A first outlook at Fintech applications to crack the code of healthcare funding: is crowdfunding a viable solution for financing medical care and vaccines?

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Acknowledgements

The authors would like to express gratitude to Andrea Baronchelli for his assistance and Scott Howell for giving strategic input into research design and overarching methodology.

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Abstract

The healthcare industry has been struggling to make research and business models sustainable for the economic systems and investors, especially in pharmaceuticals. In fact, the world is still fighting with medical care affordability and accessibility while returns for investors and corporations keep shrinking. As late stage go-to-market modelling and alternative pricing strategies are proven not sufficient to solve this puzzle, we argue the answer may lay in alternative funding approaches and Fintech. Crowdfunding in particular is emerging as an alternative way to intermediation, with a new kind of agent, raising capital directly from a broader and more diverse audience of investors. In this paper, we systematically search and review the literature to define state of the art around the practice of crowdfunding in healthcare. Analysing and clustering extant evidence on the matter, we identify major emerging themes: from the application of crowdfunding methods to finance pharmaceutical and healthtech research and development, to regulatory and policy. In addition, our findings suggest there is no undisputed evidence in the healthcare domain on the utilization of lending and equity crowdfunding in particular, supporting the formulation of two major hypothesis we urge the scientific community to further investigate.

Keywords: Fintech, crowdfunding, pharma, medtech, equity

1. Introduction

Life science investments seem to be more attractive than ever, with venture deals increasing steadily year by year for the last decade (PitchBook - NVCA, 2021) and pharma companies investing continuously in research and development to market new compounds and generally medical solutions. For any new potential asset, the venture commits heavy capitals to try to survive across all the steps, from early research and discovery all the way up to clinical trials and, finally, approval and marketing authorization from health authorities. The current model of revenues remunerates only the investments betting on those few compounds receiving final approval, where the price is discussed and settled at the very end, just in case of and after the negotiation is successful. This process revolves around the bilateral negotiation between the marketing authorization holder and local payers (publicly funded healthcare systems, insurance companies, sometimes both) considering the expected impact these medicines may have on patients and the overall system (e.g. cost-effectiveness analysis, budget impact models), remunerating production factors while preserving growth and innovation for the industry (Moreno and Epstein, 2019).

In a context where research is going to be riskier, less predictable and has to speed to find real near time solutions or vanquish competitors journey, it is worth noticing that such an ex post bilateral trading makes the return on investment in R&D very uncertain, limits the stability of cash flows and might address mainly to those directions where cost-effectiveness analysis is estimated to lead to pricing that supports the risks (i.e. not focusing on rare diseases). Not to mention the very risk of clinical failure any research and development journey implies, missed pricing and reimbursement negotiations, underperforming against forecasts after launch.

Inequality in the medical care and vaccine commercialization and rollout all around the globe is a reason more to believe current funding, development, and go-to-market models are not sustainable for both the healthcare systems as a whole and investors. Indeed, the global spread of 2019 novel coronavirus (2019-nCoV) made us experience a fair representation of how public health, financial and economic sustainability, and medical care accessibility are indissolubly tied together. On 30th January 2020, the WHO declared the outbreak of COVID-19 to be a Public Health Emergency of International Concern posing a high risk to health and economic systems on a global scale (Sohrabi et al., 2020; Singhal, 2020). As early as mid-2020, modelling already indicated how potential loss of income could be significant, with global GDP declining by up to 3.9%, and developing countries hit the hardest (4% on average, but some over 6.5%) not just on health, but also on trade, finance and macroeconomic policies (Maliszewska et al., 2020).

Unfortunately enough, it is not just about vaccines but also broadly on medical care and all high-end pharmaceutical products in particular. Economic systems are struggling with healthcare affordability and accessibility, in any kind of country wealth, not just in the low-income countries. Yet, the growth of spending does not match with the healthcare budgets of governments, with financial hardship faced by

establishments to cover drug expenses for their citizens, and shows concerns on the increasing out-of-pocket payments incurred by patients. Further, bilateral negotiations with no disclosure on final agreements might hinder some forms of opacity, up to citizens' wealth waste. From an investor point of view, it is not even rosier. Returns in the healthcare industry are still generous, but research and development costs keep soaring while market dynamics, as mentioned, stay uncertain (IQVIA Institute for Human Data Science, 2020). Sustainability of the healthcare systems is thus not ensured and concerns from any point of view (publicprivate systems, citizens, pharmaceutical companies, investors) raise vigorously.

A vast literature exists on potential solutions to find alternatives for affordability and accessibility to medicines and medical treatments, but it address the situation with a local optimum, highlighting different options in the direction of implementation of price models, mechanisms or regulations to ensure stability and preserve long-term profitability of companies. When late stage go-to-market model adjustments are showing to be not enough, the reliability of consistent funding mechanisms can guarantee pharmaceutical producers enough capital raising to purse R&D activities, fostering innovation, and helping every citizen in the true care of every disease, making the healthcare system more equitable.

Thus, we believe that the analysis of the problem must be done from its true root, i.e. the funding mechanisms of research, commercialization, and the resulting innovative drive. We believe that sustainable solutions are therefore related to the broader concept of funding, and can be found in the study of the more general innovation that is taking place in financial markets, commonly referred to as Fintech. Specifically, by analyzing innovative funding mechanisms, crowdfunding could prove to be a potentially applicable mechanism. Therefore, the aim of the current paper is to survey and investigate literature of innovative funding, in its relations with the healthcare industry. With this research, we aim at digging deep at the foundation of the healthcare industry funding standards, seeking for the junctions that Fintech showed to have on the affordability and accessibility of medical treatments.

The remaining of this paper is organized as follows. Section 2 highlights the background of the extant research, focusing on the relevant features of the healthcare industry, deep diving in the innovation in finance and particularly on crowdfunding, and coming in previous results in literature with more details. Section 3 indicates the methodology of the research, while Section 4 gives a first outlook at the results while in Section 5 we discuss emerging themes and trending topics. Section 6 concludes and introduces potential new research venues.

2. Background

The healthcare systems and the pharmaceutical industry do then have very peculiar features. In this Section we introduce the context of a limited accessibility to medicines and medical treatments, unveiling the union

that could spontaneously be created between healthcare and Fintech, with particular reference to the financing mechanisms triggered by crowdfunding.

