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SCUOLA DI INGEGNERIA INDUSTRIALE
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EXECUTIVE SUMMARY OF THE THESIS

What drives patients' acceptance of Digital Therapeutics?

The interplay between rational and institutional factors

TESI MAGISTRALE IN MANAGEMENT ENGINEERING – INGEGNERIA GESTIONALE

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1. Contextualization and purpose of the study

In Italy, data from 2020 show that 40.9% of the population suffers from at least one chronic disease. This trend goes together with the aging of the population, which will lead the 28% of the worldwide population being aged over65 and Italy is profoundly affected by this trend as the median age of the Italian population is the highest among all the countries in Europe, being recorded at 47.2 years.

Older people are more likely to experience poorer health conditions and chronic diseases than younger population. In Italy, around 59% of the population aged over80 years suffers from one severe chronic disease while around 64% suffers from at least three chronic conditions or comorbidities. Of the various chronic conditions that worsen with the aging of patients, the diffusion of obesity is growing, even among the youngest. In Italy, indeed, 35.5% of the population aged 18 years and older is overweight, while 10.4% is obese, profoundly impacting the healthcare expenditure as the cost for an obese patient can be up to 50% higher than one with a normal weight. In this scenario of rising expenses, also the technological aspect is playing its role. Various types of technologies might allow physicians to better manage the patients, improve diagnoses and prolong patients' life in a cost-effective way. Additionally, patients can dramatically improve their care pathways, ultimately enhancing the quality of their lives.

Indeed, World Health Organization recognized the potential of digital transformation to foster health outcomes worldwide and is working to deploy strategies to unlock these benefits.

In this framework, Digital Therapeutics is raising attention as they deliver evidence-based therapeutic interventions to prevent, manage and treat a chronic disease or disorder with cost-effective advantages [1]. For these reasons, they represent important support for current therapies, including obesity.

The scope of this dissertation is to design and test a theoretical model that could describe the behaviors determining the diffusion of the DTx, with a specific reference to a DTx for obesity, by

collaborating in the hospital setting of Istituto Auxologico.

2. Extant studies

Part of this dissertation was dedicated to the exploration of past studies and research on the diffusion of technologies in healthcare. Specifically, it was noted that just a minor part of the research focused on diffusion. Rather, as the diffusion results from the adoption of technology from a social system, most of the academic literature focuses on the adoption from the individual perspectives, exploring the phenomenon with diverse models that have very different if not even contrasting hypotheses [2].

Specifically, part of the literature explores general barriers and drivers of the adoption process. The main barriers can be classified as follows:

- *Technological barriers* are related to the technological limitation and characteristics such as the user interface and system security.
- *Funding and economic barriers* related to the deployment of a large amount of money not only for the initial investment but also for maintenance.
- *Social barriers* related to the interaction with the patients, their worries about the new technology, like the privacy of data.
- *Organizational barriers* rises when the implementation of the technology is non consistent with the organizations' objective.
- *Digital abilities barrier* as the lack of digital skills and proficiency in computer usage by professionals.

Instead, the most recurrent drivers encompass:

- *Financial dimension* for the impact on the efficiency and the chance to enter in subsidies from the government.
- *The technological dimension* creates opportunities to foster technological literacy and simplify activities and processes.
- *User-centric dimension* by enhancing human life, and often turn for collaborative solutions.

The second cluster of the extant literature has focused on studying the adoption and diffusion through theoretically based models.

One of the most diffused models is the Technology Acceptance Model (TAM) (Davis, 1989), which aims to analyze how external variables influence an individual's beliefs, attitudes, and intentions. The basic concept of TAM is that the individual carries out a rational process on the benefits and costs of adopting a technology. According to the model, the rational process is based on two predictors for adoption: Perceived Usefulness (PU) and Perceived Ease of Use (PEOU).
PU is defined as "the degree to which a person believes that using a particular system would enhance his or her job performance" (Davis, 1989). PEOU refers to "the degree to which a person believes that using a particular system would be free of effort" (Davis, 1989). The two variables predict the usage intention and, consequently, of the usage behavior.
TAM has been widely deployed in the healthcare field, together with its extended versions. For instance, some extended versions included the social influence with constructs like subjective norm, voluntariness, and image. Specifically, subjective norm represents the influence that significant people exercise on the individual who should engage a specific behavior.

On the other hand, some researchers have adopted an alternative perspective by seeing actions as a result of irrationalities coming from the institutional environment. For instance, researchers have studied the effects of institutional pressures on electronic health records (EHR) in the hospitalized setting.
Specifically, in this optic, individuals' behavior is influenced and constrained over time by institutions, which are social structures built over cultural-cognitive, regulative and normative pillars Scott (2001). More specifically, the pillars are described as follows.

- *The regulative pillar* is based on the coercion institutions can exert to constrain and regulate the actors' behavior, through proof of strength and raising fear of sanction.
- *The normative pillar* exploits the values and the norms to create social obligations.
- *The cultural-cognitive pillar* exploits imitation in environments with high uncertainty.

3. Research model

In recent years, the institutional theory included the importance of a degree or rational behavior while TAM included the importance of the social

norm, yet there is not a strong integration of the two theories in the past literature. The developed research model aims to investigate the interplay between the organizational and individual mechanisms which could influence the continued use of digital therapeutics among obese patients.
The three constructs introduced in the model coming from the TAM are the ones formerly introduced by Davis in 1989. These constructs are retrieved from the theoretical background: Intention To Use, Perceived Usefulness, and Ease Of Use.
For what concerns the institutional factors, Scott (2001) conceived institutions as made of pillars limiting the rational assessment and directing actors' behavior. These are regulative, normative, and cultural pillars, which in turn can be exploited by the organizations to exert the following influences, which are also the institutional factors in the proposed model.

Once defined the constructs, the configuration of the model was formalized with the support of existing studies, therefore the following hypotheses were stated as follows.

The basic relations of TAM were included. Specifically, the first two hypotheses test the positive influence of PU and PEOU on ITU. Also, the hypothesized positive effect of the PEOU on PU was included.

Additionally, six other positive influences were tested. Regulative Influence is expected to impact PU by stimulating how individuals perceive the benefits [2] but also on PEOU as rules can be felt as guidelines for the usage.
The normative pillar can influence PU through peer influence, as by seeing peers using technology and exploiting the benefits, one can think to have similar results [2]. Similar pressure can work on the PEOU, by leveraging on peer experience.
The positive cultural change can influence PEOU by fostering the disposition of individuals toward the new technology and the challenges arising from it. Similarly, it could be relevant to explore if the positive cultural change could be also influential on the disposition of individuals to feel that the technology is appropriate and useful (PU).
From the literature and considering the context, ten control variables were included in the model to see if the intention to use was influenced. These variables are gender, age, marital status, BMI, level of education, employment, difficulties in maintaining weight loss, ease of use digital solution, willingness to change and to be supported.

4. Materials and Methods

To test the proposed research model, a questionnaire was developed to collect data, that were eventually analyzed.

The survey included a section dedicated to collecting general information on respondents, as personal and demographic data, but also investigated the health status, the social and familiar context, their satisfaction for past cares and follow-ups, and their usage of technology. The second part, instead, measured the constructs present in the research model through items retrieved from the literature. The questionnaire aimed at exploring the adoption among obese patients, and therefore it was delivered to patients receiving obese treatments inside Auxologico. Specifically, it was delivered in two ways. A first paper-based version was distributed to individuals who were receiving inpatient treatments inside the hospitals of Auxologico. The second online version, instead, was delivered by Qualtrics to a 3.7k mail database of patients and former patients of Auxologico.
Once collected, the data were analyzed. Firstly, a qualitative analysis was performed on the questions about personal information. Secondly, a quantitative approach was applied to test the model through the software STATA 17. Specifically, a first Kaiser-Meyer-Olkin (KMO) test was applied to verify the sample adequacy for the factor analysis. Subsequently, for a first evaluation of the items measuring contracts, an Exploratory Factor Analysis (EFA) was carried out through the Principal Component Methodology, together with the Cronbach's alpha to test the internal consistency reliability. The testing of the model went through Structural Equation Modeling (SEM). The validity and consistency of the method to measure the constructs were assessed through the Confirmatory Factor Analysis (CFA). The convergence validity was assessed by two indicators: composite reliability and average variance extracted.

Lastly, the goodness of fit was proved by means of four indictors, both absolute like the square error of approximation (RMSEA) and the standardized root mean residual (SRMR), and incremental like comparative fit index (CFI) and the Tucker-Lewis index (TLI).

5. Descriptive Analysis

Respondents were 71% mainly female, and around 60% of respondents are aged between 51 and 70 years old. When looking for patients undergoing obesity treatment, most of the respondents are in a situation of moderate or severe obesity (BMI among 31-50). The school level and employment of respondents are in line with the general situation in Italy. Their digital proficiency can be positively evaluated as around 45% of the respondents can easily use the smartphone and a similar proportion use digital solutions to manage their health, representing a strong possibility to use this new tool of a DTx.

6. Results

The quantitative analysis started with the KMO test, showing that the factor analysis was worth it. Both EFA and CFA confirmed the validity of the relation between items and latent variables. Subsequently, the SEM validated the model applied. Specifically, the relation between the PU and ITU, and between PEOU and PU were confirmed, while the one between PEOU and ITU was found to be not significant. NP had a significant impact on PU, but not on PEOU, while RP positively affected both PU and PEOU. No control variables had a significant relation with the Intention to Use. Instead, CP positively influenced PEOU but was not significant on PU. All the goodness of fit indexes were shown to be inside the acceptability threshold, as presented in Table 1.

Indicator	Threshold	Value
RMSEA	< 0.08	0.046
SRMR	< 0.08	0.044
CFI	> 0.9	0.961
TLI	> 0.9	0.956

Table 1: Goodness of Fit indexes

7. Theoretical and managerial contribution

The main theoretical contribution comes from the fact that to the best of the authors' knowledge, the application of theoretical models to study the acceptance of DTx is not recurrent, also considering the innovativeness of the product. Additionally, the novel combination of two different frameworks, namely TAM and Institutional Theory, provides an original contribution. It has been proved how the institutional factors influence TAM constructs. The regulatory factor, indeed, contributes to the technology's PU on the one hand, while simultaneously making it appear easier to use on the other. Peer influence represents a great source of confidence for the patient when dealing with a new treatment fostering the PU. In the scenario, where DTx becomes a "habit" or "ritual" through the positive cultural change, it will become simple to utilize and approach (PEOU).

The interpretation of the results made it also possible to deduce some insightful managerial considerations. The fact that the DTx is easy to use does not directly affect Intention to Use. The PEOU, on the other hand, might be viewed as an added benefit that contributes to a higher PU. Auxologico should then focus on this last one by increasing the adoption of the technology: clear and effective communication for all the DTx benefits should be provided. Additionally, training, or external support may be recommended to break down the barrier of unfamiliarity with digital solutions.

The regulatory factor, in particular, has a positive impact on both PU and PEOU. As a result, the institution can encourage the patient to use the DTx both by leveraging on the perceived usefulness and by creating rules which works as guides. Indeed, the institution should establish a set of laws and regulations to safeguard patients while let them will feel guided during the application.

In addition, since peer influence impacts PU, one approach could be to form a community among Auxologico patients who are planning to adopt or have adopted DTx. The consequences are favorable since, on the one hand, collected feedbacks serve the patients to compare

themselves with peers, but it is also beneficial to the hospital in terms of continuous improvement.
Finally, the Cultural Pillar embedded in the organization has a good impact on PEOU. The key point is to make DTx "ordinary" and "familiar" for the patient so that they can be seen as simple as possible. Digital Therapeutics should not be viewed as a niche or experimental treatment for a selected few. Instead, DTx must be open to everybody, adaptable to each condition, and expandable over time, so that the patient perceives it as basic and easy to use.

8. Limitation of the study

The findings also revealed some weaknesses in the research. Firstly, the main constraint is due to the features of the sample examined. Indeed, only 341 answers were collected, and further research to widen the sample could be suggested. Another problem is related to the statistical sample characteristics. In Italy, obesity is more common among males than women. In fact, men represent the majority in the case of both overweight (44% vs. 27.3%) and obesity (10.8% vs. 9%). Among obese patients responding to the survey, about 70% were women.

Future studies can be conducted based on the gaps identified because of this work, with the goal of ongoing development. Firstly, the collaboration with the Auxologico revealed the need to collect opinions also from physicians. An additional step could be to administer a questionnaire dedicated to the doctors and repeat the analysis assuming a different perspective.
Furthermore, a possible future study can be made by paying more attention to patients over the age of 70 (only 10% in the current study), since they show the most resistance to the use of DTx due to a lack of experience with digital solutions.

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9. Acknowledgements

We would like to express our gratitude to our supervisor, Emanuele Lettieri, for the great motivation he transmitted us during this dissertation. He shared with us his invaluable experience, guiding us to shape this work in such a fascinating and stimulating topic. His passion and enthusiasm supported and inspired us continuously.

A special recognition goes to our co-supervisor, Alessandro Carrera. We are thankful for his immense availability throughout this journey and his professionalism which is a great example for us. Thanks also for the moral support, which by his calm allowed us to find back the route of our work when we were concerned and anxious.

We want to thank Emanuele Fresa, who allowed us to create such work, by giving us his complete availability and giving us the chance to work with such an important and prestigious institution. He challenged us by asking ever ending new questions that allowed us to think out of the scheme.

We want to thank all the other people which helped us in carrying out this thesis and to face the numerous problems that arose.

Finally, thanks to our family and friends, who have always believed in us and never missed an opportunity to encourage and motivate us.

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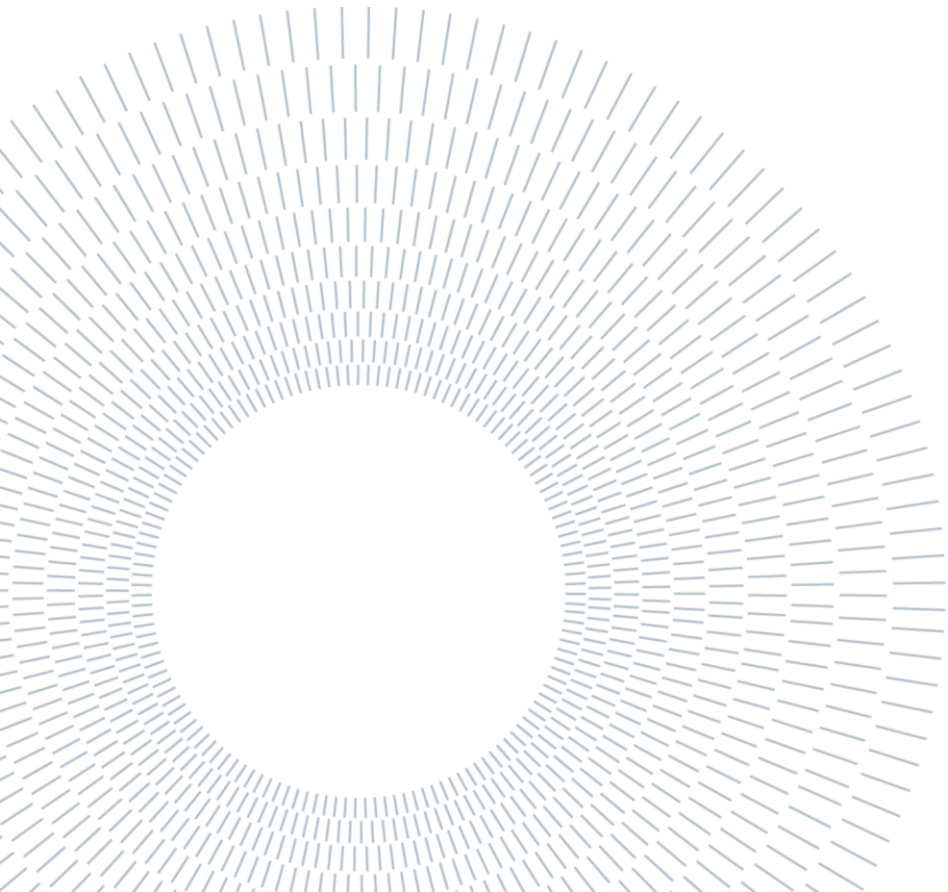

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Abstract

The rising incidence of chronic diseases among the population, considering besides the aging of the population, is an urgent challenge for the healthcare systems worldwide. The emergence of Digital Therapeutics (DTx), able to deliver evidence-based treatments to manage and treat diseases cost-effectively, open new opportunities. However, their diffusion and usage are still fragmented.
As the diffusion results from the adoption of technology from a social system and the individual acceptance, this study aims to design and test a theoretical model that investigate the intention to use DTx, with a particular focus on the treatment of obesity, as widespread and burdensome chronic condition. This research is built on a combination of organizational mechanisms, derived from Institutional Theory, and rational factors, derived from Technology Acceptance Model, that may influence the DTx usage.
The model was tested though a survey, available in both paper and digital version, which was delivered to patients and former patients of Istituto Auxologico Italiano, a healthcare facility based in Lombardy with a focus on the treatment of obesity.
The hypothesized relationships among constructs were tested and the results interpreted using the Structural Equation Modelling (SEM) technique.
The analyses confirmed the influence of Perceived Usefulness on Intention To Use, and of Perceived Ease Of Use on Perceived Usefulness, confirming the validity of the assumptions derived from TAM. On the other hand, institutional factors were introduced as antecedents of Perceived Usefulness and Perceived Ease Of Use. The results show that the Regulative Pillar influences both TAM constructs, the Normative Pillar (peer influence) has a positive effect only on Perceived Usefulness and finally, the Cultural Pillar impacts on Perceived Ease Of Use. The results contributed from a theoretical as well as a managerial point of view. In fact, the findings were operationalized into practical advice to foster the adoption and thus diffusion of Digital Therapeutics. Lastly, the gaps and open questions that emerged from this study made it possible to provide proposals for future investigations.

Keywords: Diffusion, healthcare, Digital Therapeutics, adoption, TAM, Institutional Theory

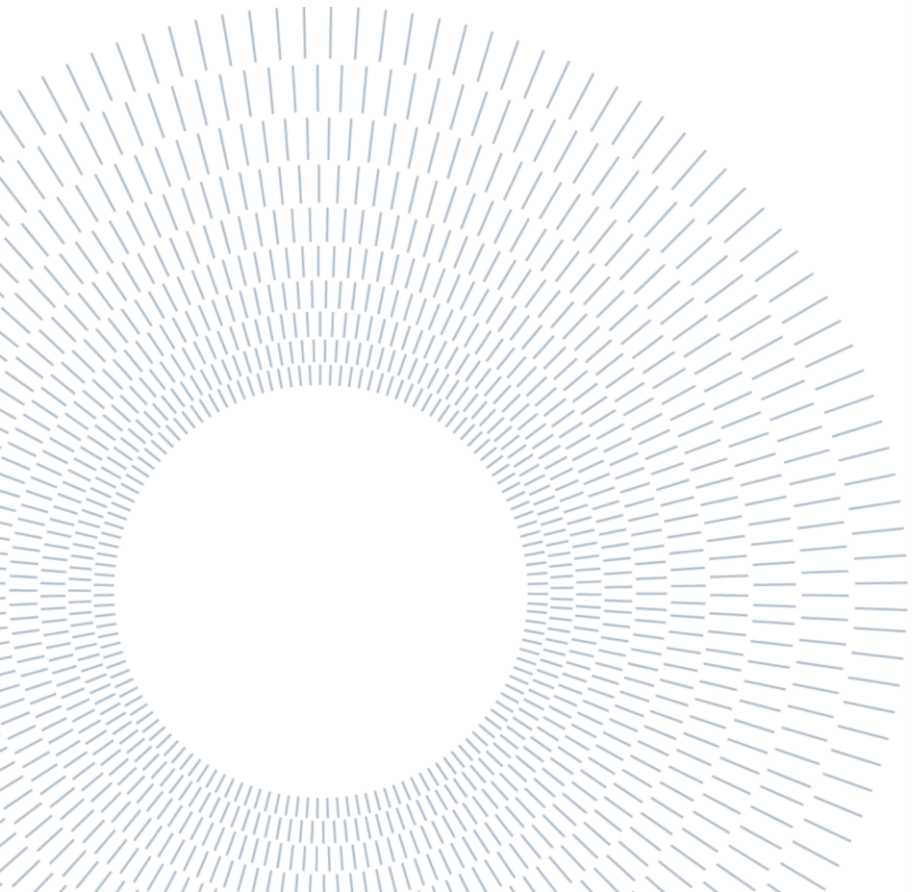
Abstract in lingua italiana

La crescente incidenza di malattie croniche nella popolazione è un fenomeno strettamente legato al suo invecchiamento, e crea un'importante sfida per i sistemi sanitari in termini di spesa. Le terapie digitali sono in grado di esercitare un trattamento basato su evidenze per trattare e curare in modo efficace diverse malattie, specialmente quelle croniche.

Poiché la diffusione è un risultato dell'adozione da un sistema sociale e dall'accettazione individuale, questo studio mira a progettare e testare un modello teorico che esamini l'intenzione di utilizzare una DTx, facendo riferimento a una sviluppata per l'obesità. Questo modello di ricerca è costruito su una combinazione di meccanismi organizzativi, derivati dalla Teoria Istituzionale, e fattori razionali, derivati dal Technology Acceptance Model, che possono influenzare l'uso delle DTx.

Il modello è stato testato attraverso un questionario, disponibile sia in versione cartacea che digitale, che è stato consegnato a pazienti ed ex pazienti dell'Istituto Auxologico Italiano, che ha sede in Lombardia e specializzato sul trattamento dell'obesità. Le relazioni ipotizzate tra i costrutti sono state testate e i risultati sono stati interpretati utilizzando la tecnica Structural Equation Modelling (SEM). Le analisi hanno confermato l'influenza della Perceived Usefulness sull'Intention To Use, e della Perceived Ease Of Use sulla Perceived Usefulness, confermando la validità delle ipotesi derivate dalla TAM. D'altra parte, i fattori istituzionali sono stati introdotti come antecedenti della Perceived Usefulness e della Perceived Ease Of Use. I risultati mostrano che il Regulative Pillar influenza entrambi i costrutti TAM, il Normative Pillar (influenza dei pari) ha un effetto positivo solo sulla Perceived Usefulness e, infine, il Cultural Pillar ha un impatto sulla Perceived Ease Of Use. I risultati hanno contribuito sia da un punto di vista teorico che manageriale. Infatti, sono stati tradotti in consigli pratici per favorire l'adozione e quindi la diffusione della Terapia Digitale. Infine, le lacune e le domande aperte emerse da questo studio hanno permesso di fornire proposte per indagini future.

Parole chiave: diffusione, adozione sanità, terapie digitali, TAM, teoria istituzionale



Contents

Introduction

The health context

An important indicator for the health status of the population in a country is the incidence of chronic diseases. In Italy, data from 2020 show that 40.9% of the population suffers from at least one chronic disease (ISTAT, 2020). This frequency rises with the aging of the population which is, in turn, generated from two main trends.

On the one side, in the last 20 years, life expectancy experienced growth by more than 6 years, reaching 73.4 years worldwide in 2019 (WHO, 2019). On the other side, in the member countries of the Organization for Economic Co-operation and Development (OECD), this major trend was associated with a decrease in the fertility rate (OECD, 2017). Therefore, while in 1960, people aged over65 years old represented 9% of the overall population, this figure is expected to reach 28% by 2050 (OECD, 2017). In particular, Italy is profoundly affected by this trend as the median age of the Italian population is the highest among all the countries in Europe, being recorded at 47.2 years (EuroStat, 2021). This means that there is the same number of people aged below 47.2 and over.

Among older people, poorer health conditions and chronic diseases are more frequently reported than among the younger population. In Italy, around 59% of the population aged 80 years and over suffers from one severe chronic disease while around 64% suffers from at least three chronic conditions or comorbidities (ISTAT, 2015). Among the several chronic conditions that worsen with the aging of patients, the diffusion of obesity is growing. In Italy, 35.5% of the population aged 18 years and older is overweight, while 10.4% is obese (ISTAT, 2020).

Generally, these trends have driven the rise of healthcare expenditures. Over the years 2000-2015, the growth of the GDP in the OECD countries has been around 2.3% and was outpaced by the health expenditure growth of 3% (OECD, 2019). Therefore,

healthcare expenditures are accounting for an ever-increasing proportion of the GDP mildly rising from 8.8% in 2015 to 10.2% expected in 2030, as shown in Figure 0.1.

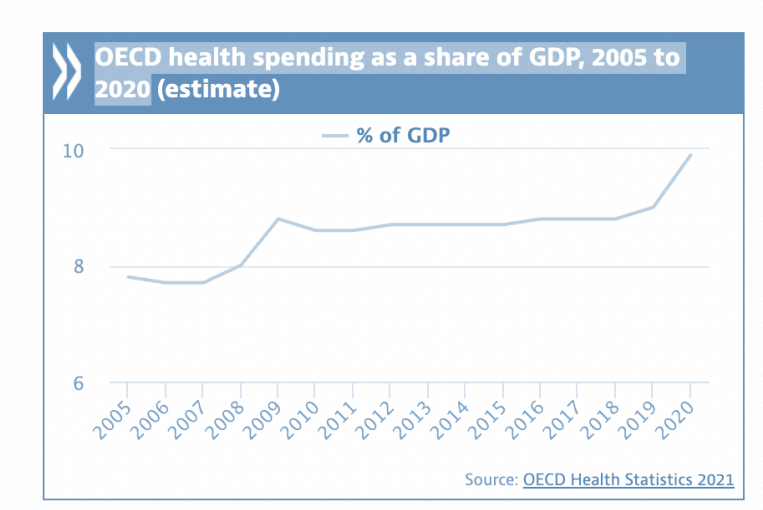


Figure 0.1: Health Spending as a share of GDP

To mention some data about how chronic conditions affect healthcare expenditures, the cost for an obese patient can be up to 50% higher than to one with a normal weight (Obesity Report, 2019). In Italy, the national healthcare system is funded through taxes by all citizens, thus just low fares should be paid when accessing a health service. Nonetheless, the resources paid directly by the citizens and not covered by the national healthcare system, the so-called out-of-pocket resources, stand for a very relevant proportion of the overall healthcare expenditure, facing a slight growth over the last years (Statista, 2019), as it is shown in Figure 0.2.

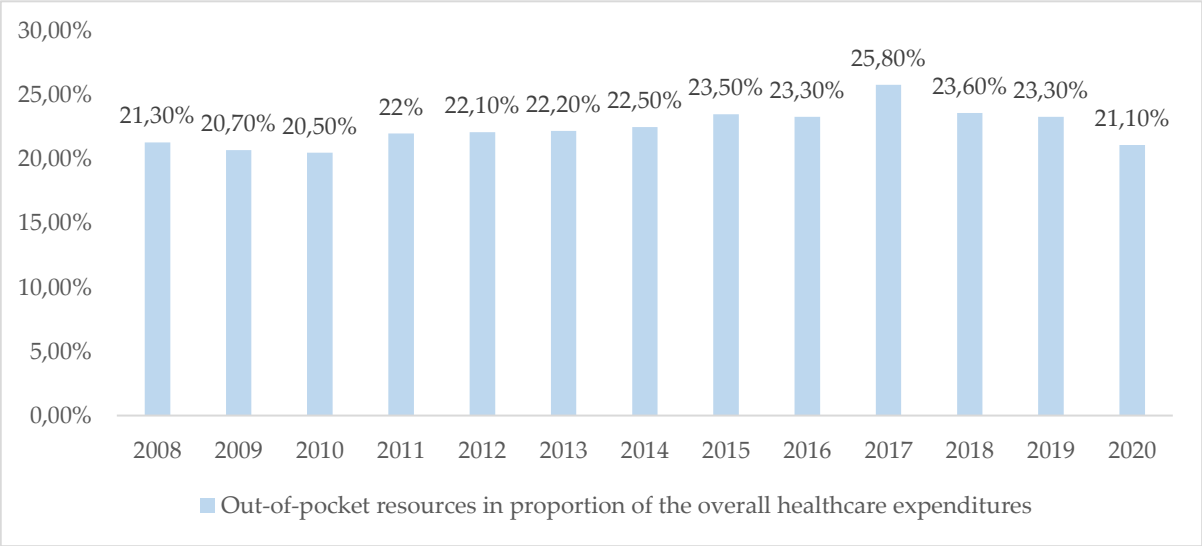


Figure 0.2: Out-of-pocket resources as a share of healthcare expenditures

These out-of-pocket expenses can negatively affect the ease of accessibility and continuity of care, as in 2019 the 10.2% of the over65 in Italy had to renounce to at least one health service for financial constraints (ISTAT, 2021).

In this general scenario of rising expenses, also the technological aspect is playing its role. Various types of technologies might allow physicians to better manage the patient, improve diagnoses and prolong patients' life. Contrastingly, the investments in these technologies are also an important driver of healthcare expenditures (OECD, 2019). To face these challenges, it is particularly relevant focusing on maximizing the value. The concept of value in healthcare is conceived as the outcomes that matter to the patient relative to the costs of achieving those outcomes (Porter and Lee, 2013). Thus, a higher value means improving the healthcare outcomes without raising costs or reaching the same outcome with lower costs (Porter and Lee, 2013). Cost-effective solutions are looked for, and they are stemming from the digital world.

The digitization of healthcare

In the last decades, the process of digitization has drastically changed the way people live and behave. As nearly 4.9 billion people can access the Internet daily[1], digital technologies are increasingly becoming indispensable in everyday life and the business models that are enabled by them are transforming multiple industries, including healthcare. Anyway, the digital transformation is happening more slowly for the healthcare sector. Although different authors might disagree on the underlying reasons for this delay, it is widely recognized that healthcare has been slow in exploiting the opportunities opened by digital transformation (Hermes et al., 2020). Just to mention one example, telemedicine has been mentioned in literature for the first time in 1969 by Raymond Murphy (Bashshur and Shannon, 2009), and only in 2020 it was widely used – in April 2020 it was used 78 times than in Feb 2020 –, with the Covid-19 pandemic as a major driver[2]. The World Health Organization recognized the potential of digital transformation to foster health outcomes worldwide and is working to deploy strategies to unlock these benefits (WHO, 2021).

The digitization of healthcare has introduced a wide variety of terms to indicate transformations and technology at different levels, although these terms are often used

[1] https://datareportal.com/global-digital-overview

[2] https://www.mckinsey.com/industries/healthcare-systems-and-services/our-insights/telehealth-a-quarter-trillion-dollar-post-covid-19-reality#:~:text=Early%20in%20the%20COVID%2D19,February%202020%20(Exhibit%201)

as synonyms or with overlapping meanings. Notwithstanding, there are some key differences in the definitions, and it is particularly important to explore the most diffused taxonomies to understand the potentialities and challenges of the various technologies. Indeed, two main frameworks introduce the most common terms, and both see digital health technologies as the most overarching term.

The term **Digital Health** includes *technologies, platforms, and systems that engage consumers in lifestyles, well-being, and wellness and health-related purposes, which serve to capture, store or transmit health data and/or support life sciences and clinical activities* (Goldsack, 2019). Recently, this term was specified as encompassing eHealth and all the other emerging fields, such as big data, genomics, and artificial intelligence[3].

Digital technologies represent a chance to improve accessibility and continuity, as well as affordability of care (WHO, 2018). Nevertheless, these technologies do not require any type of clinical evidence of efficacy and approval by regulatory agencies as they are not classified as medical devices (Verna et al. 2020).

The growing importance of digital health is represented by the continuous growth of investment year after year that reached the maximum of 24$ billion investments in 2020 or by the number of digital health apps introduced in the digital stores, with an average of 251 apps per day (IQVIA, 2021). The trend is shown in Figure 0.3.

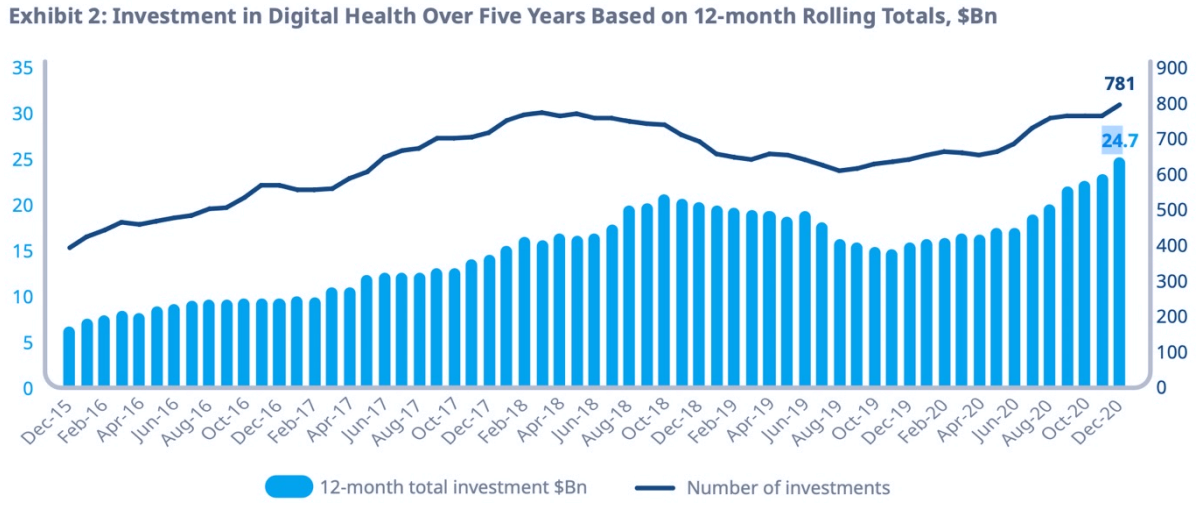


Figure 0.3: Investments in digital health

[3] https://www.ncbi.nlm.nih.gov/books/NBK541905/

Among these Apps, two macro-categories can be identified:

1) Wellness Management aims at tracking fitness behaviors, lifestyle, stress and diet.

