causes the wound to close and heal, prevents the amputation, and recurrent hospitalization."
No competitors	"Our project enables the construction of a device that does not exist in the world."
	"Our solution is unique in the market, with cost and efficiency."

Source: Prepared by the author.

As presented in Table 45, the main themes mentioned by the respondents on medical solution competitive advantage were separated into topics on solution benefits and no competitors. Solution benefits refer to the advantages of the respondents' medical solution over the existing ones. No competitors refer to the unique medical solution over the existing ones. To the development of such solutions, supplies may be available in Brazil, despite in some cases, it is necessary to import, as pointed by Jones, Wheeler, and Dimitratos (2011), Styhre and Remneland-Wikhamn (2016). As a complement, Figure 38 depicts the competitors' locations (if existing) of the medical solution developed in the project.

Figure 38 - Competitors' locations of the medical solution developed in the project

Source: Prepared by the author.

As illustrated in Figure 38, most competitors of the medical solution developed are abroad, such as established organizations, which have control over price or amount supplied in the market, as point out by Hine and Kapeleris (2006), Mittra and Williams (2007). Besides, the main distribution channels of the solution developed in the project are illustrated in Figure 39, as follows.

Figure 39 - Distribution channels of the solution developed in the project

Source: Prepared by the author.

Figure 39 demonstrates that the leading distribution channels were external organizations, hospitals, and physicians. Others comprised the Unique Health System (SUS) and health insurance. On behalf of business success, it is essential to create a stimulating environment to motivate the team to develop products in a competitive market (LI; HALAL, 2002). Thus, Table 46 demonstrates the topics mentioned by the respondents and sample findings on team motivation and structure.

Table 46 - Main topics mentioned by the respondents and sample findings on team motivation and structure

Topics	Sample findings
Accomplishment	"Transform academic research into a market product and improve people's lives." "Passion for science and doing what you like, despite the challenges." "See your project come true and the possibility of accomplishing your dreams." "I love developing, and I always wanted to make a product that makes life easier for people." "Bring an impact on a scale not only for Brazilian health but worldwide." "We have a purpose that is to improve people's lives through research, but the solution has never come to them, and it was possible with the company. The company wants people to use the solution."
Teamwork	"In twelve months, we do not intend to grow, but in twenty-four months, we want to double the number of team members." "We plan to increase the team in Phase 2." "Depends on investment, we intend to increase the research and development team." "The team is adequate."

Source: Prepared by the author.

As presented in Table 46, the main themes mentioned by the respondents on team motivation and structure were separated into topics on accomplishment and teamwork. The accomplishment topic considers the respondents' perspectives on transform health and society. Teamwork regards the team structure planning over the following twelve months. Convert academic research in business and attempt to increase or maintain the team structure were the main themes mentioned in Table 46, as identified by Lam (2011) and Shimasaki (2014), which point out the desire to act righteously for the benefit of health and society. In sum, entrepreneurs are the primary source of motivation, together with an expert team.

4.2 Data analysis

Before the development of the analyses in the following sections, it was essential to apply a strategy for the selection of variables. As presented in Table 3, there was a high number of variables to be analyzed, which would originate innumerable combinations, and indeed would be impractical to adjust all the possible models (COLOSIMO; GIOLO, 2006). From this standpoint, the researcher of the present study, together with statistical specialists, including a Full Professor and a Postdoctoral Professor, adopted a proactive stance, which implied in the selection of the variables for analyses (COLOSIMO; GIOLO, 2006), presented in Tables 47-48.

Table 47 - Selected covariates for analyses

Constructs	#	Codifications	Descriptions
Entrepreneurial company characteristics	1	TotalPIPEprojects	Total of company PIPE projects
	2	TotalCollaborativeLocations	Total of collaborative company locations
	3	TotalCollaborativeResources	Total of collaborative resources further PIPE
	4	CompanyExistedBeforePIPE	If the company existed before its 1st PIPE approval (1 = "Yes"; 0 = "No")
Team characteristics	5	PhysiciansTotal	Total of physicians partners, founders, and members
	6	HealthTotal	Total of health professionals (non-physicians) partners, founders, and members
	7	EngineersTotal	Total of engineers partners, founders, and members
	8	TechnologyTotal	Total of technology professionals (non-engineers) partners, founders, and members
	9	HardsciencesTotal	Total of hard sciences professionals (Physics, Medical Physics, Statistics, Mathematics, Chemistry) partners, founders, and members
	10	OtherTotal	Total of other areas partners, founders, and members
	11	PhysiciansPartFound	Number of physicians partners and founders
	12	HealthPartFound	Number of health professionals partners and founders
	13	EngineersPartFound	Number of engineers partners and founders
	14	TechnologyPartFound	Number of technology professionals partners and founders
	15	HardsciencesPartFound	Number of hard sciences partners and founders
	16	OtherPartFound	Number of other areas professionals partners and founders
	17	PhysiciansMembers	Number of physicians members
	18	HealthMembers	Number of health professionals members
	19	EngineersMembers	Number of engineers partners and founders members
	20	TechnologyMembers	Number of technology professionals members
	21	HardsciencesMembers	Number of hard sciences members
	22	OtherMembers	Number of other areas professionals members

continue

conclusion

Constructs	#	Codifications	Descriptions
Team characteristics	23	PostdocTotal	Total of Postdoc partners, founders and members
	24	PhDTotal	Total of Ph.D. partners, founders, and members
	25	MasterTotal	Total of Master partners, founders, and members
	26	BachelorTotal	Total of Bachelor partners, founders, and members
	27	UndergraduateTechnicianTotal	Total of Undergraduate or Technician partners, founders, and members
	28	PostdocPartFound	Number of Postdoc partners and founders
	29	PhDPartFound	Number of Ph.D. partners and founders
	30	MasterPartFound	Number of Master partners and founders
	31	BachelorPartFound	Number of Bachelor partners and founders
	32	UndergraduateTechnicianPartFound	Number of Undergraduate or Technician partners and founders
	33	PostdocMembers	Number of Postdoc members
	34	PhDMembers	Number of Ph.D. members
	35	MasterMembers	Number of Master members
	36	BachelorMembers	Number of Bachelor members
	37	UndergraduateTechnicianMembers	Number of Undergraduate or Technician members
	38	ANVISAParticipation	If some professional participated in an ANVISA process (1="Yes"; 0="No")
	39	FDAParticipation	If some professional participated in an FDA process (1="Yes"; 0="No")
	40	IPParticipation	If some professional participated in an intellectual property process (1="Yes"; 0="No")
	41	BusinessExperience	If some professional had business experience (1="Yes"; 0="No")
	42	HealthOrganizationExperience	If some professional had health organization experience (1="Yes"; 0="No")
Process characteristics	43	TotalApproaches	Total of approaches employed
	44	TotalStakeholders	Total of stakeholders
	45	RegulationPhase	If there is a regulation phase (1 = "Yes"; 0 = "No")
	46	ScaleProductionCommercialization	Scale production and commercialization project phase (1 = "Yes"; 0 = "No")
	47	SolutionSoftwareHardware	Solution more software (next do 0) or hardware (next to 100). Not applicable = ""
	48	SolutionServiceProduct	Solution more service (next do 0) or product (next to 100)
	49	ClinicalChallenge	Solution clinical challenge from low (0) to very high (100)
	50	TechnicalChallenge	Solution technical challenge from low (0) to very high (100)

Source: Prepared by the author in conjunction with statistical specialists.

Table 48 - Selected response variables for analyses

Constructs	#	Codifications	Descriptions
Innovation performance outcomes	55	TimetoMarket	The difference between the first sale date and the first PIPE date in months
	56	IPsTotal	Total number of intellectual properties
	57	PublicationsTotal	Total number of publications
	58	ProductsLaunchedTotal	Total number of products launched

Source: Prepared by the author in conjunction with statistical specialists.

Thus, Figure 40 presents the hypothesized model with the selected covariates and response variables.

Figure 40 - Hypothesized model with the selected covariates and response variables

Source: Prepared by the author in conjunction with statistical specialists.

The next sections detail the data analysis.

4.2.1 Time to market analysis

This section encompasses the analyses of H1, H2, and H3 of the hypothesized model, including which covariates of entrepreneurial company characteristics, team characteristics, and process characteristics positively influence the response variable first sale after receiving the first PIPE, i.e., the time to market, as shown in Figure 41.

