Abstract: E-Health represents one of the pillars of the modern healthcare system and a strategy involving the use of digital and telemedicine tools to provide assistance to an increasing number of patients, reducing, at the same time, healthcare costs. Measuring and understanding the economic value and performance of e-Health tools is, therefore, essential to understanding the outcome and best uses of such technologies. The aim of this paper is to determine the most frequently used methods for measuring the economic value and the performance of services in the framework of e- Health, considering different pathologies. An in-depth analysis of 20 recent articles, rigorously selected from more than 5000 contributions, underlines a great interest from the clinical community in economic and performancerelated topics. Several diseases are the object of detailed clinical trials and protocols, leading to rious economic outcomes, especially in the COVID-19 post-pandemic era. Many e-Health tools are men studies, especially those that appear more frequently in people's lives outside of the clinical mch as apps and web portals, which allow for clinicians to keep in contact with their patients. W tools and programs are increasingly studied from practical perspectives, such as in the frameworks, there is a lack of consensus regarding the recommended models to map a outcomes and performance. More investigations and guidelines by scientificate ties are advised to understand the potential and path of such an evolving and promising phenon

Keywords: e-Health; performance measurements; literature review; televedicine; economic evaluation

### 1. Introduction

The World Health Organization (WHO) estimates that life expectancy has increased by six years over the past two decades. At a global evel, the average age has risen from 67 years in 2000 to 73 in 2019 [1]. This is mainly due to improved socioeconomic and environmental conditions and better tratuments and medical care [2]. Along with the rise in life expectancy, an increase in the volume of chronic diseases has been noted. Patients affected by chronic health conditions often require frequent and specialized medical care that are not easily accessible in rural areas. All these factors increase the overall costs of healthcare services to monitor patients, communicate with them, and offer proper care.

In this frameworke-builth, defined by the World Health Organization as "the cost- effective and secure use of the organization and communication technologies (ICT) in support of health and health-related field [15] may be an essential tool for improving healthcare ac- cessibility while, at the same time, educing costs. Compared to the concept of telemedicine, which refers to a reduction in the geographic distance between the patient and medi- cal personnel, e-Health is much broader and impacts the whole health system from an organizational perspective [4,5]. Furthermore, according to the WHO, e-Health encom- passes "multiple interventions, including telehealth, telemedicine, mobile health (mHealth), electronic medical or health records (eMR/eHR), big data, wearables, and even artificial intelligence" [3].

With the outbreak of the COVID-19 pandemic and the consequent introduction of social distancing rules, the use of e-Health to monitor and assist patients has dramatically accelerated [6–13]. Since the very beginning of the pandemic, e-Health and telemedicine pols have been used for forward triage and screening, telemonitoring, infection control pochares, televisits, teleconsultation with experts, and data and report sharing [14]. Later, more sensions were implemented to increase resilience and offer adequate assistance in collecting and sharing data among citizens, healthcare institutions, decision-makers, and public entities engaged a disaster management [15].

Several medical specialities have started to implement televencine and e-Health solutions following the pandemic, for instance, for neurodegaterated disorders, such as Alzheimer's disease and amyotrophic lateral sclerosis. As these diseases progress, patients experience a loss of autonomy in daily life activities. A coming more dependent on their caregivers. The outbreak of the COVID-19 pandemic led to mecorfinement of the majority of the world population at home [7], with even longer periods of storation recommended for frail patients, thus hindering most chronic/neurodegenerative patients from being assisted in person. In order to assist patients at home, telemedicine solutions were implemented to monitor patients and support them and their caregivers. The post-pandemic lifer ture shows the potential advantages of this sincof monitoring in patient management [16–20].

All in all, the pandemic and the partagement responses to COVID-19 have sped the adoption of digital technologies in heathcare and beyond [21–24] by several years [25]. As a result, e-Health has become the third fastest-growing healthcare industry, after pharma- ceuticals and medical devices [16], with an increasing number of applications, and even gave birth to the new concept (f)le virtual Hospital [27–29].

These premises highrest the increasing importance of the e-Health concept, which should be studied more in-doubtro evaluate in detail its economic value and general performance. In fact, in the interactional literature reviews currently available, there seems to be a lack of systematic method above to analyze these aspects [30,31]. For this reason, several recent research papers have gaded for further studies and models of analysis on the topic [30,32,33].