2.1 The Healthcare Industry

As of today, the access to medical treatments is still a key topic in all healthcare systems. Sustainable Development Goals agenda considers universal health coverage as a core, with all citizens accessing the healthcare services they need, of sufficient quality to be effective, ensuring that users are not exposed to any financial burden (Kieny et al., 2017). To guarantee this fundamental right, public and private healthcare systems coexist with different configurations. Public systems include taxes and social insurance contributions and reimbursements, while out-of-pocket expenses and voluntary healthcare payments (such as voluntary health insurance, financing by non-profit institutions, and enterprise financing) sustain private expenditures (Immergut and Schneider, 2020).

In both schemes, bilateral negotiations between pharma corporations and governments or insurance companies occur in order to set the prices of each product or treatment. The starting point is the analysis on the willingness to pay or cost-effectiveness studies on the opportunity costs which have to be understood and interpreted (Siegel et al., 1996), but the final price level is also affected by market competition (Cole and Dusetzina, 2018; Rosenthal and Graham, 2016), promotion, in terms of advertisements, sales representatives, and key opinion leaders both to prescribers and to the end patients (Alves et al., 2019), and the integration mix of basic and applied research (Barigozzi and Jelovac, 2020). At the end, "incredibly complicated and non-transparent environment sets the list price for drugs with very little relation to the true resources used to produce the specific drug" (Nash, 2018). Currently, price adjustments are decided at late stages, but need to cover manufacturing and both costs raising over time due to the complexity of new drugs discovery, where R&D costs count for over billion dollars, and sunk R&D costs of products that failed to pass clinical trials (Balderrama et al., 2020; Hubbard and Love, 2004).

Such ex-post price mechanism is no longer sustainable: for citizens, which have no clear idea of the overall health mechanisms but suffer accessibility and affordability, including cost-sharing and out-of-pocket expenses (Abbott et al., 2019); for governments and insurance companies, dealing with the health budget, while complex mechanisms and negotiation may hinder more or less confidential agreements or the final price (Henry et al., 2005), willingness to follow the entire process and related uncertainty (Villa et al., 2019); for the society, where accessibility is limited in some countries, in most of cases the ones with a lower GDP per capita; for big pharma itself, which at the current state rely on IPOs and capital increases for raising capitals for financing R&D while Business Angels and Venture Capital firms mainly support smaller companies in financing their projects; and for pharma company shareholders, where risks related to new drug discovery are relevant and imply a high return (Leadley et al., 2020).

Social consequences of current schemes are therefore of outmost importance. As Covid-19 vaccines show, several concerns raise on the fair price to be paid (Balderrama et al., 2020), on the different negotiation skills of governments and insurance companies, and on the accessibility to citizens in each and all countries no matter their economic wealth.

Several alternatives have been proposed. Advance-purchase commitments, with a guarantee to buy a given amount of a drug when developed (Hubbard and Love, 2004), incentives or competition for reward and prizes (Hubbard and Love, 2004; Finkelstein and Temin, 2008), separation of distribution and marketing (Finkelstein and Temin, 2008), patent pools (Bermudez and Hoen, 2010; Cox, 2012; Childs, 2010), patent buyouts (Kremer, 1998) are among the most cited. Abbott et al. (2019) suggest discouraging pay-for-delay agreements, patent evergreening, increasing transparency, taxing advertisements to final consumers to finance research, aligning interests on the value chain, kind of revenue share mechanisms above certain thresholds, among others. Moon et al. (2011) analysed tiered prices i.e. prices of drugs systematically lower for emerging countries, arguing "policies that *de-link*" the financing of R&D from the price of medicines merit further attention, since they can reward innovation while exploiting robust competition in production to generate the lowest sustainable prices".

2.2 Fintech: a Focus on Financing and Crowdfunding

So far, the discussion related mainly to health expenditure and to the systems for assessing pricing and potential improvements, as final outcome of the entire process (see also Towse and Mauskopf, 2018), even though the idea of disentangling the relation from prices and R&D of pharma corporations is already under discussion.

However, we deem the debate should open on the entire process, potentially redesigning it in a new way. In our view, it clearly shows that an alternative way for funding R&D has to be implemented, in order to achieve sustainable and affordable prices, in any country, for any citizen, no matter the system model, while guaranteeing fair profits to pharma companies investing in research. Therefore, drug financing is becoming fundamental in the healthcare industry. In the process of funding new drugs development, Fintech – as the natural innovation displaying in the financial services industry enabled by technology – can become an enhancing factor, for smaller pharmaceutical companies that are struggling to have enough funds to purse their researches, and for bigger ones, to ensure lower risks along the research process, which will turn in a coherent risk-return profile.

Indeed, crowdfunding platforms are emerging as an alternative way to intermediation, with a new kind of intermediary (Cai, 2018), raising capital directly from a broader and more diverse audience of investors.

Although many different definitions and classifications exist, we can identify 4 major crowdfunding archetypes: charity crowdfunding, reward-based crowdfunding, lending crowdfunding, and equity crowdfunding.

- 1. Charity (or donation-based) crowdfunding is an internet-based non-profit fundraising mechanism soliciting (small) monetary contributions from crowd donors to help other people or organizations across the globe in trouble or with dreams (Zhao et al., 2019); in this very case, return for funders can be considered purely social and ethical. This method is frequently related where single name individuals have not the chance to afford a given treatment, mainly in relation with a (rare) disease whose treatments are not included in a full coverage of the public health system or in the boundaries of the insurance contract.
- 2. Reward-based crowdfunding is another online channel for venture fundraising together with equity crowdfunding the most leveraged model by start-ups where funders receive non-monetary benefits in return for monetary contributions (Shneor and Munim, 2019); often, especially in the IT industry, the benefit is early access to the product or prototype. Some medical device examples can be found on several crowdfunding platforms from air masks to smartphone apps dedicated to chronic diseases and wellbeing in general.
- 3. Lending crowdfunding (or crowd-lending, or peer-to-peer lending) is the practice of liaising between borrowers and lenders through web platforms and by-passing traditional financial institutions (Ziegler and Shneor, 2020); in brief, funders get an interest in return for the money they are investing plus the capital back at the end.
- 4. Equity crowdfunding is based on the principle of a digital, online marketplace, where entrepreneurs can access a large scale of potential investors who, in return for an ownership stake (equity), may fund their ventures (Estrin et al., 2018).