2) Health Condition Management aims at facilitating the collection of information about the disease, the access to care and support the treatment, i.e., medication reminders. The majority of these apps focus on treatments dedicated to chronic disease as mental health and behavioral disorders.

First taxonomy

The first taxonomy (WHO) includes as a subset of digital health the category **eHealth**, which refers to the concept of applying information and communication technology for medical care, *cost-effectively and securely, including healthcare services, health surveillance, health literature, and health education, knowledge, and research*. (WHO)

Among the diverse eHealth applications, there is **mobile Health** (mHealth), which is defined as *medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices* (WHO, 2011).

Second taxonomy

The second taxonomy (Verna, 2020; Goldsack, 2019) studies Digital Health through different clusters, specifically it focuses on **Digital Medicine**, which *includes software and/or hardware products based on clinical evidence of effectiveness, intended to implement, measures and/or interventions that benefit human health* (Goldsack, 2019). In turn, this can include some mHealth apps. For these products, *a demonstration of efficacy is required and the regulatory pathway changes according to the classification of the product* (Verna et. Al, 2020).

The Patient Support Programs (PSP) should receive particular attention in this category too.

PSP are interventions of an organizational or other nature, without any therapeutic activity, but aimed at helping patients to better manage the course of their disease, better understand their health conditions, and/or provide advice on the course of their disease (Gussoni, 2021).

Patient Support Programs aim at optimizing the therapy, in both pharmacological and other forms. These products are usually digital Apps or Web Apps able to collect clinical parameters, facilitate physician-patient communication and interaction, offer tools for monitoring the disease, and promote the pro-active engagement of the patient along the journey of the therapy. For this reason, it is relevant to note that Patient Support Programs aim at supporting and monitoring the therapy, not providing the therapy.

In this framework, digital medicine encompasses, in turn, **Digital Therapeutics** (DTx), a type of product that is gaining much attention. The most used definition is provided by the Digital Therapeutic Alliance (DTA), 2020, a non-profit association born in 2017:

"Digital therapeutics (DTx) deliver evidence-based therapeutic interventions that are driven by high-quality software programs to prevent, manage, or treat a medical disorder or disease. They are used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes".

DTx is different from PSP for several reasons, although the main difference is that the former treats a disease by delivering a medical treatment, and for this reason, they need to be approved as a Software as a Medical Device (SaMD) (Verna et. Al, 2020).

A representation of the two taxonomies is reported in Figure 0.4.

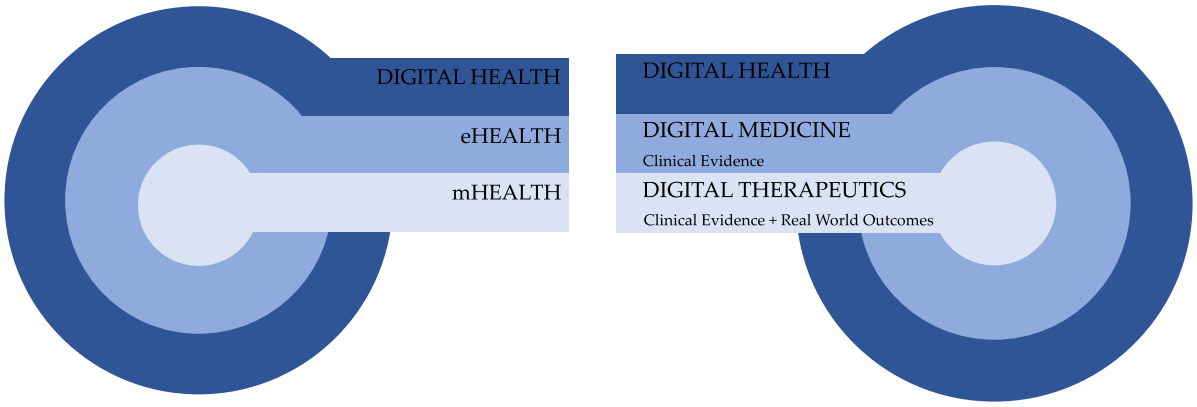


Figure 0.4: First and Second Taxonomy

Digital Therapeutics

From the aforementioned definition, some key characteristics of digital therapeutics can be highlighted.

First, DTx delivers a clinical treatment. Therefore, they can be considered as Software as a Medical Device (SaMD) – that is defined by FDA as software without a hardware medical device exerting a medical treatment[4].

Second, for these products, the demonstration of efficacy through clinical trials is required as well as clinically meaningful results obtained in the context of medical practice - Real World Evidence (DTA, 2020). The clinical effect is reached by providing content aimed at correcting dysfunctional behaviors with new habits[5], for this reason, they mainly deal with chronic diseases such as depression, anxiety, addictions, insomnia, schizophrenia, autism, attention deficit hyperactivity syndrome in children, obesity, hypertension, diabetes where the behavior impacts on the disease evolution.

DTx can be used at different phases, from prevention to the treatment of the disease. There are two ways in which a DTx can be integrated into the patients' care. The first approach is the stand-alone mode, meaning the digital therapeutic is used independently from other treatments. Otherwise, it can be a therapeutic plug-in, so the DTx is linked with another drug consumption, other therapies, or even together with other devices, fostering their effects.

By providing these results together with cost advantages[6] (Marichich et al., 2021), they represent an excellent alternative to traditional pharmacological treatment or even as a new form of combination. For these reasons, they are raising a strong interest in the market with a market value hitting U.S.D. 3.44 billion in 2020 (Statista, 2021) and around 23 approved DTx worldwide in March 2020[7]. Data are shown in Figure 0.5.

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[4] https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd

[5] https://www.advicepharma.com/news/osservatorio-innovazione-digitale-in-sanita-del-polimi-advicepharma-e-le-terapie-digitali-nel-contesto-italiano/

[6] Digital Therapeutic Alliance, DTx Product case study – reSET, last visited 9 May 2021 - https://dtxalliance.org/reset/

[7] https://www.osservatorioterapieavanzate.it/innovazioni-tecnologiche/terapie-digitali/terapie-digitali-approvate-a-che-punto-siamo-e-quali-sono

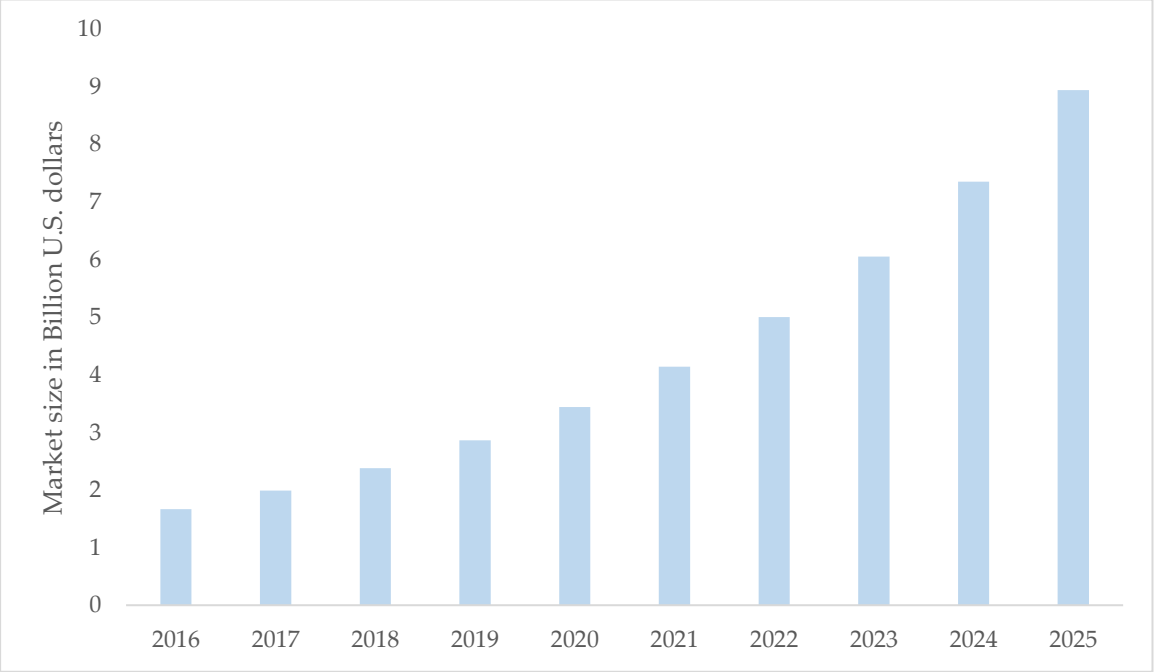

Figure 0.5: DTx market value in Billion U.S. dollars

Notwithstanding, the wide deployment of DTx products is constrained by the regulatory framework. Indeed, countries are developing different regulatory paths for such innovative products, but the pace is not shared. For instance, while in countries like the U.S. or Germany there are ad hoc regulatory frameworks to access the market, in Italy such a framework is missing.

Research objectives

Given the aforementioned premises, the present study aims at exploring the determinants driving the diffusion of Digital Therapeutics. Specifically, the final scope of this dissertation is to design and test a theoretical model that could describe the behaviors determining the diffusion of the DTx.

The diffusion results from the adoption of technology from a social system, thus this stage has a previous step of routinization from the individuals (Rogers, 1983). Most of the academic literature focuses on the adoption from the individual perspectives, exploring the phenomenon with diverse models that have very different if not even contrasting hypotheses (Gastaldi et al., 2019).

It has been studied the relevance of the individual rational assessment when engaging with a technology (Gastaldi and Corso, 2012). This is in line with one of the most used theory, which is the Technology Acceptance Model (TAM) by Davis (1989) where the intention to use is the result of two main factors: the perceived ease of use and the perceived usefulness.

On the other side, such a professionalized setting as healthcare is often studied through the lenses of organizational studies. Differently from the previous theories, in such a context, the behaviors of the individual are conceived as a result of combination of regulation, social norms and cultural systems (Butler, 2011). Each of the two streams of research have been extended to include elements of the other to enhance their interpretative capacity. For instance, both the extended versions of TAM2 (Venkatesh and Davis, 2000) and the Unified Theory of Acceptance and Use of Technology (UTAUT) (Venkatesh et al., 2003) have included the effects of social influence and organizational settings. At the same time, the self-determination of the individual plays a relevant role even in highly institutionalized settings (Radaelli et al., 2017).

However, the integration of the two theories is still very fragmented, and few examples are available in literature (Gastaldi et al., 2019). In addition, being DTx a so recent innovation, a very limited body of evidence on their diffusion is available. Therefore, these two reasons represent the novelty of the present work.

Indeed, one the one hand, this study offers a theoretical contribution to the ongoing discussion on the drivers for the adoption and diffusion of digital technologies, with the possibility to investigate how the two theories integrate each other, and its validation by the empirical means of survey. Thus, the direct effect of institutional factors on constructs of the TAM are formalized in a theoretical model and explored in the context of an institutionalized hospital, i.e., Istituto Auxologico. On the other side, the results can lead to interesting insights and practical implications on how to deploy an effective program for the adoption of a DTx.

A summary representation of the main supporting models, with their reference constructs, is shown in Table 0.1.

Theory	Author and year	Basic constructs influencing behavioral intention
TAM	Davis, 1989	Itention To Use
		Perceived Usefulness
		Perceived Ease Of Use
Institutional Theory	Scott, 1995, 2001	Regulative Pillar
		Normative Pillar
		Cultural Pillar
TPB	Harrison et al., 1997	Attitute
		Subjective Norm
		Perceived Behavioral Control
UTAUT	Venkatesh et al., 2003	Performance Expectancy
		Effort Expectancy
		Social influence
		Facilitating Condition

Table 0.1: Theoretical models and relative constructs

Obesity and Istituto Auxologico

This dissertation has been performed in collaboration with Istituto Auxologico Italiano, a Scientific Institute for treatment and inpatient care with offices in Piedmont and Lombardy. One of the disease their patients are affected by is obesity, defined by the World Health Organization (WHO) as a chronic "condition characterized by an increase in body weight due to the accumulation of fat in the adipose tissue, in excessive quantities compared to the physical and logical needs of the body, such as to adversely affect the state of health". In Italy, 1 out of 10 people is obese, and the economic burden for the State can range between 1.6% and 5.3%, and in Italy, obesity care accounts for 8.4% of total health care spending (Pozzoli et al., 2007; Obesity Report, 2019; OECD 2019).

In this framework, Istituto Auxologico has underwent a process for the development of a DTx for obese patients and this work is framed starting from this setting, to explore what could be the determinants for the diffusion of a DTx. This collaboration gives an

additional value to this work with the possibility to spread the questionnaire to those people that will be really involved in such a project.

Organization of the work

The present study is divided into 8 parts, which represent seven different types of activities and follow the logical scheme of work that has been used to achieve the result.

- Chapter 1 consists of contextual background analysis, briefly exploring the main characteristics of Digital Therapeutics and their market.
- Chapter 2 presents the results from a systematic literature review about the diffusion of diverse digital technologies in healthcare. Several papers were analyzed, and the main insights are presented, thus showing some gaps and/or that some topics were not addressed. This was the opportunity to set this study and explore uncovered areas. The results are presented together with the result of a non-systematic literature review to deep the most common theories used to study the adoption of digital technologies in healthcare.
- Chapter 3 is dedicated to the research model, the constructs, and the related developed hypotheses.
- Chapter 4 is about the methods and the materials used for the research. In particular, the model was tested by a mean of a survey delivered both paper-based and digital-based thanks to the database and to the in-presence patients of Instituto Auxologico, which opened the possibility to reach a representative sample of people. In this chapter, the survey and how it was developed are presented in detail.
- Chapter 5 is dedicated to a descriptive analysis of the obtained results, to provide an overview of the respondents' characteristics.
- Chapter 6 presents the statistical and empirical results of the analyses carried out on the model presented in Chapter 3. The proposed model was transferred into a structural equation model to analyze the relation among the constructs of the system and the goodness of the model.
- In Chapter 7 the results of the previous section are discussed to gather meaningful theoretical and managerial insights.
- In the last Chapter 8, there are the conclusions with the limitations of the study and the opportunities for the future.

1. Contextual and theoretical background

This chapter aims at presenting the context of Digital Therapeutics, starting from their main characteristics. The chapter continues with the exploration of some of the main legal frameworks which have been developed to differentiate DTx from products like Patient Support Programs and guarantee the proper level of safety and efficacy to both physicians and patients. In addition, some insights from the market are highlighted, indeed most of the DTx developed are here presented with their areas of focus and their main characteristics. Additionally, it is showed how the development of the DTx environment is in line with the new paradigms of care delivery. Indeed, the patient and person-centric approaches are creating shifting the focus on the patients' reported outcomes, empowering the patients to manage their health and disease, and creating new roles and relationships among the actors. Digital Therapeutics, engaging with the patients and caregivers from their design phase, monitoring the reported outcomes, and empowering the patient to improve their health, are in line with the deep shift in the healthcare field.

1.1 DTx components

DTA, in 2020, defined Digital Therapeutics by the following sentence:

"*Digital therapeutics (DTx) deliver evidence-based therapeutic interventions that are driven by high-quality software programs to prevent, manage, or treat a medical disorder or disease. They are used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes*".

In particular, DTx aims at correcting dysfunctional behaviors derived from chronic pathologies. Therapy acts on the patient's behavior and lifestyle; thus, intensive patient involvement is needed.

To achieve these benefits, the functioning can be explained metaphorically to one of the drugs (Verna et el., 2020). In the case of a digital therapeutic, there is not a physical drug, but an app for smartphones or tablets or even videogames, but still, an active principle and one or more excipients (e.g., app) can be identified.

In the active principle for a DTx, there are no molecules, but a software exerts the clinical treatment, with an effect that might be both positive - clinical benefit, or negative - side effect. The active principle acts similarly to Cognitive Behavioral Therapy (CBT)[8], which is a psychological treatment that aims at modifying the patterns among thought, feelings, and physical sensation changing the thinking and behavioral patterns. There are two main methods to design the active principles (Verna et el., 2020):

- The utilization of a treatment that is already available and applied in the medical practice. The example might be the case of all those DTx that are based on the principles of Cognitive Behavioral Therapy.
- The creation of a new active principle, that is created ex novo by merging different techniques. This is the example, instead, of utilizing Cognitive Behavioral Therapy with motivational interviews as well as psychoeducation. This innovative approach is created through the experience of patients, caregivers, medical specialists, and family doctors.

As in traditional drugs, the digital excipients give shape to the active principle allowing the patient to access it by making the active principle digitally available. Excipients can assume very different forms, from rewarding to gamification modules, reminders for DTx and complementary therapies assumption, as well as virtual assistants or modules to connect the patients with their doctors and other patients. The user interface of the DTx is part of the excipients as it profoundly affects the therapy acceptability, thus impacting the outcomes as well. As excipients can modify the patients' adherence and compliance to the therapy, it is expected that different

[8] https://www.apa.org/ptsd-guideline/patients-and-families/cognitive-behavioral

https://www.nhs.uk/mental-health/talking-therapies-medicine-treatments/talking-therapies-and-counselling/cognitive-behavioural-therapy-cbt/overview/

combinations can produce a different therapeutic effect, given the same active principle (Verna et al., 2020).

This distinction between the active principle and the excipient is particularly relevant in the confirmatory trials as the active principle cannot be changed, except within windows of possible modification, whilst the excipients can be updated less strictly. Indeed, being not active themselves, an update would not require a new clinical trial (Verna et al., 2020; Torous, 2019).

An additional important component in the DTx structure is the site from which the patient is able to download and use the DTx. This is called the delivery platform, which assumes a role of relevance as the patient is going to share in that platform a considerable amount of sensitive data to make the treatment as personalized as possible. The same data are shared, with the patients' authorization, with physicians who can monitor through the physician platform the patients' evolution.

1.2 Classification and delivery of a DTx

The DTA[9] has defined a product categorization for DTx products. These categories are linked to the way in which the products could be distributed among patients, based on the characteristics of the DTx itself.

- Access to the therapy can be by prescription, meaning that the allowance by the doctor is needed. This class of device is categorized under medium to high risk and would imply a reimbursement by a regulatory authority.
- The access can be even without prescription by the physicians in the case of lower risk, thus the path would be direct to consumer (DTC). These therapies would be over the counter, therefore paid for by the patients.

In the first case, the reimbursement is accounted in the budget of national health systems, thus a high level of medical or clinical evidence must be demonstrated. Some examples are already available, as Moovcare – 6 months for lung cancer in France and Zanadio – 3 months for obesity in Germany. They cost respectively 1000 and 499 euros per patient per plan (Chillè, 2020).

[9] https://dtxalliance.org/wp-content/uploads/2021/01/DTA_FS_DTx-Product-Categories_010521.pdf

The second case is instead paid by the patient, shifting the focus on a stronger consumer appeal and on perceived value. This model might have some drawbacks, as consumers might not understand the difference between DTx and products like wellness products, and no examples are available now.

In the between among the two paths, there is the possibility of DTx being paid by private insurance or corporate welfare programs. In this case, some data are required to support the medical benefit, in particular, to prove business productivity. One example is Sleepio, a program to treat insomnia, and such programs account for around 2-5 euros per month/user (Chillè, 2020).

1.3 Regulatory framework

To access the reimbursement paths, a proper regulatory framework is needed.

The international IMDRF/SaMD WG/N10FINAL:2013 guideline defined Software as a stand-alone Medical Device (SaMD) as software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device (Gussoni, 2021). Subsequently, on May 2021 the European Regulation 2017/745, known also as MDR (Medical Device Regulation), took effect. This included in the Medical Device Softwares (MDSW) also those devices designed for the prediction and prognosis of diseases. These definitions include Digital Therapeutics into the larger class of MDSW. As for MDSW and their usage, approval and market authorization are necessary, as well as reimbursement is recommended for a more widely deployment. Although different countries have developed different paths in which Digital Therapeutics can be evaluated and approved, DTx should follow some international standards for safety, benefit, and quality. In particular, ISO 13485 works to demonstrate a consistent system quality over time. ISO 14155 refers instead to the demonstration of clinical benefit on a target population. Safety, instead, should be demonstrated by ISO 62304 together with the application of ISO 14791 on risk management when dealing with design, testing, and updating activities.

In addition to these international standards, institutions like the Food and Drug Administration (FDA) in the U.S. and other equivalents around the world are looking for the way in which these devices should be assessed, and the most relevant examples are presented here below.

CE mark

As previously mentioned, through the Medical Device regulation MDR 2017/745, every DTx has to prove the safety, effectiveness, and performance measures for the market authorization. For this reason, every DTx must submit a clinical evaluation to get to the market. This process requires time and creates a notable burden for companies producing DTx, but there is one example of a State in Europe that has tried to fast up the process.

Indeed, the new **Germany**'s Digital Healthcare Act (Digitale-Versorgung-Gesetz — DVG) is an attempt to ease access to the market. Indeed, developers can register their devices with the CE-mark at a level that does not require clinical reports. The Federal Institute for Drugs and Medical Device (BfArM) examines all the information the manufacturer sent, including app security, quality, functionality, data security, and protection. It should be included also the clinical evidence, but if it is not yet available, the manufacturer can provide a plausible justification together with a 12–24-month plan to collect the needed information to be permanent in the digital health application (DiGA) directory. In the meanwhile, doctors can prescribe these DTx which can also be reimbursed through insurance plans.

United States

Digital health and medical devices are regulated by the FDA's Center for Devices and Radiological Health (CDRH). In 2017, a new body was created, the Digital Health Program, with the aim of defining the policy and regulation for digital health. In this scenario, a pilot program called Digital Health Software Precertification (pre-cert) was launched. The idea is to create a more streamlined and efficient regulatory approval for those developers who have demonstrated a robust culture of quality and organizational excellence, and who are committed to monitoring the real-world performance of their products once they reach the U.S. market (FDA). Therefore, thanks to this Pre-Cert program, the software is assessed through the performance of the developer.

There are two ways to access the Pre-Cert program. (FDA)

The first is the De-Novo classification process for some devices that are new, with a low to medium risk, and that can be approved as a lower class of risk devices rather than waiting for the premarket approval of higher risk classes.

The other path is 510(k) premarket submission. This is a declaration that the device is safe and effective, but most of all, it is substantially equivalent to an already marketed

device. Accordingly, FDA expects that review of a "Pre-Cert 510(k)" would be more efficient than the review of a traditional 510(k) submission. (FDA)[10]

The U.K.

The National Institute for Health and Care Excellence (NICE) worked from June 2018 to December 2019 in collaboration with NHS England, Public Health England, and MedCity for the definition of an Evidence standard framework (ESF) for Digital Health Technologies (DHTs). This is a framework that should be used to prove the value a new DHT provides to the UK health and social care system. A more important step was the collaboration between NICE and NHSx, one of the largest programs in the world for health and social care transformation. This agreement was aimed at creating a lean regulatory pathway for digital health technologies. It is also relevant that NHSx has developed one of the first assessment frameworks, the Digital Technology Assessment Criteria (DTAC), that validates the sustainability and value of DHT through 5 main areas, clinical safety, data protection, technical assurance, interoperability and usability, and accessibility.

Other countries

Other examples might come from Asia, where for instance Japan approved CureAPP through the Ministry of Health, Labour and Welfare (MHLW).

At the same time, Korea published in November 2020 a guideline on approval and renewal standards on Digital therapeutics. This guideline defines the DTx similarly to the DTA, but most of all define all the characteristics and data that are required. Indeed, a DTx should be available on a PC, mobile device, or commercially available devices, it should tackle one disease that is recognized by the international classification of diseases and the DTx should come with a Clinical Practice Guideline, clinical articles published in peer-reviewed journals, and materials from the clinical trials.

[10] https://www.fda.gov/media/119724/download

The main highlights of the regulatory framework are summarized in Table 1.1.

Country	Act	Regulator	Features
Germany	Digital Healthcare Act	Federal Institute for Drugs and Medical Device (BfArM)	Examination of app security, quality, functionality, data security, protection, clinical evidence (max delay 12-24 months)
United States	Digital Health Program	FDA's Center for Devices and Radiological Health (CDRH)	Examination of quality, real-world performances
UK	Evidence Standard framework (ESF) for Digital Health Technologies (DHTs)	National Institute for Health and Care Excellence (NICE)	Examination of sustainability and value in five areas: clinical safety, data protection, technical assurance, interoperability, usability and accessibility

Table 1.1: Recap of regulatory framework around the world

1.4 Overview of the market

In March 2020, a snapshot of the available DTx[11] reported 23 approved DTx, while another one[12] of June 2021 reported 25 with market authorization and many more in the pipeline. The lists were slightly different, as the discrepancy was not only in the 2 additional ones in the 2021 snapshot. The numbers that map the approved and under development DTx might slightly change based on the source, as the DTx development requires diverse actors (Mandolini et. Al, 2021) and different forms of collaborations, between startups and pharma and biotech companies. This complex environment makes it difficult for external sources to map wholly and update the DTx products. From the IQVIA database[13], in June 2021 a total of 137 DTx were in any phase of the development. These hundreds of DTx are spread on different areas of considerations, as reported in the Figure 1.1.

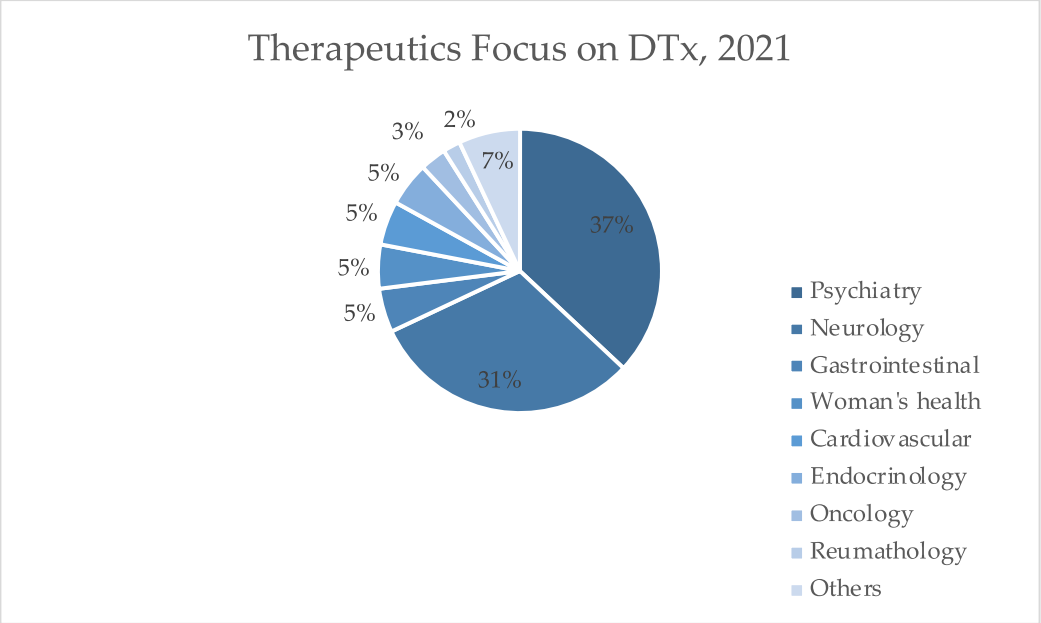

Figure 1.1: DTx areas of intervention

[11] https://www.osservatorioterapieavanzate.it/innovazioni-tecnologiche/terapie-digitali/terapie-digitali-approvate-a-che-punto-siamo-e-quali-sono

[12] Digital Health Trends, 2021 – Innovation, evidence, regulation, and adoption. IQVIA report, 2021.

[13] Digital Health Trends, 2021 – Innovation, evidence, regulation, and adoption. IQVIA report, 2021.

For what concerns the around 30 DTx already approved, they are spread in different countries, but mostly in Germany and U.S. thanks to their ad hoc regulatory paths. At the same time, the majority of the approved DTx is available in the form of mobile apps. The full list and the main characteristics of the available DTx are presented in the Annex A. Figure 1.2 and 1.3 shown a classification according to the type and geographical area of the DTx.

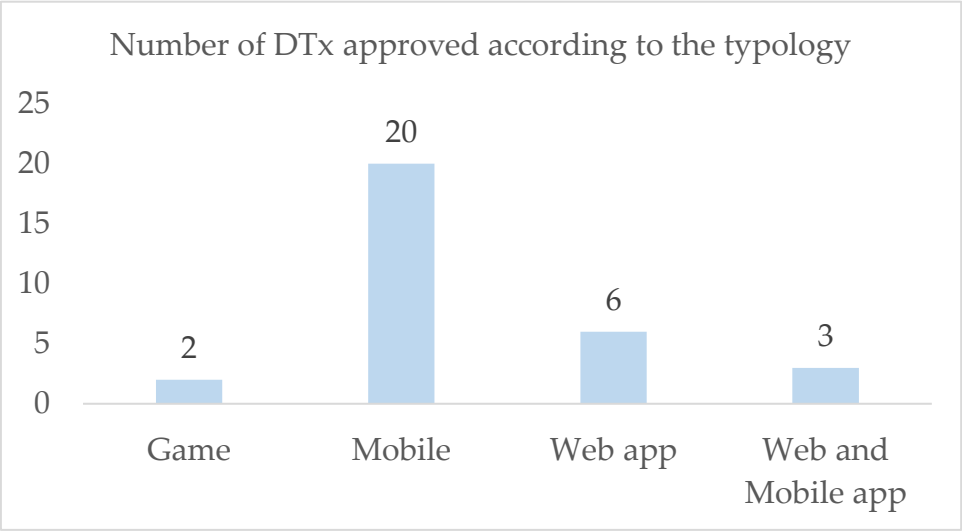

Figure 1.2: Number of DTx approved according to typology

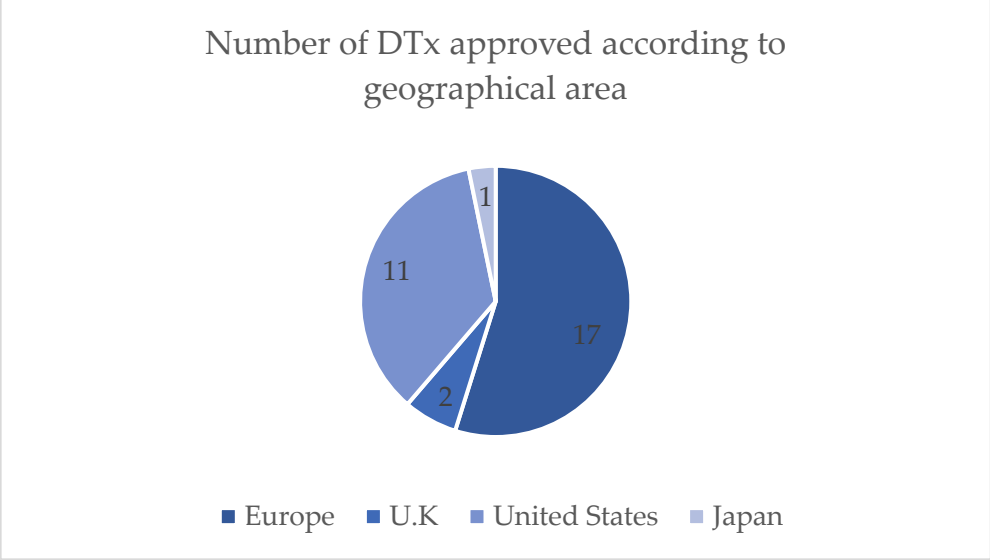

Figure 1.3: Number of DTx approved according to geographical area

1.5 The changing roles

The traditional paternalistic healthcare setting has seen passive patients versus doctors and professionals delivering care and making decisions based on symptoms, prescribing treatment, and assessing the outputs (Kumar and Chattu, 2018). Discontinued care leads the patient to move to different fragmented specialists, with unsatisfactory results (Meskó et al., 2017). This approach started to change in the half of the 20th century and the main reason was the rise of chronic diseases. Indeed, proper managing of these diseases was built over effective coordination among diverse physicians and patients. At the same time, this change was allowed by technological change (Meskó et al., 2017). Technological advances have not only revolutionized how care was delivered but have also led to a profound change in the responsibilities of the patient and in the way he or she interacts with the professionals. From that moment on, the approaches changed, and new paradigms emerged to take care of patients, like the patient-centered and person-centered approaches.

The former is respectful of the preferences and needs of the individual, and there is an increased priority on the patient-reported outcomes (OECD, 2020). This approach fosters patients' empowerment and promotes access to personal information through updated technology such as computers, wearables, mobile phones and keeps the patient actively engaged and participative. This changes the paternalistic care structure between patients and doctors and allows patients to become patients become partners able to plan their care journey as well as take responsibility for their own health (Kumar and Chattu, 2018).

A person-centered approach widens, even more, the focus of care, as the patient is seen as a whole person, and highlights the social, mental, emotional, and spiritual needs together with the health one (Kumar and Chattu, 2018).

Therefore, in both approaches, the role of the individual shifts at the center of care, from a passive stakeholder to a proactive player.

