

Research Article



Pharmaceutical Companies' Use of Commercial Adherence Programs

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ABSTRACT

Nonadherence to medications increases healthcare costs and decreases revenue for pharmaceutical companies. To prevent such losses, pharmaceutical companies may use commercial means to improve patient adherence. The market has developed hardware and software solutions to improve medication adherence and patient outcomes. The purpose of the review is to elucidate the pharmaceutical industries' involvement with the top 25 medication adherence programs. Data were gathered from 2015 to 2018. Commercial adherence programs were categorized, based on their primary mechanism of increasing adherence, into forgetfulness/behavior modification, care coordination/medication fulfillment, and cost reduction and were ranked according to their Crunchbase rank. Pharmaceutical companies' involvement with the top 25 adherence programs was identified and counted. **s:** We identified 6 commercial adherence programs that were used by 13 pharmaceutical companies. The most common type of adherence program that was used by a pharmaceutical company was forgetfulness/behavior modification; one company used care coordination/medication fulfillment. No adherence program involved with a pharmaceutical company addressed medication costs to improve adherence. Pharmaceutical companies are using commercial adherence programs to improve patient compliance. Given the importance of adherence to patients' outcomes and to pharmaceutical sales, we expect to see greater focus on promoting adherence in the future.

Keywords: Adherence, Medications, Pharmaceutical companies, Involvement.

INTRODUCTION

Nonadherence can lead to medical complications and increased healthcare costs. Approximately 50% of patients fail to use their prescribed medication.¹ The United States spends 17.6% of its GDP on healthcare. In 2016, healthcare spending was estimated at US\$3.3 trillion of which US\$329 billion was spent on prescription drugs.² Rising medication costs and out-of-pocket expenses increase the risk of nonadherence. In 2017, the healthcare system lost US\$100 to 290 billion whereas pharmaceutical companies lost \$637 billion in potential revenue secondary to nonadherence.³

To address this issue, many approaches are being developed to improve patient adherence. For example, increasing the frequency of office visits improves patient adherence.⁴ Although a majority of solutions to improve adherence are healthcare provider-oriented, pharmaceutical companies may also play a role in improving patient adherence.

Many technology companies are pursuing digital applications as potential low cost, scalable interventions to circumvent the adherence problem.³ Adherence innovations including digital application development, smart pill bottles, cloud-based platforms, robotic coaches, and on-demand prescription delivery have been tested. How pharmaceutical companies are using commercial services to increase patient adherence is not well

characterized. The purpose of this review was to elucidate pharmaceutical companies' involvement with the top 25 medication adherence programs.

METHODS

Data were obtained from Crunchbase, Bloomberg, Ventureradar, PDF files, and news sources. Data from websites and journals were considered relevant between 2015 to July, 2018. Adherence programs were ranked according to their CrunchBase rank (CB rank) in July, 2018. CrunchBase is a website that lists over 100,000 company profiles and industrial applications. The website assigns the company or program a CB rank, devised by an algorithm that takes into account the popularity of a profile by measuring the number of connections and contacts, community engagement, funding, news articles, and acquisitions.

Fifty adherence programs from the website "mobihealth" were sorted from lowest popularity to highest popularity. The top 25 programs were searched on Crunchbase, Google, and Bloomberg databases to collect information on date founded, status, lead investors, total funding amount, headquarters, key executives, and company acquisitions, or partnerships. Once all the information was collected, programs were categorized based on the approach to improve adherence: forgetfulness/behavior modification, care coordination/medication fulfillment, and cost reduction. Adherence programs categorized into the forgetfulness/behavior modification group specifically



bridge barriers for nonadherence through behavioral concepts. Adherence programs in the care coordination/medication fulfillment category reduce unfilled prescriptions by informing patients and healthcare providers. Adherence programs in the cost category improve patient access to medications by offering coupons, rebates, and discounts.