Among the most common methods reported by the literature for the economic assess- ment of e-Health [14], we can mention:

The cost-effectiveness analysis (CEA), which compares the costs of a program with its nonmonetary outcomes (e.g., life years gained, diseases avoided) [30,32,35–37];

The cost-benefit analysis (CBA), which compares the costs and the benefits in mone- tary terms. Results gathered from this method may later be converted into broader measures of value [32]:

The cost–utility analysis (CUA), which measures the benefits in terms of utility (e.g., qualityweighted life years gained) through the quality-adjusted life years (QALY) method. This analysis requires a study of direct, indirect, and lost productivity costs [30,32].

Starting from these premises, the aim of this study was to investigate the evolution of the different methods proposed in the literature for the economic and performance evaluation of e-Health, by conducting a structured review of the most recent literature on the topic, especially in a pre- and post-pandemic scenario.

### 2. Materials and Methods

mehr

A structured literature review was performed [38] using the Scopus database, the largest dataset of abstracts and citations of peer-reviewed literature in the fields of science,

technology, medicine, social sciences, arts, and humanities [39], as well as the datasets Web of Science (WoS) and Pubmed.

A preliminary research protocol was established to document the procedures that were followed in conducting the literature review in order to make it reproducible and reliable (validity). Preliminary research questions were developed to provide new insights [40]. The formalization of the research protocol helped us to identify the central question to be investigated, defined as follows:

Research Question (RQ): What are the most frequent methods for measuring the economic value and the performance of services in the framework of e-Health in a pre- and post- pandential scenario?

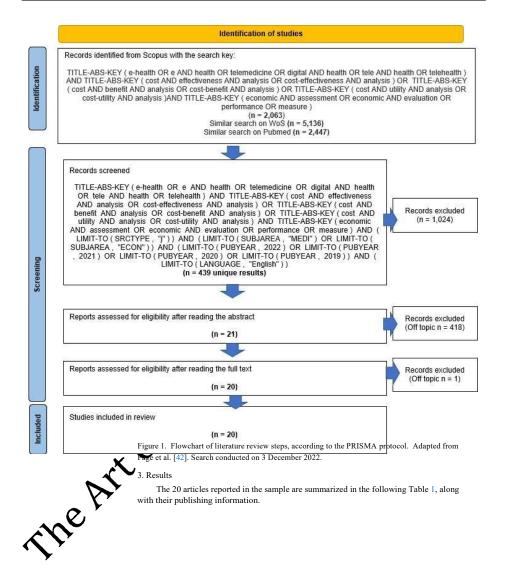
The query terms "e-health", "telemedicine", "digital health", and "telehealth" we'e used in combination with words that represented the three evaluation methods and perturn mance measurement indications. The same search, tailored to the specific search agin characteristics, was conducted on Scopus, WoS, and Pubmed.

The findings from the first step of the analysis, which targeted entrept titles, abstracts, and keywords, gave 2063 results on Scopus, 5136 on WoS, and 2447 on Fronted. The search was then further refined by including only journal articles written in Enorsh, related to topics in medicine, economics, econometrics, and finance published after 2019 reporter to obtain a framework that mirrored the context of the study, also considering the host evelopment of the latest technologies and the COVID-19 booster effect. The new search led to 480 unique results, excluding duplicates.

Once all the titles and the abstracts were read, at papers were finally selected and analyzed by two authors (HB and FD). As a result of this latter tep, reading the full text, 20 papers were considered eligible, while on was naked as off-topic. Figure 1 below summarizes the process of analysis and selection of contributions to be included in the sample according to the PRISMA methodolog [4, 42].

according to the PRISMA methodolog [4,42]. The selected articles were coded and analyzed using Nvivo software (version 12). The main nodes and subnod server selected according to the literature [43–45] and adapted to the aim of the present study.

The first node collected internation on the author's profile, such as academics, clin- icians, and multidisciplinary groups, while the second contained information about the location in which the reported studies were conducted [44,46–49]. Details about the ana- lyzed sector (public or private) were included in the fourth one [45]. The fifth and sixth nodes collected information about the applied research methodology das oded in the fourth one [45]. The fifth and sixth nodes collected information about clinic daily plane and pathology targeted mentioned by the 20 papers under review [43], while the second contained information on research implications, practices, policies, and outcomes. In the last node, the e-Health tools used were mapped.



Reviews

Table 1. Articles analyzed and coded.

