LOW-COST CONNECTIVITY IN PHARMACEUTICAL AND DRUG **DELIVERY**

Successfully Navigating Cost Barriers to Deliver Low Cost Connectivity

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Phillips Medisize

a molex company

Abstract

Nearly half of all adults currently manage one or more chronic health conditions, for which there is no cure, but the condition is managed through daily medication and/or treatment. However, in situations where the patient is unable to successfully adhere to a medication regimen, unexpected costs of Emergency Room (ER) visits and hospitalizations may be tens of thousands of dollars per year, per patient. Focusing only on those patients with a diabetes diagnosis, unmanaged hypoglycemic events cost over US$5 billion per year. Connected medical devices, which allow tracking of medication and communication between patient and physician are an important and emerging technology to minimize the costs of unmanaged health conditions. While patient acceptance of connected devices is improving, high costs associated with converting a traditional medical device to a connected medical device have remained a barrier to adoption of this technology.

Current research demonstrates that design and selection of connected health device components is a major driver in incremental costs associated with connectivity, but that it is possible to drive these costs down through selection of components that deliver value to the patient at low unit cost. Partnering with Contract Design and Manufacturing Organizations (CDMOs) with an integrated model of cross-functional development and manufacturing helps the pharmaceutical industry in attaining low-cost connectivity in pharmaceutical and medical devices with as little as $0.75 per unit additional cost, making connectivity an economically viable pathway for the pharmaceutical industry, patients, and healthcare payers. In delivering low-cost connectivity to the pharmaceutical industry, it will be possible to (i) help patients and payers save significantly through better management of chronic health conditions (ii) allow pharmaceutical companies to ensure patients take all medication as prescribed (iii) assist physicians in improving patient healthcare outcomes and quality of life.

Introduction

Long-term conditions, or chronic diseases, are conditions for which there is currently no cure, and which symptoms are managed through daily medication or treatment. It is estimated that approximately 6 in 10 US adults have one chronic disease, and that 4 in 10 US adults have two or more chronic diseases.[1] Based on NHS, approximately 15 Million adults in the UK currently manage one or more chronic conditions.[2] Examples of common long-term conditions include: diabetes, certain mental health conditions (e.g. depression, PTSD), respiratory illness (e.g. COPD, asthma), cardiovascular disease, osteoporosis, HIV/AIDS, Alzheimer's.

Adherence to a medication regimen is critical to managing the symptoms and effects of these chronic conditions. When patients do not take medication as prescribed, it can lead to Emergency Room visits, hospitalizations, and adverse health outcomes. The financial cost of non-adherence to a medication regimen is variable and can cost as much as US$43,000 in per patient costs for unexpected treatment stemming from a patient failing to take medication (c.f. Figure 1).[3]

Diabetes is one of the most common chronic medical conditions in both the US and UK. It is estimated that 34.2 million Americans currently have diabetes[4], and 88 million have pre-diabetes.[5] Within the UK, approximately 3.9 million people, or 1 in 16 of the population, have diabetes.[6] Patients living with diabetes can experience both hyperglycemic and hypoglycemic events, though it is hypoglycemic events that are more prevalent when patients do not take medication as prescribed. Per patient, it is estimated that each hypoglycemic event caused by medication non-adherence is in excess of US$30,000 (c.f. Figure 2), with the cost only increasing over time.[7] Each year, total costs for non-adherence for just this condition alone, is over US$5 billion.