Patients are co-responsible for their health; indeed, an effort is required for maintaining healthy habits after the care to prevent as much as possible the disease or postpone the use of care delivery. To mention an example of this profound transformation, the National Institute of Clinical Excellence (NICE) in 2017 elaborated a guideline on how to make possible the collaboration between professionals and patients, how these actors could take "shared decisions".

During the decision-making process, what is important is:

- Care and treatment option are fully explored, with their risks and benefits.
- Different choices available are discussed with the patient.
- A decision is reached together with a health and social care professional.

In this scenario, new figures emerge as expert patients and patients' representatives, who both collaborate with doctors to co-generate value in the whole healthcare supply chain (Grigolo et al, 2021). Additionally, caregivers become more important, as they are close to their beloved ones, and are sometimes a leading and key role in the life of the patients. Therefore, they acquire experience that can be used to improve care. To support the new roles and the new relations among the actors to enable their dialogue, new technologies and algorithms are needed (Grigolo et al, 2021).

This transformation is supported and allowed by technologies such as Digital Therapeutics. They engage with patients and caregivers from the development phase of co-design, to foster and build the "Bring your own device" (BYOD), therefore delivering their own clinical data directly from the wearables and smartphones (Grigolo, 2020). DTx creates new interactions and new relationships among the actors by the sharing of data and empowers patients to improve their health, maintaining the relation with other stakeholders (Grigolo et al, 2021).

2. Literature review

The literature review of this dissertation aims to investigate which methods are used to study the diffusion of technological innovations in healthcare. The objective is to bring out the theories and frameworks that are able to enhance the factors of a diffusion process. The study of the literature allows to acquire in-depth knowledge on the topic of interest and highlight potential gaps and open questions to be explored.

2.1 Methodology

The literature review is mainly organized in two parts. The first phase focuses on how the process of diffusion of digital technologies in healthcare takes place. In this part of the work, the diffusion dynamics of several technological innovations were analyzed. It is important to underline that as the diffusion results from two key previous moments, acceptance and adoption, most of the analyzed literature focuses on these last two. For this purpose, a systematic literature review was carried out, with the aim of investigating the drivers and barriers affecting technology dissemination and the theoretical contributions of greatest relevance to the study of diffusion processes. In the second phase, gaps and missing concepts from the analysed papers were explored through a non-systematic literature review, with the aim of providing more completeness to the analysis.

2.2 Systematic review

In order to analyze the state of the art of the topics of interest, a systematic literature review was carried out. The systematic approach made it possible to identify, select, and critically appraise all relevant findings and construct an analysis that was accurate, relevant, rigorous, and replicable. The systematic literature review was conducted via Scopus by Elsevier, a curated abstract and citation database.

The starting point was the selection of the keywords of interest in order to accomplish the research query. The selection of keywords was guided by the objective of combining the dynamics of digital technologies diffusion and applications in the

healthcare field. The choice to remain generic and include multiple digital innovations, and not the specific case of DTx, was justified mainly for the novelty of DTx. The topic under analysis can be considered innovative and consequently, scarce material was obtained from the initial search "Digital Therapeutics" AND Diffusion. Specifically, only one article was generated from this combination of keywords, and it was out of scope with respect to the current analysis. In order to grasp the relevant acknowledgments in terms of digital technologies in healthcare, the choice was to use terms such as 'e-health', 'digital health', 'telemedicine', and 'm-health'. As mentioned in the introduction, the meanings of these terms are partially overlapping but boundaries remain blurred, therefore their combined usage could capture all the facets of the topic. More specifically, they are the most frequently used terms to deal with digital innovations in the field of health in a general sense, and therefore, they can be considered a good reference to be confronted with the case of DTx. In fact, since the purpose of this dissertation is to analyze the process of technology diffusion applied in the healthcare field, the confrontation between these technologies can be significant to bring out some useful elements for the case of DTx.

The combination of the keywords selected has been:

1. **Healthcare AND Technology AND Diffusion** that is the reference research. The decision to remain broad was justified by the desire to collect a wide variety of contributions. The other researches were identified by applying some modifications to this one. In fact, more specific terminologies were introduced to include aspects comparable with DTx.
2. **"Digital health" AND Diffusion**. Digital health includes both the digital and the health-related aspects. Because it encompasses numerous concepts, the name "digital health" was adopted. The following combination of keywords represents a higher level of specificity with respect to the reference research, while still remaining broad enough to collect as much material as possible.
3. **e-Health AND Diffusion**. The term 'e-health' embraces both health-related and technological aspects. It was included in the research because, as shown in the taxonomy proposed in chapter 1, it represents a higher level of specificity than "Digital Health" research.
4. **Telemedicine AND Diffusion**. Telemedicine includes both the technological and the health-related aspects. It was included because it is one of the most recurrent terms in the literature and in past studies. Therefore, it is valuable in order to provide an overview of the topics.

5. **m-Health AND Diffusion.** m-Health includes both the technological and the health-related aspects. The considerations are the same as described for research 3 which adopts the term 'e-health'.

It is evident that the keywords that guided the literature review are the same as those that emerge from the taxonomy defined in Chapter 1. This consideration is valid, with the exception of the term "Digital Medicine" which did not produce the expected results, both in number and in content. In fact, the search generated only 5 results, all of which were duplicates of other searches. For this reason, the search "**Digital Medicine" AND Diffusion** will not be included in the next analysis.

Research Query	Number of results
Healthcare AND Technology AND Diffusion	1141
"Digital Health" AND Diffusion	65
e-Health AND Diffusion	152
Telemedicine AND Diffusion	909
m-Health AND Diffusion	106

Table 2.1: Number of results per research query

A substantial number of articles (Table 2.1) emerged from the abovementioned searches. The study was lightened through the application of some filters consistent with our analysis objective, without neglecting papers of significant relevance.

As mentioned above, DTx is an emerging technology. In order to gain as much insight as possible from the conducted research, the most recent applications have been considered of greatest interest, in order to better compare them with the case of DTx. Therefore, the choice of a time frame of 10 years has been considered reasonable, from the beginning of 2012 until today. Consistently with the objective of this dissertation, the most compliant subject areas selected have been: Computer science, Social science, Business, Management and Accounting, Decision Science, Economics, Econometrics, and Finance. Subsequently, among all possible document types, only books, articles, reviews, book chapters and conference papers published in the English language have been selected.

At this point, to ensure the maximum reliability of the analysis, papers with a ranking between Q1 and Q2 were selected. To assess the robustness of the Journal of each article, SCImago Journal Ranking was used. The SCImago Journal Rank or SJR

indicator is an indicator that measures the degree of scientific influence of academic journals. The number of documents selected is shown in Table 2.2.

Keywords	#Articles selected
Healthcare AND Technology AND Diffusion	142
"Digital Health" AND Diffusion	8
Telemedicine AND Diffusion	54
e-Health AND Diffusion	31
m-Health AND Diffusion	27

Table 2.2: Number of articles selected per research query

After removing duplicate articles, through a preliminary reading of the abstract, it was possible to exclude the papers that did not meet the objective of this dissertation and therefore were considered irrelevant. For the sake of transparency, several exclusion criteria were identified:

- **Out of scope**: in this category, articles that were distant from the topic of interest were considered. In particular, articles that did not focus on the healthcare sector and in digital technologies dissemination were excluded from the analysis.
- **General challenges for healthcare**: papers that do not analyze diffusion dynamics and that focus on industry trends and challenges in a generic and narrative way were included in this category.
- **Focus on technology characteristics**: This section includes case studies that investigate specific functional characteristics of the technology, not focusing on its diffusion.
- **Context or country-specific**: articles that focus on a specific geographic area or context. Procedures in the healthcare field change considerably based on the geographic area. In fact, each country has its own regulatory framework to be followed. This category also includes articles describing diffusion dynamics in rural areas, where the setting is excessively divergent from the developed world. In addition, also papers describing specific organizational settings were excluded from the analysis, due to inconsistencies derived from different policies and actors involved.
- **Focus on cybersecurity**: in the healthcare sector, one of the most common issues when introducing digital technologies is the treatment of data. Several articles

focus on this aspect and how it could be improved, rather than the deployment itself.

- **Focus on a specific disease**: this section includes articles that bring attention to the specific disease in question. In these cases, the technology analyzed is dependent on the disease under analysis.
- **HTA for diffusion**: papers focused on health technology assessment (HTA) were included in this category. Among the abstract review, the context in which HTA is applied is usually the hospital setting.
- **Healthcare costs**: articles included in this category focus on purely economic evaluation of the technology. The cost is the main driver that shapes decision-making processes both within organizations and at the national level.
- **Reconfiguration of operations post-diffusion**: in this section all those contributions dwelling on the post-dissemination phase and consequences were included. The core is to investigate possible reconfigurations following a spread that has already taken place and not the factors that led the diffusion.

Table 2.3 shows the number of articles excluded for each category.

Exclusion criteria	#Articles excluded
Out of scope	25
General challenges for the healthcare	22
Focus on technology characteristics	53
Context or country-specific perspective	15
Focus on Cybersecurity	8
Focus on a specific disease	4
HTA for diffusion	6
Healthcare costs	3
Reconfiguration of operations post-diffusion	4
Total number of articles excluded due to reading of abstract	140

Table 2.3: Number of articles excluded according to the criteria selected after the reading of the abstract

Consequently, among the articles selected as relevant, the papers not downloadable and not available were discarded. At this point, the reading of 64 full papers was carried forward. Through analysis of the complete articles, further skimming was performed as before. A set of exclusion criteria were identified, considering factors that had not emerged from simply reading the abstract. Specifically, the reasons for rejection are as follows:

- **Out of scope**: the first reading of the abstract did not reveal a distance from the topic of interest. With a complete reading, this category was excluded from the analysis because the articles dealt with a specific topic that was not coherent or useful for the research question.
- **Out of target:** articles ultimately found to be applied in fields of application different from healthcare. The article appeared attractive from the abstract, but the collectible and usable information proved to be poor for the purpose of the research.
- **Absence of data or results available**: in this section papers that do not present validated results were considered. Typically, these are articles in pre-print or still in progress and, for this reason, the results are not yet available.
- **Absence of useful results**: although these articles present an analysis of the results, they did not prove useful for research. These case studies usually analyze a sample of data that is excessively small or specific. In other circumstances, this type of paper focuses more on considerations and opinions about the topic.
- **Non-generalizable considerations**: this category contains those cases where the considerations are not applicable to other contexts (e.g., focused on an organizational setting, focused on hospital procedures, focused on national regulations).

The number of articles excluded for each category is shown in Table 2.4.

Exclusion criteria	Number of articles excluded
Out of scope	12
Out of target	4
Absence of data or results available	2
Absence of useful results	3
Non-generalizable considerations	8
Total number of articles excluded after full-paper reading	29

Table 2.4: Number of articles excluded according to the exclusion criteria selected after the reading of full paper

Ultimately, the number of articles approved and deemed relevant resulted to be 35. The funneling process is shown in Figure 2.1.

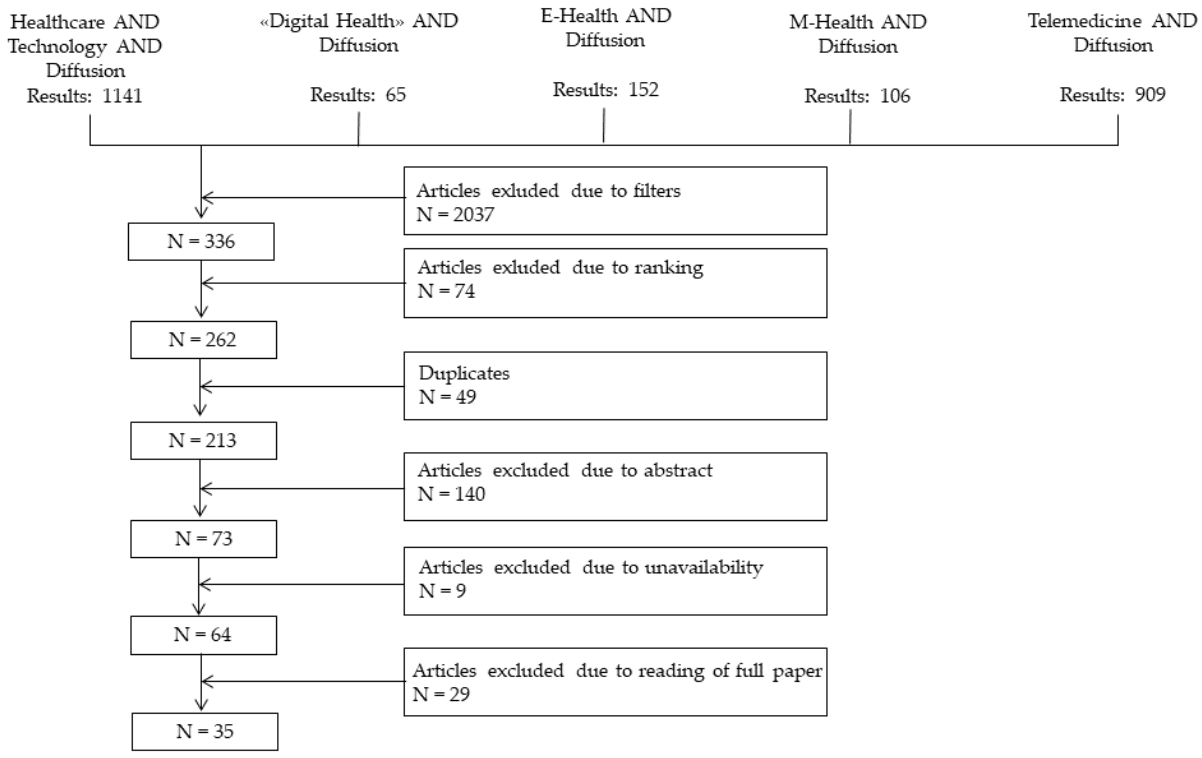

Figure 2.1: Funneling process

2.3 Qualitative analysis

In the time span of interest, from 2012 to the date, the number of documents published per year has increased. The growth can be attributed to technological advancement and an increasing interest in health care services that aims to be cost-efficient and to increase the quality of care. Although for the first few years the trend is to be considered stable, a significant increase could be noticed between the year 2018 and 2019, with more than 77% of papers published compared to the previous year. In 2021 the results drop again, probably because this analysis was carried out in mid-year, between April and May. Significant growth in publications is expected in the coming years as the need to generate innovative healthcare solutions through the use of advanced technologies has emerged in response to the health emergency. Covid-19 has laid the foundations for a transformation in all sectors and, with particular emphasis, in the health sector. Therefore, new technologies and new digital services are revolutionizing the way care is delivered and consequently, greater interest in this field can be expected in the next future. Data are shown in Figure 2.2 and 2.3, respectively for full-paper read and all papers selected.

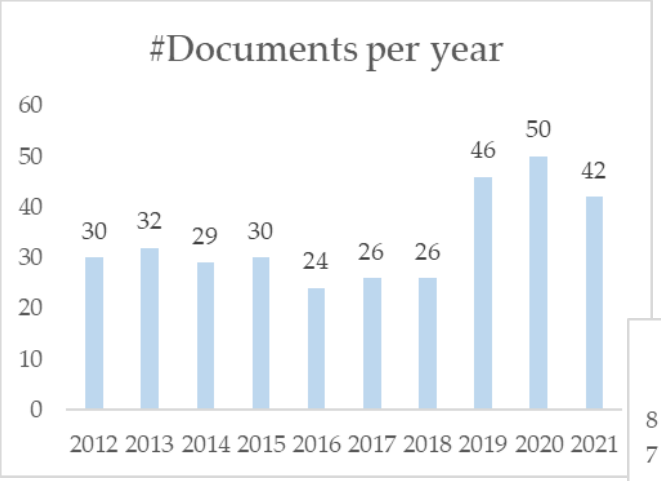

Figure 2.3: #documents per year among the selected ones

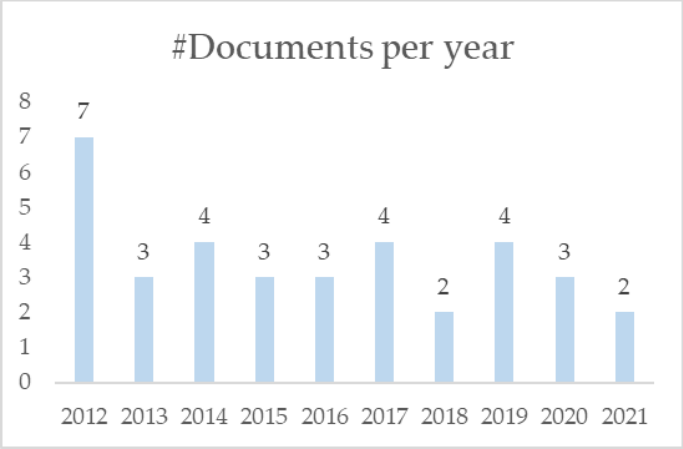

Figure 2.2: #documents per year among the full read

For each article selected after reading the full paper, the number of citations was calculated. This analysis was carried out because the number of citations is considered to be a good indicator of the "prolificacy" of an article in a specific field. Furthermore, a higher number of citations also enhances the scientific impact that a paper has generated. Even in this case, Scopus by Elsevier was the source used for this analysis. In particular, among the 35 approved papers, the number of citations of 4 articles was not available through Scopus. The number of articles per citation is shown in Figure 2.4. In particular, articles were collected in 5 clusters, according to the number of citations received.

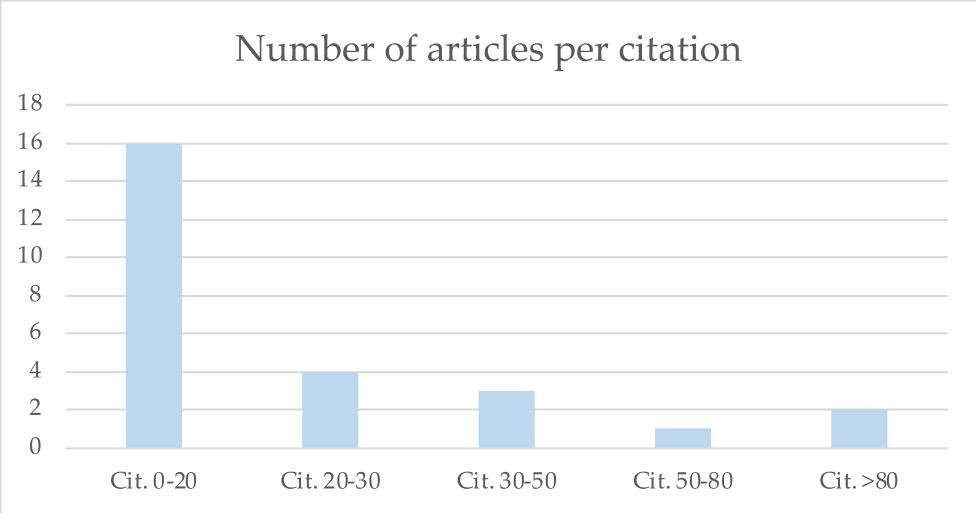

Figure 2.4: Number of articles per citation

The average number of citations per article is 21, with a minimum and maximum value of 0 and 109, respectively. Articles with a higher than the average number of citations were mainly introduced in the year 2012, and a few contributions in the years 2017 and 2018. All data are shown in Figure 2.5.

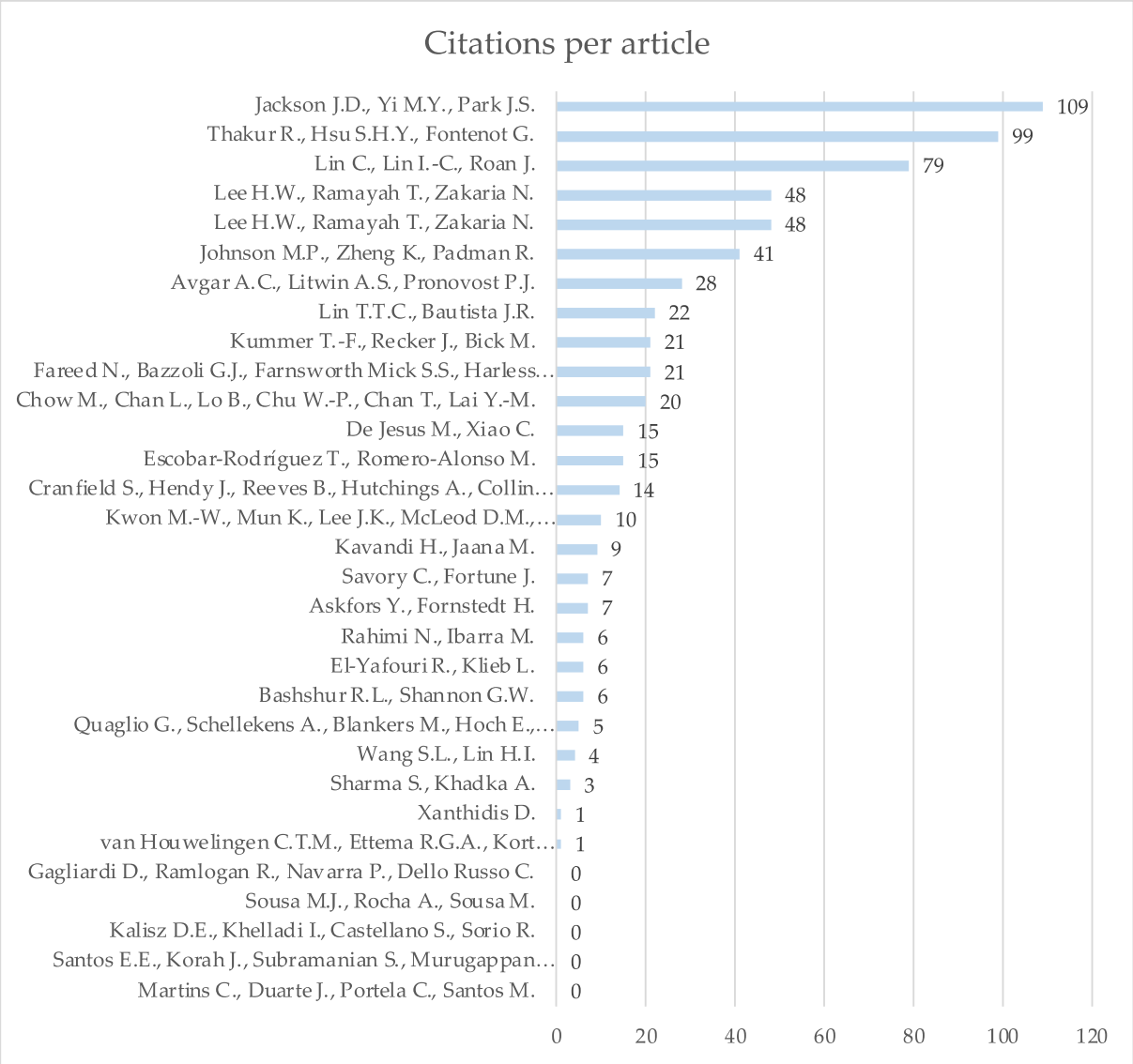

Figure 2.5: Number of citations per article

In addition, most cited papers are published in the following journals: Journal of Health Communication, Applied Clinical Informatics, Decision Support Systems, Journal of Medical Systems, Journal of Business Research, Information, and Management, Journal of Management Information Systems.

The number of citations per journal is shown in Figure 2.6.

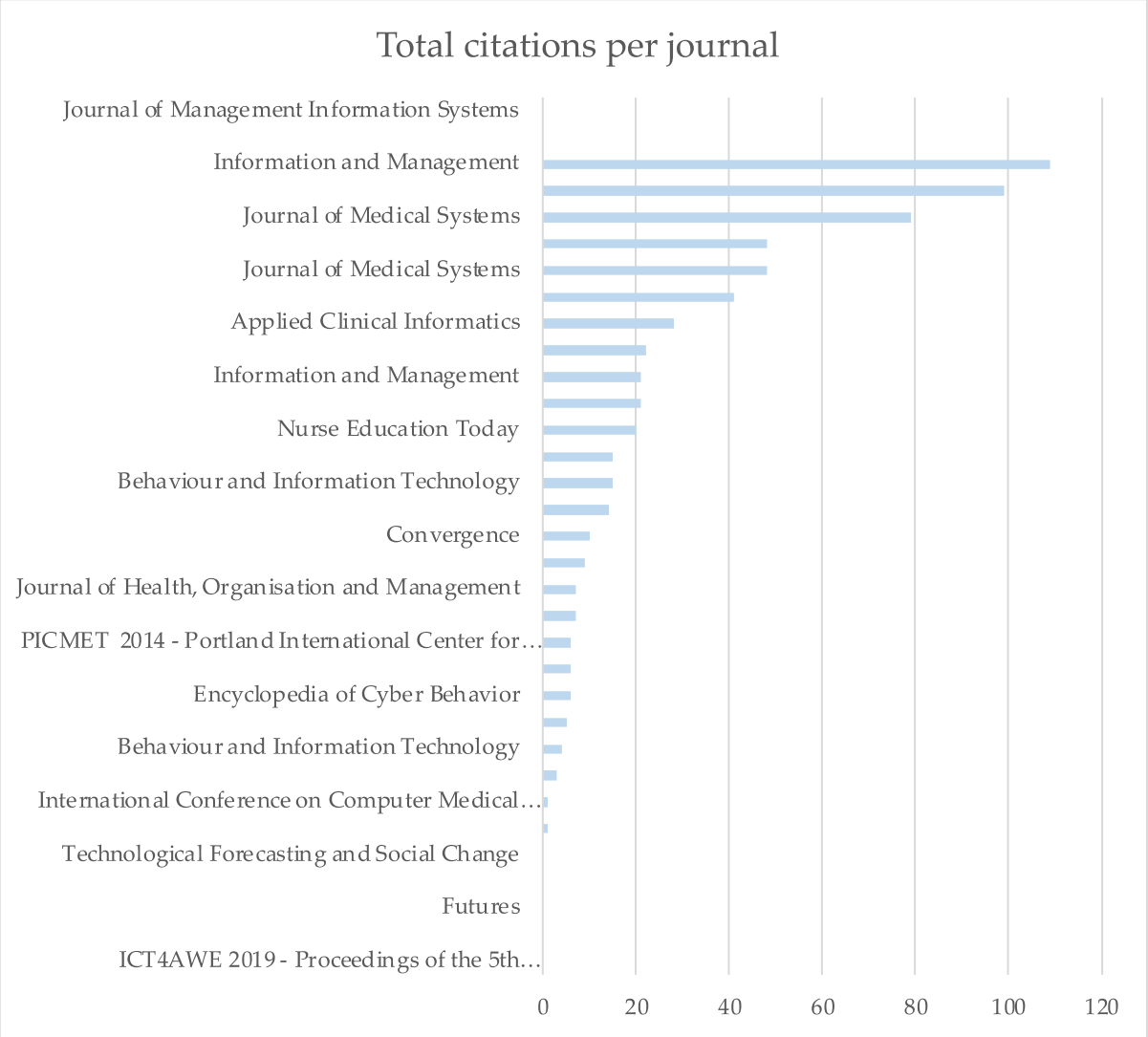

Figure 2.6: Total citations per journal

2.4 Content analysis

The studies resulting from the funneling process have been read and analyzed. Specifically, these studies can be categorized into two macro areas.

As the way in which these papers explore the innovation process is very different, authors decided to adopt this following categorization. The first cluster which will be presented studies the drivers and the barriers of adoption in general terms, while the second studies diffusion and adoption process through several specific models.

Indeed, the first part is divided, in turn, into papers focused on the barriers for adoption and use, and those focused on the drivers. Instead, the second part is divided into three main parts, following the three most recurrent theories: the Technology Acceptance Model and its extensions, the Theory of Planned Behavior, and Institutional Theory. This second part is integrated with the results of the non-systematic literature review.

2.4.1 Non-Model Based Theories

For what concerns the non-model-based studies, they explore drivers and barriers with different lenses and perspectives, but they do not apply any defined model. Another sub-categorization of these studies can be based on the focus on the process undertaken by physicians and hospitals versus one of patients and users. Indeed, the considered perspective implies different characteristics and different elements. However, only a small part of studies (Trisha et al., 2017; Sharma et al., 2019) assume this latter perspective, and they will be presented in the last separated cluster of this paragraph, as they deal with mHealth application.

The other studies are focused on different phases of the innovation process – they start from the pre-implementation, adoption and implementation to post-implementation, and diffusion. They can be organized between those mainly exploring the barriers and those exploring the drivers of new technology adoption. Some barriers are then mentioned also among the drivers, as they can be exploited in different ways, for instance, some challenges arising from the technology characteristics (Kalisz et al., 2021). The drivers and barriers will be presented accordingly to how they are studied in past studies. Generally, these studies deal with diverse technologies, from telemedicine (Steinhauser et al., 2020, Xanthidis 2013), RFID (Yao et al., 2012), clinical information systems (Or at al., 2014), technology-based intervention (Quaglio et al., 2017), social robots (kalisz et al., 2021), health information systems (Lee at al., 2012) and pharmaceutical products (Gagliardi et al., 2018).

Barriers

Decision-making is a complex activity that is driven by multiple factors, as medical, social, cultural, economic, and behavioral ones. The effects they have in the adoption process of technology are complex, dynamic, and change over time (Santos et al., 2021). The innovation adoption process is divided into stages, such as the initiation and pre-adoption activities, adoption decision, and implementation with post-adoption activities. Each phase is influenced by the previous one and has specific characteristics implying different needs, and therefore, different barriers and resistance to the implementation of new technologies emerge in the process (Avgar et al., 2012). The barriers in literature are presented for the different phases of the adoption process, and they are structured and clustered.

Part of the attention is given to considerations to be taken into account before starting the analysis of the implementation and adoption process. Indeed, the pre-implementation phase is valuable for managers as it produces information that can prevent potential conflicts and barriers in the future implementation and adoption process (Avgar et al., 2012). In particular, in this phase, a predictor of the usage intention can be identified in the positive usage acceptance. This, in turn, can be affected by potential and existing anxieties for the implementation of new systems. Indeed, the identification of such anxieties is relevant to anticipate conflicts and barriers and maximize the chances of implementations success. It has been shown that among the main types of anxieties some influence the intention to use, while others do not.

Specifically, work anxiety, referring to the concern of negative changes in the job, and relational anxiety, referring to the worry that the system will modify the relational values for the de-personification of patients, substantially influence usage intention (Kummer et al., 2017). While surveillance anxiety, referring to the perception of surveillance for all the daily activities tracked, does not influence the usage intention (Kummer et al., 2017).

The following phases, the **adoption phase** (Yao et al., 2021; Kalisz et al., 2021; Lee et el., 2012; Quaglio et al., 2017) and **implementation phase** (Avgar et al., 2012, Or et al., 2014), have common main classes of barriers which are recurrent in most of the articles.

The main types of barriers that have been identified in this phase are:

- *Technological barriers.*
  Technological limitations and technological challenges (Yao et al., 2021; Kalisz et al., 2021) are often a limitation to the adoption of some technologies. These are very specific with respect to the technology considered, but they include aspects as the reliability and security of the system. It also refers to the hardware-software computing infrastructure itself, as physicians might find the characteristics like long response time and instability of the system inadequate for their purpose (Or et al., 2014). These characteristics include the usability, ease of use, the usefulness of the technology, and compatibility of the technology with reality (Lee et el., 2012) and affect the adoption. In this sphere, the interface was found to play a key role to affect the behavior toward the technology (Lee et el., 2012, Or et al., 2014).

- *Funding and economic barriers.*
  This challenge refers to the need for the deployment of a large amount of money, that covers not only the initial investment but also continuous maintenance (Yao et al., 2021). This goes together with the fact that a lot of technologies are new and there is a lack of cost-effectiveness data and the fact that the initial phase of development happens to be expensive (Quaglio et al., 2017).
  Particular attention is given to financially supportive governmental incentives. Indeed, the lack of these incentives has been found to be significant in the non-adoption process (Or et al., 2014). This is different if the incentives are together with policies that might foster the technological component. Indeed, these latter are not found to be significant in telemedicine, as Steinhauser et al. 2020 reports that specific regulation does not significantly impact the adoption of the technology.

- *Social barriers.*
  This challenge refers to the interaction with the patients, their worries about the new technology. For instance, there is the need to guarantee that the collected data will be not misused (Yao et al., 2012). This has also been called the "consumer side", and the fact that there might be a lack of trust (Kalisz et al., 2021). Differently from what is presented in the patients' perspective, this is

considered as a barrier from experts, rather than direct opinionof interviewed users.

- *Organizational barriers.*
  Organizational barriers are the ones that have been more thoroughly explored, and they have been studied at three different levels (Avgar et al., 2012).
  The first is at a strategic level, therefore these barriers arise from a misalignment between the organizational objective and the actual usage of the technology. Therefore, it is very relevant that the implementation of the technology is consistent with the objective of the organization and reinforces the delivery of care (Avgar et al., 2012).
  The second level is the operational one, related to the managerial process and decision on the use of the technology. In this, implementing new technology is a sort of collective learning process. Therefore, better results can be seen by the organization with a culture emphasizing change and facilitating learning at both individual and collective levels, with support and encouragement, as for instance in the form of training (Lee et el., 2012; Avgar et al., 2012). Lack of such organizational support or trust issues generate barriers (Yao et al., 2012). When the organization does not encourage the full exploitation of the potentiality of similar technologies with proper coordination, there is the risk of misusing or incompletely using the technology – e.g., with no mandatory adoption, there has been a result of an incomplete usage result (Or et al., 2014; Avgar et al., 2012).
  The third level is about the frontline or workforce level, which is related to the structures of work in a broader sense. At this level, the acceptance of the technology from the frontline workforce is mandatory for the success of a technology, thus the focus is not the human capital. Similarly, as Avgar et al. (2012), this was explored also by (Lee et el., 2012).
  The human capital might be unfamiliar with changes, and if they feel them as threatened, they tend to show intolerant behavior (Lee et el., 2012; Quaglio et al., 2017). Similarly, it is important to ensure to these people that by adopting new technology, they are not going to substitute their or their colleagues' job. Those organizations that are able to maintain workforce stability are going to present an advantage in their implementation and use of the technology (Avgar et al., 2012).