Research on pharmaceutical companies were conducted through Google, Venture Radar, Bloomberg, and PDF files. Companies associated with collaborations, partnerships, or acquisitions with adherence programs, company overview, headquarters, annual revenue, program involvement, noteworthy people, and relevant news were recorded and analyzed. Pharmaceutical companies were included if they collaborated with, partnered with, acquired, or invested in adherence programs.

RESULTS

Of the top 25 adherence programs, we identified 6 that were engaged with 13 pharmaceutical companies (Table 1 and Table 2). The 6 adherence programs included mySugr, Gecko Health Innovations, Propeller Health, Medisafe, Proteus Digital Health, and Health Prize Technologies (Table 2). The 13 pharmaceutical companies involved with the adherence programs included Roche, Aptar Pharma, Teva Pharma, Merck, GlaxoSmithKline, Boehringer Ingelheim, Novartis, Otsuka, Harbin Gloria, Novo Nordisk, Mylan, Galderma, and Daiichi Sankyo (Table 2).

Of the 13 pharmaceutical companies reviewed, 12 used forgetfulness and behavioral modification through 5 different adherence programs. One company, Roche, acquired mySugr an adherence program using care coordination and medication fulfillment intervention (Table 2). None of the adherence programs used cost reduction as an adherence modification strategy.

DISCUSSION

We reviewed pharmaceutical involvement with the top 25 medical adherence programs between 2015 to 2018. All 13 pharmaceutical companies either collaborated with, partnered with, acquired, or invested in adherence programs, particularly those focused on forgetfulness and behavior modification. Nonadherence to medications results in a significant loss in revenue to big pharmaceutical companies. The increased interest in adherence companies suggests pharmaceutical companies recognize the importance of adherence as one way to improve revenue.

Forgetfulness and behavioral modification is the primary focus to address nonadherence by pharmaceutical companies. Forgetfulness is a common cause of unintentional nonadherence. Games, apps, analytics, and reminder devices can help patients remember complex treatment regimens. Despite advances in sensor technology and reminder devices, such intervention strategies have limited supporting evidence.⁶ In a randomized control trial looking at the effects of

medication reminder devices, subjects were randomly selected to receive 1 of 3 medication reminder devices (a pill bottle with toggles, digital timer lap, or standard pill box) whereas the control group did not receive a reminder device. Findings revealed no difference in adherence between those without reminder devices and those who received a standard pill box [OR, 1.03; 95% CI (0.95-1.13)].⁷

Despite the lack of evidence, forgetfulness modification is attracting pharmaceutical company investment. Propeller Health, a medical adherence company in the forgetfulness/behavior modification category, received \$US20M in funding led by a \$US10M investment from Aptar Pharmaceuticals in May, 2018 to make digital applications.⁸ Aptar Pharma, Boehringer Ingelheim, Novartis, and GlaxoSmithKline have collaborated with Propeller Health to improve adherence. Another medical adherence company, Medisafe, has partnered with Boehringer Ingelheim and Merck to advance Medisafe's digital applications.⁹ Patients can now monitor their blood pressure and glucose levels while receiving instant feedback on their health status.¹⁰ Gecko Health Innovations, Proteus Digital Health, and Health Prize Technologies are three other pharmaceutical companies in the category invested in medical adherence companies (Table 2).

Care coordination and medication fulfillment is the second largest focus for pharmaceutical companies interested in adherence. Digital Pharmacy, mySugr, TinyRx, Seamless MD, RxAnte, and C3 Healthcare Rx are all companies who have integrated a mail-order pharmaceutical system for on-demand delivery of prescription drugs. mySugr, a medication adherence company, was acquired in 2017 by Roche. mySugr helps coordinate care for people with diabetes as they offer digital health services allowing users to update blood glucose levels automatically. The platform will become an integral part of Roche's new patient-centered health services.¹¹

Cost reduction is the third largest category of focus for addressing adherence. Blink Health, Clinical Ink, and RxSavings Solution work with pharmacy benefit managers and electronic medical records to transfer rebates intended for payers and consumers to make healthcare products more affordable.⁵ Although no relevant sources contained pharmaceutical involvement, finding ways to reduce cost or add cost reduction incentives is a marketable strategy to improve profit margins in prescription drug sales.¹²