N.	Authors	Title	Year	Journal	Ref.
	Marcuzzi, A., Bach, K.,	Individually tailored self-management			
	Nordstoga, A.L., Bertheussen,	app-based intervention (selfBACK) versus a			
1	G.F., Ashikhmin, I., Boldermo,	self-management web-based intervention	2021	BMJ Open	[50]
1	N., Kvarner, EN., Nilsen, T.I.L.,	(e-Help) or usual care in people with low back	2021	BND Open	[30]
	Marchand, G.H., Ose, S.O.,	and neck pain referred to secondary care:			0
	Aasdahl, L., Kaspersen, S.L.,	Protocol for a multiarm randomised clinical trial			$\mathcal{V}_{\mathcal{C}}$
2	Buntrock Kählke, F., Smit, F. Ebert, D.D.	A systematic review of trial-based economic evaluations of internet- and mobile-based	2021	European Journal of P blic	[51]
		interventions for substance use disorders		Health	
		E-health ecosystem with integrated and stepped		~°0^	
3	Ochoa-Arnedo, C., Medina, J.C., Flix-Valle, A., Anastasiadou, D.	psychosocial services for breast cancer survivors: Study protocol of a multicentre randomised controlled trial	2021	MJ Open	[52]
		Ç	$O^*$		
	Cadilhac, D.A., Sheppard, L.,	Economic evaluation protocol and statistical		Frontiers in	
4	Kim, J., et al.	analysis plan for the cost-effectiveness of a novel	2021	Neurology	[53]
	- *	Australian stroke telemedicine (VST) program		1.carology	
	Ionov, M.V., Zhukova, O.V.,	Value-based approach to blood pressure			
5	Yudina, Y.S., et al.	telemonitoring and remote courseling in	2021	Blood Pressure	[54]
	, ,	hypertensive patients			
	Rubee, D., Jinghua, L., Donglan,	An economic evaluation of a mobile text messaging intervention to improve mental		BMC Health	
5	Z., et al.	health care in resource-poor communities in	2020	Services	[55]
		·X.Y		Research	
		Shina. a cost-effectiveness study		Research	
		Clinical and cost-effectiveness of a guided			
	Tankanat V Daarra I Titali I t	internet-based Acceptance and Commitment			
	Terhorst, Y., Braun, L., Titzler, I	Therapy to improve chronic pain–related			
7	et al.	disability in green professions (PACT-A): study	2020	BMC	[56]
	$\sim$	protocol of a pragmatic randomised controlled trial			
	$\sim$ $\sim$	Evaluation of the efficacy of an internet-based pain			
	$\sim$	education and exercise program for chronic			
	Seragio to, B.T., Reis,	museuloskeletal pain in comparison with online		BMC	
	aginto, b. 1., Reis,			Direc	
	Fiorti, L.	self-management booklet: a protocol of a	2020	Musculoskeletal	[57]
Ś	F.J.J., et al.	randomised controlled trial with assessor- blinded, 12-month follow-up, and economic	2020	Disorders	[57]
,		evaluation			
9	Birkemeyer, R., Müller, A.,	A cost-effectiveness analysis model of Preventicus atrial fibrillation screening from the point of view of	2020	Health Economics	[50]
9	Wahler, S., et al.	statutory health insurance in Germany	2020	Review	[58]
		Effectiveness and cost-effectiveness of stratified		BMC	
0	Koppenaal, T., Arensman, R.M.,	blended physiotherapy in patients with non-	2020	Musculoskeletal	[59]
	van Dongen, J.M., et al.	specific low back pain: study protocol of a cluster randomized controlled trial		Disorders	[]
		Effectiveness and cost-effectiveness of telehealth in			
1	Tsou, C., Robinson, S., Boyd,	rural and remote emergency departments: a	2020	Systematic	[ <mark>60</mark> ]

systematic review protocol

J., et al.