- *Digital abilities barrier.*
  The lack of digital skills is identified in multiple studies. Proficiency in computer usage and its relationship with higher utilization of IT tools has been identified by Or et al. (2014), Avgar et al. (2012), and Quaglio et al. (2017). This goes together with a lack of national regulation with medical guidelines for digital skills, which has been identified as a problem to increase better digital literacy (Quaglio et al., 2017). This theme is particularly interesting, as some contrasting elements might emerge. Xanthidis (2013) showed most of the practitioners believed that technology literacy was not an obstacle for the usage of similar technologies agreeing that there was not any kind of technology literacy gap among them. At the same time, when asked if they felt completely comfortable with such technologies, none of them answered positively

- *Ethical barrier.*
  Differently from the previous barriers, these ones have been mentioned only in Kalisz et al., 2021 with no further deepening the theme.

Differently from the explained category, Or et al. (2014) include some elements, which are present in the previous groups, in a group called process-based barriers. These encompass the people dimension, the human-computer interface, clinical content, and workflow and communications. Indeed, there will be resistance to technology if it is perceived to be not in line with users' expectations and needs. For this reason, it is important to integrate the technology into the existing workflow and people's needs to avoid inefficiencies and rejection.

Drivers

Drivers are identified in different elements that can positively affect the adoption process. A taxonomy similar to the one presented in the barriers is mentioned in only one study (Kalisz et al., 2021), as drivers are often studied as a positive effect of some elements, such as the complementary assets (Steinhauser et al., 2020).

For the drivers, there is not any consideration on the pre-implementation phase as in the barriers. Anyway, the bridge from this phase to the implementation and adoption is the investment decision phase. In this stage, the top managers' expectations and vision are shaped about how the organization will be able to effectively use the technology. This is the first phase where organizational factors start playing a role.

Stated that general health IT is not a strategy itself, the more the strategic objective of the organization (i.e., hospital) can be accomplished by the technology, the more the investment is likely to happen (Avgar et al., 2012).

Entering the adoption phase itself, three main categories of drivers have been identified (Kalisz et al., 2021).

- *Financial dimension.*
  Differently from what has been seen in the barriers, digital technologies can sometimes impact efficiency and decrease price, entering in subsidies from the government and creating new business model possibilities for value creation. This possibility of cost-saving has been foreseen also by (Yao et al., 2021; Kalisz et al., 2021).

- *Technological dimension*
  It creates opportunities to foster technological literacy and simplify activities and processes (Kalisz et al., 2021).

- *User-centric dimension*
  It enhances human life and often turns to a collaborative solution (Kalisz et al., 2021).

As already discussed, the lack of technology literacy could be a barrier. Therefore, to foster the continued usage of technology and its institutionalization in the practices, the healthcare organization should focus on both retention and the recruitment of health IT-capable workforces so that the IT technology can be perceived as additional support rather than a barrier for their work. In addition, organizations should also leverage coordination across providers, to promote information sharing and learning. (Avgar et al., 2012). To guarantee proper skills, the presence of complementary assets plays a relevant role, indeed they are an important driver and an influencing factor for the adoption of technologies. Indeed, complementary assets to a given technology that are employed in an organization allow physicians to acquire competencies that can ease and foster the adoption process (Steinhauser et al., 2020).

In addition, the adoption behavior of professional physicians is influenced by their network. Although this changes over time, it has been shown that peers have a strong influence as well as socio-cultural factors (Santos et al., 2021).

Indeed, these networks together with multiple other stakeholders profoundly impact the diffusion trajectory of technologies. Indeed, it has been studied that those decisions are also mediated by agencies of stakeholders that operate in the system and transform the diffusion trajectory into a result of intertwined decisions (Gagliardi et al., 2018).

Users' attitude

This section assumes the patients' or users' perspective, which was explored differently from what happened in the previous section, i.e., as already stated, Kalisz et al. (2021) considered the consumers' perspective. The reason why this content is different can be found in the fact that researchers interviewed users about their attitude and what influences their behavior. Indeed, Kalisz (2021) interrogated experts about what they thought might be a barrier to the implementation, and the answer was the reasons for resistance by those users. These two articles instead explore why users engage or not with a given technology by interviewing users, in this case, both are kinds of mHealth app.

Starting from the very beginning of the engagement, the previous stage of adoption is trialability. This assumes relevance especially in the cases of mHealth apps, where a trial version is mostly available to potential users who might try them. This method is a sort of promotional strategy that aims at increasing the adoption rate, thus trialability can be seen as a previous and essential step for adoption. Trialability is affected by peer influence in the form that high visibility of usage and desirable outcomes, so especially young users are more prone to try these innovations. At the same time, relative advantage, complexity, and compatibility have no impact on trialability and thus the adoption of mHealth. Instead, the results suggest that trying mHealth apps can contribute to mHealth literacy of the youth through enhanced health information seeking and appraisal skills (Trisha et al., 2017).

Other attention is given to the continued use of a given technology. In this case, it is referred to an online social support group for managing chronic disease. In this case, members are profoundly affected by the characteristic of the group, such as the provided emotional, network, and esteem support but even more from the accuracy, speed, and timing of the information. In particular, the sense of community positively impacts the intention to continue using the online social support group, which in turn has been associated with the knowledge quality generated by the group. Also, this

research found that patient empowerment would positively impact their intention to continue using the online health community (Sharma and Khadka, 2019).

2.4.2 Model Based Theories

In this section, the aim is to guide the reader towards the most frequent patterns when discussing the adoption of innovations in healthcare. In particular, these theories aim at analyzing the factors influencing the behavior of the individual towards the acceptance and usage of new technology. In this chapter, a combination of systematic and non-systematic reviews has been adopted. In fact, the topics were explored in depth through a non-systematic review to offer a comprehensive and accurate theoretical overview. The theoretical explanation of each theory has then been complemented with case studies and empirical references on the use of the model. Among the model-based theories emerging from the literature, more attention has been devoted to the Technology Acceptance Model, Theory of Planned Behavior, and Institutional theory.

Technology Acceptance Model

The Technology Acceptance Model (TAM) is derived from the Theory of Reasoned Actions (TRA) introduced by Fishbein and Ajzen (1975), which aims to investigate and predict individual behavior in different domains. The TRA is one of the most impactful approaches describing human behavior (Sheppard et al., 1988). The model's key assumption is that a person's Behavioural Intention is affected by Subjective Norm and Attitudes. In 1986, Davis implemented some adaptations to the TRA, in order to orient the model towards the acceptance of information system technology (IS). TAM has its deepest roots in social psychology and aims to analyze how external variables influence an individual's beliefs, attitudes, and intentions (Choopravoon and Fung, 2010). TAM continues to be one of the most widely used models for defining and predicting user acceptance of a technology (Holden and Karsh, 2010).

According to the model, there are two main predictors of the user's intention to adopt an innovation: Perceived Usefulness and Perceived Ease Of Use. Perceived Usefulness (PU) is defined as "the degree to which a person believes that using a particular system would enhance his or her job performance" (Davis, 1989). Specifically, PU defines the usefulness, thus the productivity and the effectiveness, that the individual perceived in using the technology for his/her work. In turn, Perceived Ease Of Use (PEOU) refers to "the degree to which a person believes that using a particular system would be free of effort" (Davis, 1989; Davis et al., 1989). This means that the perception of the person

who uses the technology is free from physical and mental pain. In addition, PEOU is considered a causal antecedent of PU, as the greater the Perceived Ease Of Use of technology the higher the usefulness perceived by the user. According to TAM (figure 2.7), PEOU and PU are affected by external variables such as design and user features, task characteristics, nature of development and implementation process, political influences, and others. The two variables are considered the main predictors of the usage intention and, consequently, of the usage behavior. In fact, they directly impact Attitude Toward Using (ATU) which, in turn, influences Behavioral Intention to use (BI). This intention is also directly affected by PU and determines the Actual System Use (ASU).

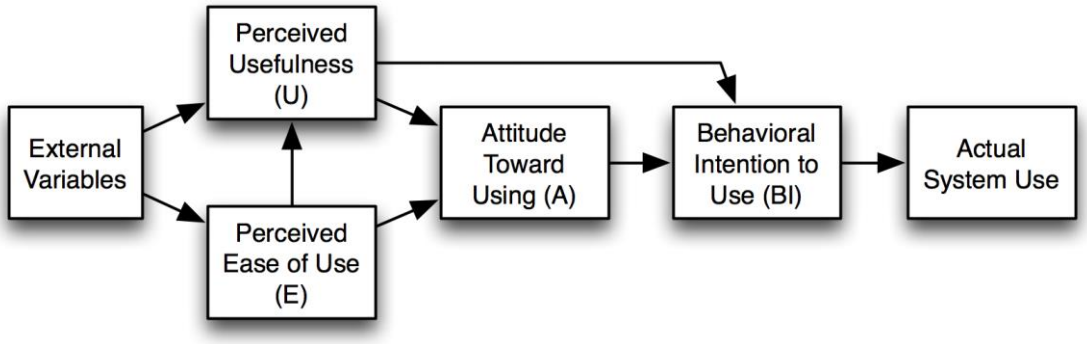

Figure 2.7: TAM Framework

TAM in the Healthcare domain

The aim of the systematic literature review was to supplement the theoretical knowledge of a model with empirical applications, especially in the healthcare sector.

The use of TAM in the healthcare field can present challenges. As mentioned above, TAM is one of the most exploited approaches to investigate the dynamics of acceptance for IS technologies. With a specific focus on healthcare, the theory has usually been used to analyze the acceptance of technologies such as hospital information systems, electronic medical records, telemedicine, and computerized patient order entry, all of which represent some of the most complicated information systems. Being among the 'most complicated IS' mainly means that both PU and PEOU are not known exactly at the moment of use, but through a longer process (Lee H.W., Ramayah T., Zakaria N., 2012).

An additional factor to be considered is the organizational context and, in particular, the stakeholders concerned in the adoption process. It has been shown that if the actors involved perceive both usefulness and ease of use toward the technology then the

uncertainty in the use of technology will be reduced. The actors involved are usually executives, such as senior managers and administrators, and practitioners, such as professionals and nurses (Ramendra Thakur; Sonya H.Y. Hsu; Gwen Fontenot, 2012). In this case, the healthcare organization must maintain a high level of familiarity between professionals and technologies, by investing in continuous on-job training and enhancing the introduction of innovation within the company (TamayoTorres et al., 2010; Ha and Stoel, 2009).

Furthermore, Lin et al., 2012 investigated the nature of certain correlations between variables. Especially in the healthcare field, the direct correlation between PEOU and PU was explored. In this regard, results showed that PU proved to have a greater influence on Behavioral Intention to Use than PEOU. This is because professionals tend to take a more pragmatic attitude when evaluating the adoption of technology. Indeed, Keil et al. (1995), Chau and Hu (2002b), Chismar and Wiley-Patton (2003) state that physicians devote more attention to the usefulness of a Health Information Technology (HIT) rather than on the ease of using it.

Extended TAM: TAM2 and TAM3

Starting from the direct link between Perceived Usefulness and Intention To Use, TAM has undergone extensions in the last decade. Specifically, Venkatesh et al. (2000) questioned and examines the antecedents of PU. In order to strengthen the relationship between Perceived Usefulness and BI, new variables were introduced such as social influence and cognitive instruments. Social influence variables include Subjective Norm, Voluntariness, and Image. As far as cognitive instruments are concerned, the variable introduced were Job Relevance, Output Quality, and Result Demonstrability. On the other hand, some constructs were removed, in particular ATU. In this way, the link between PU, PEOU, and BI became no longer mediated by attitude, but a direct one.

The new version of the model, TAM2, introduced by Devis and Venkatesh (2000), is shown in figure 2.8. The first objective of the TAM extension was to overcome the limitations of the previous model (Lee et al., 2012). Indeed, in the seminal version of TAM, the biggest limitation is represented by the inability to include also external variables which can affect positively or negatively the PU, and consequently the BI of a technology.

In addition to the introduced variables, new relationships were examined in TAM2. In particular, a direct link unites Subjective Norm with both Image and Intention To Use. Firstly, Subjective Norm (SN) is a construct already present in the TRA, and it is defined as a "person's perception that most people who are important to him/her think

he/she should or should not perform the behavior in question" (Fishbein and Ajzen, 1975). In other words, Subjective Norm represents the influence that significant people exercise on the individual who should engage in a specific behavior. In this regard, Johnson et al., (2014), pointed out that, due to the fact that the aforementioned variable is usually measured by self-reported judgments, it is often difficult to trace the structure of the network and the pressures arising from it.

Subjective Norm is directly connected with Intention To Use (ITU) and Image (I), other than PU. SN is connected to ITU both directly and mediated by PU. In the case of direct connection, if a person close to the individual expresses agreement with the performance of the behavior, the person will be more inclined to perform the behavior. In addition, the link is direct because the individual can be influenced even without necessarily perceiving a benefit, but simply driven by social pressures. On the other hand, it is also possible to identify a connection between SN and Image. Image is a variable defined as "the degree to which the use of an innovation is perceived to enhance one's [...] status in one's social system." (Moore and Benbasat, 1991). The relationship is supported by the fact that if influential people think it is right to perform a behavior, then the perception of the individual will be to have a better image in relation to the social context.

Similar to SN and I, Voluntariness (V) falls into the category of social influence variables. Voluntariness is defined as "the extent to which one perceives the adoption decision as non-mandatory" (Venkatesh and Davis, 2000). In other words, the assumption is that the behavior is not compulsory and that the individual has the freedom to judge whether to perform the behavior or not.

Concerning the category of cognitive tools, the introduced antecedents are Job Relevance, Output Quality, and Result Demonstrability.

Job Relevance (JR) is defined as "the degree to which an individual believes that the target system is applicable to his or her job" (Venkatesh and Davis, 2000). The variable has a direct connection with PU. Indeed, a technology or a system, in order to be perceived as useful, must certainly be applicable in the field of work. It represents therefore one of the pre-requisites for perceiving an advantage in the usage. Reinforcement of this concept is provided by the Output Quality (OQ) construct, which is defined as "the degree to which an individual believes that the system performs his or her job tasks well" (Venkatesh and Davis, 2000). In this case, not only is the technology or system applicable to the field of work, but it also allows the quality of the output to be improved.

The Perceived Usefulness is also influenced by the Result Demonstrability (RD). The definition, provided by Venkatesh and Davis (2000) states "the tangibility of the results

of using the technology". This means that the higher the ability to demonstrate the results obtained through the use of technology, the greater the perception that it is useful. In fact, if the results obtained cannot be made tangible, there may be a lack of argument for the usefulness of the system usage.

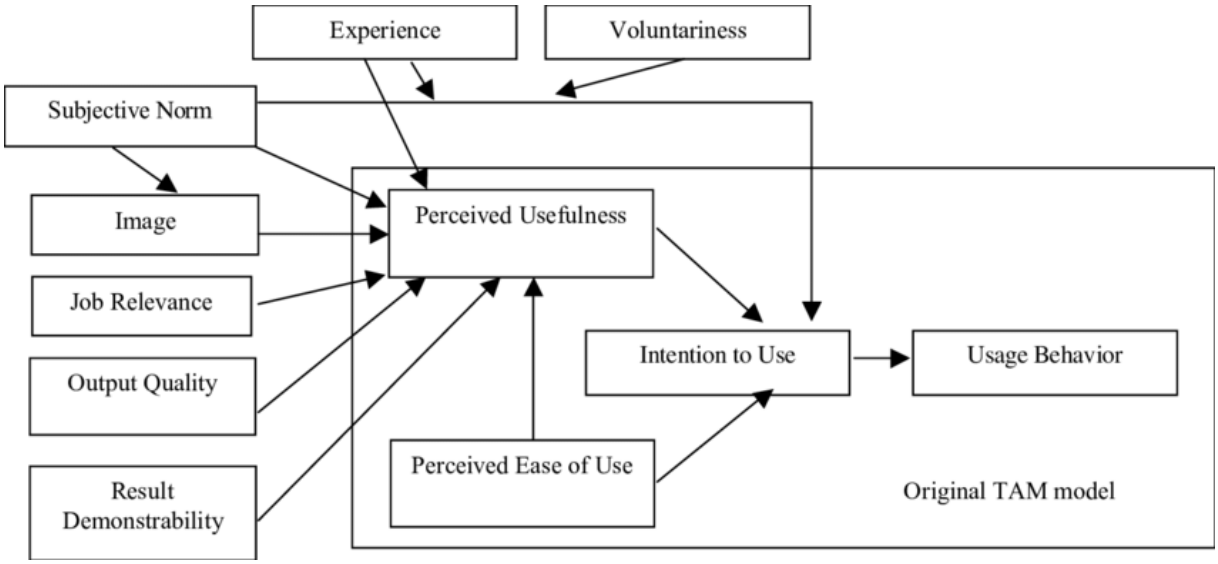

Figure 2.8: TAM2 framework

Starting from TAM2, a further extension was introduced by Venkatesh in 2000, leading to a new version, called TAM3. The main variables included refer to the usage of IT solutions, indeed they are Computer Self-efficacy, Computer Anxiety, and Computer Playfulness.

The construct of Computer Self-efficacy was introduced by Compeau and Higgins in 1995. Taking its cue from a social cognitive theory developed by Bandura (1986), the basic idea is that self-efficacy influences the behavior and motivation of the individual. Computer Self-efficacy is defined as "the degree to which an individual believes that he has the ability to perform a specific task/behavior using the computer". In relation to the healthcare setting, one of the major applications of this construct relates to the study of the adoption of the web-based clinical imaging portal. In particular, Chow et al. in 2013 emphasized the relevance of Computer Self-efficacy for the usage of that specific technology. Indeed, the perception of the ability to use a computer in the accomplishment of a task represents a key antecedent of the PEOU of the system under analysis (Compeau and Higgins, 1995).

As regards Computer Anxiety, it is defined as "the degree of an individual's apprehension, or even fear, when she/he is faced with the possibility of using computers" (Venkatesh, 2000). It could be considered a barrier that prevents the adoption of IT solutions, due to unfamiliarity with the technology.

Instead, Computer Playfulness refers to "the degree of cognitive spontaneity in microcomputer interactions" (Webster & Martocchio, 1992). It is related to the positive side of using a computer, then interactions with the computer that trigger positive feelings for the individual.

Lastly, Perception of External Control is defined as "the degree to which an individual believes that organizational and technical resources exist to support the use of the system" (Venkatesh et al., 2003). In addition, two adjustments were introduced by Venkatesh in 2000. They are Perceived Enjoyment (PE) and Objective Usability (OU). The main difference with respect to the previous constructs resides in the fact that an experience is required in order to measure them. In fact, both PE and OU, contrary to the above-mentioned variables, are based not on perceptions, but on actual use of the system. Venkatesh in 2000 define PE and OU respectively as "the activity of using a specific system is perceived to be enjoyable in its own right, aside from any performance consequences resulting from system use" and "comparison of systems based on the actual level (rather than perceptions) of effort required to complete specific tasks" (Venkatesh 2000).

TAM3 framework is shown in Figure 2.9.

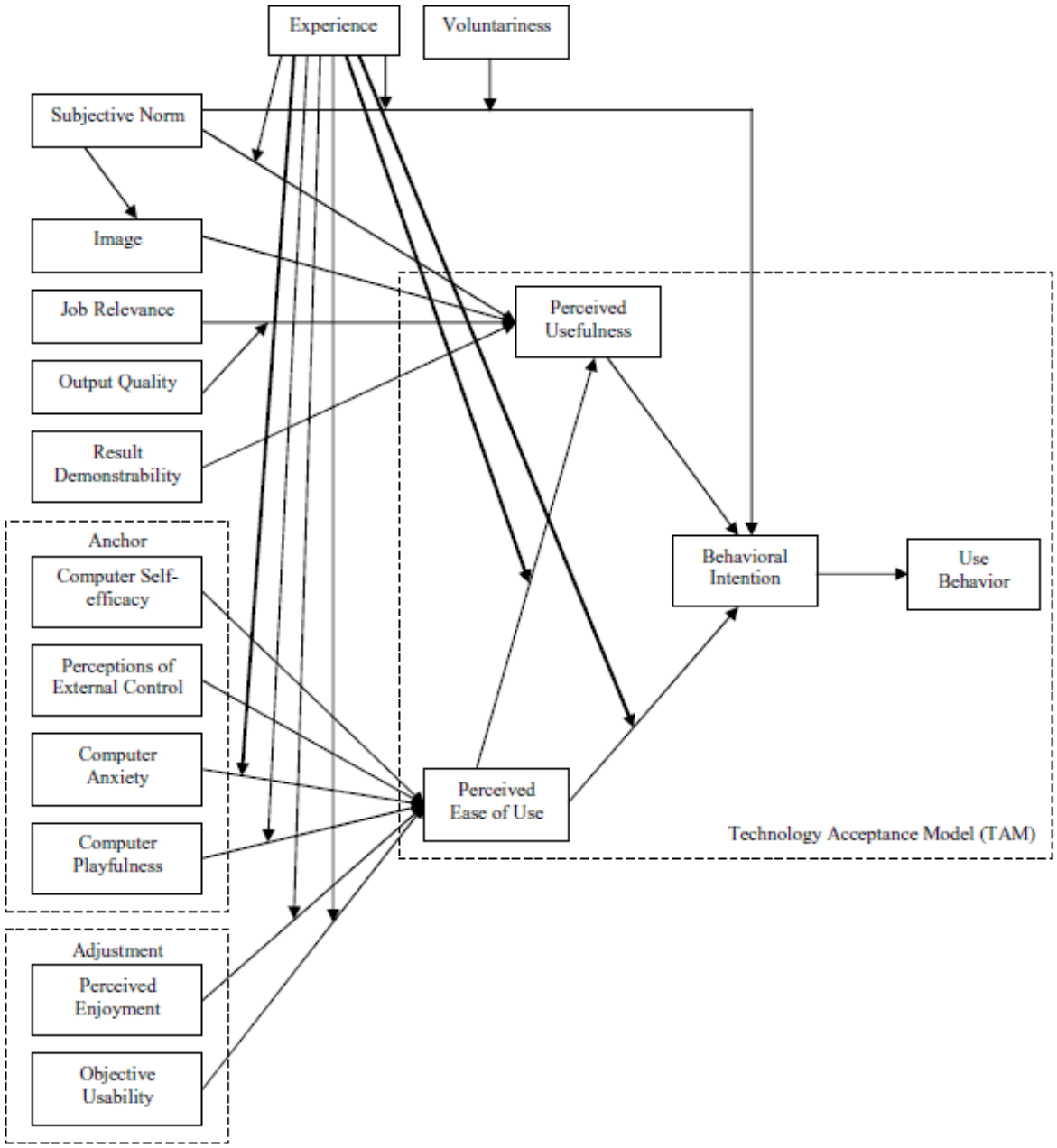

Figure 2.9: TAM3 Framework

Theory of Planned Behavior

Similar to TAM, the Theory of Planned Behaviour (TPB) is derived from the Theory of Reasoned Action (TRA) (Ajzen and Fishbein, 1980; Fishbein and Ajzen, 1975). The TPB aims to investigate what personal dynamics drive the individual's behavior in different contexts (Harrison et al., 1997). In particular, TPB explains that behavior is determined by the intention the individual has to perform that behavior. Behavioral Intention in this case refers to "indications of how hard people are willing to try of how much of an effort they are planning to exert, in order to perform the behavior" (Ajzen, 1991). The assumption is that the behavior is not compulsory and there is no obligation to perform it.

Behavioral performance may also depend on a range of resources available to the individual, such as time, capital, skills. The combination of these factors represents Actual Behavioral Control. It is important to distinguish between the latter and Perceived Behavioural Control (PBC) (Ajzen, 1991). This construct was added to the TRA and it was introduced to stress that using innovation might result in specific advantages and benefits that can be jeopardized by a lack of control during implementation (Joyce et al., 2013). The definition was proposed by Ajzen in 1991 and explained PCB as "perceived ease or difficulty of performing the behavior and it is assumed to reflect past experience as well as anticipated impediments and obstacles". PBC has often been compared to different constructs derived from other theories. To mention a few examples, interesting references are Atkinson's expectation of success (1964) and Bandura's perceived self-efficacy (1977 and 1982). Both of them try to link a given behavior to the user's belief in their ability to accomplish it, bringing them closer to the concept of Perceived Behavioral Control.

In addition to the PCB, Subjective Norm and Attitude Toward Behavior influence intention. In particular, Attitude Toward Behavior (ATB) is defined as "the degree to which a person has a favorable or unfavorable evaluation or appraisal of the behavior in question" (Ajzen 1991). In other words, ATB seeks to explain how behavior is frequently connected with an outcome, and how the intention is influenced by the expected outcome of that behavior. This indicates that the individual acquires an instinctively favorable or unfavorable attitude toward the behavior (Fishbein and Ajzen, 1975).

Finally, the construct of the Subjective Norm (SN) is related to the opinion that people in the individual's social context have about the performance of a behavior. The individual is influenced by the beliefs of others, especially of people s/he cares about and who are close to her/him. It refers to "the perceived social pressure to perform or

not to perform the behavior" (Ajzen, 1991). In Figure 2.10 the graphical representation of the model is shown.

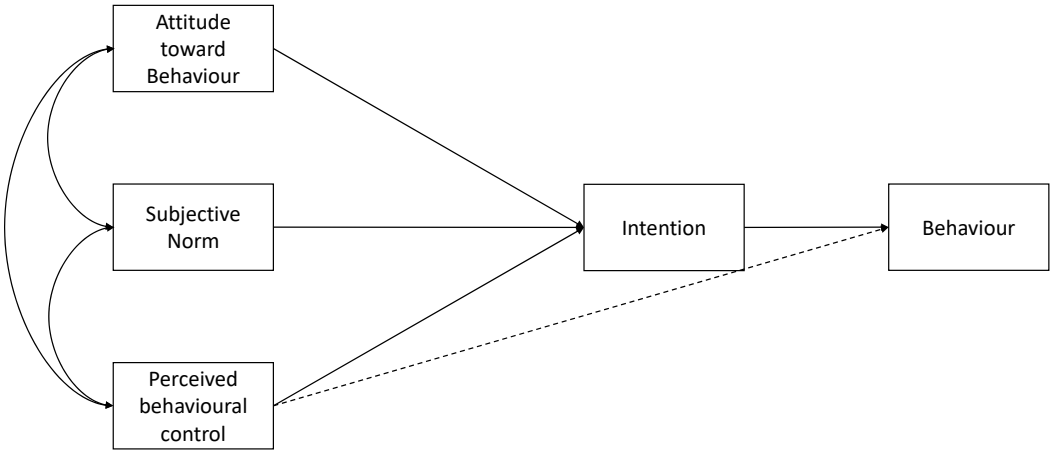

Figure 2.10: TPB Framework

Taylor and Todd proposed a decomposition of TPB in 1995. The goal of this study was to investigate the antecedents of the three constructs that influence intention and, as a result, behavior. Such antecedents of attitude, in particular, include Relative Advantage, Complexity, and Compatibility. Relative Advantage is defined by Rogers (1983) as "the degree to which an innovation provides benefits which supersede those of its precursor and may incorporate factors such as economic benefits, image enhancement, convenience, and satisfaction". This is frequently related to the above-mentioned concept of Attitude Toward Behavior, as it entails weighing the benefits and drawbacks of a certain behavior's performance. With regard to Complexity, it refers to "the degree to which an innovation is perceived as difficult to understand, learn or operate (Rogers, 1983)". This variable, in contrast to the prior antecedent, has a negative impact on attitude. In this view, the higher the level of complexity necessary to complete a behavior, the more unpleasant the behavior becomes. Lastly, Compatibility stands for "the degree to which the innovation fits with the potential adopter's existing values, previous experiences, and current needs (Rogers, 1983)". The idea is that an individual's behavior must be consistent and compatible with his or her social and cultural norms.

The Normative Influences are the antecedents that affect the Subjective Norm. The inclusion of this component is primarily motivated by the fact that multiple perspectives might emerge within the same social setting and should be included (Todd and Taylor, 1995).

To conclude, Efficacy and Facilitating Conditions are the factors of Perceived Behavioral Control. Efficacy is derived from Social Cognitive Theory, developed by Bandura in 1989, which states that personal, behavioral, and environmental factors all influence behavior. The term "Self-efficacy" refers to a set of behavioral variables.

Facilitating Conditions refer to those conditions and resources necessary to control behavior, i.e., time, money, and others. In Figure 2.11 the model is shown.

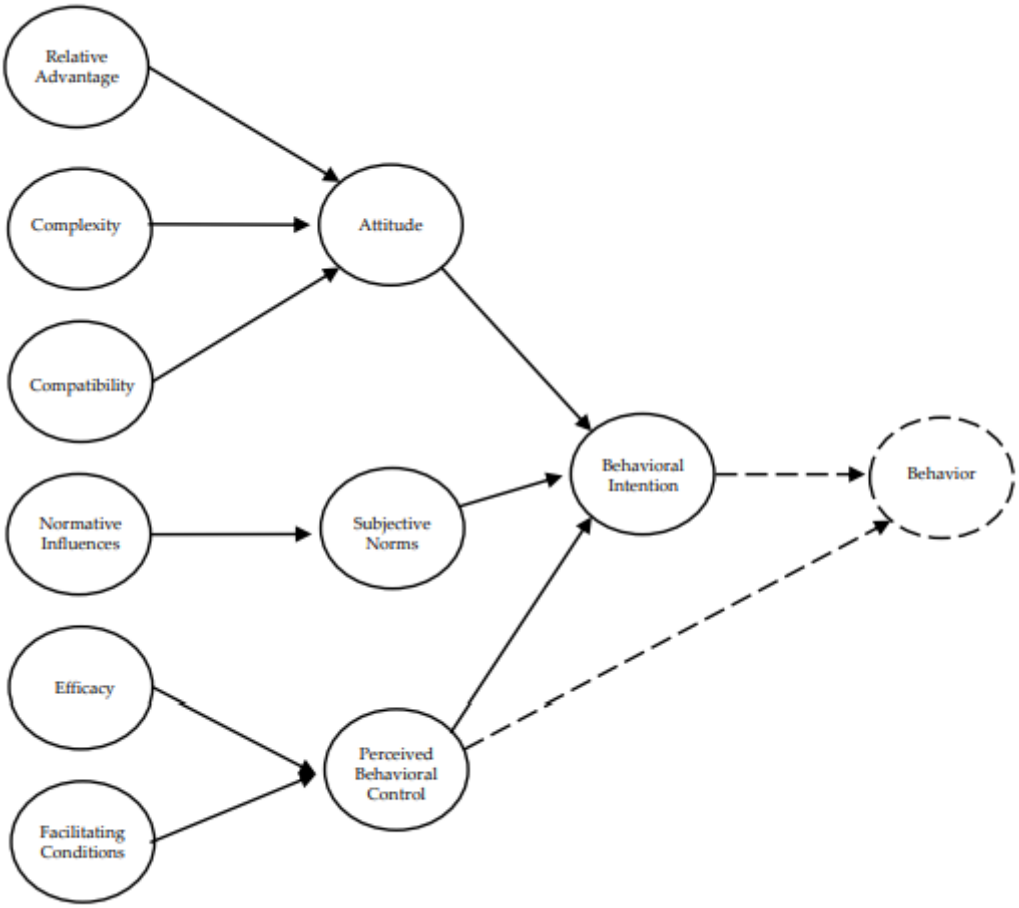

Figure 2.11: TPB Extended Model

Institutional Theory

Some researchers have adopted an alternative perspective to the one explaining decisions as to the result of rational assessment aimed at maximizing efficiency and effectiveness. Indeed, there are cases one cannot explain what happens in organizations only considering the rational actions of the managers, but irrationalities coming from the institutional environment should be considered (Mignerat and Rivard, 2015).

Indeed, the establishment, evolution, and decline over time of institutional structures as guidelines for actions is explored in the institutional theory (Scott, 2005). Specifically, the core concept of the institutional theory is legitimacy (Barley, 2008) and how organizations and organizational actors act to gain it in their environment to be accepted and ensure long-term survival (Meyer and Rowan, 1977).

Institutions have been defined by Scott (1995, 2001) as:

> "*Social structures that have attained a high degree of resilience. [They] are composed of cultural-cognitive, normative, and regulative elements that, together with associated activities and resources, provide stability and meaning to social life. Institutions are transmitted by various types of carriers, including symbolic systems, relational systems, routines, and facts*."

In this perspective, organizations are built over a set of values, norms, and beliefs (Barley and Tolbert, 1997) which affect and constrain actions over time. In this way, institutions constrain the options available to individuals and collectives (Barley and Tolbert, 1997).

From Scott's definition, the analytical components the institutions are built upon are three pillars - regulative (coercive), normative, and cultural-cognitive (Mignerat and Rivard, 2015).