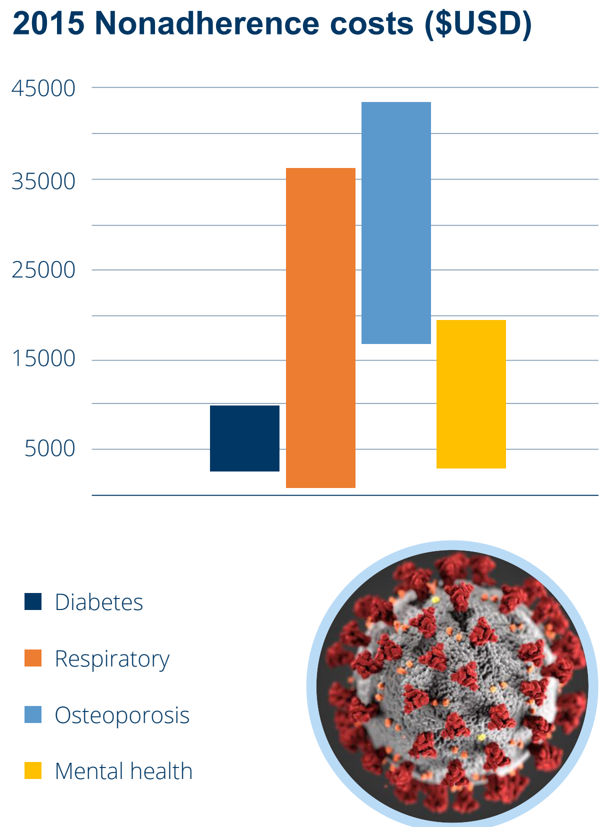

Figure 1: Non-adherence costs of select chronic healthcare conditions.

[1] "Chronic Diseases in America", www.cdc.gov/chronicdisease/resources/infographic/chronic-diseases.htm, accessed Jun 9, 2020.
[2] Department of Health, 2012. Report. "Long Term Conditions Compendium of Information: 3rd edition."
[3] Cutler, et al. BMJ Open. 2018. 8(1), e016982.
[4] Statistics About Diabetes, www.diabetes.org/resources/statistics/statistics-about-diabetes#:~:text=Prevalence%3A%20In%202018%2C%2034.2%20million,of%20the%20population%2C%20had%20diabetes.&text=Undiagnosed%3A%20Of%20the%2034.2%20million,and%207.3%20million%20were%20undiagnosed, accessed June 8, 2020.
[5] National Diabetes Statistics Report, 2020. www.cdc.gov/diabetes/library/features/diabetes-stat-report.html, accessed June 8, 2020.
[6] Diabetes: Facts and Stats. mrc.ukri.org/documents/pdf/diabetes-uk-facts-and-stats-june-2015/, accessed June 8, 2020.
[7] Lipska, et al. JAMA Intern Med. 2014. 174(7), 1116-1124.

Clearly, a means of assisting patients in better managing medication for chronic conditions is critical to not only improving patient health, but to ensuring they don't miss doses of their medications, and saving both patients and healthcare payers significant money by preventing non-adherence ER visits and hospitalizations. In the era of COVID-19, the importance of remotely monitoring patient health through telehealth is only increasing; since March 2020, in-person medical appointments have decreased by 60%, whereas telehealth appointments have increased by 14%.[8] It is likely that connected healthcare devices will not only improve the quality of the increased 14% in existing telehealth appointments, but may serve to bridge the gap of the current ~46% of patient appointments that are not being served by either in-person nor telehealth.

Adults are increasingly turning to smart, or connected, devices to help manage their daily routines. It is estimated that half of all homes will be connected by 2022.[9] These devices are often controlled through smartphone apps, connected devices manage everything from grocery lists, to light bulbs, to summer reading, to thermostats. When users forget to change a furnace filter, their thermostat sends a reminder.

With increased familiarity of connected devices in their daily lives, adults managing chronic conditions are expected to turn to this same technology to assist in managing and improving their health.

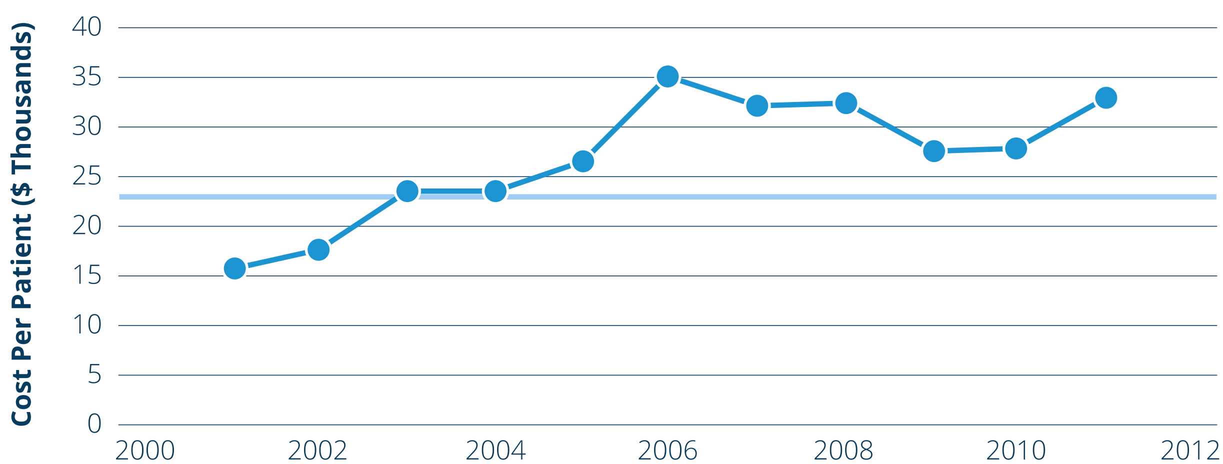

Figure 2: Cost per patient of hypoglycemic events for unmanaged diabetes.