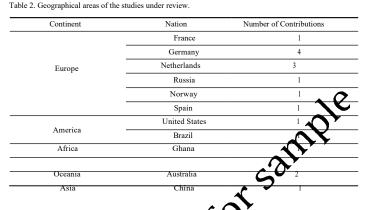
Table	1	Cont

N.	Authors	Title	Year	Journal	Ref.
12	Yang, Y., Chen, H., Qazi, H., et al.	Intervention and Evaluation of Mobile Health Technologies in Management of Patients Undergoing Chronic Dialysis: Scoping Review	2020	JMIR mHealth and uHealth	[61]
	Thao, V., Nyman, J.A., Nelson,	Cost-effectiveness of population-level proactive tobacco cessation outreach among			0
13	D.B., et al.	socio-economically disadvantaged smokers: evaluation of a randomized control trial	2019	Addiction	
		The (cost) effectiveness of guided internet-based			<b>\$</b>
14	Nadort, E., Schouten, R.W., Dekker, F.W., et al.	self-help CBT for dialysis patients with symptoms of depression: study protocol of a randomised controlled trial	2019	HWS Psychiatry	[56
	D., Hoving, C., Evers,	An economic evaluation of a computer-tailored	<b>~</b>	Patient	
15	de Ruijter, S., et al.	e-learning program to promote smoking cessation counseling guideline adherence among practice nurses	<b>O</b> <sup>2019</sup>	Education and Counseling	[63]
	itzler, I., Ebert, D.D., Braun, L., T	Clinical and cost-effectiveness of guided internet-based interventions in them licated			
16	et al.	prevention of depression in green professions (PROD-A): study protocol of 36-month follow-up pragmatic randomized controlled trial	2019	BMC Psychiatry	[56
		Cost-Effectiveness of Web-Based		Journal of	
17	Lizée, T., Basch, E., Trémolières,	Patient-Report d Outcome Surveillance in	2019	Thoracic	[64
	P., et al.	Mients with Lung Cancer		Oncology	
18	Roehr, S., Berg, F., Golchert, J., et al.	HTLP@APP: development and evaluation of a silf-help app for traumatized Syrian refugees in fermany—a study protocol of a randomized	2019	BMC Psychiatry	[65
19	Williams, A., Van Dong J.M., Kamper, S.A., al.	controlled trial Economic evaluation of a healthy lifestyle intervention for chronic low back pain: A randomized controlled trial	2019	European Journal of Pain	[66
17	illco, Moorthy,	Mobile Technology for Community Health in Ghana: Is Maternal Messaging and Provider Use		Journal of	
Ŝ	Mohan, D., et al.	of Technology Cost-Effective in Improving Maternal and Child Health Outcomes at Scale?	2019	Medical Internet Research	[67

A total of 19 out of 20 articles (95% of the sample) were published in medical journals, and only 1 (1 of the 2 systematic reviews) was published in the journal of Systematic Reviews.

The average number of authors per paper analyzed was approximately eight. Specifically, papers that were written only by clinicians or academics (5 in total) had, on average, 7.6 authors, which is slightly lower than the number of authors of the papers written by multidisciplinary groups (15 in total), which was 8.4. From this perspective, it is interesting to note that even though the majority of papers were published in medical journals, the authors of the studies were not only clinicians. On the contrary, different competencies were brought together.

Geographically, it is crystal clear that most of the studies were conducted in European countries, specifically in Germany and the Netherlands, where there is a peak of contribu- tions. As for Oceania and America, only two contributions were found, and only one for Africa and Asia continents. Results are reported in Table 2.



More than half of the contributions analyzed are releared pr otocols (11 contributions, 55% of the total sample), which present methods that will ter be applied in order to pro- ceed with the performance analysis of programs in the e-Health field. Seven contributions (35% of the total therefore, apply the identified evaluation sample) are instead quantitative clinical cases methods to the practical case. Four of the titative clinical cases analyze non-European situations: two Australian, one American. African.

pathology treated under study, it can be seen In analyzing the content of the papers, in relation to the clinical discipline and the that the medical fields most affected are pain medicine and mental health, as represented ure 2.

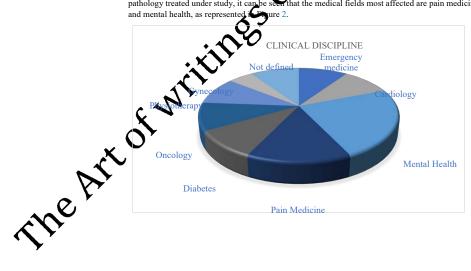


Figure 2. Clinical disciplines covered in the reviewed papers.

The most frequently mentioned treated pathologies are pain, such as low back and neck pain, psychological problems, including depression, schizophrenia and post-traumatic stress, and alcohol and smoking addictions, as shown in Figure 3 below.



Addictions TREATED

PATHOLOGY

(smoking.

alcoholis

Cancer

Chronic kidney

disease

quantitative clinical cases but not press he protocols and reviews, which instead report state of the art in the field. The e-Health tools presented in the reviewed articles, or which are used by described rams, vary, but with a high diffusion of mobile apps, phone calls and online sessions, as

programs, vary, but with a high illustrated in Figure 4 below

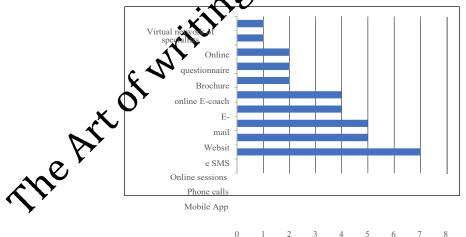


Figure 4. E-Health tools presented in the reviewed articles.