In order to investigate the literature of crowdfunding in its relations with the healthcare industry (Fig. 1), also known as medical crowdfunding (Ren et al., 2020), and to clarify whether some innovative crowdfunding mechanisms for healthcare already exist, to frame the novelty and our contribution, we systematically reviewed the literature.



Fig. 1 – Literature-based theoretical Framework.

3. Methodology

We performed a systematic literature review and clustered the evidence to identify any significant subtrend, as shown in Fig. 2. This literature review served the purpose of addressing our objective by defining the state of the art in the application of crowdfunding methods to the healthcare industry. The literature search was systematic to minimize the risk of overlooking potentially relevant contributions.



Fig. 2 – Systematic literature review phases.

The first phase aimed at preparing the ground for the literature review by running a database research founded on appropriate search terms on Scopus. To ensure capturing of the cross-disciplinary nature of the study, both crowdfunding and healthcare domains were included in the search strings, supported with concept mapping and looking for synonyms via Thesaurus search. As shown in Table 1, the final search query included both the dimensions of "crowdfunding" and "health*", but also "pharma*", "drug*", "medicine*", "device*". Based on SciVal research performance assessment, results were not limited to a specific timeframe, as focusing on years that are more recent would cause loss of significant contributions.

Search query:	(crowdfunding AND (health* OR pharma* OR drug* OR medicine* OR device*))
Database:	Scopus
Keywords in:	title, abstract, keywords
Year restriction:	none

Language restriction:	English
Subject areas:	[Medicine], [Social Sciences], [Engineering], [Business, Management and Accounting], [Biochemistry, Genetics and Molecular Biology], [Economics, Econometrics and Finance], [Pharmacology, Toxicology and Pharmaceutics]
Document and source restriction:	none

Table 1 – Literature review database searching.

The research identified 155 papers, filtered basing on language and subject areas (Table 1). We cleaned the resulting items excluding duplicates (1 paper), records escaping the filters (1 Spanish article) and not otherwise identifiable contributions (missing authors, sources, DOI, 17 cases).

The inclusion criteria were assessed to maximize specificity on the rough selected database resulted from the previous cleaning. To assess eligibility, the review of titles and abstracts was based on two major criteria. First, we considered explicit healthcare references only, excluding any kind of non-medical application (27 papers not eligible e.g. references to financial or economic health). Second, we selected studies that investigated the specific field of crowdfunding (15 papers not eligible e.g. crowdsourcing as a general process in which a firm outsources pieces of a given work leveraging hard skills of the crowd), while no further screening between crowdfunding archetypes was applied given our objective. The final 94 papers, selected applying the aforementioned inclusion criteria, are mainly articles (66) with some reviews (7), notes (7), letters (6), short surveys (4), editorials (2), conference paper (1) and book chapter (1).

4. Results

The analysis of the final sample, showed first publications are dated 2012, consistent with the relatively recent area of study for crowdfunding in healthcare. The concentration is unbalanced towards recent years with 2019-2021 weighting for the 54% of the publications, and feeding its vitality. For 50 papers, the focus was mainly at global level or with no relation with specific geographical areas; 44 papers are instead related to some local specificities: 24 based in the US, 10 in Canada, 3 in the UK and 2 at European level, while limited are the discussions in the context of Asian areas such as China (3) and Indonesia (2).

Eighteen publications are related to economic and social science outlets, 8 to engineering fields and multidisciplinary journals but healthcare-related journals were the vast majority of outlets for publication (68), consistently with the current scope of the researches, mainly focused on charity crowdfunding for supporting out-of-pocket medical expenses incurred by individuals with rare or severe diseases (71 overall, 51 in healthcare journals; Table 2). The remaining ones refer to crowdfunding in general with no mention

to archetypes or any other classification (13 overall, 10 in healthcare journals), some others discussing all the 4 archetypes (6, 4), or focusing on a specific model: 3 were focused on lending and equity crowdfunding (2 in healthcare journals) and 1 on reward-based crowdfunding (1).

	Medicine; Pharmacology, Toxicology and Pharmaceutics; Biochemistry, Genetics and Molecular Biology	Social science	Business, Management and Accounting	Multidisciplinary	Engineering
Charity crowdfunding	51	10	3	5	2
Reward-based crowdfunding	1	-	-	-	-
Lending crowdfunding	2	-	-	1	-
Equity crowdfunding		-	-		-
All the archetypes	4	1	1		
No reference to any classification	10	3	-	-	-

Table 2 – Descriptive information on crowdfunding archetypes and research subject areas.

No matter the healthcare journals as main target, most of the articles address the topic from a wider perspective focusing on healthcare in general (6), accessibility (45) and research (17) across all the diseases in order to investigate the traits of crowdfunding in the medical sector. Some focused on a specific target of crowdfunding campaigns, such as cancer care (13), transgender assistance (4), pharmaceutical support (4), covid-19 (3), stem cell treatments (2).

To sum up, we started analyzing all items resulting from systematic search considering major archetypes of crowdfunding as our lenses. Interestingly enough, this analysis showed a strong discussion on charity and donation-based models, which however might be of limited support in the funding of healthcare R&D given its overall magnitude, and no undisputed evidence on the practice of lending and equity crowdfunding in healthcare. To deepen our understanding in studying crowdfunding based mechanisms for healthcare, we went back to the final sample and re-clustered manually all the records, adopted an inductive approach based on the research domain, main objective and major findings of each contribution which we will present in Section 4.

5. Concept mapping and discussion

A detailed analysis of the reviewed studies led us to divide the papers into four groups, according to emerging themes in the selected body of knowledge: crowdfunding as an alternative instrument to access medical treatments (17 contributions); support to medical research and development (23); performance review of platforms and funding campaigns (18); concerns and reflections around policy and ethics in the field of medical crowdfunding (36). This framework forms the basis for the presentation and discussion of our findings.