[8] www.medscape.com/viewarticle/929396, accessed June 21, 2020.
[9] P. Austin. "What Will Smart Homes Look Like 10 Years From Now?", Time. July, 2019.

The Promise of Connected Health Devices

As detailed in Figure 3, there are many benefits to incorporating connectivity into medical devices, which not only the patient, but physicians and payers alike will gain. Medical devices, for example smart autoinjectors, that have connectivity to a healthcare provider and system are expected to provide a means to improve patient adherence to medication regiments and treatment plans. By providing a means of connecting these devices to the physician, patients may receive dosing reminders, interact with adherence trackers, and be provided education regarding their chronic condition and the medications they are taking for management. With connected medical devices, physicians may have better ability to monitor patient condition or disease and make earlier treatment decisions to improve patient outcomes. Healthcare payers, in turn, may have reduced uncertainty in treatment cost and may save tens of thousands of dollars per patient in unexpected hospitalizations.[10]

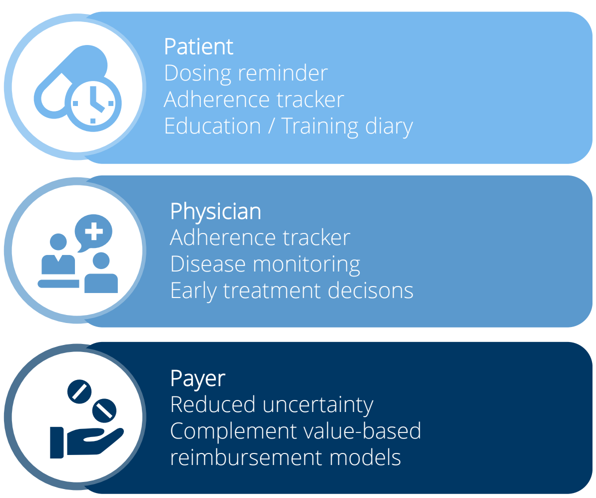

Figure 3: Benefits of connected capability in medical devices.

To achieve connectivity in these medical devices, additional device components are required to enable the device to send the dosage time of a medication, and amount of the dose, to a companion smartphone app and then onto a cloud database, or directly to a cloud database for those users without smartphone capability. Three device components are critical to connected medical device design: one or more sensor to measure dose activation and amount, a Bluetooth low energy radio, and a battery.

Because of the added device components and successive complexity, connected medical devices may be best leveraged in high-volume applications, including: pre-filled insulin pens, albuterol metered-dose inhalers, COPD dry powder inhalers, high-volume autoinjectors. Additionally, pharmaceutical companies developing connected health platforms will require manufacturing capabilities that not only rely on knowledge of medical device, but will also have in-depth knowledge of the interplay of medical device manufacturing with electronics, software, mechanics, and human-factors design.

[10] Bittner, et al. Medical Devices: Evidence and Research. 2019, 12, 101-127.

Current Challenges

Despite the many benefits of device connectivity, some barriers to adoption of this remain, here described in Figure 4.[11] With the integration of connected devices in the home, patient-driven barriers (i.e. motivation to use, privacy and connectivity concerns) are diminishing. With it, physician confidence in reliability of data is increasing. However, reimbursement and data on economic benefit remain as barriers to adoption of connectivity of medical devices.

Currently, it is estimated that configuring a device to achieve connectivity results in an increase of US$3-5 per unit. For a high-volume device (e.g. 100 million units per year), such as a pre-filled insulin pen, this represents a more than ten-fold increase in manufacturing cost. Such a cost increase challenges the economic benefits of a connected medical device.