- The regulative pillar is based on the coercion institutions can exert to constrain and regulate the actors' behavior. This is done through proof of strength and raising fear of sanctions.
- The normative pillar exploits the values and the norms to create social obligations on actors.
- The cultural-cognitive pillar exploits imitation. Indeed, where there is uncertainty, organizations are willing to copy those organizations which are considered leaders.

Institutional effects and institutionalization are the two main processes that are studied in institutional theory (Jepperson, 1991; Devereaux and Greenwood, 2003). While the former is about the process of how institutions affect other institutions, organizations, and organizational entities, the latter explores the stages in an institution formation (Devereaux and Greenwood, 2003).

The institutional effects can be analyzed by three different institutional pressures that one organization can exert on others and on organizational actors (DiMaggio and Powell, 1983).

- Coercive pressures come from the legal environment and the existence of standards applied by superior structures.
- Normative pressures are related to the process of professionalization, as inter-organizational network, backgrounds, and the coercive and mimetic pressures on professionals.
- Mimetic pressures rise especially in environments with high uncertainty. Indeed, in these cases, organizations may model themselves on other organizations that are felt to be more legitimate.

From some researchers, these three pressures have been coded as control mechanisms exploited by regulative, cognitive, and normative structures on other organizations to limit their behavior (Haggerty and Golden, 2002; Mignerat and Rivard, 2015).

Institutional theory has been exploited in the healthcare field as healthcare organizations are institutions that together constitute an institutional field (Currie and Guah, 2007). Indeed, in this field, at the individual, organizational and inter-organizational level, institutional behaviors emerge (Marchington and Vincent, 2004).

For instance, Naleef et al., 2015 analyzed the effect of institutional pressures on electronic health records (EHR) in hospitalized settings. The framework exploited a set of elements to encompass the main characteristics of an institutional pressure: cause, constituents, content, context, and control. These factors are:

1. Cause is defined as “the underlying rationale behind institutional pressures” (Oliver, 1991). Organizations' willingness to accept possible advantages in social legitimacy or economic power may influence their decision to comply with institutional constraints.
2. Constituents refer to an “organization's ability to manage the various expectations of its stakeholders in the environment” (Oliver, 1991). In this circumstance, firms will actively evaluate the demands of a powerful stakeholder before deciding whether to comply with institutional pressure or not.

3. Content is identified through “the nature of the pressure to which an organization is forced to conform” (Oliver, 1991).
4. Context construct is associated with the concept of Interconnectedness. Interconnectedness is described as the "density of inter-organizational relations among residents of an organizational area" and is an important feature of the constructed context” (Oliver, 1991; p. 170). Hospitals may be required to comply with norms that have been collectively agreed upon by all parties within a network because highly networked ecosystems have various formal and informal channels via which institutional norms can quickly diffuse (DiMaggio and Powell, 1983; Oliver, 1991).
5. Control is defined as “the means through which institutional pressures are imposed” (Oliver, 1991). The environmental field, in which a company works, is a recognized source of institutional control even in the absence of legal coercion (Ingram and Simons, 1995).

3. Hypotheses development and theoretical framework

3.1 Introduction

The presented literature review served as a starting point to develop the model that will be empirically tested. While TAM mainly aims at investigating the acceptance and usage of a certain technology through a rational and deliberate assessment, organizational studies conceive the individual behaviors as a result of an overarching system, such as the combination of social norms, regulation, and cultural systems.

This study aims to investigate the interplay between the organizational and individual mechanisms which could influence the continued use of digital therapeutics among obese patients. For this reason, the proposed model integrates elements from the Institutional Theory, i.e., the Organizational Expectation, Peer Influence, and Change Culture, with others from the Technology Acceptance Model, i.e., the Perceived Ease Of Use, Perceived Usefulness and Intention To Use. This innovative combination allows the investigation of the mediated effect of institutional and individual factors in the usage of DTx. These effects can generate interesting practical insights on how to create a more effective adoption process of a Digital Therapeutics in healthcare settings, such as Istituto Auxologico. In the following paragraphs, the model will be briefly introduced, and each construct will be analyzed in-depth, formulating the list of tested hypotheses.

3.2 Definition of the constructs

The model incorporates constructs retrieved from two diverse theories. For this reason, they are introduced in their belonging theory.

Technology Acceptance Model Factors

TAM explains the adoption and use of technology through a rational assessment. The three constructs introduced in the model coming from the TAM, are the ones formerly introduced by Davis in 1989. These constructs are retrieved from the theoretical background: Intention to Use, Perceived Usefulness, and Ease Of Use.

- ***Intention To Use - ITU.***

It is the individual motivation and willingness and effort to use the given technology, i.e., the digital therapeutics.

- ***Perceived Usefulness - PU.***

It is the individual perception of how much using a particular technology, i.e., digital therapeutics, can enhance the performance. The definition of this construct comes from Davis (1989) who defined it as: "the degree to which a person believes that using a particular system would enhance his or her job performance". Indeed, Davis explains how the more a person feels the item can enhance the performance, the more the person is willing to use it.

- ***Perceived Ease Of Use - PEOU.***

It is the individual perception of how much using the technology, i.e., digital therapeutics, can be easy for the individual. Davis (1989) defined this construct as "the degree to which a person believes that using a particular system would be free of effort". Davis shows how the more a person feels the item is easy and free of complexity, the more the person is willing to use the technology. Davis suggested that this construct can positively impact PU, as the more a person feels the item is easy to use, the more the person is prone to feel the item is able to improve the performance.

Institutional Factors

The institutional theory provides a non-rational explanation of the adoption of technologies in organizations. Indeed, the decisions are not based on the assessment of cost and benefits. According to Scott (2001), institutions are made of "cultural-cognitive, normative and regulative elements, which together with associated activities and resources offer stability and meaning to social life". The actors who are embedded in those contexts modify their choices and opinions within the environment (Barley and Tolbert, 1997; Scott, 1995; Scott 2008), and therefore, institutional analysis allow researchers to understand "how institutions influence the design, use, and consequences of technologies, either within or across organizations". As healthcare

organizations represent institutions (Currie and Guah, 2007), the actors' behaviors have been studied through institutional lenses, especially in the form of how physicians are influenced by such pressures. (Heinsch et al., 2021; Klecun et al, 2019; Fareed et al., 2015). Scott (2001) conceived that there is an iron cage made of pillars limiting the rational assessment and directing actors' behavior. These are regulative, normative, and cultural pillars, which in turn can be exploited by the organizations to exert the following influences, which are also the institutional factors in the proposed model.

- ***Regulative Influence***

The regulative pillar exists as there are rules, norms, and regulations that establish what can be done and sanctions for breaches when rules are not respected. Organizations can exert their regulative influence with strategic documents that outline the expectations in the short, middle, and long term (Scott, 2003). Hospital managers usually develop an instrument that incorporates their re-elaboration of internal and external pressures (Frooman, 1999; Jensen et al., 2009; Oliver, 1991). The regulative pillar can be exerted through semi-coercive mechanisms, clarifying the organizations' expectations. Physicians, being more powerful actors, can informally pressure patients toward the usage of technology and increase the effectiveness of care (Bozan et al., 2015).

- ***Normative Influence***

This dimension includes the expectations and norms elaborated from social groups about what could be appropriate behavior in some circumstances, i.e., in the organization. Therefore, this pillar is about what the actor is expected to do to fit in the social group. Organizations, typically, exert the normative influence through forms of peer influence, like mentoring, training with specialists and frequent interactions with colleagues (Bauer et al., 2007; Cable and Parsons, 2001). Peer influence is meant to align individuals to the belief of the necessity of the new technology. This normative influence has been proved to be of relevance in shaping professionals' behavior (Abbott, 1988), as the more the meaning system is cohesive, the more individual professionals are likely to adhere to the new social norm. Similarly, patients can generate large enough network where the physical health can be discussed. Therefore, the more the belief is diffused, the more the individual is going to adhere to the social norm.

- ***Cultural Influence***

The cultural pillar includes the common mental schemes and the symbolic representations shared among the social group. Typically, organizations exert this

influence through activities to shape and normalize the practical use of technology (Schein, 2010). The more the idea that the status quo must be changed, the more the individual is likely to adhere to the cultural change.

3.3 Research model and hypotheses

Figure 3.1 offers a synoptic view of the research model that this study aims at testing. The research model integrates the basic constructs of the TAM, Intention To Use, Perceived Usefulness, and Perceived Ease Of Use with the presented institutional constructs, the Normative, Regulative, and Cultural Influences. Specifically, the Perceived Usefulness is expected to positively impact the Intention To Use, together with the Perceived Ease Of Use. Indeed, the institutional influences are expected to have a positive influence on both the Perceived Usefulness and Perceived Ease Of Use.

These relationships hypostasized among the constructs are presented below through past studies.

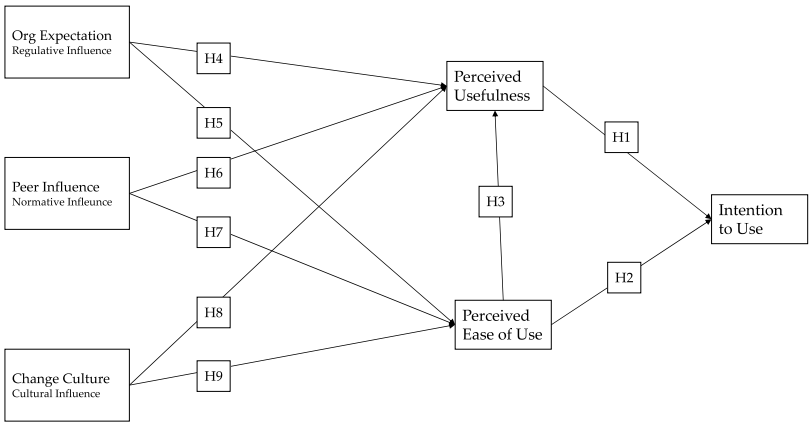

Figure 3.1: Model tested

TAM was applied in many studies in the healthcare field and the main relationships have been validated by substantial empirical evidence. The basic relationship in all these studies is the direct positive effect of Perceived Usefulness and Perceived Ease Of Use on the Intention To Use. This relationship has been proved in diverse past studies (Davis 1989, Davis and Venkatesh 1996, Venkatesh & Davis 2000, Venkatesh et al. 2003) but also in more recent ones. Indeed, the positive effect of the Perceived Usefulness on Intention To Use has been validated (de Veer & Francke, 2010; Liag et al., 2003) as well as the Perceived Ease Of Use on Behavioral Intention (Yi et al., 2006).

Furthermore, some studies have proven the effect of both those factors on the intention to use (Tsai, 2014; Wu et al. 2007). Based on these considerations, the first two hypotheses were developed.

H1: *Perceived Usefulness has a positive influence on the Intention To Use a Digital Therapeutics.*

H2: *Perceived Ease Of Use has a positive influence on the Intention To Use a Digital Therapeutics.*

The third hypothesis has been widely validated by empirical evidence too (Venkatesh & Davis, 2000). This relation sees the positive influence of the Perceived Ease Of Use in the Intention To Use, meaning that if a system is considered easy to use, it is also considered adequate to be used. Again, this relation has been proved even in more recent studies, as Dünnebeil et al. (2012) in the literature review found that 10 out of 12 studies found a significant correlation between these two variables. Consequently, this hypothesis was added to the model to understand whether the Perceived Ease Of Use could influence the Perceived Usefulness also in this case.

H3: *Perceived Ease of Use has a positive influence on the Perceived Usefulness of Digital Therapeutics.*

The second part of the model explores how the regulative, normative, and cultural pillar influences the Perceived Usefulness and Perceived Ease Of Use of new technology. Past research has shown how individuals in organizations with stronger institutional influences are more prone to perceive the PU and PEOU, although they still demonstrate a high tendency to rationalize the adoption (Pozzebon, 2004; Lawrence and Suddaby, 2006).

Organizations can delineate their expectations on the behavior individuals should adopt to reach their target. Indeed, they can actively stimulate how individuals perceive the benefits (Gastaldi et al., 2019). Additionally, these regulations can work as a guide toward the usage, allowing the individual to perceive the ease of using such a new technology. For these reasons, H4 and H5 were developed, to explore the effect that the regulative pillar can have on PU and PEOU.

H4: *Regulative Influence has a positive influence on the Perceived Usefulness of a Digital Therapeutics.*

H5: *Regulative Influence has a positive influence on the Perceived Ease Of Use of Digital Therapeutics.*

It has been studied that peer influence among professionals can impact their perceived usefulness as they see their peers exploiting new technology and the generated benefits. Indeed, they can be convinced that they could have similar results by imitating the behavior (Ajzen, 1991; Gastaldi et al., 2019) and this phenomenon is leveraged on by hospital managers to generate and motivate change in a virtuous cycle (De Benedictis et al. 2020). It was assumed that the same peer influence could work on the patients who feel the peer pressure by their social group as they could perceive the related benefit of the technology, indeed H6 was developed. Similarly, experience from peers could even influence the PEOU, by leveraging on peer experience.

H6: *Normative Influence has a positive influence on the Perceived Usefulness of a Digital Therapeutics.*

H7: *Normative Influence has a positive influence on the Perceived Ease Of Use of a Digital Therapeutics*.

The individuals' disposition toward new technologies and the challenges arising from using them can be positively influenced by a changing culture (Damschroder et al., 2009; Nilsen, 2015; Tucker et al., 2007). Similarly, it could be relevant to explore if the positive cultural change and could be also influential on the disposition of individuals to feel that the technology is appropriate and useful. For this reason, H8 and H9 explored the positive impact that the cultural influence could have on PU and PEOU, respectively.

H8: *Culture influence has a positive influence on the Perceived Usefulness Of a Digital Therapeutics*.

H9: *Culture influence has a positive influence on the Perceived Ease of Use of a Digital Therapeutics*.

3.4 Control variables

The research model additionally includes some control variables. This was aimed to increase the explanatory power of the model, as diverse studies proved the influence that some control variables could have on user acceptance (Venkatesh & Bala, 2008; Morris & Venkatesh, 2000). For this reason, a set of control variables could highlight the individual differences, which are the dissimilarities across people, including the differences in perceptions and behaviors, including the demographics, situational variables (Agarwal & Prasad, 1999).

The control variables are listed here below, and they are included in the model in Figure 3.2.

- *Gender – GEN*

Past research has shown that gender can produce differences in the acceptance of the technology. Although some studies show a higher acceptance from females, some state the contrary (Venkatesh and Morris, 2000; Yuen and Ma, 2002), there are cases where gender difference cannot be under-considered (Goswami and Dutta 2016), thus gender was included as a control variable.

- *Age – AGE*

Younger individuals tend to be more familiar with new technologies, and indeed it might be that age can negatively affect the use of such new technologies. (Chung et al., 2010)

- *Marital Status - MS*

Ma et al., in 2016 found that the Marital Status could influence the adoption of smartphone technology among older people, thus this control variable was included.

- *Level of education - EDU*

It refers to the highest level of education achieved. The influence it has on the adoption of the technology has been proved in diverse studies (Mahmood et al. 2001; Sun and Zhang 2006).

- *BMI*

BMI is one the most important yet basic indicators to monitor the health status of obese patients. It has been shown that those who have a high BMI and are in need to lose weight prove the willingness to lose weight but not to use weight-related care (Tol et al. 2014). Indeed, it was investigated if the BMI could influence the intention to use digital therapeutics.

- *Difficulties in maintaining results - DIFF*

Although weight loss programs might be effective, long-term maintenance is a more difficult step (Wu et al., 2009). For this reason, previous difficulties in maintaining the weight loss could be positively correlated with a higher intention to use digital therapeutics.

- *Employment status - JOB*

The employment status has proven to have a direct effect on the intention to use technologies (Porter & Donthu, 2006), especially through the influence this status can have on the interactions of the individual

- *Ease of use of digital solution -EAS*

This control variable refers to the ease of using existing digital devices. People with higher experience in using technological solutions are more prone to using new digital solutions, as they are more comfortable and familiar to change and digital usage (Venkatesh & Morris, 2000).

- *Willingness to change and to being supported – CHNG, SUPP*

The motivational factor has been indicated among the individual differences in the work of Sein et al. (1987). For this reason, a control variable to measure the motivation and attitude toward change was included. Similarly, a very context-specific control variable was included to test the attitude of patients toward a solution that could support their health maintenance. In figure 3.2, the control variables are introduced in the model.

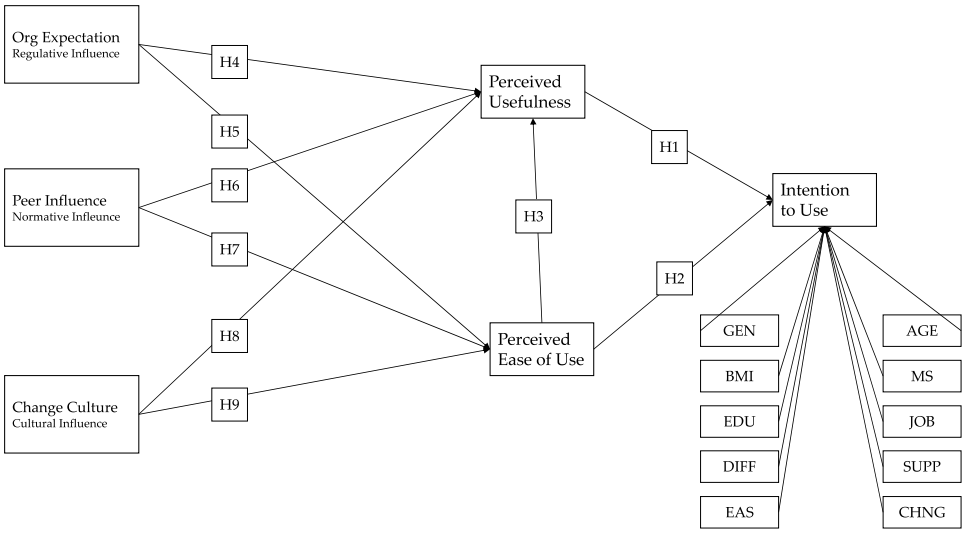

Figure 3.2: Research Model and Control Variables

4. Materials and methods

The aim of this study is to test the theoretical model presented in Chapter 3. The methodology applied to validate the model is presented hereafter in this section. Therefore, the research design is presented, followed by the methods to measure constructs and collect data.

4.1 Research design

The model was validated relying on a survey, which was available both in online and paper-based version. The survey was self-administered, non-experimental, cross-sectional, and explanatory. Additionally, the survey was anonymous to allow respondents to be completely free in expressing their opinions and believes and reduce the risk of biased answers (Bush and Hair, 1985).

The survey was self-administered both in the case of the online and physical version, therefore respondents had the possibility to answer anywhere and anytime. This choice was led by its ease and its efficiency as it does not require an interviewer for each interview and it allowed researchers to share the questionnaire to a wider geographical area of respondents, especially through the digital format.

The research is defined non-experimental as the researchers cannot control or manipulate neither the control nor the independent variables. Thus, the researchers measure the variables as they occur. Moreover, this type of research is based on observation and interpretation to get a conclusion, with the objective that the results can eventually be generalized to wider population.

The study is defined as cross-sectional as it is a one-time observational measurement, which pictures a snapshot of the population in a specific point in time, allowing the researchers to make inferences about the population of interest.

The methodology can be defined explanatory as the questionnaire tries to explore the cause-effect relationships among the constructs of the models, allowing the researchers to study and analyze them in depth.

4.2 Respondents and sample construction

Respondents were chosen to be a representative subset of the population of interest, so the available results could be extended to the whole population. As this latter is intended to be all those people that could engage with a DTx for obesity, the respondents were searched among current and former patients of Auxologico Institute. The questionnaire was made available in different forms to the patients, indeed, although the survey was administrated both physically and digitally, the two versions had the same questions.

The choice of the double format was led by the expectation to ease and foster the collection of data of those patients who were receiving inpatient treatment. Indeed, while the physical version was easily distributed during inpatient treatment in the hospitals of Auxologico, the digital version was delivered to past or in-house treatment patients. The digital version of the questionnaire was designed through the innovative platform Qualtrics, which optimized the interface easing the answering process and showing the respondent's process. The link was sent to a list of 3.7k email addresses that were retrieved from the database of the hospital with the addresses of patients that were in treatment in the hospital and were registered in the last three years. In this case, the link to the Qualtrics survey was sent by email to the patients through an institutional account that could be recognized as the property of the hospital.

It is worth noticing that the survey was written in both cases in Italian to allow all the patients to properly understand the text and answer all the questions.

4.3 Survey Questionnaire

The survey questionnaire is made available in Appendix B and is built though 44 questions. Structurally, the questionnaire can be divided into two parts. The first part is dedicated to collect information and insights about the characteristics of the respondents, while the second part was designed to test the 6 constructs presented in Chapter 3.

The first 26 questions of the survey assessed the general characteristics of the group, which gather information on the behavior of the participants. These variables remain constant in the study, thus enable the researchers to better understand the relations among other variables. These includes questions exploring the demographic variables of the group, as well as their attitudes toward technologies and the care path and the knowledge and eventual usage of similar products. The answers were collected by multiple answer systems, that included open-ended questions, single and multiple-

choice questions, as well as some Likert scales, as they will be presented in the next section.

The second part was dedicated to 18 statements to measure the constructs presented in the model: Intention to Use, Perceived Usefulness, Perceived Ease of Use, Regulative Pillar, Normative Pillar, Cultural Pillar. In this case, all the answers were collected through a Likert scale answer system presented in Table 4.1. This scale was chosen for the easiness of answer and analysis of collected data. The scale consisted in 5 answer options ranging from 1 for complete disagreement to 5 complete agreement with the statement.

Complete disagreement	Disagreement	Indifference	Agreement	Complete agreement
1	2	3	4	5

Table 4.1: Likert Scale from 1 to 5

These questions were asked after a brief explanation of what a DTx for obesity would be. Indeed, to ease the process and the understandability for patients, the term digital therapeutics was never mentioned but the expression "medical app that could help in improving the health status" was employed a thought to be more easily understandable.

In the following paragraphs, a general overview of the survey is reported, and the main macro-areas will be explored and presented in their measurement process, and eventually, each construct will be presented and explained.

4.4 Personal Variables

The first part of the survey has been developed to have a deeper understanding of the characteristics of the responding sample and it was conceived as a set of questions regarding demographics, health-related behaviors, the path of care, and technology use. These findings regarding several aspects of the life of the individual can act as contributory support for the contextualization and interpretation of the results. Indeed, this part aimed at investigating whether the constructs are influenced by specific characteristics of the population. Hereafter, the variables are presented as divided into some subgroups measuring similar aspects of the respondents.

4.4.1 Demographic and Personal Information

The first cluster comprehends the demographic information (Table 4.2) needed to characterize the groups being studied and understand if it could be generalizable. In particular, elements like gender, age, education, occupation, sentimental status and residence were asked. Additionally, elements like weight and age were asked in order to compute the BMI - Body Mass Index[14], a very important body indicator when dealing with obesity.

Question	Measurament scale						
Gender	male	female					
Age range	<18	18-30	31-40	41-50	51-60	61-70	>70
What is your highest level of education?	elementary school	middle school - low level	middle school- high level	degree	PhD or post-lauream		
What is your occupation?	student	worker	unemployed	household	retired		
What is your sentimenatl relationship?	single	I have a stable partner	other				
Region of residence	open question						
Weight (Kg)	open question						
Height (Cm)	open question						

Table 4.2: Demographic and Personal variables

4.4.2 Health Status

A set of variables explored the health status of the respondent as well as which was their treatment inside the path of Auxologico. Indeed, as obesity is often related to other types of comorbidities (Obesity Report, 2019), these conditions were explored. Additionally, it was asked to patients which was the type of treatment they received in Auxologico in the last year and if they receive any pharmacological treatment.

[14]https://www.salute.gov.it/portale/nutrizione/dettaglioIMCNutrizione.jsp?lingua=italiano&id=5479&area=nutrizione&menu=vuoto

Health Status items and responses are shown in Table 4.3.

	Question	Measurament scale								
health status	Are you suffering from one or more of these pathologies	cardio-cerebrovascular disease	hypertension	diabetes	liver disease	osteoarthitis	osteoporosis	renal disease	other	none of the above
	Have you provided one of the following health services in the last year? (you can tick multiple answers)	ambulatory	mac/Day Hospital	inpatient tratment (auxologico)	bariatric surgery					
	Do you take or have you taken drug therapy for obesity?	yes	no							

Table 4.3: Health Status variables

For what concerns the second question of this group, it is worth noticing how it is strictly related to the paths available in Auxologico. They are briefly described in the following Table 4.4.

Path	**Features**
Outpatient	Patients with BMI < 35 kg/m^2 and no comorbidity are referred for outpatient treatment and follow-up usually at the Obesity Centers
Inpatient	In-depth assessment of the comorbidities accompanying obesity, the setting of therapies and the treatment of these comorbidities
MAC/Day Hospital	Organizationally complex (multidisciplinary and multi-specialist) semi-residential rehabilitation treatment with a more intensive educational approach than can be provided in a 'simple' outpatient setting
Bariatric Surgery	Obese patients for more than 5 years with BMI ≥ 40 kg/m^2 or 35-40 kg/m^2

Table 4.4: Description of possible path in Auxologico

4.4.3 Social and Familiar context

The social context might be important, especially in terms of family (Obesity Report, 2019) and close environment support. For this reason, respondents were asked how much their families or close others influence their behaviors (Table 4.5).

	Question	Measurament scale				
social and familiar context	Do you consider yourself a person who loves to be with others?	very little	little	avarage	much	very much
	With whom do you consume the main meals of the day?	alone	with family	with friends/ colluegues		
	Does your family support/motivate you in maintaining/improving your state of health?	yes	no			
	Does your family support/motivate you in maintaining/improving your state of health?	yes	no			
	Does your family support/motivate you in maintaining/improving your state of health?	yes	no			

Table 4.5: Social variables and familiar context

4.4.4 Patient Satisfaction

Additional questions were asked to understand whether respondents are actually improving their health status and if they are satisfied with the work they are doing to improve their health.

Patient Satisfaction items are shown in Table 4.6.

	Question	Measurament scale				
patients satisfaction	Has your state of health improved during the management by Auxologico?	very little	little	avarage	much	very much
	Are you satisfied with the results obtained?	very little	little	avarage	much	very much

Table 4.6: Patient satisfaction variables

4.4.5 Follow-up

In obese patients, the regain of weight loss is frequent when they finish their inpatient treatment. For this reason, it was asked patients if they were facing these difficulties and their propensity to have longer care at home to maintain their health status (Table 4.7). Similarly, participants were asked the degree they agree to how much they are responsible for their health. These questions showed their propensity to actively engage in care outside the inpatient treatment.

	Question	Measurament scale					
follow-up	Once you get home, do you have difficulty managing the maintenance/improvement of results over time	I do not have any difficulty	yes, I have - in maintain/reduce the weight	yes, I have - about the feeding behavior and habits	yes, I have - about the motivation to change	yes, I have - Other reasons	
	I would like to be followed by healthcare professionals even from home, remotely, also through technological-digital tools	I don't care	yes, for 1 month	yes, for 3 months	yes, for 6 months	yes, for 12 months	yes, for my whole life
	How much do you agree with the following statement: "I am the main architect of my health"	very little	little	avarage	much	very much	

Table 4.7: Follow-up variables

4.4.6Use of technology

This section of the questionnaire was particularly meaningful to understand the profiles of the interviewed in terms of technological ability. Low abilities could arise a problem in the usage of a technological solution, thus it was important to explore their confidence with technological devices.

Additionally, they were asked if they know similar solutions, such as Noom, an app that can help people to better manage their health, lose or maintain weight[15]. Also, the knowledge of the app for intermitting fasting was understood. Intermitting fasting consists mainly of the consumption of two meals per day but can be applied in different ways. It is raising consensus, thus there are some apps helping in following the main principles (Patterson and Dorothy, 2017). For this reason, their awareness was measured (Table 4.8).

	Question	Measurament scale								
use of technology	How much do you agree with the following statement: "I use the Apps on my mobile phone (smartphone) with great simplicity"	very little	little	avarage	much	very much	I do not have a smartphone where i can access internet			
	How many hours a day per week do you use your mobile phone (smartphone)?	less than 1h	1-2h	3-5h	5-10h	>10h				
	Do you use digital solutions (such as APP, wearable devices such as smartwatches, smart bracelets) for the management of your health (e.g. to follow a diet or do physical activity)?	never	rarely	sometimes	frequently	always				
	Do you know an APP called "Noom"?	never heard about that	some megazines mentioned it, but I have never downloaded it	my familiy / friends / collegues mentioned it, but I have never downloaded it	some doctors mentioned it, but I have never downloaded it	web or social media mentioned it, but I have never downloaded it	some megazines mentioned it, and I have downloaded it	my familiy / friends / collegues mentioned it, and I have downloaded it	some doctors mentioned it, and I have downloaded it	web or social media mentioned it, and I have downloaded it
	Do you know about the APP for "intermittent fasting" ("fasting" in English) such as Fasting; DoFasting; Zero; Vora; 21 day hero?	never heard about that	some megazines mentioned it, but I have never downloaded it	my familiy / friends / collegues mentioned it, but I have never downloaded it	some doctors mentioned it, but I have never downloaded it	web or social media mentioned it, but have never downloaded it	some megazines mentioned it, and I have downloaded it	my familiy / friends / collegues mentioned it, and I have downloaded it	some doctors mentioned it, and I have downloaded it	web or social media mentioned it, and I have downloaded it

Table 4.8: Use of technology variables

4.5 Construct measurement

The second section of the questionnaire has been designed to measure the 10 constructs of the model through the 31 items. Specifically, each of these 10 constructs was measured through items, which tended to have overlapping meanings. This was done as each group of items was intended to measure the same underlying construct. In this

[15] https://web.noom.com/about-us/

section, there will be an accurate description of the items. In addition, for each construct, there will be a table reporting the main elements as the code and the corresponding item questions, the source, and the possible answers.

All the items were retrieved from the literature and adapted to the context, then translated into Italian to be understandable by the target group.

4.5.1 Intention to Use (ITU)

The target construct for the following items is the intention to use the medical APP briefly described before these items. The items used are three (Table 4.9), all in line with the items provided in the original study of Davis & Venkatesh (2004).

item	question					source
ITU1	I intend to use this medical App					Davis & Venkatesh (2004)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
ITU2	I predict I would use this medical App					Davis & Venkatesh (2004)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
ITU3	I would consider to use this medical App for the maintenance of my physical well-being					Davis & Venkatesh (2004)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	

Table 4.9: Items related to ITU

4.5.2 Perceived Ease of Use (PEOU)

The perception of the easiness of use of the solution is one of the fundamentals constructs of TAM. To measure the perceived ease of use of the DTx, three items were considered (Table 4.10). These questions were retrieved from Davis et al., 1989 and Davis (1993) and adapted to the context, in order to explore the effort and easiness in using such an App.

item	question					source
PEOU1	Using this medical app would not require a big effort					Davis et al. (1989)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
PEOU2	Using this medical app would be easy and intuitive for me					Davis et al. (1989)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
PEOU3	Using this medical app on my smartphone, I would find it easy to do what I want					Davis et al. (1989)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	

Table 4.10: Items related to Perceived Ease Of Use

4.5.3Perceived Usefulness (PU)

The Perceived Usefulness is another construct coming from the TAM and it explores how useful is perceived the utilization of digital therapeutics (Table 4.11). The construct was measured in three items selected from Davis's (1989) work and elaborated in order to meet the reference context. The authors focused on the usefulness and efficacy to improve health and care path.

item	question					source
PU1	Using this medical App would improve my lifestyle and my health					Davis (1989)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
PU2	Using this medical App wouold enable me to manage my path more effectively					Davis (1989)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
PU3	I would find this App useful to manage my health					Davis (1989)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	

Table 4.11: Items related to Perceived Usefulness

4.5.4 Regulative Pillar (RP)

This construct is one of the institutional factors which have been explored. This was mainly retrieved from the work of Gastaldi et al. (2019) and adapted to the context. The items to measure this construct were originally inspired by the work of Ajzen (1991), and this choice was made as in past research institutional factors are investigated through qualitative methodologies. Thus, scales from non-institutional studies were adapted. Here, the conflicts and agreements with the doctors' priorities and guidelines are explored (Table 4.12).

item	question					source
RP1	I always agree with what my physicians tell me, even on using this medical App					Ajzen (1991)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
RP2	I am often in conflict with my doctors priorities, even on using this medical App					Ajzen (1991)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
RP3	I always agree with the therapies that my doctros prescribe, even on using this medical App					Ajzen (1991)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	

Table 4.12: Items related to Regulative Pillar

4.5.5 Normative Pillar (NP)

The normative pillar is again retrieved from the institutional factors. Again, it was adapted from the items used in Gastaldi et al. (2019), which in turn were retrieved from the work of Ravlin and Meglino (1987). The same issue of the adaptation of a non-institutional scale emerged here. Items are shown in Table 4.13.

item	question					source
NP1	People who I most esteem think I should use this medical App to improve my health path					Ravlin and Meglino (1987)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
NP2	If it was presbribed them, people I most esteem would use this medical App to improve their health path					Ravlin and Meglino (1987)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
NP3	People I most esteem think that approved and certified medical App could imrpove care path					Ravlin and Meglino (1987)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	

Table 4.13: Items related to Normative Pillar

4.5.6 Cultural Pillar (CP)

The last institutional factor is the cultural pillar, in the form of culture for change. The three items were inspired and adapted from the work of Gastaldi et al. (2019), which in turn used the construct of the work of Khoja et al (2007), who used again a non-institutional scale. Here, how the change and the innovation are perceived by closest friends and relatives is explored (Table 4.14).

item	question					source
CP1	My closest friends, relatives and colluegues trust technological innovation (e.g., this medical App)					Khoja et al. (2007)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
CP2	My closest friends, relatives and colluegues are not worried by tring new things (e.g., this medical App)					Khoja et al. (2007)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	
CP3	My closest friends, relatives and colluegues are open to new digital solutions (e.g., this medical App)					Khoja et al. (2007)
	1 - complete disagreement	2 - disagreement	3 - indifference	4 - agreement	5 - complete agreement	

Table 4.14: Items related to Cultural Pillar

4.6 Data analyses

The process used to test the research model is presented in this chapter, together with the analyses and tools which have been applied to the collected data.