	CROWDFUNDING IN HEALTHCARE, 94 results			
Access to medical treatments, 17 results				
	Alternative access		4 results	
		Imanulrachman et al. (2019); K (2020a)	imseylove et al. (2020); Renwick and Mossialos (2017); Snyder et al.	
	Pitfalls in he	althcare systems	13 results	
		Cohen et al. (2019); Coutrot et a Lublóy (2020); Lukk et al. (2018 Sisler (2012); Snyder et al. (202	al. (2020); Di Carlo et al. (2020); Ho et al. (2019); Kenworthy (2019); 8); Palad and Snyder (2019); Rajwa et al. (2020); Saleh et al. (2021); 20c); The Lancet Oncology (2017)	
Support to	Medical res	earch and development, 23 resu	llts	
	Alternative s	ourcing	16 results	
		Afshinnekoo et al. (2016); Byı Dragojlovic and Lynd (2016); (2015); Özdemir et al. (2015); R (2020); Sharma et al. (2015); Sh	rnes et al. (2014); Cameron et al. (2013); Chetlen et al. (2018); Hidayat et al. (2020); Kamajian (2015); Koole et al. (2018); Otero ay and Özdemir (2016); Riccardi et al. (2017); Schuhmacher and Kuss nith and Merchant (2015); Wiebe and FitzGerald (2017)	
	Neglected di	seases and orphan drugs	7 results	
		Del Savio (2017); Dragojlovic a al. (2015); Loucks (2013); Rajpu	nd Lynd (2014); Fumagalli and Gouw (2015); Hahn (2015); Isakov et ut et al. (2015)	
Performan	nce review of	platforms and funding campaig	gns, 18 results	
	Crowdfundir	ng platforms	1 result	
		Bassani et al. (2019)		
	Predictors of	success	17 results	
		Ba et al. (2021); Berliner and K al. (2019); Loeb et al. (2018); C Proelss et al. (2020); Ren et al. (2020); Thompson et al. (2015);	enworthy (2017); Durand et al. (2018); Fong et al. (2020); Holmes et Drtiz et al. (2018); Park (2012); Peng et al. (2021); Pol et al. (2019); (2020); Saleh et al. (2020); Saxton and Wang (2014); Solotke et al. Vassell et al. (2020)	
Policy and	Ethics, 36 re	esults		
		Gonzales et al. (2018); Snyder a	nd Crooks (2020); Snyder et al. (2016)	
	Non-approve	ed treatments	12 results	
		Iqbal and Collins (2020); Murdo and Cohen, I.G. (2019); Snyder (2020b); Song et al. (2020); Tan	cch et al. (2019); Smith (2015); Snyder and Caulfield, T. (2019); Snyder and Turner, L. (2019); Snyder and Turner, L. (2018); Snyder et al. aner et al. (2019); Vox et al. (2018); Zenone et al. (2020)	
	Regulatory c	oncerns	9 results	
		Dressler and Kelly (2018); Jin Young and Scheinberg (2017); Z	(2019); Kubhek (2020); Mercer (2019); Moore (2019); Ross (2020); Zenone and Snyder (2019); Zonia (2016)	
	Social inequa	alities	12 results	

	Barcelos (2020); Barcelos (2019); Barcelos and Budge (2019); Burtch and Chan (2019); Kenworthy
	et al. (2020); Lee and Lehdonvirta (2020); Silver et al. (2020); Snyder (2016); Snyder et al. (2017a);
	Snyder et al. (2017b); Van Duynhoven et al. (2019); Zenone and Snyder (2020)

Table 3 - Descriptive information for studies included in the systematic review.

5.1 Access to medical treatments

The world is struggling with access to medical care, with the World Health Organization (WHO) reporting that as of today nearly 2 billion people have no access to basic medicines, causing a cascade of preventable misery and suffering (World Health Organization, 2017). As reported (Moon, 2017), there is serious concern that current funding and business models (especially in pharmaceuticals) will break health system budgets, with worldwide spending outpacing both overall health expenditures and economic growth. However, what has recently been headline news in high-income countries has long been a concern everywhere else; unaffordable medicines and inadequate innovation have become global issues, and business as usual is no longer an option. It is no surprise access to treatment is one of the burning emerging themes when studying current practice of crowdfunding in healthcare. At a closer look, we identified two very distinct perspective on this matter: crowdfunding as an alternative way to access unaffordable (sometimes not-yet approved) treatments, and the study of medical crowdfunding to spot coverage gaps and weak spots in the economic and healthcare systems.

5.1.1 Alternative access

The right to health founding principles comprehends availability, accessibility, quality and equality as the four core elements (World Health Organization, WHO). However, access to healthcare is most of the times prevented by economic and financial condition of patients. Kimseylove et al. (2020) demonstrated how patients looking for support to transgender medical services through online campaign are significantly more represented in those areas of the United States where these practices are not falling within the health coverage programs for low-income residents procedures.

Costs remain one of the major constraints to these patients, and crowdfunding could foster and facilitate the practice of the "right to try" pathway, although the evidence suggest there is no practical benefit in comparison to the more regulated FDA expanded access programs (Snyder et al., 2020a). Imanulrachman et al. (2019), studying real world campaigns in Indonesia on one of the most common crowdfunding platforms, similarly conclude how crowdfunding is indeed a viable and fair alternative path to access healthcare services, in respect of all WHO guiding regulations. To be underlined, the two local contexts of the aforementioned researches show that accessibility challenges affect patients from all over the world, and not just in low-income countries.

More broadly, advantages of better accessibility will be not just for patients, but for the healthcare systems in general.(Renwick and Mossialos, 2017) argue that crowdfunding may bring many economic benefits to

healthcare, especially around deferred and underserved medical issues. Many of the benefits of crowdfunding – improving access to funding and socialize engagement, to name a few – are common to all applications across sectors; however, as we ourselves outlined before, healthcare utilization should be handled more carefully since exacerbated alternative paths of access could bias broader priority settings for public health.

5.1.2 Pitfalls in healthcare systems

It emerges from the selected body of knowledge that crowdfunding campaigns and their systematic study can tell a lot about gaps in coverage and defect in medical services all around the world, regardless of the healthcare systems archetypes (i.e. publicly funded, based on private insurance, hybrid).

The practice of crowdfunding highlights how campaigners are usually motivated by gaps in the wider social system, like traveling costs related to medical care or unpaid time off work (Snyder et al., 2020c), and this applies even in context where the healthcare system is universal and publicly funded e.g. Canada. Similarly, other authors argue how the spread of healthcare crowdfunding is nothing but a shortcoming of the Canadian welfare state provision (Lukk et al., 2018). Comparable investigations were conducted all over the world and across all healthcare systems archetypes such as the United Kingdom (Coutrot et al., 2020), Germany (Lublóy, 2020), the United States (Sisler, 2012) ones. The latter, a typical private system where citizens do pay directly (out-of-pocket) or are lucky enough to have an insurance coverage, deserves a special mention, as there is an underlying trend linking the practice of healthcare crowdfunding and health insurance coverage lack or broadness. In many circumstances, the campaign is not even a medium to get to the treatment or service but the only way to face everyday expenditures and avoid medical-related bankruptcy.