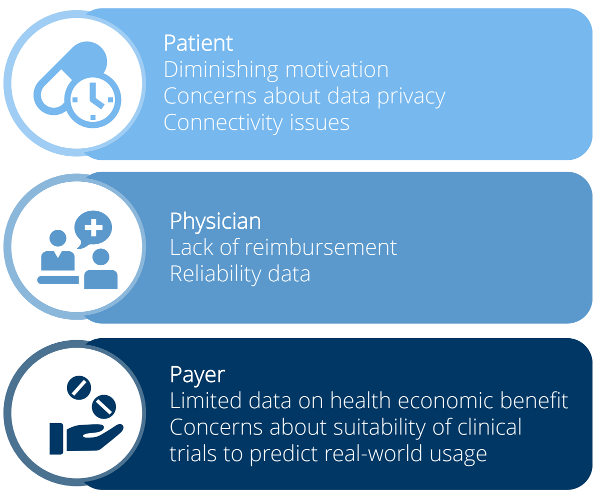

Figure 4: Current barriers to adoption of connected capability of medical devices.

[11] Bittner, et al. Medical Devices: Evidence and Research. 2019, 12, 101-127.

Solutions to Adopting Connected Health

Achieving low cost connectivity is currently the most pressing barrier to adoption of connected medical device technology. Two key drivers, selection of device components and partnering with an integrated Contract Design and Manufacturing Organization (CDMO), will allow the pharmaceutical industry to realize the goal of low-cost connectivity.

Many contract manufacturers lack expertise in one or more areas of electronics, software, mechanics (i.e. engineering), and/or human-factors design. By selecting a CDMO that has all capabilities (c.f. Figure 5) integrated into its service model, pharmaceutical customers can reduce cost of connectivity by reducing overhead and simplifying supply chain. Integrated CDMO teams rely on cross-functional project management to quickly bring projects to market, managing risk early, and creating a seamless connected device that leverages depth of expertise across the technology fields of electronics, software, mechanics, and human-factors design that are critical to success of the device as delivered to the patient.

While the above platform development competencies are all core needs for a successful connected device, Quality and Project Management Principles are also critical to connected device success, and CDMO's that incorporate these practices into the early stages of development are best positioned to quickly bring a robust connected device to market.

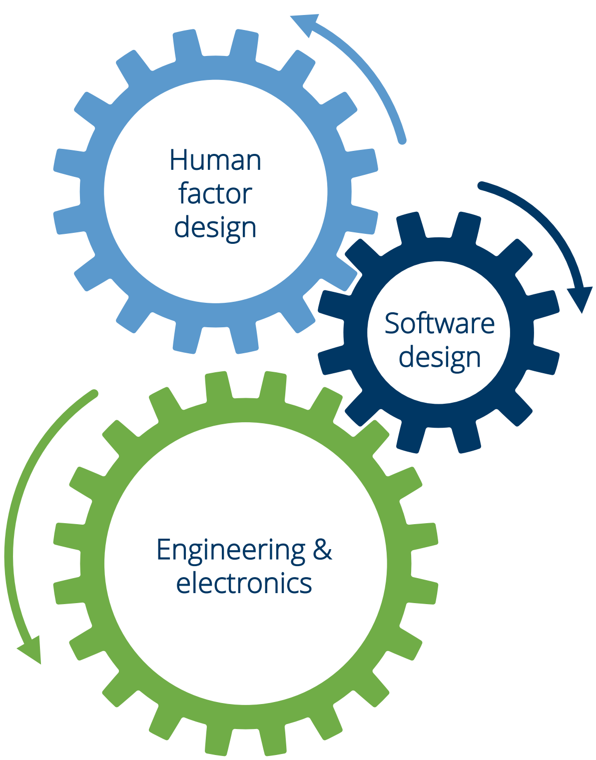

Figure 5: Integrated CDMO model for achieving low-cost connectivity of medical devices.

At Phillips-Medisize research has been conducted to select the connected device components that confer the greatest value to the customer. The Bluetooth low energy radio and sensor(s) to measure dose activation and amount have been selected to achieve an incremental product cost of US$1 per unit, a fraction of the cost of competitive connected device technologies. But design attention should first be placed on the battery selection.

Typical connected medical devices are classified as "occasional-use". Such devices are powered by a battery, but do not have an "on-off" switch. Rather, they operate in a "sleep" mode that is awoken by some type of activation function. Because of this, battery life for a connected medical device would need to be 2-3 years of latent storage life, while the device was warehoused or at the pharmacy. Once in the hands of the patient, there must be sufficient battery life for the device to be used intermittently for a 2-3-week window, to power all doses and communicate with a cloud storage system. If the battery lacks sufficient life, it must be changed, which adds device and user complexity, or the device must be discarded which adds to both cost and waste.