Figure 41 - Covariates and TimetoMarket response variable

Source: Prepared by the author.

The statistical computing and graphics in this section were developed in R software (R, 2020). Before demonstrating the analyses, it is worth introducing the concept of censoring in statistics. Censoring is a partial observation of response in situations in, which for some reason, the monitoring of something was interrupted. For instance, the patient's monitoring was interrupted because the study ended for data analysis. Consequently, it is necessary to apply methods of survival analysis, which permit to include in the statistical analysis the information contained in the censored data (COLOSIMO; GIOLO, 2006). Accordingly, in this research, companies that did not make the first sale until the collection date were considered censored. In contrast, companies that made the first sale until the collection date were considered no censored.

The time until the first sale, i.e., the time to market, was calculated considering the difference between the first sale date and the first PIPE date in months. For the censored data, the time until the first sale was computed considering the difference between the collection date and the first PIPE date. It is worth mentioning that time values should be greater than 0 in building a statistical model (COLOSIMO; GIOLO, 2006). As a result, from 79 companies, 74 were viable for developing the analysis since two of them had negative time values in months, i.e., the first sale date was before the first PIPE date. Additionally, three of them had no first sale but had negative time values in months because the project had already been approved and was expecting the conclusion of specific procedures to initiate formally. Besides, as prior mentioned, companies that did not make the first sale until the collection date were considered censored. Thus, the number of companies with the first sale and without the first sale is presented in Table 49.

Table 49 - Number of companies with the first sale and without the first sale

Company profile	Number of companies	Companies with the first sale	Companies without the first sale (Censor)
Digital health	7	2	5
Medical device	34	12	22
Pharma/biotech	33	5	28
Total	74	19	55

Source: Prepared by the author under the validation of the statistical specialist.

According to Table 49, from seven digital health companies, two made the first sale, and five did not make the first sale. From 34 medical device companies, 12 made the first sale, and 22 did not make the first sale until data gathering was performed. Lastly, from 33 pharma/biotech companies, five made the first sale, and 28 did not make the first sale. As previously mentioned, 74 companies were viable for analysis. The total of companies with the first sale was 19, and without the first sale was 55, which were considered censored data.

4.2.1.1 Descriptive analysis

Figure 42 shows the survival curve estimated using the Kaplan-Meier approach for the time variable (in months) that a company takes to make its first sale after receiving the first PIPE, i.e., the time to market.

Figure 42 - Survival function calculated from the Kaplan-Meier estimator, with a 95% confidence interval

Source: Prepared by the statistical specialist.

According to Figure 42, the maximum (registered) time a company took to make its first sale was 77 months. Note that the Kaplan-Meier curve did not reach a 0 value. Therefore, the mean survival time a given company would take until to make its first sale was underestimated. Consequently, more robust measures were employed, such as percentiles, for instance, the median survival time, as indicated in Table 50.

Table 50 - Percentiles of survival time and their respective confidence intervals

Percentile	Estimate	95% Confidence Limits	
		Lower	Upper
Percentile 30	35	22	-
Percentile 40	56	29	-
Percentile 50	77	55	-

Source: Prepared by the statistical specialist.

Table 50 specifies the estimates for the 30, 40, and 50 percentiles and their 95% confidence intervals. Accordingly, the median survival time is 77 months, i.e., there is a 50% probability that a company will not make its first sale after 77 months. Subsequently, a company has a 70% probability of not making its first sale after 35 months and 60% after 56 months. Likewise, there is a 30% probability that a company will make its first sale in the first 35 months, 40% in the first 56 months, and 50% in the first 77 months, respectively.

4.2.1.2 Regression model

In this section, a parametric regression model was implemented to analyze the relationship between the time a company takes to make its first sale after receiving the first PIPE, i.e., the time to market, and the 50 covariates aforementioned in Table 47. Consider T the time it takes a company to make its first sale, $x = (x_1, x_2, \dots, x_p)$ the covariates vector, and $\beta = \{\beta_1, \dots, \beta_p\}$ the parameters to be estimated. Thus,

$$T = \exp\{x'\beta\} \exp\{\sigma W\},$$

where σ is the dispersion parameter to be estimated, and W is a random variable that follows a probability distribution that may be used to describe $\ln(T)$. In survival analysis modeling, it is recommended to indicate a distribution for the random variable T and then check the adequacy of the model after the inclusion of the covariates (COLOSIMO; GIOLO, 2006). In this analysis, the exponential, Weibull, and lognormal distributions were considered to model the distribution of the variable T due to adapt to a wide variety of situations.

In the first analysis, the Weibull distribution was considered since there is an approximately linear relationship between $\log(t)$ and $\log(-\log(\hat{S}(t)))$, where $\hat{S}(t)$ is a Kaplan-Meier estimator (see Figure 43), and the Weibull model was appropriate (COLOSIMO; GIOLO, 2006).

Figure 43 - Plot $\log(-\log(\hat{S}(t)))$ versus $\log(t)$

Source: Adapted from Colosimo, Giolo (2006).

However, it should be emphasized that after the selection of covariates, the shape parameter of the Weibull model was not significantly different from 1 at the 5% significance level. Thus, it was necessary to repeat the analysis assuming the exponential distribution, which is a particular case of Weibull distribution when the shape parameter is equal to 1 (ALLAN; BILLINTON, 1992).

4.2.1.3 Adjustment of the regression model

Assuming T , the time it takes a company until to make its first sale follows an exponential distribution with parameter α , the survival function for T conditional on x , which is a vector of covariates, is expressed by:

$$S(t|x) = \exp\left\{-\left(\frac{t}{\exp(x'\beta)}\right)\right\},$$

where $\alpha = \exp(x'\beta)$. The percentiles of T are $t_p = -[\log(1 - p)]\exp(x'_i\hat{\beta})$. The parameters were estimated using Maximum Likelihood Estimation (MLE) since the sample size was $n=74$, and 55 cases were censored, i.e., it contained 74% of censored data. In such a case, for large sample sizes ($n>50$) and from 50-80% censoring, it is recommended to apply MLE (HELSEL, 2012).

Once considering the exponential model, the selection of covariates was carried out, as shown in Tables 51, 52, 53, and 54. In this analysis, the choice of covariates was based on Collett (2003) proposal.

In the first step, exponential models were adjusted with a single covariate. The significance of each covariate in the model was assessed, applying the Likelihood Ratio (LR) test. It is worth mentioning that when deciding whether a term should be included, the level of significance should not be too low, and it is recommended a value close to 0.10 (HOSMER; LEMESHOW, 1999).

Table 51 demonstrates the significant covariates at the level of 0.10 in this first selection step.

Table 51 - Step 1: the selection of covariates

	Covariates	p-values
Step 1	SolutionServiceProduct (X1)	0.001
	CompanyExistedBeforePIPE (X2)	0.083
	TotalAlternativeResources (X3)	0.026
	TotalStakeholders (X4)	0.037
	ScaleProductionCommercialization (X5)	<0.001
	TechnologyMembers (X6)	0.053
	HardsciencesMembers (X7)	0.083
	EngineersTotal (X8)	0.095

Source: Prepared by the statistical specialist.

In the following step, the significant covariates at the 0.10 significance level in Table 51 were adjusted together. Subsequently, reduced models were adjusted, excluding a single covariate at a time. Only the covariates that cause a significant increase in the LR statistic remained in the model for the next selection step. This second step was essential since, in the presence of certain covariates, others may cease to be significant.

Table 52 presents the results of the second step. Note that only the covariates SolutionServiceProduct (X1) and ScaleProductionCommercialization (X5) caused significant increases, i.e., p-values<0.10. Thus, in the next selection stage, these covariates were adjusted together.

Table 52 - Step 2: the selection of covariates

	Covariates	p- values
Step 2	X1+X2+X3+X4+X5+X6+X7+X8	-
	X2+X3+X4+X5+X6+X7+X8	0.006
	X1+ X3+X4+X5+X6+X7+X8	0.311
	X1+X2+ X4+X5+X6+X7+X8	0.295
	X1+X2+X3+X5+X6+X7+X8	0.666
	X1+X2+X3+X4+X6+X7+X8	<0.001
	X1+X2+X3+X4+X5+X7+X8	0.757
	X1+X2+X3+X4+X5+X6+X8	0.345
	X1+X2+X3+X4+X5+X6+X7	0.318

Source: Prepared by the statistical specialist.