The methods used for measuring performance in the analyzed e-Health programs are indicated in the identified contributions. Table 3 below provides a description of the measurement methods, placing the data side by side with the treated pathology and e- Health tools used, presenting a visual to help us determine whether there may be links

2

3

4

Hypertension Mental

disorders

(schizophrenia,

post-trauma

7 8

6

Α

Concerning pre- and post	(s) of performance		e by pathology, reporting f the sample) were			
published between 2020 and 2	naining 8 papers were	published in the				
pre-pandemic era. Still, only one of the papers [54] explicitly mentions the pandemic. In particular, the study by Ionov and colleagues [54] underlines the need to find solutions for patients confined at home. Concerning the tools used, telemonitoring with or without						
remote counseling may impro-	remote counseling may improve blood pressure control and adherence to protocols, es-					
pecially in force majeure even or cost calculation is reported	-	mic outbreak. Still, no	specific impact on ts			
Table 3. Performance measureme           analyzed (excluding literature rev	· •	athology, and tools used t	for each contribution			
			$\overline{\mathcal{N}}$			
Title	Treated Pathology	Tools Used	Measurement Methods			
Economic evaluation protocol and statistical analysis plan for	runology	<u> </u>	CEA			
the cost-effectiveness of a novel Australian stroke telemedicine (VST) program	Ictus	Virtuel vetwork of specialists	CB A			
	•	1	CU			
Value-based approach to blood pressure telemonitoring and		$\mathbf{N}$	А			
remote counseling in hypertensive patients	Hypertension	App, Website	CUA			
An economic evaluation of a mobile text messaging intervention to improve mental health care in resource-poor communities in China: a cost-effectiveness study	Schizophrenia	SMS	CEA CUA			
Clinical and cost-effectiveness of a guided internet-based Acceptance and Commitment Therapy to improve chronic pain- related disability in green professions (PACT-4); Sudy	Chronic pain	E-mail, Phone calls, Online sessions, E-coach	CE A			
art			A CU			
protocol of a pragmatic randomised controlled trial						
Evaluation of the efficacy of an interpet-based pain education and exercise program for chronic nusculoskeletal pain in		SMS, Phone calls,				
comparison with online see management booklet: a protocol of a randomised cardrolled trial with assessor-blinded,	Chronic pain	Website, Online brochure	CEA CUA			
12-month Wowp, and economic evaluation		biochure				
A cost-frequeness analysis model of Preventicus atrial	Ictus	Арр	CEA			
Some tion screening from the point of view of statutory health insurance in Germany						
	Lumbago	App	CEA			
health insurance in Germany ffectiveness and cost-effectiveness of stratified blended physiotherapy in patients with non-specific low back pain: study protocol of a cluster randomized controlled trial Effectiveness and cost-effectiveness of telehealth in rural and remote emergency departments: a systematic review protocol	Lumbago Multiple pathologies	App Not defined	CEA CEA			
health insurance in Germany ffectiveness and cost-effectiveness of stratified blended physiotherapy in patients with non-specific low back pain: study protocol of a cluster randomized controlled trial Effectiveness and cost-effectiveness of telehealth in rural and	Multiple					