The healthcare systems gaps emerging from the application of crowdfunding in healthcare have been investigated specifically in the different fields of medicine, not only across geographies. Unsurprisingly, oncological care stands out, as surely technological innovations and epidemiological factors have all contributed to the raise in costs hence financial burden on patients (Cohen et al., 2019). Chimeric antigen receptor T cells (CAR-T) therapies, the novelty of cancer treatment, do not escape this analysis, where evidence suggest patient may deal with unforeseen indirect costs associated and should then be advised on all resources to handle these costs – even unconventional resources, like crowdfunding (Ho et al., 2019). Similar examples can be found in other therapeutic areas, from urology (Di Carlo et al., 2020) to drug abuse and addiction-related services (Palad and Snyder, 2019).

The extraordinary circumstances of the COVID-19 pandemic are aggravating the distress of economic and healthcare systems in regards of access to medical care. It is reported that the online crowdfunding response was remarkable, with an exponential growth of patients relying on web campaign to support their expenses

– mostly related to services or protective equipment (Rajwa et al., 2020); again, the thoughtful study of this practice should be the pulse-check tool governments and policy makers should use to spot underserved needs and better define the social distress, especially in the face of a global health threat (Saleh et al., 2021). Different views emerge on healthcare crowdfunding, as a complex innovation, not simply and purely a good innovation, reshaping systems, influencing disparities, even shifting political norms (Kenworthy, 2019), or as a practice (just like charity) meant to be a last resort, or even a signal of the failure of healthcare systems – especially those which are universal and publicly funded (The Lancet Oncology, 2017). It is undisputed that, when studying the evidence, no matter what is the aim of the authors, ethical concerns emerge strongly (please refer to Section 5.4 for a coherent discussion).

5.2 Support to Medical research and development

Second trending theme emerging from our review is the application of crowdfunding to support medical research and development, in general as an alternative or complementary source of funding for scientists and small ventures, or, in particular, as a novel option for financially backing orphan drugs research and underserved diseases. None of the papers in this area specifically refers to equity or lending, where majority of the studies maintains a high perspective on crowdfunding or alludes to donation-based (charity) crowdfunding, highlighting some phenomena related to the role of social media or gaps in economic and healthcare systems worldwide.

5.2.1 Alternative sourcing

In the recent years, an increasing number of healthcare researchers has been relying on crowdfunding to support their activities, leveraging personal motivation of the crowd to see these initiatives taking off and, in a few cases, a general appetite for some type of financial and monetary reward. Real worlds examples are described in the niches of genomics, bioinformatics, microbiome and meta-genomic research, infectious diseases (Afshinnekoo et al., 2016; Cameron et al., 2013; Riccardi et al., 2017). There is a common sentiment when studying the application of crowdfunding principles to medical research this could be a booster for healthcare innovation (Kamajian, 2015).

It is interesting to get a better understanding of what the predictors of success in this specific area are, similarly to the case of single campaigns or platforms. Dragojlovic and Lynd (2016) studied what are the preferences of prospective donors in North America in regards of drug development campaigns. Their findings suggest, although there is predilection for non-profit research organizations, the crowd is not averse to donating to the so-described for-benefit corporations. As the authors highlighted, we agree this behavior can reinforce the usage of crowdfunding to support early stage biotech ventures and seed funding, in

particular when the market potential of the assets at stake has yet to be established (Dragojlovic and Lynd, 2016). Evidence from Chetlen et al. (2018) and Sharma et al. (2015) confirms the hypothesis, demonstrating how these limited funds are often used to trigger and finance small initiatives, bridge and complement to larger grants or funding, support early stage clinical trials. This perspective may be relevant not only for small new ventures but for large established pharmaceutical companies too, where mobilizing the general public through crowdfunding to prioritize and focus on what the system really values (Schuhmacher and Kuss, 2020).

In fact, if crowdfunding campaigns cannot replace yet the more traditional archetypes of funding for medical research, the evidence suggest these small amounts of money can serve as a starting point and ensure survival of early-stage start-ups. To achieve this goal, campaigners are required to bring to the cause, beyond proper technical knowledge of the medical science and the ability to translate in the language of the crowd, a certain ability in the matters of social media engagement (Otero, 2015). Building an audience, actively engaging, nurturing and broadening it, is key to success like in any other real world application of crowdfunding (Byrnes et al., 2014). Medical scientists, like any other campaigner, should then focus on visibility and consistently increase social media presence, investing best efforts in identifying and engage with key stakeholders in the relevant community and beyond the interest in a tangible financial support (Smith and Merchant, 2015). The phenomenon seems to apply broadly regardless of the disease and research area, where successful cases in the domain of hearth diseases are reported to be critically linked to the ability of fostering connections with professional organizations (patient advisory groups) and, again, the ability of delivering the message through a simple and straightforward narrative (Koole et al., 2018).

An interesting perspective emerging from the current body of evidence is considering this phenomenon from the angle of the service it may bring to the communities and social participation. In fact, medical crowdfunding can represent an opportunity for the crowd to support directly ventures trying to address major health problems in their communities; to achieve this vision of social empowerment, current funding models should be reshaped and embrace concerted efforts bringing together angel investors and common citizens to pool their resources for the good of public health and innovation without overlooking a favorable return on their investments (Özdemir et al., 2015). The COVID-19 pandemic is again exacerbating the need for a different approach to healthcare funding, where some practical example of how crowdfunding can support fast-track development of medical assets in the extraordinary circumstances are reported, leveraging the community spirit of social entrepreneurship and collaboration of the crowd (Hidayat et al., 2020). On a scale larger than single case application, socializing healthcare funding and empowering financial communities has the potential of massively reshaping research direction, beyond patient centricity and partnership on trial design and enrollment, with all the ethical and integrity questions this scenario poses (Wiebe and FitzGerald, 2017). Ray and Özdemir (2016) seem to share same view when claiming

crowdfunding has the potential to fill current gaps in the systems through large scale social engagement, although in some countries like China or India despite their vast population this kind of financial contribution is still very infrequent (Ray and özdemir, 2016).