As a consequence, in the final model, the covariates SolutionServiceProduct (X1) and ScaleProductionCommercialization (X5) were considered.

Table 53 - Step 3: the selection of covariates

	Covariates	p- values
	X1+X5	-
Step 3	X1	<0.001
	X5	<0.001

Source: Prepared by the statistical specialist.

Table 53 demonstrates that none of these covariates (X1, X5) should be removed from the model since $p\text{-values} < 0.001$. Finally, the covariates excluded in step 1 were considered again to confirm whether any of them should be in the final model. However, none of them caused a significant increase in the LR statistic, i.e., $p\text{-values} > 0.10$. The interactions between the final covariates (X1 and X5) were also not significant.

It is worth noting that before establishing the final model, new explanatory covariates were defined based on the covariates "total professions", "partners/founders" and "members", for instance, PhysiciansPartFound + HealthPartFound, PhysiciansMembers + HealthMembers. The following is an example of the new covariates when considering combinations between two professions in the total team group.

Y1 = PhysiciansTotal + HealthTotal

Y2 = PhysiciansTotal + EngineersTotal

Y3 = PhysiciansTotal + TechnologyTotal

Y4 = PhysiciansTotal + HardsciencesTotal

Y5 = HealthTotal + EngineersTotal

Y6 = HealthTotal + TechnologyTotal

Y7 = HealthTotal + HardsciencesTotal

Y8 = EngineersTotal + TechnologyTotal

Y9 = EngineersTotal + HardsciencesTotal

Y10 = TechnologyTotal + HardsciencesTotal

Other covariates were also considered as the result of combinations of three professions, for instance, PhysiciansTotal + HardSciencesTotal + EngineersTotal.

Exponential models were adjusted with new single covariates (the new covariates total, partners/founders, and members were considered), and the significance of each covariate in the model was assessed applying the LR test. Consequently, Table 54 indicates only the covariates that were significant at the 0.10 significance level.

Table 54 - Significant covariates

Covariates	p- values
Z1	0.040
Z2	0.006
Z3	0.004

Source: Prepared by the statistical specialist.

Where, Z1 = PhysiciansPartFound + EngineersPartFound; Z2 = HealthPartFound + HardsciencesPartFound and Z3 = EngineersPartFound + TechnologyPartFound. To check if these new covariates should be added in the final model, they were adjusted together with covariates X1 and X5 (significant from the first selection of covariates), and then reduced models were adjusted, excluding a single covariate at a time. However, none of the new covariates (Z1, Z2, Z3) caused a significant increase in the LR statistic (see Table 55).

Table 55 - Selection of covariates

Covariates	p- values
X1+X5+Z1+Z2+Z3	-
X5+Z1+Z2+Z3	<0.001
X1+Z1+Z2+Z3	<0.001
X1+X5+Z2+Z3	0.601
X1+X5+Z1+Z3	0.841
X1+X5+Z1+Z2	0.486

Source: Prepared by the statistical specialist.

Hence, in the last step, the effects of covariates Z1, Z2, Z3 were considered individually in conjunction with X1 and X5, to confirm which one should be in the final model. It was noted that when only the covariate $Z2 = \text{HealthPartFound} + \text{HardsciencesPartFound}$ was significant at the 0.05 significance level. Thus, in the final model, the covariates X1, X5, and Z2 were considered.

The covariate `SolutionServiceProduct` (X1) is continuous and assumes values between "0" and "100", i.e., the closer the value is to "0", it indicates that the project solution is more service-oriented. The closer the value is to "100", the project solution is more product-oriented. Additionally, the covariate `ScaleProductionCommercialization` (X5) is dichotomous that assumes the value "1" if the project is in scale production and commercialization phase and "0" otherwise. Finally, the `HealthHardsciencesFound` (Z2) covariate is continuous and indicates the proportion of partners and founders whose profession is the sum of Health and Hard Sciences.

It is noteworthy that all covariates were individually tested. The covariate `ScaleProductionCommercialization` was significant and should be included. If the covariate `ScaleProductionCommercialization` would not be considered, the results were biased, and it did not mean that other covariates would be significant. For instance, an analysis of lung cancer depends on whether the individual smokes or not (KOSHIARIS C. et al., 2017), and suddenly the effect of the covariate `Smoke` is removed. As a result, covariates will appear and might influence but are not significant due to the effect of smoking be removed from the model. Consequently, the results of the analysis will be biased (MEEKER; ESCOBAR, 1998; COLOSIMO; GIOLO, 2006). In sum, it was essential to consider the covariate `ScaleProductionCommercialization`. As previously mentioned, the covariate `ScaleProductionCommercialization` is dichotomous that assumes the value "1" if the project is in scale production and commercialization phase and "0" otherwise. Thus, if it is not necessary to consider such a covariate, assume the value "0".

Table 56 presents the parameter estimates of the exponential regression model.

Table 56 - Parameter estimates of the exponential regression model

	Estimative	Std. Error	p-value
Intercept	5.642	0.706	<0.001
SolutionServiceProduct X1 ($\hat{\beta}_1$)	0.023	0.006	<0.001
ScaleProductionCommercialization X5 ($\hat{\beta}_2$)	-2.318	0.653	<0.001
HealthHardsciencesFound Z2 ($\hat{\beta}_3$)	-1.363	0.641	0.033

Source: Prepared by the statistical specialist.

As indicated in Table 56, note that all covariates are significant at the 0.05 significance level. The interpretation of the estimated parameters for the covariates SolutionServiceProduct, ScaleProductionCommercialization, and HealthHardsciencesFound will be further described in section 4.2.1.5. Previously, the next section describes the residual analysis.

4.2.1.4 Residual analysis

Before interpreting the parameter estimates of the adjusted model, a residual analysis was developed to confirm the model adequacy of the data. If the final exponential model is well adjusted, then the Cox-Snell residuals must follow a standard exponential distribution. Cox-Snell (1968) residuals for the exponential regression model are specified by:

$$\hat{e}_i = t_i \exp\{-x_i' \hat{\beta}\}$$

Thus, if the model is well adjusted, the graph of the survival function of residuals obtained by the Kaplan-Meier estimator versus the survival function obtained by the exponential model should be approximately a straight line. Similarly, the closer these survival curves are, the better it is considered the model fits the data, as demonstrated in Figure 44.

Figure 44 - Survival of Cox-Snell residues estimated by the Kaplan-Meier method and by the standard exponential model (Figure 44.a) and respective estimated survival curves (Figure 44.b)

Source: Prepared by the statistical specialist.

Thus, the graphs presented in Figure 44 indicate that the exponential regression model with covariates was well adjusted to the data.

4.2.1.5 Interpretation of the estimated parameters

The survival function estimated by the exponential regression model for a given company is specified as follows, to calculate the time a company would take to not make its first sale, with specific covariates values X1, X5, Z2.

$$\hat{S}(t|x) = \exp \left\{ - \left(\frac{t}{\exp(5.642 + 0.023 X1 - 2.318 X5 - 1.363 Z2)} \right) \right\}$$

Thus, the following expression may be applied to calculate the median survival time, which in the context would be the median time a given company takes to not make its first sale, according to the covariates.

$$\hat{t}_{0.5} = -\log(0.5) \exp(5.642 + 0.023 X1 - 2.318 X5 - 1.363 Z2)$$

Where $X1$ is the covariate `SolutionServiceProduct`, $X5$, `ScaleProductionCommercialization`, and $Z2$ the covariate `HealthHardsciencesFound`. Note that for $(\hat{\beta}_1)$, the parameter estimate for the `SolutionServiceProduct` covariate is positive (0.023), as demonstrated in Table 56. This parameter indicates that the time it takes for a company not to make its first sale increases as the `SolutionServiceProduct` covariate increases, i.e., companies with lower `SolutionServiceProduct` (more service-oriented projects) make their first sale faster. These findings are in agreement with Cusumano, Kahl and Suarez (2015), since services may assist and accelerate new market entrances and improve competitiveness.

Setting the covariates `ScaleProductionCommercialization` and `HealthHardsciencFound`, $\exp(\hat{\beta}_1) = 1.023$, i.e., with each increase of one unit of the covariate `SolutionServiceProduct` on a logarithmic scale, the median time that a given company takes not to make its first sale increases by 2.3%. Each time `SolutionServiceProduct` increases (more product-oriented solutions), the time for not making the sale increases, i.e., it takes longer to make a sale.