Phillips-Medisize conducted a study to evaluate two standard battery types for an insulin injector pen application. Both batteries were coin cells, approximately 11 mm in diameter, to achieve a small device profile that would be suitable for everyday use while maintaining device portability.

The battery life cycle was segmented into 3 phases: manufacturing and testing, warehouse and storage, and dose (c.f. Figure 6).

Warehouse storage represents an approximately 2 year window, wherein the complete connected device would be maintained at temperature and humidity per manufacturer, after battery manufacture and quality test was complete, but before the 2-3-week window where the finished connected device was in the hands of the patient. To account for usage variability, a goal was set to identify a battery that maintained a minimum of 20% charge at the end of Phase 3, corresponding to the end of life for the device.

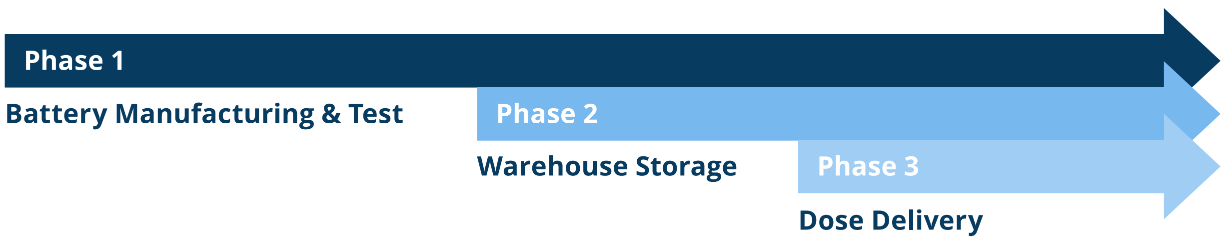

Figure 6: Phases of battery life for low-cost connectivity study.

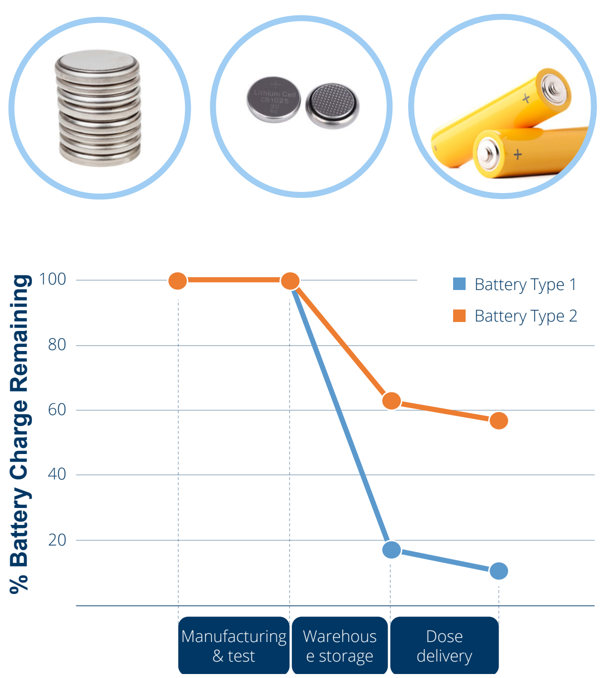

Figure 7: Battery-life study to achieve low-cost connectivity for medical devices.

As shown in Figure 7, Battery Type 2 was able to maintain greater than 60% charge at the beginning of Phase 3, and maintained greater than 50% battery life by the completion of the 2-3 week window it would be expected to be used by the patient. However, Battery Type 1 had less than 20% remaining battery at the end of the device's life.

The study showed that Battery 2 met the requirements and further allowed estimation of the per unit cost for a connected device that was developed with an integrated CDMO model, and relied on current research into low cost, and high customer value, designs.

One of the main component-based cost drivers for connected devices is Bluetooth processors. Bluetooth processors are the critical mechanism for linking the device to a mobile device or cloud storage, from which a physician can obtain patient data for improved healthcare management. A typical Bluetooth processor relies on a short-distance radio that is combined with a microprocessor into a single, integrated, chip, called a "system-on-a-chip" (c.f. Figure 8). Because of the ubiquity of IoT (i.e. "Internet of Things") devices, cost of the featured driver components has drastically decreased. Systems-on-a-chip may include a number of sub-components, including but not limited to: a power management unit, a Bluetooth protocol core, an RF transceiver, a cybersecurity engine, an ARM processor, memory, oscillators, timers, clocks, interrupts, and peripheral components. To ensure connected devices are low-cost, it is critical to select a Bluetooth component that has no additional memory or feature beyond what is necessary to maintain basic functions and features of the device.