5.2.2 Neglected diseases and orphan drugs

Although there is no universally accepted definition for rare diseases and the term may present different legal hence access implication across the different geographies, in our analysis we refer to neglected diseases as those medical conditions with low prevalence, about 1 in 1,500 people according to the Rare Disease Act of 2002 (107th Congress Public Law 280, 2002), or, more generally, underserved because of missing resources and support to research and development efforts. According to the US Food and Drug Administration (FDA), orphan drugs are those pharmaceutical agents intended for the prevention, diagnosis or treatment of rare diseases (U.S. Food & Drug Administration, 2018). More than 300 million people live with rare diseases globally, and crowdfunding is considered an effective alternative to fund and boost medical research in an area currently facing, like many others, significant limitations in resources (Rajput et al., 2015). Despite the many incentives provided by the FDA – from longer patent times to tax breaks, drug development is an expensive business and orphan drugs make no exception hence, where as highlighted before extra funding to early-stage biotech companies is key to success (Loucks, 2013) and where medical crowdfunding could become a tremendous surrogate for financing innovation (Dragojlovic and Lynd, 2014).

As further discussed in the policy and ethics section, it is opinion of some that massive adoption of crowdfunding methods in the medical research domain may lead to systemic shortcutting of existing expertbased scientific valuation processes – like prioritization of resources based on disease burden. We agree with other authors (del Savio, 2017) and strongly believe this practice has the potential of bringing new life to this industry especially in those areas affected by resistant failures of standard funding systems such as neglected diseases. A number of different and specific real world cases are reported, from rare genetic conditions to preeclampsia (Fumagalli and Gouw, 2015; Hahn, 2015; Isakov et al., 2015).

5.3 Performance review of platforms and funding campaigns

Third dominant theme emerging from the review is performance, namely how crowdfunding campaigns perform in the healthcare area in real world, what are the most suitable platforms across the countries and, most important, what are predictors of a successful funding campaigns – from social behaviors and environment, to basic demographics of campaigners and their diseases. We focus our discussion on the two major trending areas: platforms (or any complementary technical features) and their correlation to the campaign performance, and predictors of success across different geographies and disease areas.

5.3.1 Crowdfunding platforms

Most studies focused on one single platform search, a few at most, with one single research adopting a comprehensive approach to the investigation of platforms and the environmental factors influencing them. Unsurprisingly, research shows a direct correlation between the spread of medical crowdfunding platforms and the healthcare system archetypes, with authors describing a real substitution effect when the coverage is poor – in line with what has been described in regards of the systemic gaps spotted through the investigation of medical crowdfunding campaign all around the world. However, it is surprising the effect of crowdfunding platforms on the chances to run a successful campaign; in fact, the evidence suggest that investment-based platforms (e.g. equity crowdfunding) and healthcare-dedicated ones are less likely to be successful when it comes to medical crowdfunding campaigns (Bassani et al., 2019).

5.3.2 Predictors of success

Predictors of success for medical crowdfunding campaigns have been studying from many different angles, in various countries and circumstances. In China, medical information (low mortality rate, high frequency) and epidemiological details around the campaigners and clinical cases were found to be one of the most relevant determinants of success, same for some demographic and social attributes, like age or location (Ba et al., 2021). Association between demographics of project initiators and epidemiological characteristics with funding success was thoroughly assessed in other countries as well: the United States, Canada, the United Kingdom. Although the reasons behind the single individuals look very different in the different countries and social disparities emerge from the study, in general medical campaigns raised more funds in the Unites States – with black individuals, female, and routine care commonly less successful. It is worth noting that campaign for inaccessible and experimental care, more common for cancer treatments, raised more than routine care (Saleh et al., 2020). To test these individual factors on the largest scale and make more clarity around the actual impact on fundraising performance, alternatives for patterns and clusters rely on machine learning where first results, although not conclusive, are encouraging and support further efforts in this direction (Peng et al., 2021).

Determinants of medical crowdfunding campaigns success in relation of specific disease areas were also investigated. In fact, certain conditions seem to perform better than others – even within the same disease area; it is the case of organ transplantation, where liver transplants on average hit half of the campaign target versus kidney transplants reaching a mere 11.5% (Pol et al., 2019). When it comes to cancer treatments and complementary costs, a similar phenomenon can be observed. These medical crowdfunding campaigns are more often triggered and managed by relatives or friends of the affected, with breast cancer campaign raising more funds than prostate cancer (Loeb et al., 2018). Malignancies in general tend to attract

the donors attention more, as evidence from thyroid surgery related crowdfunding suggest, where indeed thyroid cancer campaign raised the highest amount of funds when compared to other diseases in the same area (Fong et al., 2020). Other factors appear to have an influence on outcomes: a positive emotional sentiment in the narrative, third-person description and length, higher goal amount (Durand et al., 2018).

Narratives i.e. how initiators and promoters describe the illness and financial need play a major in determining the success of a medical crowdfunding campaign. Different authors have highlighted the importance of a compelling and accurate narrative, mastery in medical jargon and proficiency in the language of media (Berliner and Kenworthy, 2017). On average, medical crowdfunding campaign perform better when the subject is an infant girl, or children in general (Ren et al., 2020), the wording accurate but not technical; in addition, images depicting the patients, especially when diagnosed with more sever diseases, plays in favor of better outcomes. Most successful campaigns are usually the one started around holidays, with a peak for Christian holidays (Proelss et al., 2020). Similar trends seem to emerge in the rare disease space. Vassell et al. (2020) studied systematically medical crowdfunding campaigns in support to Lyme disease treatment or diagnosis, looking for common themes into these narratives. Beyond medical technicalities, wording appears very personal and emotional in nature, centered on the loss in quality of life, missing support and care, what is sought and hoped (Vassell et al., 2020).

The network is natural environment of every medical crowdfunding campaign, every crowdfunding campaign lives and prosper through the internet by definition, and it described by many authors how the ability of campaigners to build and leverage the social media effect is key for ultimate success. In fact, online donors behave differently: tend to follow the media stream more than anything else, privilege certain categories over others (healthcare in particular), give small contributions (Saxton and Wang, 2014). A strong social media network, taking advantage of social media contents, plays an important role in all medical crowdfunding campaigns (Ortiz et al., 2018; Park, 2012), in general and in the area of oncology and hematology in particular (Thompson et al., 2015). Regardless of the disease area, although media attention still emerged as a relevant predictor of success, certain goods seem to be less attractive than others, where pharmacy-related products (like anything related to patient medication and medication management) appear to have a low success rate (Holmes et al., 2019).