Additionally, note that $(\hat{\beta}_2)$ is negative (-2.318), according to Table 56, indicating that companies with `ScaleProductionCommercialization` "yes" in the project phase take less time not to make their first sale when compared to companies with `ScaleProductionCommercialization` "no" in the project phase, i.e., companies with the covariate `ScaleProductionCommercialization` "yes" in the project phase makes the first sale faster. These findings are in accordance with El-Haik and Mekki (2008) and Pietzsch et al. (2009), considering the product production and distribution to the market.

Setting the covariates `SolutionServiceProduct` and `HealthHardsciencesFound`, the result is as follows.

$$\frac{t_{0.5}(\text{ScaleProductionCommercialization (yes)})}{t_{0.5}(\text{ScaleProductionCommercialization (no)})} = \exp(\hat{\beta}_2) = \exp(-2.318) = 0.098$$

Thus, the median time that a company with `ScaleProductionCommercialization` project phase would take not to make its first sale is approximately 0.098 times the median time it would take the company without `ScaleProductionCommercialization` project phase. For instance, the median time that company with a project "A (`ScaleProductionCommercialization=yes`)" takes is 0.098 median times a company with project "B (`ScaleProductionCommercialization=no`)", assuming `SolutionServiceProduct` and `HealthHardsciencesFound` covariates with the same characteristics.

Figure 45 illustrates the survival curve (survival probability) according to `ScaleProductionCommercialization`, assuming, for instance, `SolutionServiceProduct` equal to 0.0 (more service-oriented project solutions) and `HealthHardsciencesFound` equal to 20%.

Figure 45 - Survival probability according to ScaleProductionCommercialization, assuming SolutionServiceProduct = 0.0 and HealthHardsciencesFound=20%

Source: Prepared by the statistical specialist.

Figure 46 - Survival probability according to ScaleProductionCommercialization and SolutionServiceProduct assuming HealthHardsciencesFound=20%

Source: Prepared by the statistical specialist.

Figure 46 shows the Survival probability according to ScaleProductionCommercialization and SolutionServiceProduct, setting the HealthHardsciencesFound covariate to 20% ($Z_2 = 0.20$). From Figures 45 and 46, it is noted that companies with ScaleProductionCommercialization "yes" in the project phase take less time to make their first sale after receiving their PIPE when compared to companies without ScaleProductionCommercialization in the project phase. Finally, it is observed that companies with less SolutionServiceProduct (more service-oriented project solutions) take less time to make their first sale.

Lastly, $(\hat{\beta}_3)$, the parameter estimate of the covariate HealthHardsciencesFound is negative (-1.363), as indicated in Table 56. This parameter suggests the time that a given company takes not to make its first sale decreases when the sum of the health and hard sciences partners and founders increases, i.e., when there are more professionals in both areas, the first sale is faster. Such findings expanded the existing literature on the fundamental role of physicians and physicians with engineers in developing medical solutions (WHO, 2010; YODA, 2015; SHLUZAS; LEIFER, 2014).

Setting the covariates `ScaleProductionCommercialization` and `SolutionServiceProduct`, $\exp(\hat{\beta}_3) = 0.256$, indicates that with each increase of one unit of the `HealthHardsciencesFound` covariate in the logarithmic scale, the median time that a given company takes not to make its first sale decreases 25.6%, i.e., more professionals in these areas sell faster.

Figure 47 - Survival probability according to `ScaleProductionCommercialization` and `HealthHardsciencesFound` assuming `SolutionServiceProduct=10%`

Source: Prepared by the statistical specialist.

Figure 47 indicates the survival probability, according to `ScaleProductionCommercialization` and `HealthHardsciencesFound`, assuming `SolutionServiceProduct=0.10`. Note that companies with `ScaleProductionCommercialization` "yes" in the project phase take less time to make their first sale after receiving their PIPE when compared to companies without `ScaleProductionCommercialization` in the project phase. In conclusion, it is observed that companies with a greater sum of health and hard sciences partners and founders take less time to make the first sale.

In sum, the results in this section provide empirical and statistical support for H2 (team characteristics), involving health and hard sciences partners and founders exclusively, and H3 (process characteristics), concerning particularly more service or more product solutions, together with the scale production and commercialization project phase. The results do not support H1 (entrepreneurial company characteristics).

4.2.2 IPs, publications, and products launched analysis

This section encompasses the analyses of H1, H2, and H3 of the hypothesized model, including which covariates of entrepreneurial company characteristics, team characteristics, and process characteristics positively influence the response variables total of IPs, publications, and products launched, as shown in Figure 48.

Figure 48 - Covariates and response variables total of IPs, publications, and products launched

Source: Prepared by the author.

The following statistical computing and graphics in the following sections were executed in Minitab software (MINITAB, 2020), considering 79 companies, as there was no presence of negative values. Thus, it was possible to apply statistical techniques of correlation, regression, and chi-square (COLOSIMO; GIOLO, 2006).

4.2.2.1 Correlation analysis

Firstly, correlation analysis was applied to identify the strength of the linear relationship between the total of IPs, publications, and products launched, respectively, together with each covariate aforementioned in Table 47. The results are demonstrated in Table 57, as follows.

Table 57 - Linear relationship between each covariate and response variable
(*insignificant correlation, ***fairly correlation, ***significant correlation)

Covariates	Response variables					
	IPsTotal		PublicationsTotal		ProductsLaunchedTotal	
	Pearson correlation	p-value	Pearson correlation	p-value	Pearson correlation	p-value
PhysiciansTotal	-0.068	0.549	-0.088	0.441	0.152	0.180
HealthTotal	-0.021	0.857	0.122	0.285	-0.163	0.151
EngineersTotal	0.233*	0.039	0.054	0.639	0.091	0.426
TechnologyTotal	-0.059	0.608	-0.053	0.644	0.126	0.270
HardsciencesTotal	-0.179	0.114	-0.065	0.569	-0.017	0.879
OtherTotal	0.143	0.209	-0.088	0.443	-0.098	0.390
PostdocTotal	0.143	0.208	0.058	0.614	-0.094	0.410
PhDTotal	-0.140	0.219	-0.076	0.504	-0.095	0.405
MasterTotal	-0.101	0.375	-0.084	0.463	-0.021	0.855
GraduateTotal	0.105	0.356	0.100	0.379	0.104	0.361
UndergraduateTechnicianTotal	-0.126	0.270	-0.084	0.463	0.180	0.112

continue

continuation

Covariates	Response variables					
	IPsTotal		PublicationsTotal		ProductsLaunchedTotal	
	Pearson correlation	p-value	Pearson correlation	p-value	Pearson correlation	p-value
PhysiciansPartFound	0.067	0.555	-0.054	0.634	0.089	0.435
HealthPartFound	-0.078	0.496	-0.070	0.538	-0.167	0.140
EngineersPartFound	0.144	0.204	0.024	0.834	-0.071	0.533
TechnologyPartFound	-0.016	0.889	-0.024	0.833	-0.011	0.925
HardsciencesPartFound	-0.068	0.552	0.125	0.272	0.226*	0.045
OtherPartFound	-0.056	0.626	-0.062	0.588	-0.069	0.547
PhysiciansMembers	-0.126	0.269	-0.072	0.530	-0.096	0.400
HealthMembers	0.018	0.872	0.128	0.261	-0.118	0.300
EngineersMembers	0.136	0.231	0.036	0.750	0.112	0.324
TechnologyMembers	-0.047	0.683	-0.049	0.668	0.129	0.256
HardsciencesMembers	-0.188	0.096	-0.100	0.381	-0.028	0.808
OtherMembers	0.207	0.067	-0.080	0.481	-0.089	0.436
PostdocPartFound	0.207	0.067	0.066	0.565	0.150	0.187
PhDPartFound	-0.065	0.566	0.098	0.391	-0.047	0.682
MasterPartFound	-0.142	0.211	-0.090	0.430	-0.045	0.695
GraduatePartFound	-0.026	0.819	-0.096	0.400	-0.127	0.265
UndergraduateTechnicianPartFound	-0.060	0.600	-0.033	0.774	0.256*	0.023
PostdocMembers	-0.018	0.872	-0.054	0.638	-0.099	0.387
PhDMembers	-0.100	0.381	-0.073	0.521	-0.136	0.231
MasterMembers	-0.103	0.364	-0.065	0.568	-0.088	0.442
GraduateMembers	0.123	0.281	0.105	0.358	0.118	0.301
UndergraduateTechnicianMembers	-0.115	0.312	-0.062	0.589	0.004	0.975
ANVISAParticipation	0.135	0.236	0.178	0.117	-0.089	0.433
FDAParticipation	0.031	0.785	-0.044	0.700	-0.045	0.696