First, a qualitative analysis of the sample was performed. This evaluation was based on the questions presented in Chapter 4.5, which were designed to assess the general characteristics of the sample. The main instrument for this first part has been Excel, and bar and pie charts are the main instruments to display results, which are presented in Chapter 5.

A different path has been pursued for the analysis of the model and related construct. For each construct, also known as a latent variable, three items were developed, and the related results were collected. Having multiple items for each construct allowed a better accuracy in the measurement. The relations are reflective, meaning that a change in the construct implies a change in its measure, thus implying a causal relationship between the two (Edwards and Bagozzi, 2000). The collected answers on the items were analyzed through the numeric values associated with the Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). In this second part, the tool for the entire investigation is the main general-purpose statistical software Stata17.

The first step of the analysis is the evaluation of whether the dataset is suitable for applying a factor analysis. The test exploited for this assessment is the Kaiser-Meyer-Olkin (KMO) (Williams et al., 2010). With the positive result of this first step, an Exploratory Factor Analysis was performed to have a preliminary assessment of the defined construct.

Subsequently, the appraisal of the construct measurability and consistency was calculated through a Confirmatory Factor Analysis (CFA). This analysis was executed in the framework of the Structural Equation Modeling (SEM), which aimed at verifying the developed hypotheses. For the analyses, the level of significance was set at 95%. In the following paragraphs, all the steps of the analysis are presented more in detail.

4.6.1 Exploratory Factor Analysis

Before the Factor Analysis, the adequacy of the sample and suitability of data for the factor analysis should be verified. The Kaiser-Meyer-Olkin (KMO) (Kaiser 1970) test can assess the sampling adequacy, with values ranging from 0 to 1. The minimum

threshold for the suitability for factor analysis is 0.5, and above 0.6-0.7, it is considered adequate for analyzing EFA output (Taherdoost et al. 2014).

Once performed the KMO test, the Exploratory Factor Analysis (EFA) was accomplished. This is a multivariate statistical method that aims at determining:

- The number of factors influencing the set of collected measures.
- The constructs validity and their relationship with the observed measure.

This is why EFA does not require a priori specification of the number of factors (Kline, 2016).

In this study, EFA was applied to understand which items were better measuring the latent variables. Among the several available methodologies for EFA, the chosen one was principal components analysis (PCA), which is one of the most common ones (Taherdoost et al., 2014). In this technique, principal components are identified, which are the components accounting for as much variability in the data set as possible. The PCA was applied through the Kaiser rules for retention (Kaiser, 1960), where the principal component is retained with an eigenvalue greater than one. Additionally, to facilitate the interpretation of the factor loadings, an orthogonal rotation was applied in order to cluster items correlated to a particular factor. Specifically, factor loadings of the items had to be over the threshold of 0.7.

Additionally, it was important to assess the internal consistency of the items for each construct. This was tested through Cronbach's alpha (Cronbach 1951), computed for each construct. This measure assesses the Internal Consistency Reliability of a summative rating scale (Likert 1932) made of a set of items called test items. The formula (4.0) is:

(4.0)

$$\alpha = \frac{N \cdot \bar{c}}{\bar{v} + (N-1) \cdot \bar{c}}$$

Where:

- N = number of items
- $\bar{c}$ = average co-variance between item-pairs
- $\bar{v}$ = average variance

The reference for the acceptability of the alpha values is retrieved from the work of Nunnally and Bernstein's, (1994, p 265). Accordingly, the constructs are considered reliable with values of the Cronbach's alpha higher than 0.7.

4.6.2 Structural Equation Modeling

The second part of the analysis was based on Structural Equation Modeling (SEM). This term does not designate a single statistical technique but instead refers to a family of related procedures (Kline, 2016). SEM aims at testing a theory, which is explained through a model with the predictions among the possible constructs measured through observed variables (Hayduk et al., 2007), but it also represents a tool to carry out the confirmatory analysis (Hair et al 2010). In this phase of the analysis, the model presented in chapter 3 was designed through the graphical interface for SEM builder in STATA 17, exploring two main models:

- The *measurement model*, therefore, the relations between the latent variables and the observable items.
- The *structural model*, therefore, explores the relations between the constructs of the model.

4.6.3 Measurement model and Confirmatory Factor Analysis

The validity and consistency of the method to measure the constructs were assessed through the Confirmatory Factor Analysis (CFA). In STATA17, this analysis is carried out by listing all the latent constructs and linking them to their observed variables through a set of arrows. Indeed, different from the EFA where there is no need for specification, in the CFA the number of items for each construct has to be defined before the analysis. Additionally to the arrows between latent variables and items, the relationships between the different constructs have to be introduced too. The results of this analysis should be used to assess the validity of construct convergence; indeed, the latent variable is better defined if the measures are more strongly correlated (Weston, 2006). This is proven from the factor loadings, generally interpreted as regression coefficients. The convergence validity was assessed by two indicators:

- Composite Reliability – CR

This measures the internal consistency of the measured items and is computed in the formula (4.1).

$$CR = \frac{(\sum_{i=1}^{p} L_i)^2}{(\sum_{i=1}^{p} L_i)^2 + \sum_{i=1}^{p} V(e_i)} \quad (4.1)$$

Where:

- Li = factor loading of the variable i in the construct.
- p = number of the variables in the construct.
- $V(e_i)$ = error variance of the variable i, and it is computed as V(ei) = 1 – (Li)2.

The values for the acceptability of CR should be 0.7 or higher to ensure the internal consistency by the Fornell & Larcker criterion (1981).

- Avarage Variance Extracted – AVE

This value measures the how much the construct is able to capture variance with respect to the overall variance of the overall variance of its indicators (Henseler et al. 2015) and it is measured as shown in the formula (4.2).

$$AVE = \frac{\sum_{i=1}^{p} L_i^2}{p} \quad (4.2)$$

Where:

- L_i = factor loading of the variable i in the construct.
- p = number of the variables in the construct.

To support the convergent validity, the acceptability level for AVE is 0.5 or higher.

4.6.4 Structural Model and Goodness of Fit

The second part of the SEM aimed at assessing the structural model, where the hypotheses of the model have been tested. The relation was considered verified when the p-value was below the threshold of 0.05. Additionally, several indexes have been developed to evaluate the fit and these measures are intended as continuous measures of model-data correspondence. (Kline, 2016). Specifically, the following indexes have been used for this analysis: square error of approximation (RMSEA), the standardized root mean residual (SRMR), the comparative fit index (CFI), the Tucker-Lewis index (TLI).

The RMSEA is an absolute fit index, therefore it measures how well an a priori model explains the data. This indicator is scaled as a badness-of-fit and it measures the amount of unexplained variance, therefore, values closer to zero represent best results (Kline, 2016). Indeed, 0.01 is considered as a maximum threshold for excellent fitness. Values below 0.05 are usually defined as a good fit, while values ranging from 0.05 to 0.08 are usually considered acceptable fit. The threshold for poor fitting is 0.1 (MacCallum et al., 1996)

SRMR is an absolute fit index too and it measures the standardized difference between the observed correlation and what was hypnotized in the model. As it is an indicator for the badness-of-fit statistics, lower values imply the model better fits the data (Kline, 2016). A good fit is usually limited to 0.08 (Hu and Bentler, 1999).

The Bentler CFI is an incremental fit index, therefore it measures the relative improvement in the fit of researchers' model over the baseline model (Kline, 2016; Bentler, 1990). It is also a goodness-of-fit, therefore a better fit implies values closer to 1. A related statistic is the TLI (Tucker & Lewis, 1973), and they are both recommended to be >0.9 (Bentler & Bonett, 1980).

4.6.5 The control Variables

To assess if the intention to use digital therapeutics could be influenced by some specific characteristics of the population, some control variables were included in the model. Data for these control variables were retrieved by the data collected in the first part of the survey which aimed at gathering personal information. Specifically, these variables explored the following characteristics of the respondents.

- Gender
- Age
- Marital status
- Level of education
- Employment status
- BMI
- Difficulties in maintaining weight loss after the received treatment
- Ease of use of digital solutions
- How much they are prone to change, measure though how much they feel they are responsible for their health.
- Willingness for being supported.

5. Descriptive analysis

The delivery of the survey allowed firstly to investigate some characteristics of the sample considered. This information was used to identify the limitations of the sample and to determine if the results could be generalized and extended to a larger sample. Furthermore, it should not be ignored that these control variables deeply influence the model and the relationships between the different constructs. To carry out the following analyses, the software used was mainly Microsoft Excel.

5.1 Demographic analysis

The initial questions of the survey were dedicated to the collection of demographic information. In particular, respondents were asked to state their gender, age range, level of education, occupation and relationship status (Table 5.1). Furthermore, since the sample was composed of patients and former patients of the Istituto Auxologico Italiano, they were asked to indicate their region of residence, assuming Italian nationality for all respondents. An additional feature of interest for this specific case was to define weight in kg and height in cm, in order to calculate the BMI of each patient. BMI is computed as the weight in kilograms divided by the height in meters squared, as shown in formula (5.1).

$$BMI = \frac{Weight\ [kg]}{Height^2\ [m^2]} \tag{5.1}$$

Variable	Responses (#) N = 341	Responses (%)
Gender		
Female	241	71%
Male	93	27%
I prefer not to say	7	2%
Age Range		
<18	5	1%
18-30	17	13%
31-40	19	6%
41-50	59	17%
51-60	121	35%
61-70	83	24%
>70	37	11%
Level of education		
Elementary	11	3%
Lower secondary	67	20%
Secondary school	191	56%
Degree	52	15%
Doctorate or postgraduate	20	6%
Occupation		
Unemployed	47	14%
Housekeeper	32	9%
Student	8	2%
Worker	159	47%
Retired	95	28%
Relationship status		
Single	118	34,71%
Stable partner	194	57%
Other	29	8,3%
Region of residence		
Lombardia	251	77%
Piemonte	36	11%
Liguria	7	2,15%
Sicilia	7	2,15%
Toscana	6	1,84%
Puglia	5	1,53%
Lazio	3	0,92%
Marche	3	0,92%
Veneto	2	0,61%
Abruzzo	2	0,61%

Table 5.1: Demographic and Personal variables results

Among the respondents, the majority are female, accounting for 71% of the total. The number of male respondents was 27% and only 2% preferred not to indicate their gender. From this characteristic of the model, the first limitation of the study might arise. Specifically, a significant female majority in the sample creates difficulties in generalizing the result. In addition, the problem of obesity appears to be more common in men than in women, so the difference in level between males and females may represent a constraint for the analysis.

With regard to the age range, the majority of respondents belong to the 51-60 age range representing 35% of the total followed by the 61-70 age range (24 % of the total). The objective of the survey is to investigate the dynamics of acceptance of a new medical APP, and usually, the older age groups are also the ones that present the greatest resistance to change towards digital solutions. Therefore, it may be interesting to understand the attitude towards the adoption of these age groups. At the same, 17% and 13% of the respondents belong to the 41-50 and 18-30 classes respectively. This distribution depends above all on the type of patients taken care of by Auxologico since a significant number of surveys were distributed in paper form by patients hospitalized at the Institute. On the other hand, some answers were collected by e-mail, thus attracting also younger age groups.

As far as the level of education is concerned, the majority of respondents have a high school diploma as their highest qualification, representing 56% of the total. Only 3% have an elementary level of education and only 6% have doctoral or postgraduate degrees. Respondents with a university degree account for 15%, which can be compared to the situation in Italy, where only 20% of the population aged 25-65 has a university degree[16] (ISTAT, 2021).

Among the respondents, only 2% were students, probably because the number of respondents under 18 years of age corresponds to 1% of the total. The majority is represented by the working class, which amounts to 47% of the total, followed by retired people (28%). Finally, the unemployed class accounts for 14% and housewives for about 9% of the total. Also, in this case, the data are more or less heterogeneous, and the results can easily be generalized for a larger sample.

Moving to BMI is considered a key characteristic for the analysis. It was computed by asking respondents to enter their weight in kilograms and their height in centimeters. BMI can give an indication about the several needs, objectives, and care pathways of

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16 https://www.ansa.it/sito/notizie/cronaca/2021/10/08/istat-in-italia-solo-il-201-di-laureati-contro-il-328-ue_51620548-b30a-4657-b347-2b6cb60348e1.html

the different patients in the sample. the majority of respondents had a BMI between 31 and 40 kg/m2, i.e., patients with moderate and severe obesity. Cases of very severe obesity account for 32% of the total, i.e., with a BMI > 40 kg/m2. This implies that the results are not representative of the entire Italian population but rather of a typical patient who might resort to, is turning to, or has gone to a facility like Auxologico.

5.2 Health status

The burden of obesity cannot be considered as an isolated one. An obese patient is also one with an increased risk of other associated diseases. In particular, obesity can lead to various disorders such as metabolic, cardiovascular, and respiratory diseases.[17] The higher the patient's BMI, the higher the risk of incurring other diseases. The investigation was carried out to map all the obesity-associated diseases the patients suffer from.

The patient was able to identify one or more of the following diseases associated with obesity: hypertension, diabetes, hepatic disease, kidney disease, cardio/cerebrovascular disease, others. The analysis of the results was carried out by comparing male and female cases. In particular, data show that the most common disease in both men and women is hypertension. In particular, 14% of women and 19% of men are affected by this condition. For 19% of men, diabetes is a frequent disease, a fact that is not confirmed in the case of women. Only 5% of women, indeed, have that pathology. Many of the male respondents (19%), did not find the appropriate disease among the options and therefore selected "other".

The alarming fact, which confirms what has been said previously, is that the majority of the participants state that they have more than one disease at the same time. Indeed, 58% of the women and 1/4 of the men selected more than one disease. Isolated cases of liver disease, kidney disease, osteoporosis and osteoarthritis were less common.

[17] http://www.centro-obesi.com/it/rischi_del_paziente.php

The incidence of different pathologies among men and women is represented in Figure 5.1.

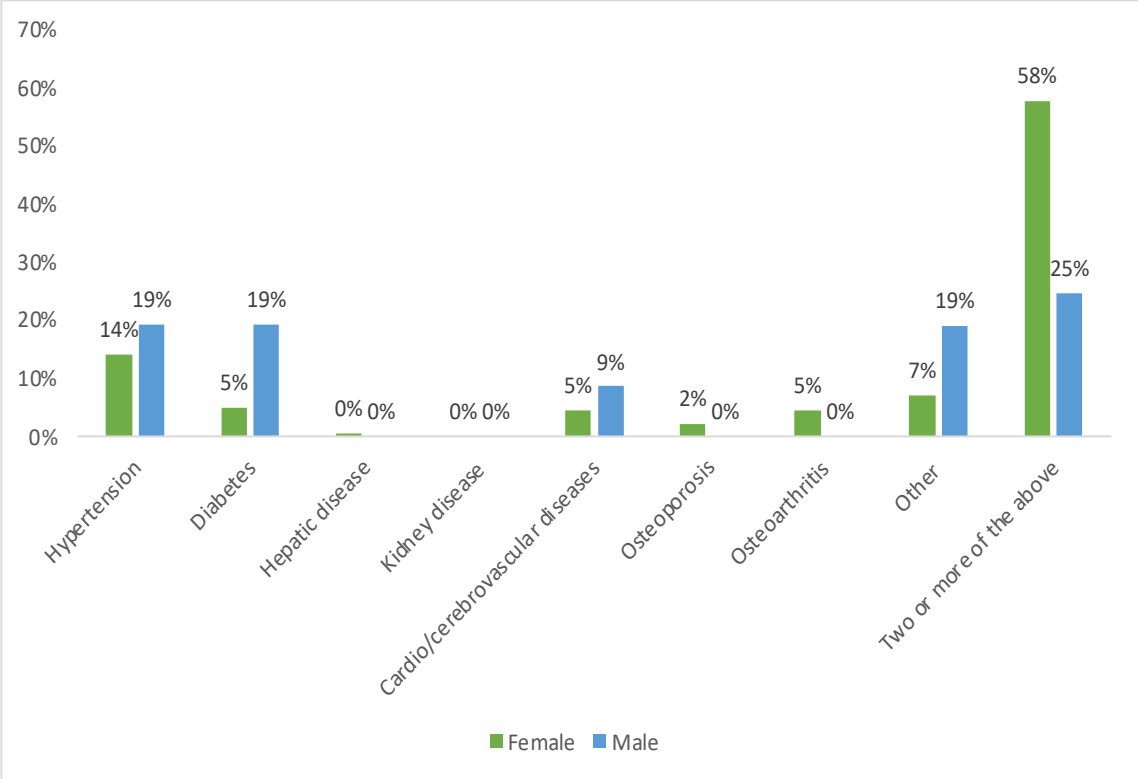


Figure 5.1: Incidence of pathologies on respondents according to gender

The previous analysis yielded a precise description of the patient's state of health. The next step was to analyze the type of therapeutic pathway carried out within the Auxologico Institute in the last year. The patient had the possibility to choose between one or more of the following options: Outpatient pathway (Obesity Centre), Inpatient (e.g. Piancavallo), MAC/Day Hospital, Bariatric surgery. All paths are explained in Chapter 4.4.2.

The analysis was carried out by comparing the pathway and the age range the patient belongs to. The results show that for the majority of age categories a significant percentage (on average about 30%) of the respondents declare having crossed two or more steps within Auxologico. The exception is the age range between 51- and 60-years interval, of which 62% state to have crossed two or more paths within the Institute, a number considerably higher than the average value. Among the most frequent pathway, Outpatient can be included, especially for interviewers belonging to the age group between 18-30 years (about 41%) and 41-50 years (about 34%).

Similarly, hospitalization or Inpatient pathway is considered very common in patients from 61 to 70 years (54%) and in the over 70 (41%). In a much lower frequency, the MAC/Day hospital pathway is however important, especially for patients between 31-40 years of age. Almost negligible can be considered the cases of bariatric surgery, usually associated with very severe cases of obesity. Figure 5.2 shows the findings.

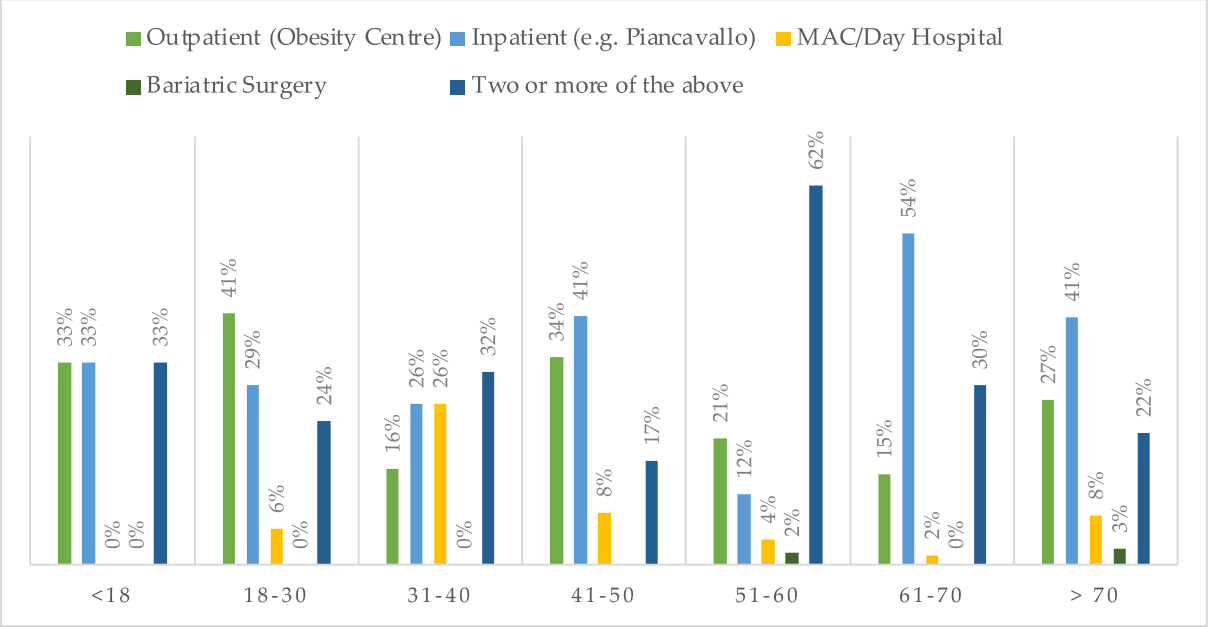


Figure 5.2: Experienced path in Auxologico according to age range

In order to complete health status sphere, respondents were asked to indicate whether they had taken or were taking medication to treat obesity. The majority of patients do not use drug therapies. On the other hand, 76 patients (about 22% of the total) responded positively. Results are shown in Figure 5.3.

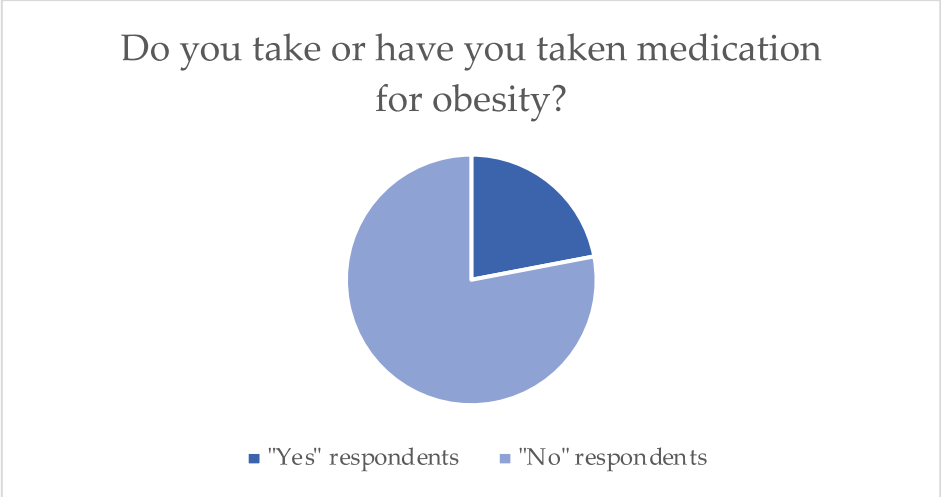


Figure 5.3: Drug intake among respondents

5.3 Social and familiar context

When treating conditions such as obesity and related pathologies, the level of involvement by the patient's family or loved ones cannot be ignored. Indeed, the social context of the patient definitely has an influence on the patient's adherence to treatment and psychological support can be considered crucial for the effectiveness of care(Björn Meyer, 2015).

The first question of the survey dedicated to the social aspect of the patient is "*Do you consider yourself a person who likes to be in company?*". For the measurement of this item, the answer can change from 1 (very little) to 5 (very much).

Among the respondents, 31% declare to like much and 14% very much to be in company. The majority of respondents, however, are in the middle ground, accounting for 48% of the total. An irrelevant proportion of respondents consider themselves little and very little sociable, respectively 6% and 1% of the total (Figure 5.4).

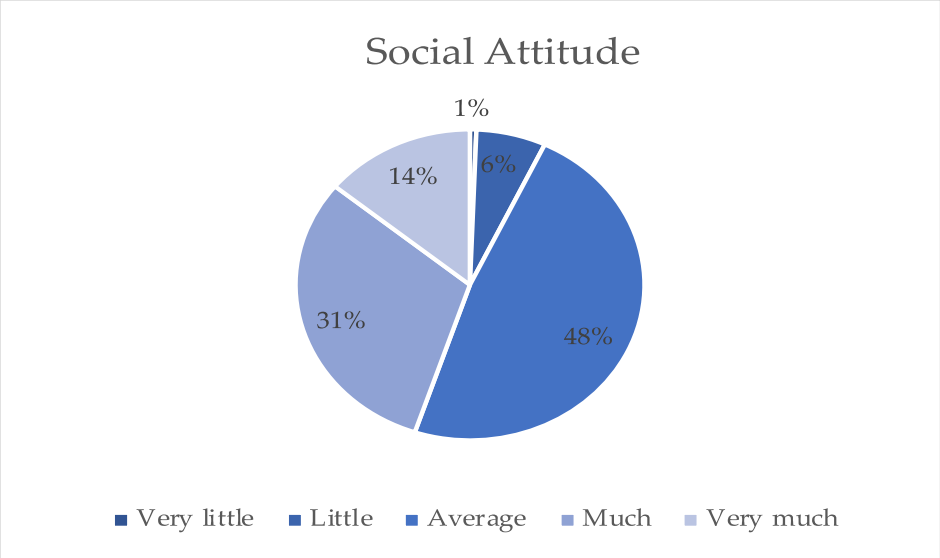


Figure 5.4: Results of social attitude

Analyzing more in-depth the context of the obese patient, one of the survey questions focuses on who the people are who join the respondent in eating his/her daily meals (Figure 5.5). The results show that more than 200 people, i.e., 62% of the total, spend their daily meals with their families. About 105 respondents, i.e., 31% of the sample, declare to eat meals alone and only 7% of the interviewees are accompanied by family and friends.

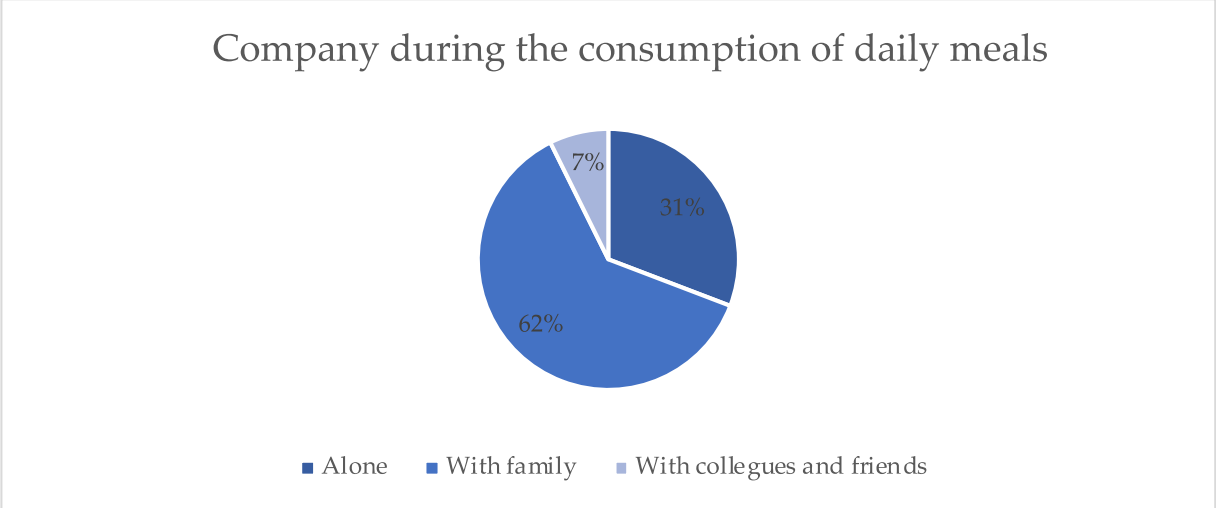


Figure 5.5: Results about the company during consumption of daily meals

Afterward, the analysis of the patient's perception of the psychological support and the level of involvement with a precise focus on family context was carried out. Three questions were constructed to investigate the influence of family members on the care pathway. The patient had the possibility to answer "yes" or "no" to the three questions. The first question (item "*Is/would your family be involved in the treatment process?*") refers to the level of involvement of the family context in the care pathway. About 61% of the patients declare to have family members involved in the care process. The second question (item "*Does your family NEGATIVE influence your eating behavior*?") focuses on the negative influence that the family can have on the patient's eating behavior. A bit less than 1/4 of respondents state that they receive a negative influence from the family context. Finally, the third question (item "*Does the family members support/motivate you in maintaining/improving your health?")* tries to investigate the psychological support and motivation received from the family members. About 81% declare that they are helped and stimulated by the family in maintaining and improving their health. It is interesting to note that, from the results collected (Figure 5.6), few patients feel the need for more psychological support. What emerges is the need for a higher level of involvement and the need to resolve the negative influences that family members may

have on eating behavior. Overall, the results lead to positive considerations, as no significant criticalities are present.

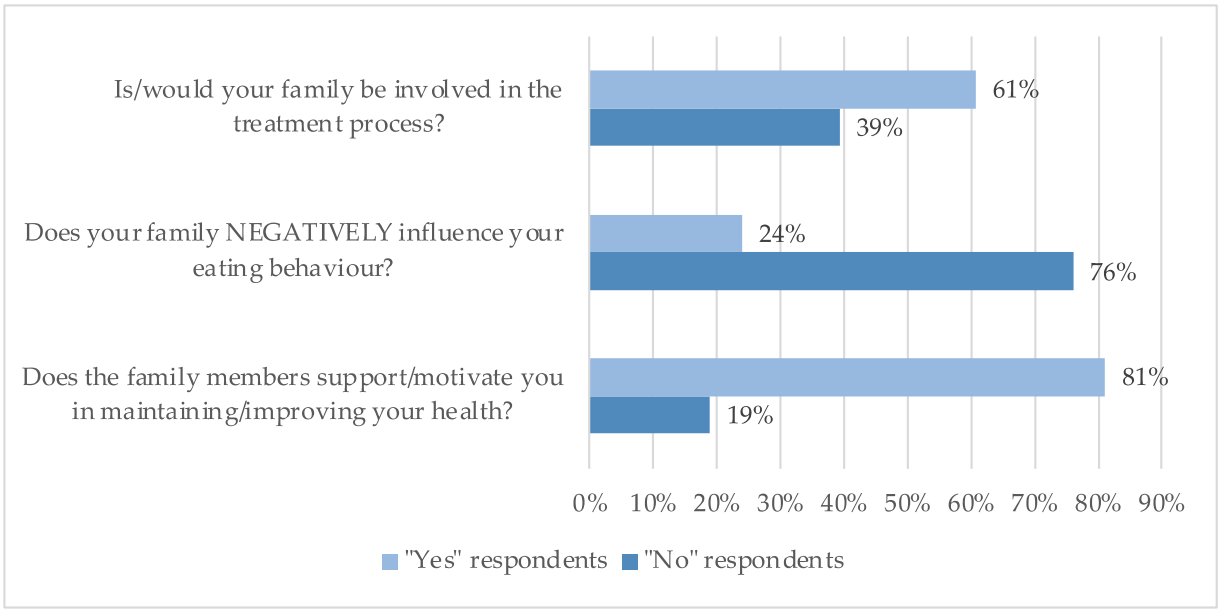


Figure 5.6: Family influence on treatment

5.4 Patient satisfaction

In order to assess the current level of patient satisfaction, the respondents were asked to express an opinion about the results obtained during their stay at Auxologico and their level of satisfaction with the achieved results. The answer varies, again, from 1 (very little) to 5 (very much) according to the client's opinion. In particular, two questions were dedicated to this objective and were analyzed jointly. The choice of studying the two questions together is mainly due to the fact that they are interconnected. In fact, the assumption is that if the patient has noticed improvements in his or her state of health, he or she will probably also be satisfied with the results obtained. On this account, it is reasonable that the trend in results is consistent and comparable between the two questions. In particular, the majority of the respondents declare that they have noticed enough improvement in their health status and, consequently, that they are quite satisfied. This case is represented by about 40% of the sample, for both items. On average, about 28% of respondents claim to have experienced many improvements in their health and show a high level of satisfaction. However, a not negligible proportion of patients did not see any improvement and was not satisfied at all. These are about 8% of the total. Although the patient's perception of the treatment provided by Auxologico is in overall positive, the

percentage of those who saw a lot of improvement and a very high level of satisfaction remains low, 11% and 13% respectively for the first and second question. Therefore, the analysis shows a possible margin for improvement (Figure 5.7).