Title	Treated	Tools Used	Performance
	Pathology		Measurement Methods
Clinical and cost-effectiveness of guided internet-based interventions in the indicated prevention of depression in green professions (PROD-A): study protocol of a 36-month	Depression	SMS, Phone calls, Online sessions, E-coach	CE A CU 🔨 🖉
follow-up pragmatic randomized controlled trial			
Cost-Effectiveness of Web-Based Patient-Reported Outcome Surveillance in Patients with Lung Cancer	Lung cancer	Online questionnaire	
HELP@APP: development and evaluation of a self-help app for traumatized Syrian refugees in Germany—a study protocol of a randomized controlled trial	Post-traumatic stress	App	CE A CBA
Economic evaluation of a healthy lifestyle intervention for		3	~
chronic low back pain: A randomized controlled trial	Lumbago	Phone care	CEA
Individually tailored self-management app-based intervention (selfBACK) versus a self-management	•	JT	
web-based intervention (e-Help) or usual care in people with low back and neck pain referred to secondary care: protocol for a multiarm randomised clinical trial	Lumbago neck pain	Aup, Website	CEA
E-health ecosystem with integrated and stepped psychosocial	5		
multicentre randomised controlled trial	<b>y</b> •		
Table 4. Possibility relationships an used.	nong the treated patho	logies, tools, and perfor	mance measurement meth
		logies, tools, and perfor	Performance Measurement Methods
used.	Treated	Tools Used Virtual network	Performance Measurement Methods CEA CB
used. Title	Treated	Tools Used	Performance Measurement Methods CEA
Used. Title conomic evaluation protocol and statistical analysis plan for the cost-effectiveness of a novel Australian stroke telemedicine (VST) program	Treated Pathology	Tools Used Virtual network	Performance Measurement Methods CEA CB A CU
used. Title conomic evaluation protocol and statistical analysis plan for the cost-effectiveness of a novel Australian stroke telemedicine (VST) program Australie flectiveness analysis model of Preventicus atrial forillation screening from the point of view of statutory	Treated Pathology	Tools Used Virtual network of specialists	Performance Measurement Methods CEA CB A CU A
used. Title conomic evaluative protocol and statistical analysis plan for the cost-effectiveness of a novel Australian stroke telemedicine (VST) program restructiveness analysis model of Preventicus atrial forillation screening from the point of view of statutory health insurance in Germany An economic evaluation of a mobile text messaging intervention to improve mental health care in resource-poor	Treated Pathology	Tools Used Virtual network of specialists App SMS	Performance Measurement Methods CEA CB A CU A CU A CEA CEA
Title Title conomic evaluative protocol and statistical analysis plan for the cost-effectiveness of a novel Australian stroke telemedicine (VST) program Appost the triveness analysis model of Preventicus atrial forillation screening from the point of view of statutory health insurance in Germany An economic evaluation of a mobile text messaging intervention to improve mental health care in resource-poor communities in China: a cost-effectiveness study The (cost) effectiveness of guided internet-based self-help CBT for dialysis patients with symptoms of depression: study	Treated Pathology	Tools Used Virtual network of specialists App SMS	Performance Measurement Methods CEA CB A CU A CU A CEA
Title Title iconomic evaluative protocol and statistical analysis plan for the cost-effectiveness of a novel Australian stroke telemedicine (VST) program Tristorffectiveness analysis model of Preventicus atrial Nitillation screening from the point of view of statutory health insurance in Germany An economic evaluation of a mobile text messaging intervention to improve mental health care in resource-poor communities in China: a cost-effectiveness study The (cost) effectiveness of guided internet-based self-help	Treated Pathology	Tools Used Virtual network of specialists App SMS CUA	Performance Measurement Methods CEA CB A CU A CU A CEA CEA

CBT for dialysis patients with symptoms of depression: study

			9 of	
protocol of a randomised controlled trial	Depression	Online sessions	CU	HELP@APP: development and eval
An economic evaluation of a computer-tailored e-learning program to promote smoking cessation counseling guideline			А	for traumatized Syrian refugees i protocol of a randomized
adherence among practice nurses	Smoking	Online sessions	CE	
			A	
			CU	
			A	

HELP@APP: development and evaluation of a self-help app		CE
for traumatized Syrian refugees in Germany-a study	App	А
protocol of a randomized controlled trial		CB
		А

Table 4. Cont.

	Treated		Performance
Title	Pathology	Tools Used Mea	surement Methods
Clinical and cost-effectiveness of a guided internet-based Acceptance and Commitment Therapy to improve chronic pain– related disability in green professions (PACT-A): study protocol of a pragmatic randomised controlled trial		E-mail, Phone calls, Online sessions, E-coach	CE A CU 🔨 🖉
Effectiveness and cost-effectiveness of stratified blended			
physiotherapy in patients with non-specific low back pain: study protocol of a cluster randomized controlled trial		App	A A A
Evaluation of the efficacy of an internet-based pain education			$\sim$
and exercise program for chronic musculoskeletal pain in comparison with online self-management booklet: a protocol of a randomised controlled trial with assessor-blinded, 12-month follow-up, and economic evaluation	Pain	SMS, Phone calls, Website, Online brochure	CE A CU
Economic evaluation of a healthy lifestyle intervention for		ςΟ <sup>γ</sup>	А
chronic low back pain: A randomized controlled trial	•	Phone calls	CEA
Individually tailored self- management app- based intervention (selfBACK) versus a self- management web- based intervention (e-Help) or usual care in people with low back and neck pain referred to secondary care: protocol for a multiarm randomised clinical trial	, o <sup>r</sup>	App, Website	CEA
Cost-effectiveness of population-level proactive tobacco	5		
cessation outreach among socio-economically disadvantaged	5	E-mail, Phone calls	CEA
smokers: evaluation of a randomized control trial	Smoking		
An economic evaluation of a computer-tailored e carning	• -		CE
program to promote smoking cessation counsering guideline adherence among practice nurses		Online sessions	А
Cost-Effectiveness of Web-Based Patient Reported Outcome		Online	CU
Surveillance in Patients with Lung Cancer		questionnaire	Α
E- health ecosystem with integrave land stepped psychosocial services for breast cancer survivors: study protocol of a multicentre readomised controlled trial	Cancer	Website	CEA
$\sim$			CE
4. Discussion			A CU
$\mathbf{V}$			A