continue

conclusion

Covariates	Response variables					
	IPsTotal		PublicationsTotal		ProductsLaunchedTotal	
	Pearson correlation	p-value	Pearson correlation	p-value	Pearson correlation	p-value
IPParticipation	0.251*	0.026	0.098	0.389	0.086	0.453
BusinessExperience	0.027	0.812	0.010	0.927	0.136	0.233
HealthCompanyExperience	0.137	0.230	0.069	0.545	-0.123	0.281
TotalPIPEprojects	0.239*	0.034	0.559***	0.000	0.258*	0.022
TotalCollaborativeLocations	0.083	0.465	-0.013	0.911	-0.179	0.115
TotalCollaborativeResources	0.160	0.158	0.251*	0.025	-0.026	0.818
TotalApproaches	0.053	0.645	-0.050	0.661	-0.025	0.826
TotalStakeholders	0.289	0.010	0.167	0.141	0.081	0.477
RegulationPhase	0.373**	0.001	0.224	0.047	-0.053	0.642
ScaleProductionCommercialization	0.321**	0.004	0.237	0.036	0.234	0.038
SolutionSoftwareHardware	0.088	0.517	0.178	0.185	0.202	0.132
SolutionServiceProduct	-0.085	0.458	0.063	0.582	-0.111	0.330
ClinicalChallenge	0.080	0.485	0.145	0.201	0.011	0.925
TechnicalChallenge	0.071	0.531	0.118	0.302	0.159	0.162
CompanyExistedBeforePIPE	0.065	0.572	0.099	0.386	-0.165	0.146

Source: Prepared by the author under the validation of the statistical specialist.

Pearson correlation coefficients are the most used measure of association between two variables. The analyses in Table 57 demonstrates that in most of the cases, there was no linear relationship between variables since $p\text{-value} > 0.05$. Additionally, there were insignificant correlations, such as IPsTotal versus IP Participation, IPs Total versus TotalPIPEprojects, and Products Launched Total versus TotalPIPEprojects. Fairly significant correlations, such as IPsTotal versus ScaleProductionCommercialization, were also computed. However, Publications Total versus TotalPIPEprojects had a strong correlation, indicating that the total of PIPE projects influences the total of publications (WALKER; ALMOND, 2010).

4.2.2.2 Regression analysis

In this section, regression analysis was executed to evaluate the relationship among the total of IPs, publications, and products launched, respectively, together with the covariates aforementioned in Table 47. The results are demonstrated in Table 58, as follows.

Table 58 - Regression analyses among covariates and response variables

**Low value indicates a weak linear fit for the model*

Covariates	Response variables		
	IPsTotal	PublicationsTotal	ProductsLaunchedTotal
PhysiciansTotal HealthTotal EngineersTotal TechnologyTotal HardsciencesTotal OtherTotal	All terms were removed from the model.	All terms were removed from the model.	All terms were removed from the model.
PostdocTotal PhDTotal MasterTotal Bachelor's degreeTotal UndergraduateTechnicianTotal	All terms were removed from the model.	All terms were removed from the model.	All terms were removed from the model.
PhysiciansPartFound HealthPartFound EngineersPartFound TechnologyPartFound HardsciencesPartFound OtherPartFound	All terms were removed from the model.	All terms were removed from the model.	$R\text{-sq}=5.12\%^*$ $R\text{-sq}(adj)=3.88\%^*$
PhysiciansMembers HealthMembers EngineersMembers TechnologyMembers HardsciencesMembers OtherMembers	All terms were removed from the model.	All terms were removed from the model.	All terms were removed from the model.

continue

conclusion

Covariates	Response variables		
	IPsTotal	PublicationsTotal	ProductsLaunched Total
PostdocPartFound PhDPartFound MasterPartFound GraduatePartFound UndergraduateTechnicianPartFound	All terms were removed from the model.	All terms were removed from the model.	$R\text{-sq}=10.07\%^*$ $R\text{-sq}(adj)=5.21\%^*$
PostdocMembers PhDMembers MasterMembers GraduateMembers UndergraduateTechnicianMembers	All terms were removed from the model.	All terms were removed from the model.	All terms were removed from the model.
ANVISAParticipation FDAParticipation IPParticipation BusinessExperience HealthCompanyExperience	$R\text{-sq}=6.28\%^*$ $R\text{-sq}(adj)=5.06\%^*$	All terms were removed from the model.	All terms were removed from the model.
TotalPIPEprojects TotalCollaborativeLocations TotalCollaborativeResources TotalApproaches TotalStakeholders	$R\text{-sq}=12.68\%^*$ $R\text{-sq}(adj)=10.38\%^*$	$R\text{-sq}=31.29\%$ $R\text{-sq}(adj)=30.40\%$	$R\text{-sq}=12.13\%^*$ $R\text{-sq}(adj)=9.82\%^*$
SolutionSoftwareHardware SolutionServiceProduct ClinicalChallenge TechnicalChallenge CompanyExistedBeforePIPE	All terms were removed from the model.	All terms were removed from the model.	$R\text{-sq}=9.03\%^*$ $R\text{-sq}(adj)=5.66\%^*$

Source: Prepared by the author under the validation of the statistical specialist.

The analyses in Table 58 demonstrate that in most of the cases, all terms were removed from the model, and most R-sq and R-sq(adj) low values indicated a weak linear fit for the model. As a final result, the covariate TotalPIPEProjects explains 30.40% of the variation within the data, and it is significant since $p\text{-value} < 0.001$ (CHATTERJEE; HADI, 2012). Lastly, the regression equation is:

$$PublicationsTotal = -7.62 + 5.194 TotalPIPEProjects$$

Setting the variable TotalPIPEProjects = 3, the number of publications is approximately 8. Accordingly, the total of PIPE projects affects the total of publications.

The findings demonstrated that PIPE projects promote publications. In medical innovation, publications may be essential to foster the proposed solution acceptance and dissemination, in line with OECD/Eurostat (2005), Hine and Kapeleris (2006), Schmoch, Rammer and Legler (2006), Terziovski and Morgan (2006), Yock et al. (2015), and Thompson, Ziedonis, and Mowery (2018). The residual analysis was developed to verify the model adequacy, as indicated in Figures 49-50.

Figure 49 - Normal Probability Plot

Source: Prepared by the author under the validation of the statistical specialist.

Figure 50 - Versus Order

Source: Prepared by the author under the validation of the statistical specialist.

The residuals in Figures 49-50 are well-behaved and confirmed the model adequacy of the data. A mere outlier in both Figures 49-50 was due to an established small medical device company with a proportion of 0.25 engineers and 0.75 hard sciences partners and founders, and the proportion of 0.26 engineers and 0.74 health members.

In sum, the results provide empirical and statistical support for H1 (entrepreneurial company characteristics), involving the total of PIPE projects exclusively. The total of PIPE projects affects the total of publications. The results in this section do not support H2 (team characteristics) and H3 (process characteristics).

4.2.3 Chi-square tests of independence

Chi-square tests are versatile and widely used because they may be applied in a wide variety of analyses of categorical data. As a complement, this section applies the standard Pearson chi-square test of independence (WALKER; ALMOND, 2010) to assess the following relationships.

Claim 1: there is a relationship between the clinical challenge and the company profile

H₀: the clinical challenge is independent of the company profile.

H₁: the clinical challenge depends on the company profile.

Table 59 - Clinical challenge chi-square results
Expected values between parenthesis

Company profile	Clinical challenge		Total
	from 0 to 50	from 51 to 100	
Digital health	5 (3.544)	3 (4.456)	8
Medical device	18 (15.506)	17 (19.494)	35
Pharma/biotech	12 (15.949)	24 (20.051)	36
Total	35	44	79
P-value	0.170		

Source: Prepared by the author under the validation of the statistical specialist.

Table 51 provides the contents and expected values between parenthesis. As a result, the $p\text{-value} > 0.05$ and failed to reject H₀, i.e., the clinical challenge, is independent of the company profile. There is not enough evidence to confirm the claim that the clinical challenge and company profile are related.