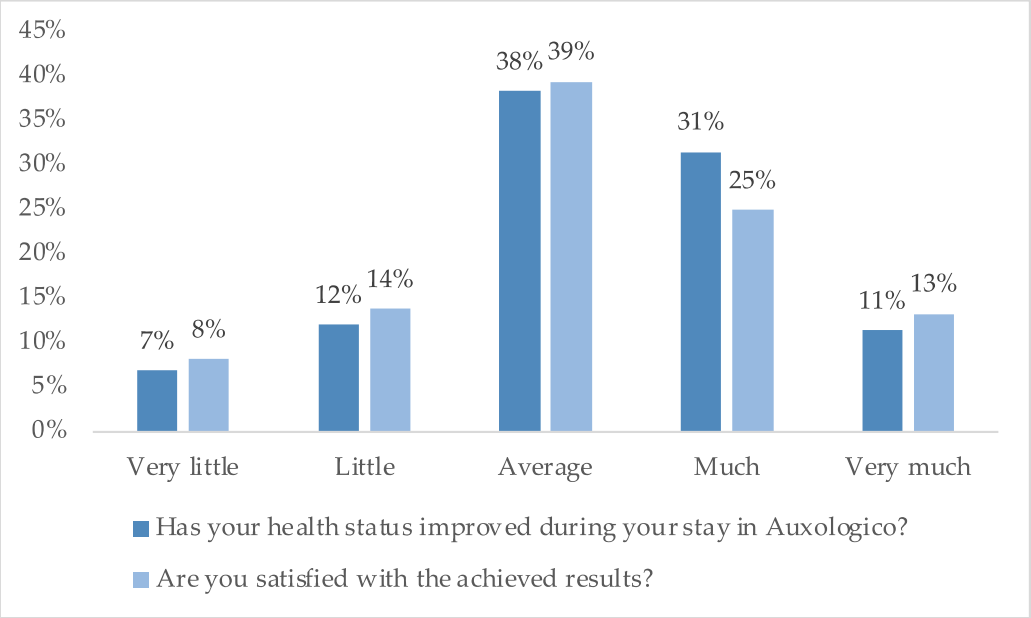


Figure 5.7:Health improvements

5.5 Follow up

The subsequent questions of the survey aimed at investigating the patient's attitude towards health maintenance. First of all, the results should reveal what is the most critical and constraining domain in maintaining and improving health outcomes. The answers show (Figure 5.8) that the majority of the respondents, about 28% of the total, find it difficult to manage the area of weight maintenance/reduction once they return home. Similarly, 23% of the interviewees stated that they had difficulties in managing their eating habits and behavior. However, the same percentage of responders states that they do not have any kind of difficulty and do not need external support. The problem of motivation to change seems to be of little relevance for the sample and the proportion of patients who declare to have difficulties at home, but in areas not mentioned above, is not negligible (about 23%).

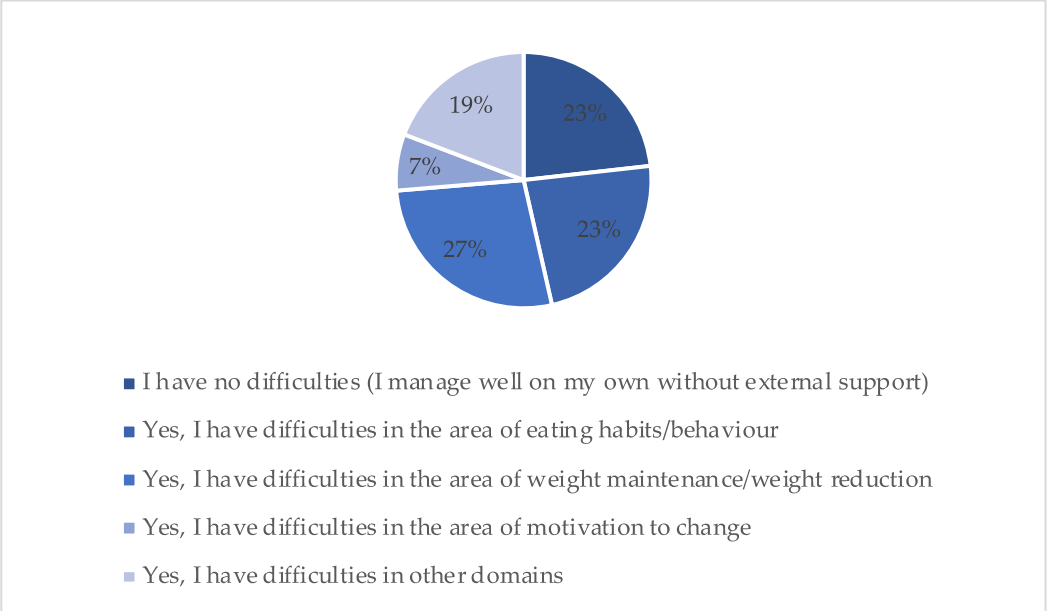


Figure 5.8: Follow-up variables

Once the patient's areas of concern, if any, were mapped, the aim was to investigate the respondent's attitude towards adopting digital solutions to solve these problems. In particular, the patient's willingness and intention to be followed at home or remotely by health professionals through technological tools and other digital innovations were analyzed (Figure 5.9). About 20% of the respondents stated that they

were not interested, which is reasonable considering that 23% have no problems in managing health maintenance once back home. Few patients, 3% and 7% of the total considered it useful to be followed by health professionals from home for short periods, 1 and 3 months respectively. A much higher proportion of respondents, about 14%, though that 6 months of follow-up through the proposed solutions was sufficient. The majority, however, perceives the advantage of solutions applied in the long term. Indeed, 26% of the respondents like to be followed up for an indefinite period, comparable to a lifetime. The remaining 29% believe that one year is sufficient.

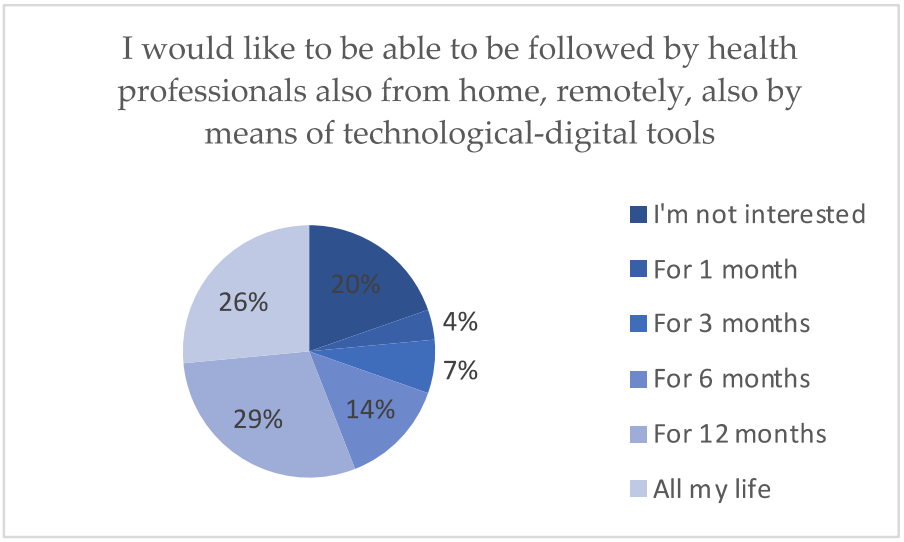


Figure 5.9: Willingness to be supported

The last question devoted to this domain aims at investigating patients' perception of their responsibility for their own health. Respondents were asked to express their degree of agreement with the expression: *'I am the man responsible for my own health'*. As already stated, also this item was measured by a Likert scale from 1 (very little) to 5 (very much). The aim of the question was to find out how responsible the patient feels for his or her own health. There are many considerations that can be built around this question. First of all, the answer gives an idea of the degree of motivation for change that the patient possesses. In fact, patients who consider themselves responsible for their own health may feel more motivated to change but recognize that they themselves are a significant limitation and are aware that the most significant change has to come from oneself. Therefore, they are likely to find it more difficult to manage on their own once they return home and may need external support for longer periods. The results show that the majority of respondents claim to be "very much" and " much" in charge of their own health, respectively 34% and 37% of the total. About

24% of the interviewees felt “quite” responsible and a negligible proportion disagreed with the statement. Results are shown in Figure 5.10.

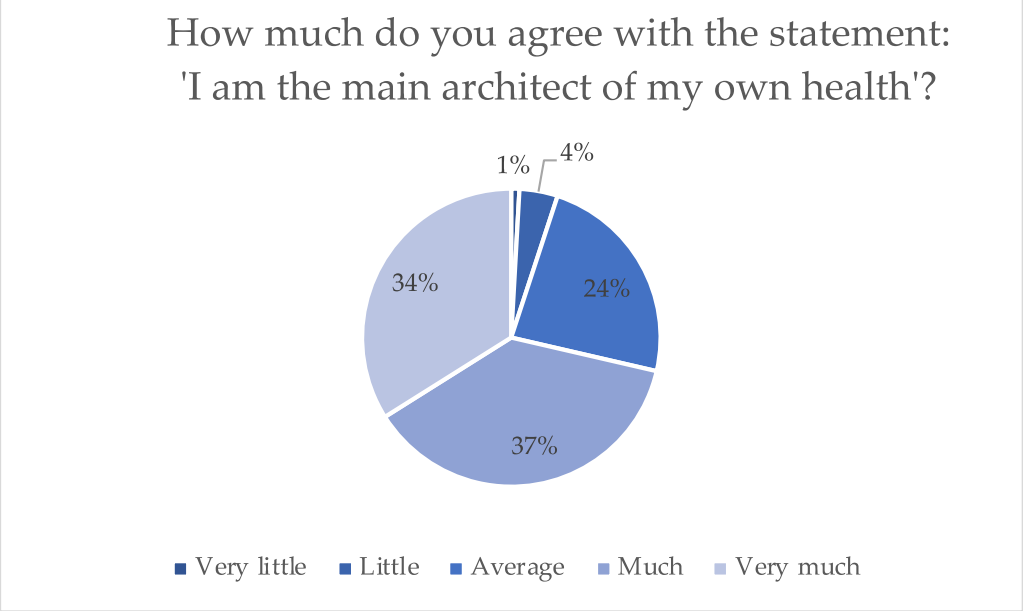


Figure 5.10: Sense of responsibility toward health status

5.6 Digital related variables

In order to assess the attitude towards digital solutions, the first step was to ask the interviewees whether he/she can use his/her smartphone easily. Answers ranged from 1 (strongly disagree) to 5 (strongly agree) but, in this case, a sixth response option was added: "*I do not own a smartphone*". The results show (Figure 5.11) that only 10 patients, about 3% of the total, do not own a smartphone. The majority claimed to use the smartphone quite easily, accounting for 34% of the total. In addition, those who agree and very much agree with the statement "*I use my smartphone with ease*" turn out to be 24% and 23% of patients. However, 5%, some 18 respondents, felt that they strongly disagreed with the above statement and the proportion of those who disagreed, 11%, was not negligible.

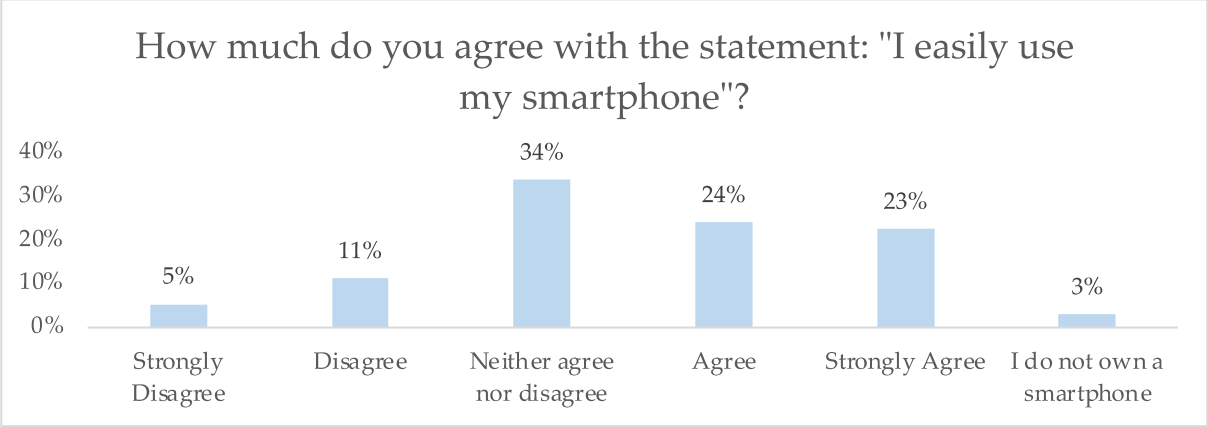


Figure 5.11: Simplicity in using the smartphone

Excluding those who do not own a smartphone, the sample of 331 respondents was analyzed to investigate the number of hours per day spent using a smartphone. It is important to note that since this is a personal statement, it may not always correspond to the actual time of use. In fact, it is plausible that perception is slightly underestimated compared to practice. About 37 % of the interviewees claim to spend time on their smartphone in the two ranges: 1-2 hours, 3-5 hours. Only 4 % claim to spend more than 10 hours a day using their smartphone. Those who claim to spend less than one hour a day and between 5 and 10 hours are comparable, 11 and 12 % of the patients surveyed respectively. Data are summarized in Figure 5.12.

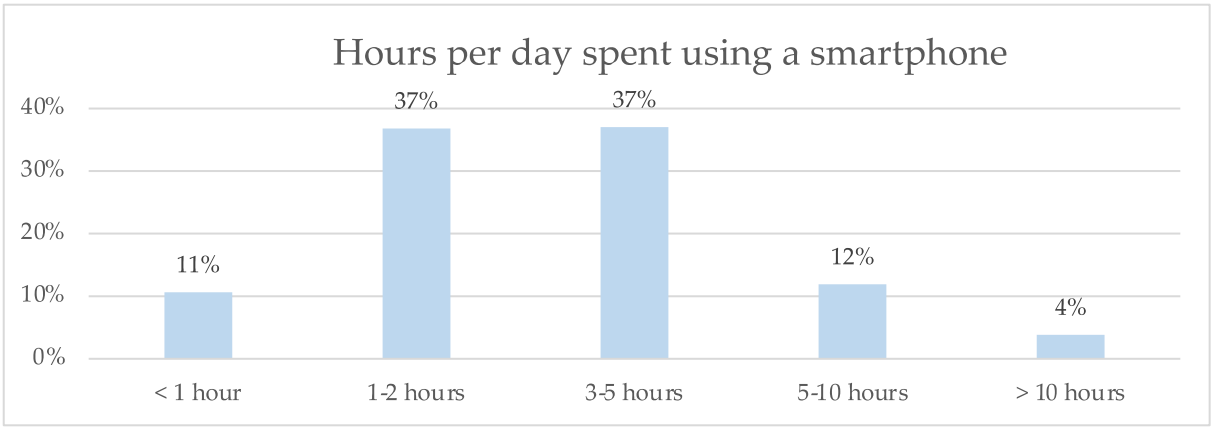


Figure 5.12: Hours per day spent in using a smartphone

In order to analyze patient orientation towards digital solutions more in-depth, respondents were asked to indicate how often digital innovations are used for health purposes. The focus shifts to the care and monitoring functionality of the device, APP, or other solutions.

Few patients currently use digital solutions for health purposes, accounting for 11% of the total. About 13% say they often use technologies, apps, devices to manage their health and 12% rarely use them. A higher proportion of patients (21%) sometimes use digital health technologies, but the proportion of respondents (around 44%) who have never used digital solutions to manage their health is still significant. Results are represented in Figure 5.13.

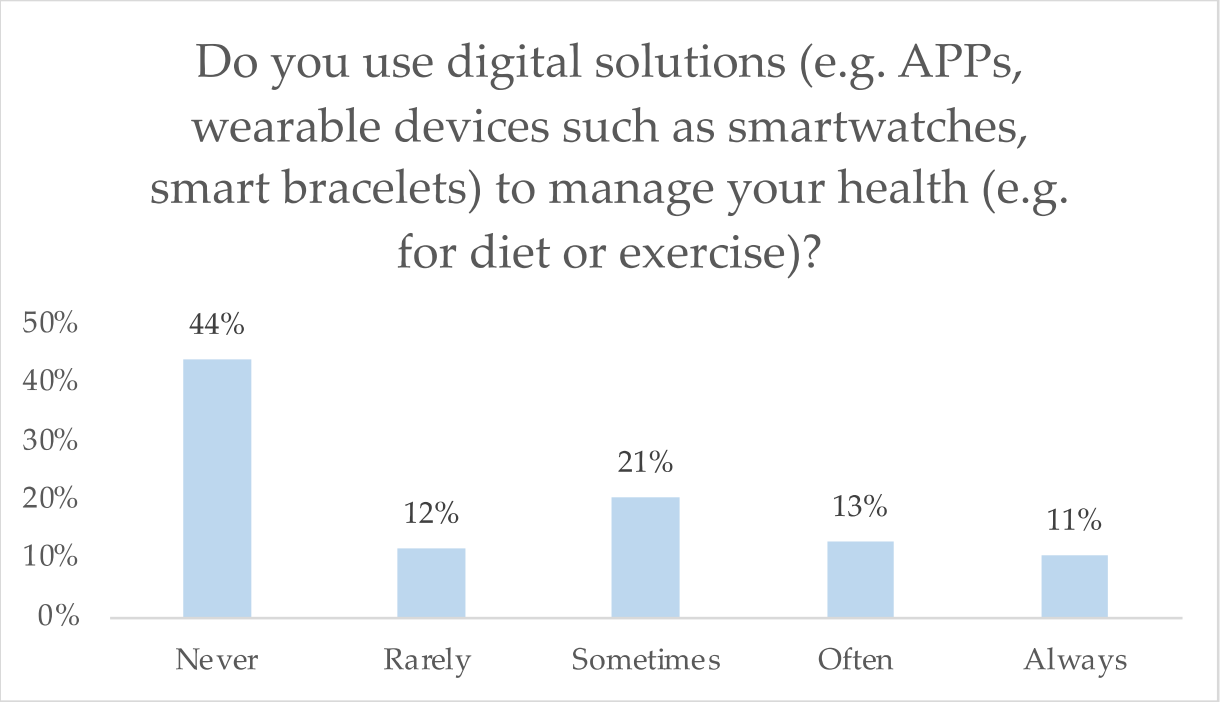


Figure 5.13: Usage of digital solutions to manage health

To conclude, the last two questions of the survey aimed to investigate the popularity of certain APPs, respectively "Noom" and intermittent fasting APPs, among the patients in the sample. The majority, in both cases, stated that they had never heard of them, 94% for Noom and 77% for intermittent fasting APPs respectively. In the case of Noom, none of the respondents had ever downloaded the app, but 2% had heard about it from some magazines and a further 2% from the web/social media. In the case of intermittent fasting apps, the data are more promising, although not very significant. 10% of patients heard about it from the web/social media, which is the most known source among respondents. 2% of respondents heard about it either from magazines and from the web/social media and also downloaded it to try it out.

Responses are shown in Figure 5.14.

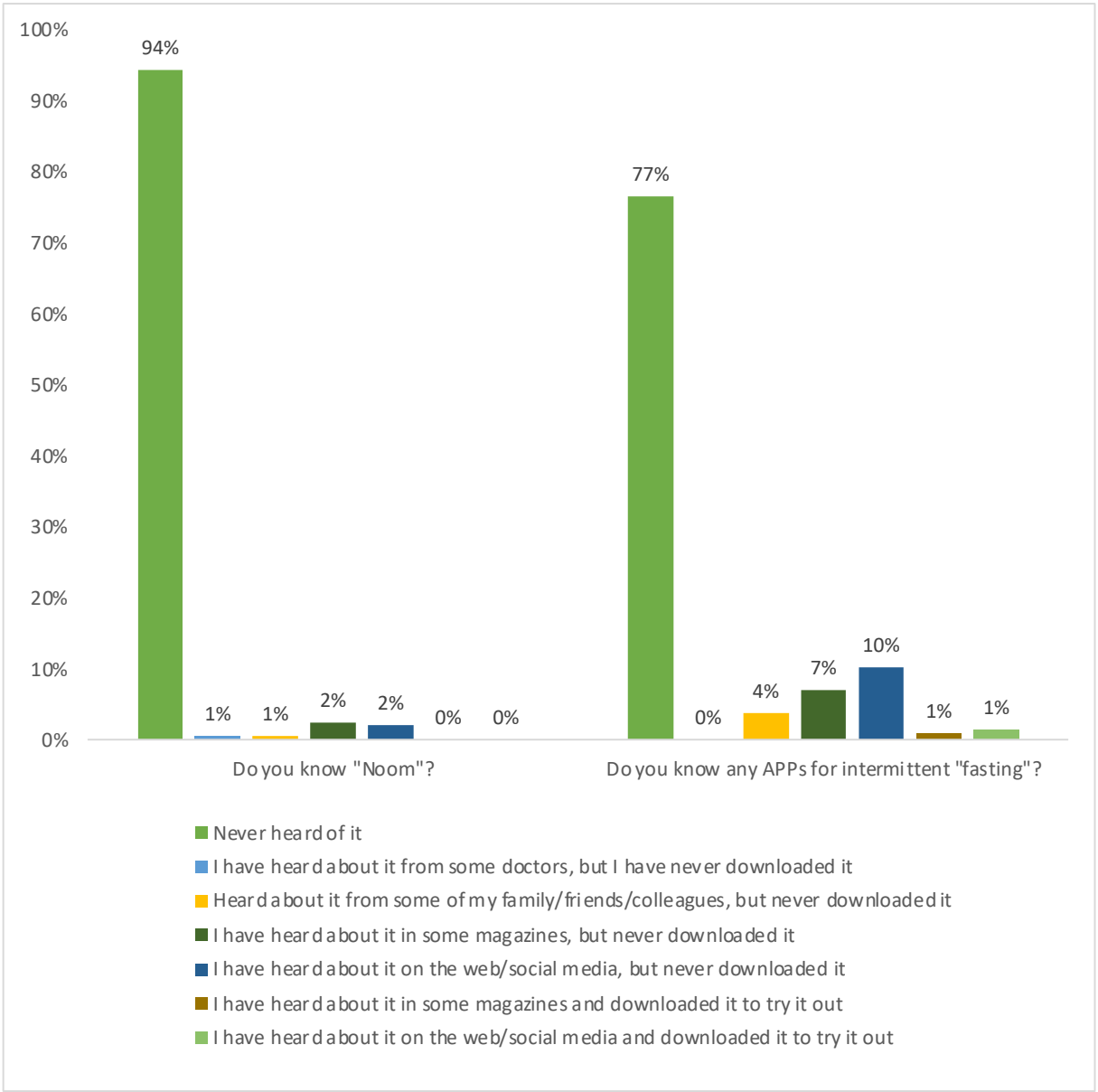


Figure 5.14: Awareness of Noom and Intermittent “fasting”

6. Results

As mentioned above, the data analyses were carried out using the software STATA 17 and, to support specific calculations, Excel. The results of the Exploratory Factor Analysis (EFA), Confirmatory Factor Analysis (CFA) and Structural Equation Modeling (SEM) analyses will be introduced in the following sections.

6.1 Preliminary analysis

The starting point was to assess whether it would be appropriate to conduct an Exploratory Factor Analysis. To do so, the Kaiser-Meyer-Olkin (KMO) test was carried out, with the aim of analyzing the adequacy of the sample (Table 6.1). In fact, this is a statistic that indicates the proportion of variance between the variables in the model. A KMO value between 0.8 and 1 indicates that the sample is adequate and therefore a factor analysis is considered useful.

Variable	kmo
ITU1	0.8952
ITU2	0.9084
ITU3	0.9502
PU1	0.9666
PU2	0.9468
PU3	0.9546
PEOU1	0.9394
PEOU2	0.9376
PEOU3	0.9505
RP1	0.9400
RP2	0.9119
RP3	0.9443
NP1	0.9325
NP2	0.9242
NP3	0.9305
CP1	0.9580
CP2	0.8896
CP3	0.8935
Overall	**0.9332**

Table 6.1: KMO Test

On the other hand, a KMO value below 0.5 indicates that the sample is not adequate, and some action needs to be undertaken and, consequently, this could be problematic for factor analysis. The results show that, for all items, the KMO is higher than 0.8, specifically with a minimum value of 0.8896 and a maximum value of 0.9580. For this reason, it can be deduced that factor analysis is worthwhile.

Once the adequacy of the sample had been verified, an Exploratory Factor Analysis was carried out. The objective of the EFA was to understand how well the items are valid in representing certain constructs for exploratory purposes, in the sense that the relationships between items and constructs can be investigated from the data. The results showed that ITU is defined by 3 items and, similarly, all the other constructs, namely PU, PEOU, CP, RP, NP. The logic was to select all items with a factor loading greater than 0.7. Indeed, factor loading represents the saturation, more specifically the "intensity" of the relationship between the factor and the measured variable (Joyce, 2013). A factor loading lower than 0.7 indicates the absence of correlation or makes the link between the two variables negligible. In the current case, no item from the proposed model was removed due to factor analysis as they all had factor loading above the acceptability threshold (Table 6.2).

In parallel, to assess the reliability of the survey constructs, Cronbach's alpha was used as the main statistical indicator. In particular, assessing the reliability (or trustworthiness) of the questionnaire means assessing how accurate the data are. The value of the indicator is usually between 0 and 1. A high alpha value expresses high data quality, vice versa, if the value is closer to 0, it indicates low reliability of the available data. The indicator aims to investigate how reliable the items actually are in representing the construct and therefore, it was measured for each construct. Usually, an acceptable Cronbach’s alpha has a value greater than 0.7 (Tavakon and Dennick 2011).

Construct	Items	Measurement Items	Factor Loading	Cronbach's alpha
Intention to use (ITU)	ITU1	I will want to use this medical APP	0.9350	0.9029
	ITU2	I plan to use this medical APP in the future	0.9128	
	ITU3	I would like to use this medical APP to keep fit	0.7352	
Perceived Usefulness (PU)	PU1	Using this medical APP will improve my lifestyle and health	0.8054	0.9215
	PU2	The use of this medical APP will allow me to manage my care pathway more effectively	0.9223	
	PU3	The use of this medical APP will help me to manage my health	0.9202	
Perceived Ease of Use (PEOU)	PEOU1	Using this medical APP will NOT require much effort from me	0.8121	0.8811
	PEOU2	Using this medical APP will be intuitive and easy for me	0.8126	
	PEOU3	When I use this medical APP on my mobile phone I will easily be able to do what I need to do	0.8391	
Regulative Pillar (RP)	RP1	I always agree with what the doctors who treat me tell me, including the use of this medical APP	0.8558	0.9108
	RP2	I always agree with the priorities given to me by the doctors treating me, including on the use of this medical APP	0.8874	
	RP3	I always agree with the therapies prescribed by the doctors treating me, including when using this medical APP	0.8424	
Normative Pillar (NP)	NP1	People I rate most highly think I should use this medical APP to improve my care pathway	0.8087	0.8855
	NP2	People I estimate most would use a medical APP to improve their care pathway if prescribed by their doctor	0.8422	
	NP3	People I value most think that medical apps can help improve their care pathway if certified and validated	0.8274	
Cultural Pillar (CP)	CP1	In my circle of family/friends/colleagues there is full confidence in technological innovation (like, for example, this medical APP)	0.7309	0.8578
	CP2	There is NO fear in my circle of family/friends/colleagues to try new things (like, for example, this medical APP)	0.8145	
	CP3	**In my circle of family/friends/colleagues there is full openness to digital solutions (like, for example, this medical APP)**	**0.8388**	

Table 6.2: Factor loadings and Cronbach's alpha

6.2 Structural equation modeling

The next step after EFA was a Confirmatory Factor Analysis (CFA). In particular, through the CFA it is possible to identify the goodness of the model, thus, contrary to the previous case, the starting point is not only the data but also the structure of the model itself (Mueller, 1996). As a matter of fact, the aim is to understand if the model is suitable with respect to the observed sample. The above-mentioned analysis is therefore designed to confirm the relationships between constructs and items identified through the EFA. In the CFA instead, factor loading was calculated in order to derive convergent validity indicators such as Average Variance Extracted (AVE) and Composite Reliability (CR). The calculations useful for this section were supported by Excel software. As shown by the results in Table 6.3 for each construct, the indicators respect the limits of acceptability. In fact, an AVE higher than 0.5 and a CR higher than 0.7 are indicatives of good measurement quality. Notably, the factor loadings for all the items are above 0.7. Furthermore, for all constructs, the CR and AVE exceed respectively the values 0.8 and 0.6. This is representative that convergent validity is verified.

Construct	Item	Factor Loading	CR	AVE
Intention to use (ITU)	ITU1	0.942	0.912	0.777
	ITU2	0.939		
	ITU3	0.750		
Perceived Usefulness (PU)	PU1	0.810	0.926	0.806
	PU2	0.941		
	PU3	0.938		
Perceived Ease of Use (PEOU)	PEOU1	0.822	0.886	0.722
	PEOU2	0.847		
	PEOU3	0.878		
Regulative Pillar (RP)	RP1	0.862	0.936	0.774
	RP2	0.894		
	RP3	0.885		
Normative Pillar (NP)	NP1	0.825	0.886	0.721
	NP2	0.858		
	NP3	0.865		
Cultural Pillar (CP)	CP1	0.806	0.861	0.674
	CP2	0.813		
	CP3	0.843		

Table 6.3: Factor loadings, CR and AVE

The results showed that the construct with the lowest AVE and CR is the Cultural Pillar (CP) from Institutional Theory. CP construct presents a CR equal to 0.861 and an AVE amounting to 0.674, which can nevertheless be considered acceptable values.

The subsequent analysis was carried out using the Structural Equation Modelling (SEM) technique. Starting from the construction of the model through the design of the path diagram (Figure 6.1), it was possible to emphasize the relationships between the different constructs assumed in Chapter 3.2 and the links between the items and the reference factors. In more detail, the purpose of the analysis is to verify the significance of the hypothesized relationships with reference to the sample analyzed. To accomplish this, several parameters were analyzed. Firstly, the p-value relative to a 5% confidence interval has the function of testing the statistical significance of the path in question. In particular, a p-value of less than 0.05 is indicative of statistical significance, therefore for the sample under analysis, the correlation is supported. In the opposite case, i.e., a p-value higher than 0.05, the hypothesis is not verified. In addition, the β coefficient was taken into the analysis as it expresses the strength of the relationship between the variables and thus the intensity of the influence between one construct and another.

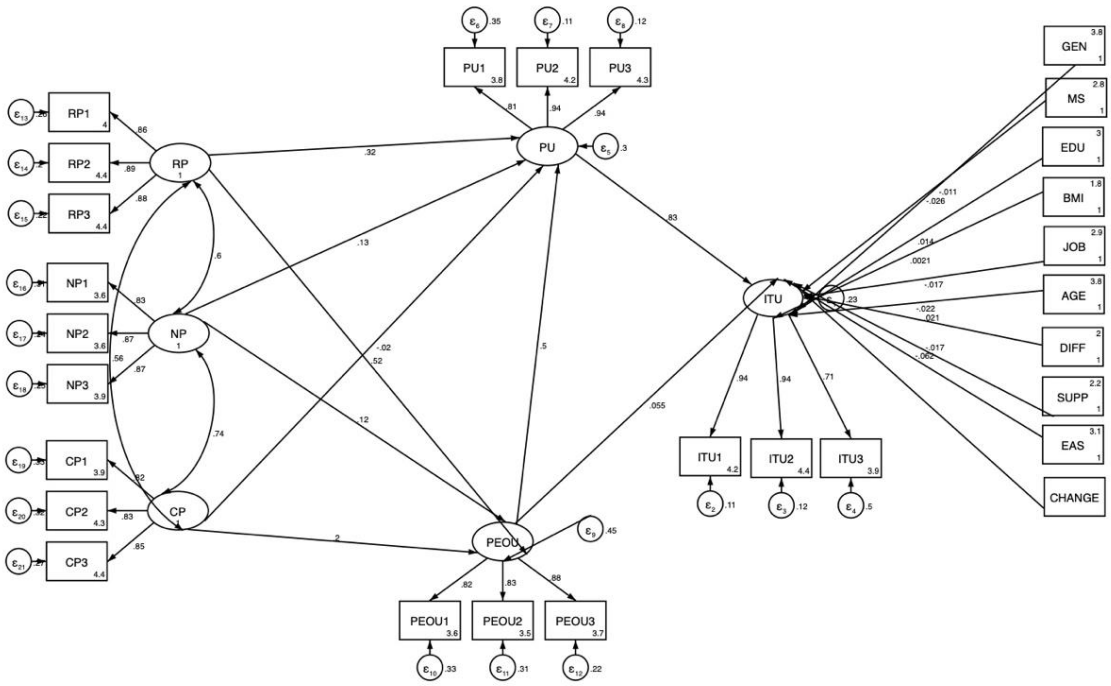


Figure 6.1: Tested Model

The findings are shown in Table 6.4.

Hypothesis	Path	Coef.	Std. Err.	p-value	Results
H1	PU → ITU	0.830	0.057	0.000***	Significative
H2	PEOU → ITU	0.057	0.070	0.414	Not Significative
H3	PEOU → PU	0.491	0.058	0.000***	Significative
H4	RP → PU	0.297	0.062	0.000***	Significative
H5	RP → PEOU	0.527	0.061	0.000***	Significative
H6	NP → PU	0.145	0.066	0.028*	Significative
H7	NP → PEOU	0.120	0.083	0.148	Not Significative
H8	CP → PU	0.007	0.065	0.910	Not Significative
H9	CP → PEOU	0.179	0.079	0.025*	Significative

p-value representation : *** $p \leq .001$; ** $p \leq 0.010$; *$p \leq .050$

Table 6.4: hypotheses testing results

As can be seen from the reported results, the three hypotheses H2, H7 and H8 are not supported, as they have a p-value greater than 0.05. On the other hand, H1, H3, H4, H5 present a p-value equal to 0.000, which indicates maximum statistical significance. Finally, H6 and H9, although significant, have a higher p-value of about 0.025. The analysis of the hypotheses tested will be explained in Chapter 6.5.

6.3 Control variables

As far as the control variables are concerned, not all of them were included as there are few references in the literature to support the correlations.

This analysis was carried out because the ITU is influenced by some characteristics of the sample. Sex, age, sentimental situation, level of education and occupation tended to be the most recurrent. In addition, BMI, approach to digital solutions and degree of motivation to change were found to be relevant. As shown in Table 6.5, the β coefficients remain relatively low for each control variable, indicating a low influence on intention to use. Moreover, none of the correlations were statistically significant, presenting a p-value always greater than 0.05.