Almost all articles published in medical journals express an almost exclusive interest in discussing the topic solely within the boundaries of the clinical setting, presenting a gap in the managerial and statistical literature. This result leads to an interesting reflection, which underlines the increasing relevance of economic and managerial issues in the clinical literature as well. Such findings are consistent with the growing importance of the role of medical doctors as "hybrid managers" [68,69] with cost, budget, and economic outcome responsibilities. Department chiefs should, therefore, be in charge of managing such aspects, which differ from pure clinical practice, and require specific training and decision-making mindsets [70].

The geographical spread of the contributions suggests that the e-Health phenomenon may have recently been widespread in Northern Europe or that it originated in these areas first, allowing for sufficient data to make reasoning about performance evaluations. However, the fact that only four of the seven quantitative clinical cases analyze non-European situationstwo Australian, one American, and one African-suggests that it is Europe that is at an earlier stage than the other continents. A few contributions propose field studies that have already been carried out. Europe has thus been the most interested region in the topic for the past four years, but research protocols have a significant impact on the data.

Relative to the clinical discipline and the treated pathology, pain medicine and mental health appear to be the ones attracting the most interest, as described in Figure 2. For this reason, it can be assumed that these disciplines offer more possibilities for remote

# clinical pathways compared to others, that more often require direct contact with medical

personnel [71]. Still, even those specialities that require an in-person approach, such as surgery, allow for online pre-surgical consultation, follow-up, and telemonitoring in the rehabilitation phase [6,72-75], despite doubts and open questions posed by surgeons about the practical applications and "its efficacy in improving patients' health, cost-effectiveness and user satisfaction" [72].

This reflection is linked to recent studies on the possibility of launchir natient management paths according to the Virtual Hospital model [28,29]. This m assistance for the patient, carried out remotely, similar to that provided in

a physical hospital. A high level of digitalization permits early tion and analysis of diseases, enabling proactive intervention (defined as "initiative meditine") and thus improving the understanding of disease progression, resulting in at reduction in mortality and a substantial improvement in quality of life.

Moreover, in Virtual Hospitals, the number of patients who can be cared for remotely is greater than that in physical hospitals, and ecause patients can be cared for from anywhere (their own home, residences for ly, nursing homes or hospices, or other care facilities), without the need for outparent inics or hospitals [76,77]. A Virtual Hospital and high-tech environment, both for patients and offers numerous advantages due to its u healthcare providers as well as for the healthcare institution itself. Furthermore, this model ensures better accessibility and equity of care and healthcare by providing access to services there is available (thus red

erwise available (thus reducing inequalities in access

to healthcare serv greater efficiency, especially in monitoring elderly or

chronically ill pati require follow-up care [78]. In fact, it seems to be more efficient if it is aimed at a specific target group of patients, i.e., those who are in a follow-up phase. These uple, frail, elderly patients and/or those who have one or more chronic include, conditions ch as heart disease, stroke, diabetes, chronic respiratory disorders, etc. [79]. when applying Virtual Hospital frameworks to such conditions, e- Health tools ent key aspects, and so their economic and sustainability-related issues and performances be considered and monitored.