Claim 2: there is a relationship between the technical challenge and the company profile

H₀: the technical challenge is independent of the company profile.

H₁: the technical challenge depends on the company profile.

Table 60 - Technical challenge chi-square results
Expected values between parenthesis

Company profile	Technical challenge		Total
	from 0 to 50	from 51 to 100	
Digital health	2 (1.316)	6 (6.684)	8
Medical device	6 (5.759)	29 (29.241)	35
Pharma/biotech	5 (5.924)	31 (30.076)	36
Total	13	66	79
P-value	0.737		

Source: Prepared by the author under the validation of the statistical specialist.

Table 60 provides the contents and expected values between parenthesis. As a result, the $p\text{-value} > 0.05$ and failed to reject H_0 , i.e., the technical challenge is independent of the company profile. There is not enough evidence to confirm the claim that the technical challenge and company profile are related.

Claim 3: there is a relationship between a more service or product solution and the company profile

H_0 : the more service or product solution is independent of the company profile.

H_1 : the more service or product solution depends on the company profile.

Table 61 - More service or product solution chi-square results
Expected values between parenthesis

More service or product solution				
Company profile	More service (from 0 to 39)	Service and Product (from 40 to 59)	More product (from 60 to 100)	Total
Digital health	3 (2.228)	3 (1.620)	2 (4.152)	8
Medical device	9 (9.747)	9 (7.089)	17 (18.165)	35
Pharma/biotech	10 (10.025)	4 (7.291)	22 (18.684)	36
Total	22	16	41	79
P-value	0.260			

Source: Prepared by the author under the validation of the statistical specialist.

Table 61 provides the contents and expected values between parenthesis. As a result, the $p\text{-value} > 0.05$ and failed to reject H_0 , i.e., the more service or product solution is independent of the company profile. There is not enough evidence to confirm the claim that the more service or product solution and company profile are related.

Claim 4: there is a relationship between a more software or hardware solution and the company profile

H_0 : the more software or hardware solution is independent of the company profile

H_1 : the more software or hardware solution depends on the company profile

Table 62 - More software or hardware solution chi-square results
Expected values between parenthesis

More software or hardware solution					
Company profile	More software (from 0 to 39)	Software and Hardware (from 40 to 59)	More hardware (from 60 to 100)	Not applicable	Total
Digital health	7 (1.924)	1 (1.114)	0 (2.734)	0 (2.228)	8
Medical device	5 (8.418)	10 (4.873)	20 (11.962)	0 (9.747)	35
Pharma/biotech	7 (8.658)	0 (5.013)	7 (12.304)	22 (10.025)	36
Total	19	11	27	22	79
P-value	<0.001				

Source: Prepared by the author under the validation of the statistical specialist.

Table 62 provides the contents and expected values between parenthesis. As a result, the $p\text{-value} < 0.001$ and reject H_0 , i.e., the more software or hardware solution depends on the company profile. There is enough evidence to confirm the claim that the more software or hardware solution and company profile are related.

Claim 5: there is a relationship between the application of approaches and the company profile

H_0 : the application of approaches is independent of the company profile.

H_1 : the application of approaches depends on the company profile.

Table 63 – Application of approaches chi-square results
Expected values between parenthesis

Application of approaches			
Company profile	Yes	No	Total
Digital health	4 (3.540)	4 (4.460)	8
Medical device	16 (15.510)	19 (19.490)	35
Pharma/biotech	15 (15.950)	21 (20.050)	36
Total	44	35	79
P-value	0.889		

Source: Prepared by the author under the validation of the statistical specialist.

Table 63 provides the contents and expected values between parenthesis. As a result, the $p\text{-value} > 0,05$ and fail to reject H_0 , i.e., the application of approaches is independent of the company profile. There is not enough evidence to confirm the claim that the application of approaches and company profile are related.

The findings show that there is not enough evidence to confirm the previous claims, except claim 4, which points out that the more software or hardware solution and the company profile are related.

5 CONCLUSIONS

The objective of this research was to identify the factors under the medical solution project development that positively influence innovation performance outcomes. Such factors comprehended entrepreneurial health companies, teams, and process characteristics.

Thus, given the specific objectives of this research, a literature review was carried out, obtaining the constructs and the hypothesized model comprising the hypotheses H1, H2, and H3. Hypothesis 1 included the entrepreneurial company characteristics that positively influenced innovation performance outcomes. Hypothesis 2, the team characteristics that positively influenced innovation performance outcomes. Lastly, hypothesis 3, the process characteristics that positively influenced innovation performance outcomes.

Towards empirical data and statistical analyses, a survey research method was applied to researchers of entrepreneurial human health companies with PIPE projects. The results provided empirical and statistical support for H1, H2, H3 regarding specific factors.

The first hypothesis was supported involving the total of PIPE projects exclusively, i.e., the total of PIPE projects affects the total of publications. The second hypothesis was supported, involving the health and hard sciences partners and founders solely. The first sale, i.e., the time to market, is faster when there are more partners and founders in the health and hard sciences areas. The third hypothesis was also supported particularly to more service or more product project solutions, together with scale production and commercialization project phase. Companies with scale and production commercialization project phase take less time to make their first sale after receiving PIPE when compared to companies without scale production and commercialization project phase. Companies with more service-oriented project solutions take less time to make their first sale after receiving the PIPE.

The results also pointed out that the more software or hardware project solution and company profile are related. Besides, the descriptive findings provided insights into the medical innovation setting. As a complement, the main topics and sample findings on

the PIPE process, together with company growth limitations, competitiveness, and team structure, were demonstrated.

In essence, innovative entrepreneurial health companies have been developing solutions that significantly improve human health. Typically, concerning PIPE projects, Phase 1 has an expected duration of nine months and Phase 2 up to 24 months. Notwithstanding, the research findings pointed out an additional interval among PIPE project phases in entrepreneurial health companies. Medical innovation is a lengthy and complicated process, and the transformation of researches into commercial products is time and resource-consuming. From this standpoint, the guidelines and grant duration of health projects should be thoroughly reviewed, including specific requirements according to digital health, medical device, and pharma/biotech domains. Digital health projects have fewer current regulatory hurdles, and development cycles are usually faster than the medical device and pharma/biotech domains. Medical device projects have a variety of requirements and regulatory barriers, leading to longer development cycles. Pharma/biotech projects also have long development cycles and require particular attention to clinical trials and pathways throughout the compound regulatory approval process. It is noteworthy to mention that the research findings also identified that the fact of a company comprised more PIPE projects, from Phase 1 to Phase 3, did not influence the competitive time to market innovation performance outcome.

In conclusion, the whole findings containing in this research promote understanding of essential features and implications for improving medical innovation with positive outcomes. Besides, the results offer a wide variety of perspectives concerning entrepreneurial health companies. Despite the intense competition and challenges in the health sector, the researchers, also entrepreneurs, inspire to transform the pathways in successful medical solutions.

5.1 Theoretical implications

Concerning theoretical implications, the results obtained from the validated model comprising entrepreneurial company, team, and process characteristics, together with innovation performance outcomes, contribute to theory. Additionally, the main

objective, together with the support for hypotheses H1, H2, and H3, considering specific factors, also constitute contributions to the theory.

Besides, the research contributes to the existing literature on medical innovation, which had been based on case studies, and there was a lack of statistical and empirical shreds of evidence. There was limited research on innovation performance outcomes of medical domains (SHLUZAS; LEIFER, 2014), including digital health (SHARMA, 2018), medical device (BEAULIEU; LEHOUX, 2018), and pharmaceutical and biotechnology (EVENS; KAITIN, 2015) entrepreneurial human health companies.

In particular, the research provides statistical evidence on what are the factors under the medical solution project development that positively influence innovation performance outcomes concerning entrepreneurial health companies, teams, and process characteristics. First, FAPESP, together with PIPE projects, stimulate the number of publications. Second, the research also adds to medical innovation literature by presenting the importance of health and hard sciences partners and founders. The findings extend the traditional ones on the essential role of physicians and physicians with engineers in medical innovation teams, as pointed by WHO (2010), Yoda (2015), Shluzas, and Leifer (2014). Lastly, the results enhance the medical innovation literature concerning that more service-oriented project solutions, together with the scale production and commercialization project phase, make the first sale, i.e., the time to market be faster, in agreement with Cusumano, Kahl, and Suarez (2015).