We did not identify any pharmaceutical companies using commercial adherence programs based on drug cost reduction to improve adherence. Although behavioral issues account for 69% of nonadherence, reducing prescription drug cost may affect patient behavior towards adherence.¹² According to a Consumers Reports survey, subjects taking at least one prescription drug felt the need to budget their income for prescription



medication by reducing household expenses. Despite efforts to save money, a large number of subjects deferred doctor visits, delayed medical procedures, or failed to fill their prescriptions.¹³ Pharmaceutical companies' own programs to reduce patients' drug copayments may already, to some extent, fill this gap. We reviewed how pharmaceutical companies are using

adherence programs. However, the review does not evaluate the effectiveness of such programs. It also doesn't address pharmaceutical companies internal research and development to address adherence. Further investigation needs to focus on interventions that have the most promise applicable to pharmaceutical based adherence programs.

Table 1: Brief description of the top 25 adherence programs

Rank	Program	Funding Amount (\$US)	Pharmaceutical Company	Focus/Technology	Category	Pharmaceutical, Biotechnology, and Other Companies Involvement
1	Digital Pharmacist	\$12.3M	N	Uses <i>Pharmacist Saas Platform</i> to help patients connect w/doctors and pharmacists	CCMF	Active Ventures(O)
2	mySugr	\$6.6M	Acquired by Roche	Uses a digital health platform, using the mySugr App to help people manage diabetes	CCMF	Roche (P)
3	Gecko Health Innovations	\$2.1M	Acquired by Teva Pharma	Uses games and social tools to engage patients w/ poor adherence	FBM	Teva Pharma (P)
4	Propeller Health	\$69.9M	Aptar Pharma	Uses sensor, apps, analytics to improve patient outcome	FBM	Aptar Pharma (P)
5	Blink Health	\$165M	N	Negotiates drug prices with Pharmacies	Cost	Express Scripts (O)
6	Capsule	\$20M	N	Prescription Delivery via text messages	FBM	Thrive Capital (O)
7	Medisafe	\$21.5M	Boehringer Ingelheim	Cloud Platform for medication management	FBM	Boehringer Ingelheim (P)
8	Proteus Digital Health	\$422.3M	Novartis, Otsuka, Harbin Gloria	Uses Smart Pill that communicates to doctors when swallowed by a patient	FBM	Novartis (P), Otsuka (P), Harbin Gloria (P)
9	Amino	\$45M	N	Uses data and design to pair patient w/ best doctor	FBM	Highland Capital Management (O)
10	Cohero Health	\$15.3M	N	Uses sensor technology platform to help patient connect w/ doctors	FBM	Three Leaf Ventures (O)
11	Mango Health	\$8.3M	N	Uses digital platform (<i>Google Fit</i>) to find patient w/ best treatment	FBM	Kleiner Perkins Caufield & Byers (O)
12	Catalia Health	\$7.8M	N	Uses a robotic coach to educate patients	FBM	Ion Pacific (O)
13	Clinical Ink	\$29.7M	N	Uses <i>eSource</i> to eliminate paper-based data cutting costs	Cost	RTI International (O)
14	Health Prize Technologies	\$11.4M	Novo Nordisk, Mylan, Galderma, Diiachi Sankyo	Uses <i>RespiPoint</i> a digital support platform for patients	FBM	Novo Nordisk (P), Mylan, Galderma (P), and Diiachi Sankyo (P)
15	Zip Drug	\$2.6M	N	Delivers on-demand prescription medication for home delivery	FBM	Lux Capital (O)
16	Adhere Tech	\$3.8M	N	Uses smart pill bottles	FBM	Pear Therapeutics (B)
17	RxSavings Solution	\$21.1M	N	Uses web-bssed software to make epi-pens more affordable	Cost	McCarthy Capital (O)
18	Emocha Mobile Health	\$1.7M	N	Uses mobile health platform to strengthen patient-provider relationship	FBM	BioHealth Innovation (B)
19	TinyRx	U	N	Uses prescription delivery service	CCMF	U
20	Seamless MD	\$1.1M	N	Uses cloud-based platform to educate patients through surgery	CCMF	Next Canada (O)
21	RxAnte	\$4.6M	N	Negotiates with healthcare organizations to deliver the right intervention for the patient	CCMF	Aberare Ventures (O)
22	Towerview Health	\$200K	N	Uses digital pill box that alert doctor when patients forget	FBM	Ben Franklin Tech (O)
23	Medminder	\$2.4M	N	Uses smart pill boxes to improve adherence for patients	FBM	Trinnovate Ventures (O)
24	C3 HealthcareRx	\$2M	N	Focus on long-term medication management	CCMF	U
25	Healthera	U	N	Uses technology to set smart medicine reminders on patients phones and book clinical consultations	FBM	FT Capital (O)