If better socializing of a certain condition can determine the success of medical crowdfunding disease – whether media attention is focused on a disease or the financial burden someone may face handling it, same phenomenon can affect for the bad and predispose to failure. Evidence from a recent study show how success in crowdfunding campaigns to support abortion services is dramatically low in the United States, despite single state abortion policy (Solotke et al., 2020). Despite the fact a third person narrative, especially when abortion was triggered by a maternal or fetal diagnosis, raised significantly more money, campaigners should be aware the media effect could amplify the social stigma around some affections.

5.4 Policy and Ethics

Regulatory and ethical concerns is indeed the most represented topic when systematically reviewing the literature of crowdfunding in healthcare (Snyder et al., 2016), not a surprise considering how sensitive the intersection between financial and medical services can be. With markets and services evolving so rapidly, regulating such environment requires adequate technological instruments for policy makers hence this discipline is today (and tomorrow) key to the very survival of the broader ecosystem. If some authors question about privacy of patients and campaigners (Gonzales et al., 2018; Snyder and Crooks, 2020), the majority seems to be concerned with the usage of medical crowdfunding to support non-approved or alternative treatments, missing a regulatory framework where to operate, the widening of social gaps resulting from non-supervised application of the practice of crowdfunding in healthcare (especially donation-based, single-patient applications).

These contributions funnel on pure medical ethics and accessibility only, we believe the perspective on the matter should be broader and embrace ethics and regulatory in finance as well (Regtech). Considering the different archetypes of crowdfunding, equity crowdfunding is significantly different when looking at it from the investor perspective. Equity crowdfunding implies investment decisions with a prospect of a potential return on investment, meaning higher risk levels compared to reward-based crowdfunding, where, as mentioned, funders get material or immaterial rewards for their financial support or refund if the funding campaign does not reach its goal. Also, equity crowdfunding is largely characterized by information asymmetries in the evaluations of new ventures as the majority of funders are retail non-professional investors (Mochkabadi and Volkmann, 2020), with limited knowledge of funding mechanisms, shareholders duties and risks. Fintech and Regtech have been growing in relevance exponentially, hand in hand since the global financial crisis of 2008. As Fintech refers to the application of technology in general, information technology in particular, Regtech identifies the practice of leveraging such mediums in the domain of regulatory, from monitoring to reporting and compliance (Arner et al., 2016). With the financial markets and services evolving so rapidly, regulating such environment requires adequate technological instruments for policy makers hence this discipline is today (and tomorrow) key to the very survival of the broader ecosystem.

5.4.1 Non-approved treatments

There is large evidence of practicing medical crowdfunding for requesting financial support to unlicensed drug treatments or alternative therapies in general, especially in North America, especially for cancer (Iqbal and Collins, 2020). These campaigns are also supported by, or promoted through, news media. In a recent

study from Murdoch et al. (2019) roughly 20% of the articles from a combined United States-Canada newspaper sample referred to unproven or lacking regulatory approval treatments.

Findings suggest campaigners often rely on crowdfunding to get access to alternative or complementary treatments to licensed medicines, as a substitute or because licensed treatments are not available (Snyder and Caulfield, 2019). Among the other risks, this practice can be source of intrinsic inefficiency in resource allocation, especially when the driver for campaign success is a misleading narrative (Snyder et al., 2020b). Practical example is crowdfunding cannabidiol for cancer-related care, where majority of campaigns are backed by anecdotal evidence and misinformation is widespread (Zenone et al., 2020). Vox et al. (2018) assessed a broader set of treatments, and again the study demonstrated how medical crowdfunding is widely used to finance unlicensed or ineffective – sometimes potentially dangerous – treatments across different disease areas. Although these campaigns are usually less successful than the average, the way the funds are spent is far from being virtuous. A case a part is crowdfunding for stem cell treatments, employed for a number of different diseases and, despite this practice represents just a fraction of the total, these campaigns are relatively successful. Still, majority of the above-mentioned medications are unproven and misrepresented, and donations seem to be triggered by misleading narratives often leveraging a general sentiment of the crowd towards stem cells and perceived scientific value (Snyder and Turner, 2018; Tanner et al., 2019).

Authors also suggest different alternatives to mitigate and regulate the phenomenon, starting just with stem cell treatments crowdfunding where Snyder and Turner (2019) hope for targeted patient education initiatives and policies to raise the awareness and limit misuse. Education is key, not only patient education but broadly of all involved stakeholders, including physicians who should educate themselves on complementary therapies (Song et al., 2020) and the practice of crowdfunding and alternative medical funding in general. Others suggest it should be the crowdfunding platform to implement stronger regulations and avoid the spread misinformation and funding unproven medical interventions (Snyder and Cohen, 2019), and it is extremely interesting the perspective of Smith et al. (2015) advocating for early intervention of health authorities (e.g. FDA) in giving guidance to small companies seeking for alternative funding.

5.4.2 Regulatory concerns

Medical crowdfunding, given the right circumstances, can be a formidable instrument serving the healthcare ecosystem and all involved stakeholders. Alleviating the risks and embed the practice into a fair regulatory framework will not be easy though, in consideration of the many forces at stake: ambiguity in laws and policies, lack of control, reporting, awareness (Young and Scheinberg, 2017). At its worst, missing governance may leave room to deception, up to crowdfunding frauds: real world evidence is missed across

the geographical and social spectrum, and although platforms have policies to protect both donors and campaigners some argue this is not enough (Jin, 2019; Zenone and Snyder, 2019). It has been argued "virtuous donors" (i.e. self-rigor of the crowd) could be a deterrent against vicious campaigns in healthcare and mitigate associated ethical risks (Moore, 2019), and, if virtues alone cannot replace good regulatory practices, we agree it has to be part of the solution. In this regard, it is crucial to consider how medical crowdfunding seems to influence policy making at many levels, from the safeguard of patients and donors to conflict of interest mitigation in federally funded medical research (Zonia, 2016).