5.2 Managerial implications

Researchers and entrepreneurs have been facing considerable challenges in the current medical sector scenario (DAIM; BREM, 2020), including inadequate health infrastructure, continuous transformations in consumer needs, market expectations, and scientific advances (BROOKS et al., 2012; SZYCHER, 2019). Likewise, chronic diseases require new medical therapies and technologies (BARDRAM; MIHAILIDIS; WAN, 2007). Brazil and most countries have been facing the same set of challenges, together with high health costs (PEINE; MOORS, 2015; YOCK et al., 2015; WHO, 2018).

In this context, the research outcomes provide practical implications for researchers and entrepreneurs. The participation of health and hard sciences partners and

founders in medical project development, together with more service-oriented project solutions and the scale production and commercialization project phase, accelerate the time to market. Thus, investing in such factors may contribute to increasing the innovation performance outcomes, resulting in faster sales, exports, intellectual properties, publications, and product launch, among other aspects. The researchers and entrepreneurs should evaluate and manage the effectiveness of such factors during the project development regarding expectations and interests. Additionally, the results represent the current management practice scenarios, which may assist researchers and entrepreneurs in operating in the complex and dynamic medical innovation setting.

The research presented extensive results that may be applied to improve directions in upcoming research on medical innovation decisions. In sum, the whole findings may be converted into tangible guidelines, tools, and training seminars that will assist medical innovation applicants and provide guidance to further product launch and to improve their decision-making processes concerning innovation.

5.3 Limitations and further research

Although the PIPE program is characterized as the leading funding source of innovation support in Brazil (FALEIROS, 2018; FAPESP BALANCE SHEET, 2020), the research is limited to analyzing entrepreneurial health companies through PIPE projects, comprising the state of São Paulo. Medical innovation has unique features and extensive advancements that may have different outcomes. Consequently, the generalization of the findings to all entrepreneurial health companies ought to be carefully performed. Accordingly, further research on entrepreneurial companies of other domains and regions is suggested. A more in-depth understanding may assist specialists to focus on the assessment of additional specific characteristics and their influence on innovation performance outcomes.

Despite the accurate empirical support for the research results, other potential innovation performance outcome variables demand further studies, such as company growth, which may be measured by the revenue evolution, new employees, business portfolio, and stock turnovers. There may be supplementary measures, such as customers' increase, feedback, and retention. Additionally, more elaborate measures

may be included, such as Return on Investment (ROI) of R&D projects and market share. Due to the opportunities and challenges for medical innovation and other domains, further investigation of innovation performance outcomes on forthcoming innovation progress remains necessary.

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APPENDIX A - Survey questionnaire structure and respective constructs

Constructs	Factors	Survey questions
-	-	Respondent's name
		E-mail
		Position
		Company name
Entrepreneurial company characteristics	Company profile	What is the company's main product/service?
	Company size	What are the number of active partners, founders, and members of the company?
	Company existed before the first PIPE	Did the company exist before the approval of its first (oldest) PIPE project? <i>Yes/No</i>
	Quantity of PIPE projects the company had support in each phase	Select the quantity of PIPE project(s) that the company was supported. <i>Phase 1, Phase 2, Phase 3. Quantity.</i>
	First PIPE date	Select the phase(s) and month/year of the first PIPE project(s) the company had support. <i>Phase 1, Phase 2, Phase 3. Month/Year.</i>
	Collaborative company resources Total of collaborative company resources	In addition to PIPE, select other collaborative company resources. <i>Yes/No</i> <i>Personal funds</i> <i>Angel investors</i> <i>Other funding agencies</i> <i>Universities</i> <i>Hospitals</i> <i>External organizations (not hospitals)</i> <i>Accelerator/Incubator</i> <i>Venture capital</i> <i>Other (specify)</i>
	Collaborative company locations Total of collaborative company locations	Throughout its history, the company has been located in: <i>Yes/No.</i> <i>Technological parks, Incubators, Accelerators. Other (specify).</i>

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Constructs	Factors	Survey questions
Team characteristics		Are there physician(s) among partners, founders, and members? Yes/No. <i>Quantity of physicians partners and founders</i> <i>Quantity of physicians members (non-partners and founders)</i>
	Total of physicians Physicians partners and founders Physicians members	What are the medical specialties and the quantity of physicians in each one (Anesthesiology, Cardiology, Surgery, Medical Clinic, Dermatology, Neurology, Orthopedics and Traumatology, Pulmonology...)?
		Are there health professionals (non-physicians) among partners, founders, and members? Yes/No. <i>Quantity of health professionals partners and founders</i> <i>Quantity of health professionals members (non-partners and founders)</i>
	Total of health professionals Health partners and founders Health members	What are the academic background and the quantity of health professionals in each one (Biology, Nursing, Pharmacy, Dentistry ...)?
		Are there engineers among partners, founders, and members? Yes/No. <i>Quantity of engineers partners and founders</i> <i>Quantity of engineers members (non-partners and founders)</i>
	Total of engineers Engineers partners and founders Engineers members	What are the academic background and the quantity of engineers in each one (Electrical Engineering, Mechanical Engineering, Software Engineering ...)?
		Are there technology professionals (non-engineers) among partners, founders, and members? Yes/No. <i>Quantity of technology professionals partners and founders</i> <i>Quantity of technology professionals members (non-partners and founders)</i>
	Total of technology professionals Technology partners and founders Technology members	What are the academic background and the quantity of technology professionals in each one (Computer Science...)?
		Are there other areas professionals among partners, founders, and members? Yes/No. <i>Quantity of other areas partners and founders</i> <i>Quantity of other areas members (non-partners and founders)</i>
	Other areas professionals* *Including hard sciences professionals (Physics, Medical Physics, Statistics, Mathematics, and Chemistry) Total of other areas professionals Other areas partners and founders Other areas members	What are the academic background and the quantity of other areas professionals in each one (Law, Administration...)?
	Total of hard sciences professionals Hard sciences partners and founders Hard sciences members	

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Constructs	Factors	Survey questions
Team characteristics		Select the number of physicians concerning the educational attainment of the company's partners, founders, and members. <i>Quantity of Postdoc partners and founders physicians</i> <i>Quantity of Ph.D. partners and founders physicians</i> <i>Quantity of Master partners and founders physicians</i> <i>Quantity of Bachelor partners and founders physicians</i> <i>Quantity of Undergraduate or Technician partners and founders physicians</i> <i>Quantity of Postdoc members physicians</i> <i>Quantity of Ph.D. members physicians</i> <i>Quantity of Master members physicians</i> <i>Quantity of Bachelor members physicians</i> <i>Quantity of Undergraduate or Technician members physicians</i>
	Postdoc partners and founders physicians Ph.D. partners and founders physicians Master partners and founders physicians Bachelor partners and founders physicians Undergraduate or Technician partners and founders physicians Postdoc members physicians Ph.D. members physicians Master members physicians Bachelor members physicians Undergraduate or Technician members physicians	Select the number of health professionals (non-physicians) concerning the educational attainment of the company's partners, founders, and members. <i>Quantity of Postdoc partners and founders health professionals</i> <i>Quantity of Ph.D. partners and founders health professionals</i> <i>Quantity of Master partners and founders health professionals</i> <i>Quantity of Bachelor partners and founders health professionals</i> <i>Quantity of Undergraduate or Technician partners and founders health professionals</i> <i>Quantity of Postdoc members health professionals</i> <i>Quantity of Ph.D. members health professionals</i> <i>Quantity of Master members health professionals</i> <i>Quantity of Bachelor members health professionals</i> <i>Quantity of Undergraduate or Technician members health professionals</i>