FBM-Forgetfulness/Behavior Modification; CCMF-Care Coordination/Medication Fulfillment; P-Pharmaceutical Company; B-Biotechnology Company; O-Other Company; U-Unknown; N-No Company



Table 2: Category of each pharmaceutical company involvement from news sources from January, 2015 to July, 2018

Adherence Program	Category	Pharmaceutical Company	Involvement (news sources)
mySugr	CCMF	Roche	Roche acquired mySugr for \$100M. ¹⁴
Gecko Health Innovations	FBM	Teva Pharma	Teva Pharma acquired Gecko Health Innovations on Sep 25, 2015. ¹⁵
Propeller Health	FBM	Aptar Pharma, Boehringer Ingelheim, Novartis, GlaxoSmithKline	Aptar Pharma invested 10M in funding. The partnership will build, commercialize, and distribute digital therapeutics. ⁸ Boehringer Ingelheim, Novartis, and GlaxoSmithKline all collaborated with Propeller Health to improve adherence.
Medisafe	FBM	Boehringer Ingelheim, Merck	Medisafe partnered with Boehringer Ingelheim on Jun 19, 2018. The partnership will advance medisafe application platform to manage medication. ¹⁶ Merck partnered with Medisafe to improve adherence.
Proteus Digital Health	FBM	Novartis, Otsuka, Harbin Gloria	Novartis: CFO, Uneek Mehra has joined the company as CFO of Novartis to guide them with his former expertise in global finance. He will help Proteus Digital Health advance commercial footprint. ¹⁴ Otsuka: Otsuka and Proteus Digital health have FDA-approval for digital medicine on Nov 15, 2017. Otsuka is collaborating with Proteus in digital health. ¹⁷ Harbin Gloria: Harbin Gloria invests \$40M in Proteus Digital on Mar 1, 2016. ¹⁸
Health Prize Technologies	FBM	Novo Nordisk, Mylan, Galderma, and Daiichi Sankyo	All pharmaceutical companies collaborated with HealthPrize to improve adherence. HealthPrize improved adherence by 50%. ¹⁹

FBM-Forgetfulness/Behavior Modification; CCMF-Care Coordination/Medication Fulfillment

Conflict of interest:

Dr. Steven Feldman is a speaker for Janssen and Taro. He is a consultant and speaker for Galderma, Stiefel/GlaxoSmithKline, Abbott Labs, Leo Pharma Inc. Dr. Feldman has received grants from Galderma, Janssen, Abbott Labs, Amgen, Stiefel/GlaxoSmithKline, Celgene and Anacor. He is a consultant for Amgen, Baxter, Caremark, Gerson Lehrman Group, Guidepoint Global, Hanall Pharmaceutical Co Ltd, Kikaku, Lilly, Merck & Co Inc, Merz Pharmaceuticals, Mylan, Novartis Pharmaceuticals, Pfizer Inc, Quriient, Suncare Research and Xenoport. He is on an advisory board for Pfizer Inc. Dr. Feldman is the founder and holds stock in Causa Research and holds stock and is majority owner in Medical Quality Enhancement Corporation. He receives Royalties from UpToDate and Xlibris.

Dr. Adrian Pona and Lucas May have no conflicts to disclose.

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