A recent and unfortunate case in the United Kingdom aroused some reflections in the medical community and not only (Ross, 2020), and, beyond the ethical concerns purely related to the medical practice, authors observe how these applications can drive reallocation of social resources (Dressler and Kelly, 2018) as highlighted before. More important, medical crowdfunding if applied on a large scale, especially in publicly funded systems, could in fact "commodify" healthcare and make a market out of it. We believe that introducing market norms where there is none is not necessarily for the bad, if properly regulated, especially when the phenomenon is often response to structural issues (Mercer, 2019). It is true though that this market, as it is currently, is indeed influenced by unfairly distributed forces such as social media savviness, network, ability in creating compelling narratives (Kubheka, 2020), and all of this should not have any role in how essential medical services and goods can be accessed.

5.4.3 Social inequalities

Medical crowdfunding campaigns are more successful for those who are wealthier, have better access to interpersonal wealth and social media, show a superior ability to appeal to the crowd of donors and outpace the competition (Lee and Lehdonvirta, 2020; Silver et al., 2020). These studies expose the way funds coming from the crowd are not distributed universally or based on need, rewarding the more privileged ones and widening the socioeconomic gaps in access in the United States. This conclusion is further supported by a recent study of Canadian cancer-related medical campaigns, where the authors demonstrated a disproportioned use corresponding with higher income and education (Van Duynhoven et al., 2019).

Medical crowdfunding as a booster of social inequalities is a hot and well-represented topic in the existing literature around this practice. There is a mounting concern among the authors on how the practice as it is today – an alternative or complementary course to access medical care, may be cause of systemic injustices more than solution (Snyder, 2016).

The theme of social stigma influencing campaigns performance emerges. In fact, it is thoroughly described what the outcomes are when campaigners represent more vulnerable and socially stigmatized groups, such as transgender people or women in case of abortion. The evidence suggest these campaigns are indeed systematically incapable or reaching their goals – roughly 25% of the target in a pool of transgender medical

crowdfunding cases (Barcelos, 2019), based simply on *perceived worthiness*, and medical crowdfunding could exacerbate the burden on these communities (Barcelos, 2020; Barcelos and Budge, 2019; Zenone and Snyder, 2020).

Technological and social gap could create an unfair market and fuel inequities as well (Kenworthy et al., 2020). If crowdfunding can truly reduce personal medical-related bankruptcy in non-publicly funded healthcare systems like the United States, the social stigma may be wider than it seems at a first glance and embrace all *digitally divided*, disadvantaged groups (Burtch and Chan, 2019). These people are affected not only by a medical condition, not only unable to access the more basic health care, but also are affected by systematic disparities in the usage of crowdfunding and its outcomes. In this regards, Kenworthy et al. (2020) demonstrated the ultimate performance is only marginally influenced by those attributes under campaigners' control (e.g. narrative or complementary).

Crowdfunding healthcare is surely a very promising practice, with the potential of disrupting the way we access medical care, yet there are light and shades and, as emerging from this last analysis, many authors argue systematic application of these methods, if not properly controlled and regulated, may widen the existing gaps and paradoxically mask pitfalls and shortages of the economic and healthcare systems (Snyder et al., 2017a, 2017b). However, it is important to consider though that current evidence refers specifically to donation-based (mostly single-case) applications or crowdfunding in general, once again there is a huge gap on those areas specifically within the domain of FinTech, namely healthcare equity (or lending) crowdfunding.

6. Conclusions and implications for future research

Over the past decades equity investments in healthcare (across all sub-sectors, from global pharmaceuticals to nursing homes in the United States) have been dramatically increasing, where, however, this vast appetite is no guarantee of better outcomes for public health and investors' wealth. In fact, while economic and healthcare systems still struggle with accessibility to and affordability of medical care, the industry returns on investments has been shrinking over time. Social responsibility, sustainable growth, fair access to medicines, cost of medical care are still at the burning core of the worldwide healthcare agenda, and we believe focusing its solution on changing the approach to pricing and late stage business models as the sole lever to crack the code of healthcare funding will fail the expectations. These tweaks alone will not be sufficient, at least without a profound disruption of the way the industry is currently funded and engages with its stakeholders, acting early on the many signals coming from the real world evidence.

The results of this paper show that there is evidence of real world applications of crowdfunding in relation to the healthcare context. Patients and caregivers rely on web platform-based campaigns all over the world to fund their medical expenses but the review of the literature suggests that it is more on a spot-base, mainly on single-cases, and following a donation-based scheme or, at most, a reward-based scheme, regardless of the healthcare system archetype (public, private insurance-based, or hybrid). While equity crowdfunding is disrupting the way many ventures – small to medium start-ups in particular, seek for capitals in the market, proving itself a powerful instrument of risk distribution and reward socialization, no relevant and consistent data are available around the practice of equity crowdfunding in healthcare, with the exception of some anecdotal cases where platforms and funds from the crowd have been used as a medium for seeding and angel investing in early biotech start-ups.

The mass of single-case, donation-based campaigns is living proof of how the art of pricing is not enough to ensure fair access to treatment, while posing constraints which may threaten life sciences investments and, ultimately, healthcare evolution and global health. We ask ourselves and the scientific community if changing the standard funding models in the healthcare sector, importing modes typical of equity crowdfunding, broadening the base of investors and socialize risk and reward sharing, could be enough to solve the puzzle and guarantee stable returns for investors while improving accessibility and affordability of medical care, or at least trigger a new pathway to financial sustainability.

Based on our preliminary findings, we identified two major hypotheses: i) healthcare equity crowdfunding is still at a very early stage, hence it will naturally and gradually expand from small, sporadic start-up applications to capital-heavy industries, including healthcare in general and pharmaceuticals in particular; ii) healthcare ventures are simply too heavy in capitals to be fruitful and sustainable application of smaller scale intuitions. In the latter case, we suggest research to develop in other industries, like real estate, similar in regards of capital heaviness, but where equity crowdfunding is already soaring high (Montgomery et al., 2018).

To answer the question, we urge to critically assess current healthcare funding archetypes, research and development processes, go-to-market models, and test our assumptions through systematic retro engineering and testing of equity crowdfunding best practices. Some authors see this surge as the failure of economic and healthcare systems, especially publicly funded ones, we firmly believe this may be the first step towards a different way – a new ecosystem where stakeholders, from private and public investors to patients and society, play a different role for the sustainability of healthcare and the good of all.

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