Compared to other e-Health tools, the significant diffusion of apps, text messages, and phone calls is undoubtedly due to the fact that these are the most easily used devices for a wide target population. More complex techniques require more specific tools and skills on the part of both the patient and the clinical staff [71], who do not always have

adequate training in technology and data analysis [80]. In this regard, one of the major

criticalities is a poor level of digital literacy, which affects not only the population (potential patients), but also the health personnel themselves. While the acquisition of new digital skills may be easy for the younger segment of the population and for clinicians-for whom competencies may be implemented during undergraduate or postgraduate modules or in their lifelong learning education-in other cases, training and accompaniment in the use of these tools may be necessary, both among patients and caregivers [81,82]. In some cases, the accompaniment of the patient by a third-party figure (for example, for seniors) may also be necessary. Moreover, the use of complex tools implies the adoption of a new digital mindset by healthcare personnel, patients, and caregivers [71,79]. On the other hand, widely used online tools (such as those related to mobile technology) may represent facilitators in the management of the clinical relationship [83-86] and in the related communication with the patients.

The recent COVID-19 pandemic, with the reorganization of several clinical processes [10,87–90], has forced clinicians and clinical institutions to use and apply e-Health tools to monitor patients [11,14], assist them, even in end-of-life care [12], and communicate with them. The COVID-19 experience has, therefore, encouraged and promoted the use of e-Health tools, which have been named among the winning strategies for a resilient

and antifragile response to the post-pandemic healthcare system [91]. Still, the results of our literature review do not reveal any particular changes before and after the pandemic outbreak in terms of costs or cost calculation. Interesting enough, only one paper among those published after the beginning of the COVID-19 pandemic specifically mentions this issue [54]. What could be determined was that the pandemic appears to be the ideal context to foster and encourage the use of telemedicine and e-Health tools, but the economic and performance evaluation issue appears independent, as it is discussed by a specific part of the literature. Undoubtedly, the COVID-19 emergency and the subsequent increase in the use of e-Health tools and applications require a deep understanding of the surrounding economic dynamics.

In agreement with other recent studies [30,37], our literature review, albeit it have haved sample, does not reveal any link or repeatability between the pathology treated and the cylealth tool used, as shown in Table 4. Thus, it might be worthwhile to devote specific studies to determine whether there are more or less suitable or effective instruments relative to each pathology treated at a distance.

#### 5. Conclusions

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E-Health appears to be a growing phenomenon, especially in the COVID-19 postpandemic era. E-Health is destined to be one of the winning structures for caring for an increasing number of patients while controlling healthcare costs. Moreover, it is at the basis of modern phenomena such as the Virtual Hospital [79,92]. Within the context, cost dynamics are relevant, as they require measuring the performance of c-Health too.

The studies included in the search protocol of this literature review identified a combined use of the three main methods—cost-effectivenes, cost-benefit, and cost-utility— with no preference emerging for any one depending on the pathology identified. Therefore, we identified an effort in the medical literature to understand not only the clinical result but also the economic outcome of the use of e-Health tools linked on the technologies.

Although the sample selected was infinited, multiple pathologies and various techno- logical tools for patient support emerged. The fact emphasizes once again the strategic role that e-Health tools are playing in the health are landscape and their future development prospects, also from a Virtual Hospital perspective

The cross-fertilization between economic studies and clinical outcomes appears to be an efficient way to study annunderstand the phenomenon as a cornerstone for the development of the future health system. For thermore, in agreement with other literature reviews [30], the need to set standard and surreable guidelines is recalled. In this sense, the role of scientific societies could be strategic in guideling the clinical and managerial commun- nity towards certain solutions and methods that are more elevant to specific situations.

## Limitations of the Study and Future Research Avenues

As with every piece of research, our study has several limitations. Although the methodology used to select the literature for the analysis is rigorous and has already been used by multiple international studies, the sample size is far too limited. The studies did not identify a precise link between the pathology, the preferred e-Health tool, and the performance evaluation method. Still, this limitation could be overcome by changing the search keys or adding more specific ones, such as, for instance, "telepsychiatry", "telecardiology", or "telephysiotherapy". A more comprehensive article sample may also allow a comparison of methodologies and technologies applied to the different e- Health types to reveal new practical implications for healthcare institutions and clinicians. Moreover, as e-Health stands as a general topic, which today involves a variety of medical specialities and diseases, more focused research could deepen the same analysis on specific conditions or subjects.

Finally, given the speed of technological and also organizational change in the healthcare domain also following the effects and responses to the COVID-19 pandemic, it would be appropriate to repeat the investigation in the near future in order to understand innovations and, thus, paradigm shifts in the use and economic measurement of performance. All these aspects constitute interesting future lines of research. Clinicians and experts in economics, healthcare management, and statistics should combine their expertise to produce multidisciplinary results that can help the medical sphere to fully understand, map, and implement the e-Health phenomenon and its potential.

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