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Constructs	Factors	Survey questions
Team characteristics		Select the number of engineers concerning the educational attainment of the company's partners, founders, and members.
	Postdoc partners and founders engineers	<i>Quantity of Postdoc partners and founders engineers</i>
	Ph.D. partners and founders engineers	<i>Quantity of Ph.D. partners and founders engineers</i>
	Master partners and founders engineers	<i>Quantity of Master partners and founders engineers</i>
	Bachelor partners and founders engineers	<i>Quantity of Bachelor partners and founders engineers</i>
	Undergraduate or Technician partners and founders engineers	<i>Quantity of Undergraduate or Technician partners and founders engineers</i>
	Postdoc members engineers	<i>Quantity of Postdoc members engineers</i>
	Ph.D. members engineers	<i>Quantity of Ph.D. members engineers</i>
	Master members engineers	<i>Quantity of Master members engineers</i>
	Bachelor members engineers	<i>Quantity of Bachelor members engineers</i>
	Undergraduate or Technician members engineers	<i>Quantity of Undergraduate or Technician members engineers</i>
		Select the number of technology professionals (non-engineers) concerning the educational attainment of the company's partners, founders, and members.
	Postdoc partners and founders technology	<i>Quantity of Postdoc partners and founders technology professionals</i>
	Ph.D. partners and founders technology	<i>Quantity of Ph.D. partners and founders technology professionals</i>
	Master partners and founders technology	<i>Quantity of Master partners and founders technology professionals</i>
	Bachelor partners and founders technology	<i>Quantity of Bachelor partners and founders technology professionals</i>
	Undergraduate or Technician partners and founders technology	<i>Quantity of Undergraduate or Technician partners and founders technology professionals</i>
	Postdoc members technology	<i>Quantity of Postdoc members technology professionals</i>
	Ph.D. members technology	<i>Quantity of Ph.D. members technology professionals</i>
	Master members technology	<i>Quantity of Master members technology professionals</i>
	Bachelor members technology	<i>Quantity of Bachelor members technology professionals</i>
	Undergraduate or Technician members technology	<i>Quantity of Undergraduate or Technician members technology professionals</i>

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continuation

Constructs	Factors	Survey questions
Team characteristics	Postdoc partners and founders other areas Ph.D. partners and founders other areas Master partners and founders other areas Bachelor partners and founders other areas Undergraduate or Technician partners and founders other areas Postdoc members other areas Ph.D. members other areas Master members other areas Bachelor members other areas Undergraduate or Technician members other areas Postdoc partners and founders hard sciences Ph.D. partners and founders hard sciences Master partners and founders hard sciences Bachelor partners and founders hard sciences Undergraduate or Technician partners and founders hard sciences Postdoc members hard sciences Ph.D. members hard sciences Master members hard sciences Bachelor members hard sciences Undergraduate or Technician members hard sciences	Select the number of other areas professionals concerning the educational attainment of the company's founders, partners, and members. <i>Quantity of Postdoc partners and founders other areas professionals</i> <i>Quantity of Ph.D. partners and founders other areas professionals</i> <i>Quantity of Master partners and founders other areas professionals</i> <i>Quantity of Bachelor partners and founders other areas professionals</i> <i>Quantity of Undergraduate or Technician partners and founders other areas professionals</i> <i>Quantity of Postdoc members other areas professionals</i> <i>Quantity of Ph.D. members other areas professionals</i> <i>Quantity of Master members other areas professionals</i> <i>Quantity of Bachelor members other areas professionals</i> <i>Quantity of Undergraduate or Technician members other areas professionals</i>
	ANVISA participation	Have you or any of the partners, founders, and members ever submitted an ANVISA registration request? Yes/No
	FDA participation	Have you or any of the partners, founders, and members ever submitted an FDA registration request? Yes/No
	IP participation	Have you or any of the partners, founders, and members ever participated in any intellectual property registration process? Yes/No
	Business experience	Have you or any of the partners, founders, and members had previous experience (before the PIPE project and the current company) in creating new businesses (startups, small and medium enterprises)? Yes/No
	Health organization experience	Have you or any of the partners, founders, and members had previous experience working in other health organizations before the current company? Yes/No

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continuation

Constructs	Factors	Survey questions
Process characteristics	ANVISA medical device classification	Select the ANVISA classification of the medical solution developed (or under development) in the project. <i>Class I - low risk</i> <i>Class II - medium risk</i> <i>Class III - high risk</i> <i>Class IV - maximum risk</i> <i>Not applicable</i>
	FDA medical device classification	Select the FDA classification of the medical solution developed (or under development) in the project. <i>Class I - low to moderate risk</i> <i>Class II - moderate to high risk</i> <i>Class III - high risk</i> <i>Not applicable</i>
	Regulation phase	Select the current phase of the medical solution regulation process developed (or under development) in the project. <i>Submission preparation</i> <i>Pre-market evaluation submission (classification, safety, and performance principles)</i> <i>Regulatory agency approval</i> <i>Post-marketing surveillance (notifications and reports)</i> <i>No phase</i>
	Embedded software medical solution	Is there any embedded software in the medical solution developed (or under development) in the project? <i>Yes/No</i>
	Software/hardware medical solution	Is the medical solution developed (or under development) in the project more associated with the software or hardware? <i>From 0 to 100, where 0 = more software solution and 100 = more hardware solution</i>
	Service/product medical solution	Is the medical solution developed (or under development) in the project more associated with the service or product? <i>From 0 to 100, where 0 = more service solution and 100 = more product solution</i>
	Approaches Total of approaches	Was (or is) there an intentional application of any of the following project development approaches? <i>Biodesign</i> <i>Design Thinking</i> <i>Stage-gate</i> <i>Design for Six Sigma</i> <i>Scrum</i> <i>Customer Development</i> <i>None</i> <i>Other (specify)</i>

continue

continuation

Constructs	Factors	Survey questions
Process characteristics		Select the stakeholders involved in project development. <i>Yes/No</i> <i>Universities</i> <i>Hospitals</i> <i>Government entities</i> <i>Health organizations</i> <i>Others (specify)</i>
	Stakeholders Total of stakeholders	
		Select the completed phase(s) of the medical solution development process during PIPE. <i>Yes/No</i> <i>Concept generation</i> <i>Prototyping</i> <i>Technical feasibility</i> <i>Clinical feasibility</i> <i>Intellectual property registration</i> <i>Regulation</i> <i>Business model definition</i> <i>Marketing and sales strategy definition</i> <i>Scale production/commercialization</i> <i>Other phases (specify)</i>
	Project phases	
	Clinical challenge	Select the clinical challenge degree (understanding the disease, physical contact of the solution with the patient, ethical constraints for clinical testing) for the solution development. <i>From 0 to 100, where 0 = none and 100 = very high.</i>
	Technical challenge	Select the technical challenge degree (development, deadlines, technology, cost) for solution development. <i>From 0 to 100, where 0 = none and 100 = very high</i>
Innovation performance outcomes		Select the month/year of the first sale of the medical solution developed in the project. <i>Month/Year</i> <i>To be performed</i>
	First sale date Time to market (first sale date - first PIPE date) Increased sales	Select the year(s) in which the project led to increased sales in the company. <i>Yes/No/Not applicable (ongoing project)</i> <i>1st year, 2nd year, 3rd year, 4th year, 5th year, Other years</i>

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continuation

Constructs	Factors	Survey questions
Innovation performance outcomes	First export date Increased exports	Select the month/year of the first export of the medical solution developed in the project. <i>Month/Year/To be performed</i> Select the year(s) in which the project led to increased exports in the company. <i>Yes/No/Not applicable (ongoing project)</i> <i>1st year, 2nd year, 3rd year, 4th year, 5th year, Other years</i>
	Total of ANVISA registers First ANVISA date Total of FDA registers First FDA date	Select the number of registers approved by ANVISA, FDA, and the month/year of the 1st register of the medical solution developed in the oldest PIPE project. <i>ANVISA, Number of registers, 1st register Month/Year</i> <i>FDA, Number of registers, 1st register Month/Year</i>
	Total of intellectual properties	Select the number of intellectual properties resulting from the medical solution developed in the oldest PIPE project.
	Total of publications	Select the number of publications resulting from the solution developed from the oldest PIPE project.
	Total of products launched	Select the number of products launched on the market from the core technology developed in the oldest PIPE project.

continue

conclusion

Open-ended questions		
Constructs	Factors	Survey questions
Process characteristics	PIPE experiences	Tell me about the experiences in the PIPE project development.
	PIPE improvements	What suggestions do you have to improve the PIPE?
Entrepreneurial company characteristics	Company growth	What are the factors that limit the fastest growth of the company?
	Competitive advantage	What makes the solution developed in the project have a competitive advantage?
	Supplies	Are there supplies available for the project solution development?
	Competitors	Where are the competitors of the solution developed in the project?
	Distribution channels	What are the distribution channels of the solution developed in the project?
Team characteristics	Motivation	What motivates the partners, founders, and members?
	Structure	How does the company plan to structure the team over the next twelve months?

Source: Prepared by the author.