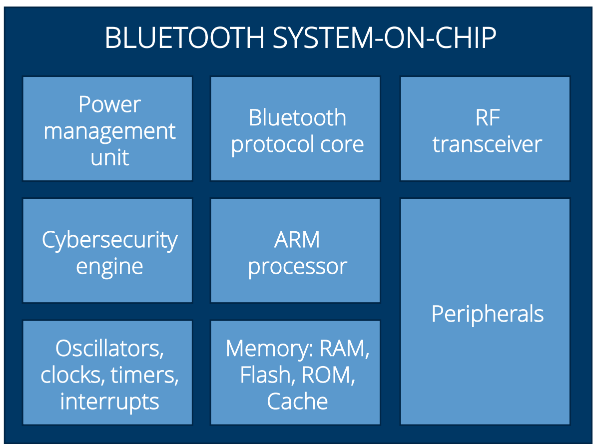

Figure 8: Block Diagram of Bluetooth Processor components.

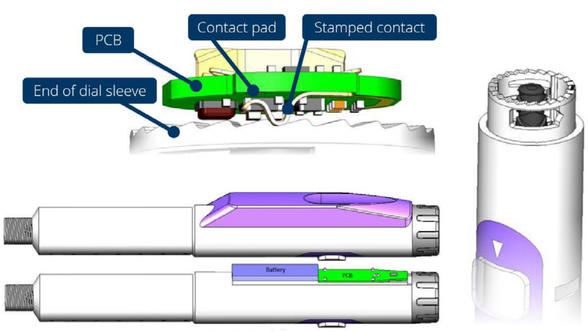

Figure 9: Example of low cost rotational sensor.

Sensors that detect the usage of connected devices are another costly component; based on the number and type of sensor, cost may dramatically increase beyond that of an unconnected device. These sensors may monitor rotational or longitudinal movements of the device, inspirational airflow, device agitation, drug temperature, or start- and end-of-dose detection. As an example of one means of developing low-cost solutions for a device with a rotational sensor, developers may evaluate capacitance sensors, mechanical switches, magnetic sensors, or optical sensors for inclusion in the final device design. Capacitance-, optical-, or magnetic-based sensors are sophisticated and significantly increase the cost of the final device design, but may not confer an economic benefit to the patient or physician. In contrast, mechanical switches manufactured from a simple stamped metal part offer a low-cost alternative that meet basic device functionality without requiring power consumption that would be needed for other sensor designs. An example of a rotational mechanical switch is shown in Figure 9, herein termed "stamped contact". The use of a stamped mechanical switch offers the added benefit of not only having a lower cost of goods for switch manufacturing but also preserves battery life (c.f. Figure 7).

Table 1 describes current, and forecast, price models, assuming a 10-100 million unit product volume per year.

	Range ($ per unit)
Conventional	3.00 – 5.00
Current Technology	1.20 – 1.45
Next Gen Tech	0.85 – 1.05
2nd Gen Tech	0.75 – 0.95

Table 1: Price models for low-cost connected devices.

The data in Table 1 show incremental cost, from a CDMO, of added cost of connectivity compared to a purely mechanical device. With future investment in emerging connected device components and technologies, it will be possible to not only achieve the desired US$1 per unit cost of connected capability, but exceed these targets by as much as 25% with second-generation technologies. In doing so, connectivity in medical devices will not only be cost effective, but will (i) help patients and payers save significantly through better management of chronic health conditions (ii) allow pharmaceutical companies to ensure patients take all medication as prescribed (iii) assist physicians in improving patient healthcare outcomes and quality of life.

Recommendations

By combining high-volume manufacturing with selection of low-cost componentry that still meets device requirements, it is possible to design and manufacture a connected device for an approximate US$0.80 per unit increase over existing device cost. Working with component manufacturers to identify further means of reducing cost of goods may further drive down cost of developing connected health devices which, in turn, may provide improved healthcare outcomes for patients and reduce cost of healthcare to payers.