Item	Control Variable	Coef.	Std. Err.	p-value
GEN	Gender	-0.010	0.032	0.757
AGE	Age	-0.020	0.035	0.554
MS	Marital Status	-0.024	0.032	0.455
EDU	Education level	0.016	0.033	0.624
JOB	Occupation	-0.016	0.033	0.619
BMI	BMI	0.006	0.032	0.852
DIFF	Difficulties in managing the weight maintenance/reduction	0.027	0.033	0.415
SUPP	Need of external support via digital technologies	-0.020	0.033	0.539
EAS	Ease of use of the smartphone	-0.063	0.034	0.065
CHNG	Motivation to change	-0.004	0.034	0.903

Table 6.5: Incidence of control variables on ITU

6.4 Goodness of fit

A further analysis was carried out using SEM to investigate the fit of the model. The goodness of fit (GOF) testing was conducted, with the aim of reporting fit indicators. The results are shown in Table 6.6, compared with the thresholds of acceptability. All fit indicators are included in the range of acceptability, so the results can be considered satisfactory. In particular, several parameters were selected:

The root means the square error of approximation (RMSEA) resulted to be 0.046, below the threshold of 0.08.

Standardized root means square residual (SRMR) with an acceptable value of 0.044, compared with a limit of acceptability equal to 0.08.

Comparative fit index (CFI) and Tucker-Lewis index (TLI) respectively of 0.961 and 0.956, i.e., very close to 1.

Indicator	Threshold	Value
RMSEA	< 0.08	0.046
SRMR	< 0.08	0.044
CFI	> 0.9	0.961
TLI	> 0.9	0.956

Table 6.6: Goodness of fit indicators

6.5 Testing the hypotheses

In this chapter, some considerations on the results reported in table X are explicated.

H1: Perceived Usefulness and Intention to Use

The first hypothesis, which correlates PU with ITU, is supported in relation to the sample considered (p-value 0.000 < 0.05 and standardized β 0.830). In fact, it presents a p-value of 0.000 is therefore strongly significant. In addition, the β coefficient is indicative of a strong relationship among the constructs, the greatest compared with the other hypotheses. More specifically, since the coefficient has a positive score, the greater the usefulness perceived by the patient towards the medical APP, the greater the Intention to use it. The results are in line with those confirmed in the literature in Chapter 3.3. In fact, it is reasonable to conclude that the perceived usefulness of a medical APP, i.e., the possibility of deriving an advantage from the usage, can positively influence the intention of the obese patients to use it.

H2: Perceived Ease of Use and Intention to Use

Unforeseen is the result of the second scenario, which links PEOU to ITU. Indeed, the hypothesis is not supported (p-value 0.414 > 0.05 and standardized β 0.057) and the correlation between the two constructs results to be weak. The outcomes show that the assumption according to the perceived ease of use (PEU) of the medical APP implies current patient adoption is not verified. This means that, in this case, the patient does not consider the easiness in the usage of the technological solution as influential, which can be considered informative for discussion. Nevertheless, this finding is in contradiction to previous assumptions and literature references of model TAM.

H3: Perceived Ease of Use and Perceived Usefulness

The third assumption expresses the influence of PEOU on PU. The parameters confirm that the assumption finds statistical evidence (p-value 0.000 < 0.05 and standardized β 0.491). From the findings, it can be deduced that the perceived ease of use (PEOU) of the medical APP has a positive impact on the perceived beneficial effect on the patient's health. Indeed, the easier it is to use the technology, the more advantages will be associated with the medical APP for the management of obese patients. This means that the perceived usefulness of the technology is positively affected by the simplicity in its use.

H4: Regulative Pillar and Perceived Usefulness

With regard to the fourth scenario, the correlation between RP and PU was found to be supported by showing statistical evidence (p-value 0.000 < 0.05 and standardized β 0.297). In this link, a combination of institutional factors and constructs from TAM was

performed. In particular, the results show how the system of norms and rules imposed by the institution to which the patient belongs, in this case, the Istituto Auxologico Italiano, positively influences the usefulness of the medical APP for the management of the obese patient. From the patient's perspective, a system that is regularized, controlled, and respected can lead to greater trust and, consequently, higher perceived benefit.

H5: Regulative Pillar and Perceived Ease of Use

Furthermore, the fifth hypothesis was also supported by statistical evidence (p-value 0.000 < 0.05 and standardized β 0.527). In this assumption, the influence of the system of institutional norms on the perception of user-friendliness is emphasized. This result can be interpreted in different ways. In fact, it means that the patient does not associate the regulatory system with a limiting pressure but rather sees the regulation as a guide towards using the medical APP, which therefore appears easier. Therefore, it is possible that the system of rules and standards itself makes the use of the medical APP unambiguous and therefore uncomplicated.

H6: Normative Pillar and Perceived Usefulness

The sixth hypothesis aims at describing the effect of the regulatory pillar on PU. From the results obtained, the hypothesis appears to be supported, showing statistical significance (p-value 0.028 < 0.05 and standardized β 0.145). The idea behind this assumption was that the social group of the patient definitely has an influence on his or her behavior. In fact, it is clear from the sample under analysis that peers experience impacts the patient's perceived advantage over technology. The patient, to be in alignment with the social context to which he or she belongs, will perceive benefits related to the use of the medical APP.

H7: Normative Pillar and Perceived Ease of Use

The further hypothesis, in which the relationship between the regulatory pillar and PEOU was tested, was found not supported by the results obtained from the sample. In fact, the parameters show a lack of statistical significance (p-value 0.148 > 0.05 and standardized β 0.120). Contrary to expectations, for the obese patient the peer experience does not affect the perceived ease of use of the medical APP. This means that even if the technology is widely used within the patient's context, the patient will not necessarily find it easy to use.

H8: Cultural Pillar and Perceived Usefulness

In the eighth scenario, the purpose was to investigate the influence of the cultural pillar on perceived usefulness. Like the previous hypothesis, this assumption also failed to find statistical evidence (p-value 0.910 > 0.05 and standardized β 0.007). From these

findings, it can be deduced that for the patient the belief system, attitudes, thoughts transmitted by an institution, although shared, do not influence the perceived benefit derived from the use of the medical APP. In particular, the usefulness of the technology does not depend on cultural infusions on behalf of the organization.

H9: Cultural Pillar and Perceived Ease of Use

Finally, the last hypothesis, which describes the influence of the institutional cultural pillar on the PEOU, finds statistical significance (p-value 0.025 < 0.05 and standardized β 0.179). The patient, in continuous contact with an institutional environment, assumes and develops thoughts and a culture increasingly assimilated to the organization itself. In the case of the medical APP, this influence from the institution may impact the patient's view of ease of use. In more detail, if the adoption of the technology is consistent with the mindset imposed by the Auxologico Institute, the obese patient will feel less fatiguing and less complicated the approach to the technology.

7. Discussion

This study offers various theoretical contributions to the current literature, and some important managerial considerations and insights can be derived.

Firstly, this research fills in numerous gaps that have not been explored previously, especially due to the degree of innovation of the technologies under consideration, namely Digital Therapeutics. From a theoretical standpoint, providing a comprehensive grasp of the technology and investigating individual and organizational aspects impacting the obese patient's Intention To Use represents one of the main contributions. To this purpose, an additional value-added of the present research is the coupling of TAM and Institutional Theory constructs.

On the other side, some managerial recommendations can be deduced from the findings. In this regard, the relationship with the Istituto Auxologico Italiano and the confrontation with a multidisciplinary team of professionals played a key role. It is critical to communicate the benefits that can be produced through the use of DTx in a clear and effective manner. The predominant stumbling blocks are a lack of familiarity with digital solutions, particularly among the seniors, and, consequently, limited knowledge about the innovation's potentialities. Finally, the patient's motivation should not be disregarded since it is a critical component of effecting a lasting change in lifestyle and habits.

7.1 Theoretical Contribution

To the best of the authors' knowledge, the application of theoretical models to study the acceptance of DTx is not recurrent. Among previous investigations, the most commonly employed approach has been the detection of factors and impediments that affect the acceptance and implementation of technologies in the healthcare field or the application of one single theory. In this regard, the current study is expected to contribute, both in terms of the technology examined and the theoretical approach is taken.

In particular, the novel combination of two different frameworks, TAM, and Institutional Theory, makes a significant contribution. On the one side, the findings affirmed the validity of the TAM constructs measured to investigate the acceptance of DTx among obese patients. On the other hand, new considerations derived from the integration of institutional elements and their mediated impact on patient Intention To Use have emerged.

The three institutional factors were introduced as the antecedents of Perceived Ease of Use and Perceived Usefulness. Both Perceived Usefulness and Perceived Ease Of Use were found to be positively affected by the Regulative Pillar, i.e., the system of norms and rules imposed by the institution to which the patient belongs. A supervised and controlled system encourages the patient to utilize the DTx in hospital settings like this one. As a result, the institution's rules can be beneficial. More specifically, the regulatory factor contributes to the technology's perceived increased advantage on the one hand, while simultaneously making it appear easier to use on the other.

Several considerations emerged in relation to the Normative Pillar. Firstly, the findings revealed that the normative factor, i.e., the social setting in which the patient lives and interacts, has a beneficial impact on the Perceived Usefulness of the DTx. As a result, peer influence represents a great source of confidence for the patient when dealing with a new treatment. If the use of DTx is recurrent among peers, and if it can change the patient's status quo within the group, the therapy will be seen as beneficial. Nevertheless, the impact of social context on the Perceived Ease Of Use of DTx is negligible. This means that DTx appears simple or complicated to use, regardless of the peers' experience. The Perceived Ease Of Use is most likely dependent on the individual's familiarity with digital solutions, and thus reflects a personal trait that cannot be easily influenced by others.

Finally, the impact of the construct pertaining to institutional culture was investigated. The Cultural Pillar, i.e., the collection of beliefs and practices belonging to the institution, has a significant impact on the individuals. This implies that the patient shares the values of the organization to such an extent that he/she is easily identifiable as a member of the institution. In this way, the DNA of the organization is absorbed by the individual and becomes his or her own culture. The findings revealed that these values affect the Perceived Ease Of Use rather than the Perceived Usefulness of the DTx. In the scenario where DTx becomes a “habit” or “ritual”, it will become simple to utilize and approach. To conclude, in order to explore the indirect influence on the Intention To Use of a DTx for an obese patient, the three institutional pillars were included as antecedents to the TAM constructs.

TAM’s embedded constructs were discovered to be quite intriguing. As expected, the obese patients’ perception of the DTx benefits will impact positively their decision to

utilize it. Patients are more inclined to use DTx if the apparent advantages are greater. Indeed, it is assumed that the patient's primary purpose is to enhance his or her own health status.

The fact that the DTx is simple to use, on the other hand, does not necessarily have a positive effect on Intention To Use. First, the patient may intend to use the technology even if it is complicated, driven by a strong motivation to change. Another possibility is that the DTx appears easy to use but the patient, not perceiving a clear and visible advantage, decides not to use it. However, it's worth noting that the Perceived Ease Of Use of the DTx has an indirect effect on the Intention to Use. In reality, the patient intuitively perceives an additional advantage as a result of the simplicity of usage. As a result, the Perceived Ease Of Use influences the Intention to Use through its effect on Perceived Usefulness. In Figure 7.1 the influence of institutional and individual factors on intention to use is shown.

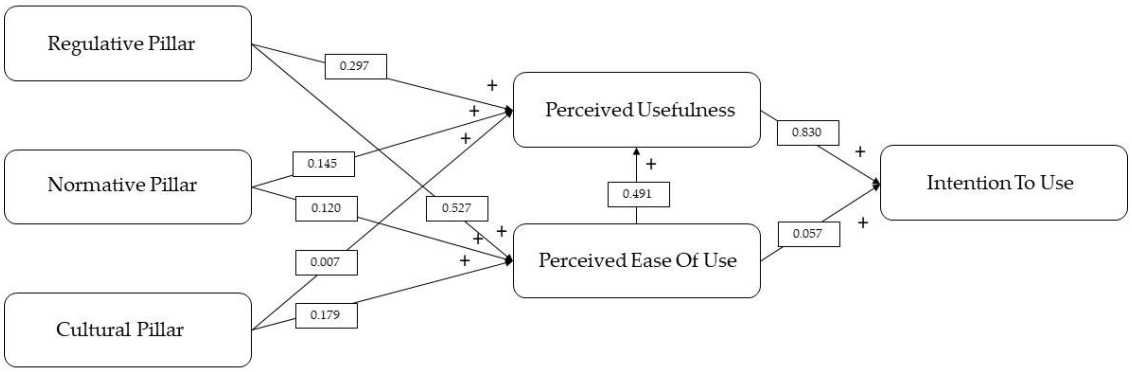


Figure 7.1: Influence among constructs

7.2 Managerial contribution

The interpretation of the results made it possible to deduce some insightful managerial considerations. The collaboration with the Istituto Auxologico Italiano, in particular,

adds practical importance to this work. In fact, several implications were shared with the professionals of the Institute in order to collaborate for the implementation of a digital therapy for the management of obese patients.

The discussion provided insights into which aspects of the technology adoption were the most critical to focus on, as well as which elements should be emphasized to encourage its use.

To begin, the SEM approach proved the statistical significance of the hypothesis that Perceived Usefulness of the DTx positively affects the Intention To Use. In order to increase the adoption of the technology, Instituto Auxologico Italiano should provide clear and effective communication of all benefits that can be derived from DTx. Since the patient's primary goal is to maintain or lose weight, the main advantages should be related to health status. Setting weekly or monthly goals that are attainable with digital therapy could be motivating in this regard. In addition to weight reduction and maintenance, additional psychological benefits should be demonstrated. Digital therapy should serve as an additional source of motivation for the patient to improve, as well as a means of correcting dysfunctional habits. Although the motivational effects are difficult to quantify, the therapy must appear as a constant support tool from the beginning of the treatment until the follow-up. In fact, even recognizing that therapy is more effective in the long run than in the short run is crucial to gaining the patient's trust. It has been shown that the greatest difficulties may emerge, in fact, once the patient has returned home. Thus, to encourage the use of DTx, it is important to show how even on its own, excellent results can be achieved by the patient.

As previously stated, the fact that the DTx is easy to use does not directly affect Intention to Use. The Perceived Ease Of Use, on the other hand, might be viewed as an added benefit that contributes to a higher Perceived Usefulness. As a result, even in this scenario, the therapy's operation must be communicated step by step in a clear and understandable manner, especially to the elderly. For patients who need it the most, training, or external support may be recommended to break down the barrier of unfamiliarity with digital solutions.

The final considerations are intended to describe which institutional factors should be emphasized and for what purpose. The regulatory factor, in particular, has a good impact on both Perceived Usefulness and Perceived Ease Of Use. As a result, the institution should establish a set of laws and regulations to safeguard patients while clearly demonstrating the technology's hazards. In this approach, the patient will feel guided during the application and will see DTx as having a secondary advantage.

In addition, since peer influence influences Perceived Usefulness, one approach could be to form a community among Auxologico patients who are planning to adopt or

have adopted DTx. In this way, different perspectives and experiences can be conveyed and shared.

The consequences are favorable since, on the one hand, collected feedbacks serve the patients to compare themselves with peers, but it is also beneficial to the hospital in terms of continual improvement.

Finally, the Cultural Pillar embedded in the organization has a good impact on Perceived Ease Of Use. The key point is to make DTx "ordinary" and "familiar" for the patient so that they can be seen as simple as possible. Digital Therapeutics should not be viewed as a niche or experimental treatment for a selected few. Instead, DTx must be open to everybody, adaptable to each condition, and expandable over time, so that the patient perceives it as basic and easy to use.

7.3 Limitation and future research

The findings also revealed some weaknesses in the research. Firstly, the main constraint is due to the features of the sample examined. The survey was administered to more than 3,000 patients who were under Auxologico's treatment. Only 341 of them responded, therefore the first restriction is the small number of interviewees. It would be valuable to collect a more substantial number of responses as the next study, so as to carry out a valid SEM and generalize the results to a larger population. This issue is also related to the way the questionnaire was delivered. In fact, a minority part of surveys was delivered in paper version to patients who, at the time of the administration, were hospitalized at the Istituto Auxologico Italiano. The remaining patients were contacted through e-mail, so only those who agreed to the Auxologico Institute's terms and conditions for receiving e-mail updates were considered. Many responses were left blank on the paper version because the mandatory answer could not be verified. As a result, many respondents were discarded, resulting in a significant reduction in the sample size.

Another problem is related to pathology. In Italy, obesity is more common among males than women. In fact, men represent the majority in the case of both overweight (44% vs. 27.3%) and obesity (10.8% vs. 9 %) (Obesity Report, 2019). Among obese patients responding to the survey, about 70% were women. This may represent a possible flaw in the work. In addition, it should be noted that one constraint is that the results are valid for obese patients and may not necessarily be confirmed by patients with other diseases.

Future studies can be conducted based on the gaps identified as a result of this work, with the goal of ongoing development. Firstly, the collaboration with the Auxologico Institute revealed the need to collect opinions also from physicians and professionals.

An additional step could be to administer a questionnaire entirely dedicated to the doctor and repeat the analysis assuming a different perspective. In fact, it could be interesting to investigate the intention of the professional towards the adoption of DTx, since this figure plays a fundamental role in the adoption process. Furthermore, a possible future study can be made by paying more attention to patients over the age of 70 (only 10% in the current study), since they show the most resistance to the use of DTx due to a lack of experience with digital solutions.

8. Conclusions

The current study's primary goal is to examine the dynamics of diffusion of Digital Therapeutics among obese patients. Since acceptance and adoption are triggering elements that influence the diffusion process, the study concentrates on the institutional and individual factors that influence the intention to adopt the DTx. The target group is represented by obese patients who show comorbidities associated with the disease and who are or have been taken care of by the Istituto Auxologico Italiano.

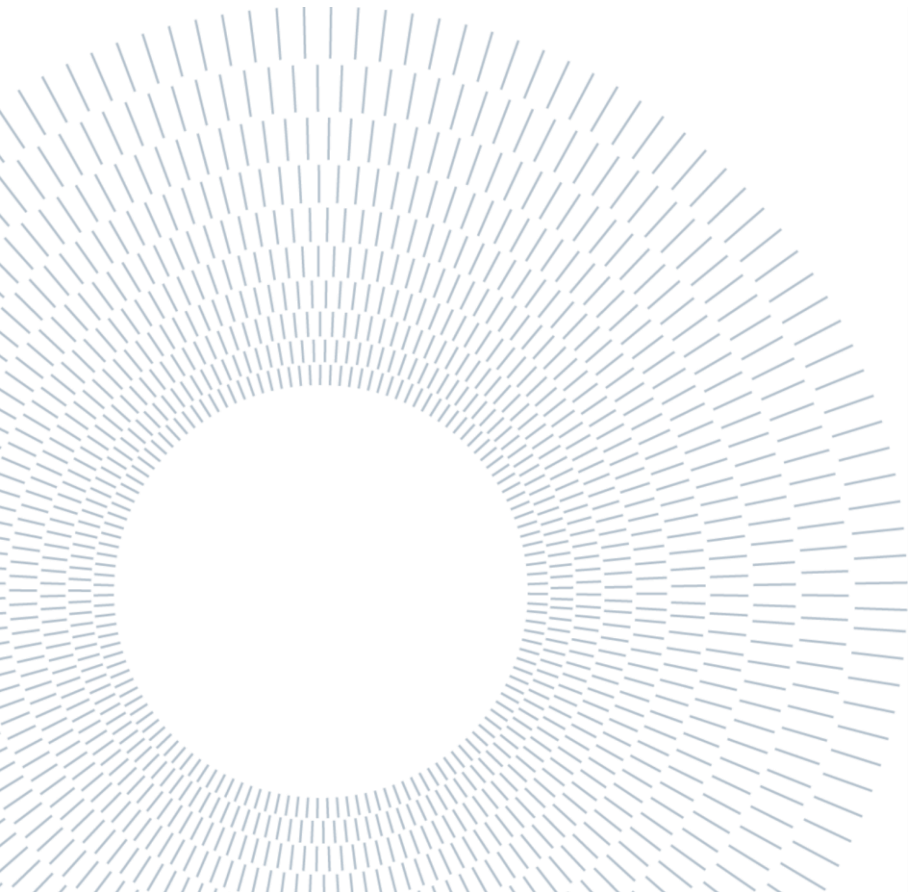
Given the limited number of studies devoted to this topic, this study provides several contributions mainly related to the combination of different theoretical models. In particular, a combination of TAM and Institutional Theory constructs is the approach used to investigate the antecedents of the patient's Intention To Use DTx. Specifically, the Normative, Regulatory, and Cultural pillars derived from Institutional Theory were introduced as precursors of the TAM's basic determinants of Intention to Use: Perceived Usefulness and Perceived Ease Of Use.

According to the results of this study, it can be proven that the Intention To Use DTx is positively related to the obese patient's Perceived Usefulness, proving that the hypotheses obtained from the TAM are valid. The same consideration cannot be made, however, for the Perceived Ease Of Use, which turns out not to be a determinant of the Intention To Use DTx in a direct way. On the other hand, the Perceived Ease Of Use affects positively the Perceived Usefulness thus, in an indirect way, also the Intention To Use. Among the institutional elements, Regulative Pillar (system of norm and rules imposed by the institution) and Normative Pillar (peer influence) have a positive effect on Perceived Usefulness. However, the hypothesis that the Cultural Pillar (system of belief, attitudes derived from the institution) influences the Perceived Usefulness results to be not statistically significant.

Perceived Ease Of Use, on the other hand, is positively influenced by Regulatory and Cultural Pillars, but not by Normative Pillar. Thus, findings show that the system of rules and habits constructed by the individual within the institution make DTx appear easier, but peer influence does not affect the Perceived Ease Of Use.

The interpretation of the findings resulted in theoretical contributions as well as managerial suggestions. As a result, this study is valuable in determining a strategy to encourage patients to utilize DTx.

In conclusion, the collaboration with the Istituto Auxologico Italiano is one of the most meaningful source of value. Furthermore, the concrete confrontation with professionals from multidisciplinary fields has substantially aided the quality of this research. Additionally, the integrating approach of institutional and individual factors accompanied by the innovativeness of the technology constitute a point of strength compared to past research.



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A. Appendix A

The following Table summarized the main characteristics of the DTx approved around the world.

DTx	Company	Type	Delivers CBT	Disease	Approved	RCT
Vorvida	Orexo	Web app	Yes	Alcol use disorder	CE mark and Diga	1
Deprexis	GAIA AG	Web app	Yes	Depression	CE mark and Diga	1
Velibra	GAIA AG	Web and mobile app	Yes	Anxiety disorder / panic /agoraphobia	CE mark and Diga	1
Elevida	GAIA AG	Web app	Yes	Fatigue in multiple sclerosis	CE mark and Diga	1
Somnio	Mementor DE gmbh	Web and mobile app	Yes	Insomnia	CE mark and Diga	2
M-sense Migrane	Newsenselab gmbh	Mobile app		Migraine	CE mark and Diga	1
Mindable	Mindeable health	Mobile app	Yes	Panic & agoraphoiba	CE mark and Diga	2
Zanadio	Aighere Gmbh	Mobile app		Obesity	CE mark and Diga	1
Kelmeda tinnitus	Cmocro/ mynoise gmbh	Mobile app	Yes	Tinnitus	Ce mark and diga	1
Rehappy	Rehappy gmbh	Mobile app	No	TIA stroke, SAH or intracerebral bleeding/hemorragic stroke	CE mark and Diga	1
Mika	Mika	Mobile app	No	QOL and psychological/psychosomatic issues from cancer diagnosis esp. Cervix/uterus/ovary	CE mark and Diga	2
Selfapys	Selfapy gmbh	Web app	Yes	Mental illness (depression, anxiety, eating disorders and burnout)	CE mark and Diga	2
Vivira	Vivira Health Lab gmbh	Mobile app	No	Pain (unspecific back, knee and hip pain, ostearthritis in the knee, hip and spine)	CE mark and Diga	2
Cureapp SC	**Cureapp**	**Mobile app**	**Yes**	**Smoking cessation (nicotine addiction)**	**MHLW (japan)**	**1**
Reset	Pear Therapeutics	Mobile app	Yes	Substance use disorder	FDA de Novo	2
Nightware	Nightware	Mobile app	No	Post traumetic stress disorder	FDA De Novo	3

Parallel	**Mahana**	**Web app**	**Yes**	**Irritable bowel syndrome**	**FDA de Novo and CE Mark (MDD)**	**2**
Endevorrx	Akili Laboratories	Game	No	Attention deficit hyperactivity disorder	FDA de Novo and CE Mark (MDD)	3
Somryst	Pear Therapeutics	Mobile app	Yes	Chronic insomnia	FDA 510 (k)	2
Reset-O	Pear Therapeutics	Mobile app	Yes	Opioid use disorder	FDA 510 (k)	2
Freespira	Freespira	Mobile app	No	Panic attack symtoms, PTSD	FDA 510 (k)	1
Mindmotion GO	Mindmaze	Game	No	Neuro-rehabilitation	FDA 510 (k) and CE mark (MDD)	N
Pivot program	Carrot inc.	Mobile app	No	Smoking cessation	Fda 510 (k) and ce mark (mdd)	N
Kaia health	Kaia health	Mobile app	No	Musculoskletal pain	Ce mark (mdd)	2
Bluestar	**Welldoc**	**Mobile app**	**No**	**Diabetes type 1,2**	**Fda 510(k), uk**	**1**
Insulia	Voluntis	Mobile app	No	Diabetes 2	U.k.	1
Invirto	Sympatient	Mobile app	Yes	Anxiety	Ce mark and diga	N
Moovcare	Sivan	Web app	No	Lung cancer	Ce mark - france	1
Oleena	Voluntis	Mobile app		Neoplasm		
Propeller	Propeller	Mobile app	No	Asthma and copd	Fda 510k	1
Sleepio	Big health			Insomnia	U.k.	1

B. Appendix B

The survey submitted to obese patients in Auxologico is reported in the original language.

Part A

#	Quesito	Risposte
1	Sesso	Maschio
		Femmina
2	Fascia d'età	< 18
		18-30
		31-40
		41-50
		51-60
		61-70
		>70
3	Peso (kg)	……..
4	Altezza (Cm)	……..
5	Qual è il tuo più alto livello di istruzione	Elementari
		Medie inferiori
		Medie superiori
		Laurea
		Dottorato o post-laurea
6	Regione di residenza	……..
7	Qual è la tua occupazione?	Studentessa/e
		Lavoratrice/ore
		Disoccupata/o
		Casalinga/o
		Pensionata/o

8	**In che relazione sentimentale sei?**	**Solo/a (single)**
		Ho un partner stabile
		Altro
9	Ti reputi una persona che ama stare in compagnia?	Pochissimo
		Poco
		Abbastanza
		Molto
		Moltissimo
10	Con chi consumi i pasti principali della giornata?	Da solo/a
		In famiglia
		Con colleghi/amici
11	Il tuo nucleo familiare ti supporta/motiva nel mantenere/migliorare il tuo stato di salute?	Sì
		No
12	Il tuo nucleo familiare influenza NEGATIVAMENTE il tuo comportamento alimentare?	Sì
		No
13	Il tuo nucleo familiare è/potrebbe essere coinvolto nel tuo percorso di cura?	Sì
		No
14	Quanto sei d'accordo con la seguente affermazione: "Io sono il principale artefice della mia salute"	Pochissimo
		Poco
		Abbastanza
		Molto
		Moltissimo
15	Quanto sei d'accordo con la seguente affermazione: "Utilizzo con grande semplicità le App sul mio cellulare (smartphone)"	Pochissimo
		Poco
		Abbastanza
		Molto
		Moltissimo
		Non ho un cellulare con accesso ad Internet e ad App (smartphone)
16	Sei affetto da una o più di queste patologie? (puoi barrare più risposte)	Malattie cardio o cerebro vascolari
		Ipertensione
		Diabete
		Malattia epatica
		Osteoartrite

17	**Assumi o hai assunto una terapia farmacologica per l'obesità?**	**Sì**
		No
18	Hai effettuato nell'ultimo anno una delle seguenti prestazioni sanitarie? (puoi barrare più risposte)	Ambulatorio (centro Obesità)
		MAC / Day Hospital
		Ricovero (es. Piancavallo)
		Chirurgia bariatrica
19	Il tuo stato di salute è migliorato durante la presa in carico da parte di Auxologico?	Pochissimo
		Poco
		Abbastanza
		Molto
		Moltissimo
20	Sei soddisfatto dei risultati ottenuti?	Pochissimo
		Poco
		Abbastanza
		Molto
		Moltissimo
21	Una volta tornato a casa, hai difficoltà a gestire il mantenimento/miglioramento dei risultati nel tempo	Non ho alcuna difficoltà (mi gestisco bene da solo senza supporti esterni)
		Sì, ho difficoltà nell'ambito del mantenimento/riduzione del peso
		Sì, ho difficoltà nell'ambito delle abitudini/comportamento alimentare
		Sì, ho difficoltà nell'ambito della motivazione al cambiamento
		Sì, ho difficoltà in altro
22	Mi piacerebbe poter essere seguito dai professionisti sanitari anche da casa, in remoto, anche tramite strumenti tecnologici-digitali	Non mi interessa
		Per 1 mese
		Per 3 mesi
		Per 6 mesi
		Per 12 mesi
		Per tutta la vita
23	Quante ore al giorno utilizzi il tuo cellulare (smartphone)?	Meno di un'ora
		1-2 ore
		3-5 ore
		5-10 ore
		Oltre 10 ore
24	Utilizzi soluzioni digitali (come per esempio APP, dispositivi indossabili come	Mai
		Raramente

25	**Conosci una APP che si chiama "Noom"? (leggi bene tutte le possibili risposte)**	**Mai sentita**
		Ne ho sentito parlare da alcuni miei familiari/amici/colleghi, ma non l'ho mai scaricata
		Ne ho sentito parlare da alcuni medici, ma non l'ho mai scaricata
		Ne ho sentito parlare sul web/social media, ma non l'ho mai scaricata
		Ne ho sentito parlare su alcune riviste e l'ho scaricata per provarla
		Ne ho sentito parlare da alcuni miei familiari/amici/colleghi e l'ho scaricata per provarla
		Ne ho sentito parlare da alcuni medici e l'ho scaricata per provarla
		Ne ho sentito parlare sul web/social media e l'ho scaricata per provarla
		Ne ho sentito parlare su alcune riviste, ma non l'ho mai scaricata
26	Conosci delle APP per il "digiuno intermittente" ("fasting" in inglese) come ad esempio Fasting; DoFasting; Zero; Vora; 21 Day Hero? (leggi bene tutte le possibili risposte)	Mai sentita
		Ne ho sentito parlare da alcuni miei familiari/amici/colleghi, ma non l'ho mai scaricata
		Ne ho sentito parlare da alcuni medici, ma non l'ho mai scaricata
		Ne ho sentito parlare sul web/social media, ma non l'ho mai scaricata
		Ne ho sentito parlare su alcune riviste e l'ho scaricata per provarla
		Ne ho sentito parlare da alcuni miei familiari/amici/colleghi e l'ho scaricata per provarla
		Ne ho sentito parlare da alcuni medici e l'ho scaricata per provarla
		Ne ho sentito parlare sul web/social media e l'ho scaricata per provarla
		Ne ho sentito parlare su alcune riviste, ma non l'ho mai scaricata

Part B

Likert Scale 1 (Completamente in disaccordo) to 5 (Completamente d'accordo)

#	Quesito	1	2	3	4	5
1	Vorrò utilizzare questa APP medicale					
2	Prevedrò di utilizzare in futuro questa APP medicale					
3	Vorrò sfruttare questa APP medicale per tenermi in forma					
4	L'utilizzo di questa APP medicale migliorerà il mio stile di vita e la mia salute					
5	L'utilizzo di una questa APP medicale mi permetterà di gestire più efficacemente il mio percorso di cura					
6	L'utilizzo di questa APP medicale sarà utile per la gestione della mia salute					
7	Utilizzare questa APP medicale NON mi richiederà un grande sforzo					
8	Utilizzare questa APP medicale sarà per me intuitivo e facile					
9	Quando utilizzerò questa APP medicale sul mio cellulare riuscirò facilmente a fare ciò che mi servirà					

10	Sono sempre d'accordo con ciò che mi dicono i medici che mi hanno in cura, anche sull'utilizzo di questa APP medicale					
11	Sono sempre d'accordo con le priorità che mi danno i medici che mi hanno in cura, anche sull'utilizzo di questa APP medicale					
12	Sono sempre d'accordo con le terapie che mi prescrivono i medici che mi hanno in cura, anche sull'utilizzo di questa APP medicale					
13	Le persone che stimo di più pensano che dovrei utilizzare questa APP medicale per migliorare il mio percorso di cura					
14	Le persone che stimo di più utilizzerebbero una APP medicale per migliorare il loro percorso di cura se prescritta dal loro medico					
15	Le persone che stimo di più pensano che le APP medicali possano aiutare a migliorare il percorso di cura se certificate e validate					
16	Nella mia cerchia di familiari/amici/colleghi c'è piena fiducia nell'innovazione tecnologica (come, ad esempio, questa APP medicale)					
17	Nella mia cerchia di familiari/amici/colleghi NON c'è alcun timore a provare cose nuove (come, ad esempio, questa APP medicale)					
18	Nella mia cerchia di familiari/amici/colleghi c'è piena apertura alle soluzioni digitali (come, ad esempio, questa APP medicale)					

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