Continuous Glucose Monitoring and U.S. Market Strategy

By

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ABSTRACT

There are about 25M (million) diabetics in the US alone, of which only 5-10% of the type 1 diabetics (1M) market has been penetrated with continuous glucose monitoring (CGM) devices. This thesis will provide an overview of the glucose monitoring, then focus on who the key market players for CGM are. Ensuing sections will explore product offerings, understanding what features patients care for and what critical limitations exist in design. It will also tackle why there hasn’t been a more widespread adoption of CGM systems considering the technology has been on the market for a decade now. It will dive into a variety of potential market drivers, such as, first mover’s advantage, pricing, product attributes and reimbursement coverage. It will emphasize the two US leaders, Medtronic and Dexcom and analyze the companies by comparing their revenue and underlying strategies. Finally the thesis will cover emerging technologies that could pose a market threat to incumbents.

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I dedicate this thesis to my parents, Shashi Humad and Dr. Sameer Humad, who dropped everything for me to be at MIT. Without my mother’s love, support and friendship I could not have immersed myself at MIT Sloan the way I did these last 2 years. And to my dad for being my biggest fan and encouraging me to always dream big.

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Lastly, to my daughter, Rhia, who has no idea yet, how she helped me become a stronger person.

Shweta
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1. Introduction

Diabetes is recognized by the World Health Organization and the International Diabetes Federation as a significant and growing health problem. In 2007, it was estimated that there were 246 million adults with diabetes throughout the world. By 2025, the number of adults with diabetes is expected to rise to 380 million and that's a conservative estimate. This continued increase in the prevalence of diabetes, combined with an expansion of insurance coverage as a consequence of healthcare reform, will cause the United States diabetes care device market to grow to nearly $16 billion by 2017.

There are many products that serve this space, such as a variety of oral and injectable medications, together with insulin pens, insulin pumps and blood glucose test strips. This thesis will only focus on continuous glucose monitoring (CGM) devices. Two companies, Dexcom and Medtronic currently dominate the dynamic CGM market, and have launched several iterations of their products, but new entrants are likely in the near future, given the available opportunities for advanced products.

The objective of the thesis is to address the strategy underlying the CGM US market. Why has Medtronic managed to capture majority market share? Is it a function of product attributes, pricing structure, advertising, patient behavior or the effect of reimbursement? Each of these factors will be studied based on historic trends for Medtronic and Dexcom to understand what has affected market diffusion. Medtronic for example was the first to enter the CGM market in the US. Their monopoly status definitely helped them in their leading market position, but is CGM considered a luxury good? In which case patients maybe resistant to trying other CGM product offerings unless it is significantly better? Dexcom is the only other company with FDA approval for their CGM product in the US since 2006. Their growth numbers were 40% higher in 2012 compared to 2011. Did they offer better product attributes or was advertising and or/ warranty a key promoter in helping them squeeze into the market?

The CGM systems market is segmented into the market for transmitters-receivers, glucose sensors and insulin pumps. Medtronic first entered the market not with CGM but with an insulin pump in 1999. Did bringing diabetic patients onboard with insulin treatment make it easier to tap into the monitoring market? How did the reimbursement landscape affect their strategy? Dexcom has followed development of a similar CGM integrated insulin pump in partnership with Johnson & Johnson (J&J), receiving CE mark (for medical products sold in Europe) approval in 2011. They are still awaiting FDA approval. Given Dexcom has better accuracy should Medtronic anticipate a strong threat? Other potential entrants may also be companies that manufacture and sell insulin, such as Sanofi and Novo Nordisk and Eli Lilly.

Given the rising diabetic population, patients can also play an integral role in driving market share. The existence of online patient communities by way of blogs and forums creates constructive feedback loops. This form of word of mouth advertising can be very powerful in patients taking ownership of product selection with their doctor. At this point it is also beneficial to understand how doctors decide to prescribe one product over the other. Given that the reimbursements have to be standard across the board, since they align with CPT (Common Procedural Terminology) codes, are doctors making device recommendations based on patient age, disease state and lifestyle?

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2 Millennium Research Group
2. Overview of glucose monitoring

People with diabetes have an increased risk of developing a number of serious health problems. Consistently high blood glucose levels can lead to serious diseases affecting the heart and blood vessels, eyes, kidneys and nerves. In almost all high-income countries, diabetes is a leading cause of cardiovascular disease, blindness, kidney failure, and lower limb amputation. But with the correct treatment and recommended lifestyle changes, many people with diabetes are able to prevent or delay the onset of complications. Therefore people with diabetes need regular monitoring.

2.1 Self-monitoring blood glucose monitoring (SMBG)

The first blood glucose meter came to market in doctors’ offices in 1965. Within a minute of placing a drop of blood on a paper strip, a color reading was produced. The doctor compared this color to a blood glucose reading chart. The first digital readout came in 1970 with home meters being produced starting in 1975. From 1975 until 2005, the device grew to be more accurate and smaller over time. Traditional SMBG devices, including meters, strips and lancing devices currently account for 70% of the diabetes devices market. These products are widely reimbursed. They are becoming commoditized products, which has led to strong price competition and the entry of low-cost competitors.

2.2 Continuous glucose monitoring (CGM)

CGM has evolved since 1999 from reviewing blood profiles retroactively to real-time monitoring. Currently CGM devices utilize constant feedback of analytical information from a glucose sensor to activate an insulin delivery pump, thereby ultimately realizing the concept of an artificial pancreas. Depending on whether the CGM device penetrates the skin, these devices can be categorized as totally invasive, minimally invasive, and noninvasive.

Continuous glucose monitoring (CGM) systems use a tiny sensor inserted under the skin (usually on the abdomen) to check glucose levels in interstitial tissue fluid. The sensor stays in place for several days to a week and then must be replaced. A transmitter sends information about glucose levels via radio waves from the sensor to a pager like wireless monitor (Figure 1). Because currently approved CGM devices are not as accurate and reliable as standard blood glucose meters, users confirm glucose levels with a meter before making a change in treatment. The key advantage of CGM is that it can help identify trends and minimize fluctuations (hypo and hyperglycemia). These fluctuations may otherwise go unnoticed with standard HbA1c tests and intermittent finger stick measurements. For diabetic patients, less time spent in hypo and hyperglycemia is correlated with less risk of short and long term diabetes related complications. But adoption may have been limited by factors like issues with cost and accuracy and a lower level of reimbursement than traditional glucose monitoring technologies, not to mention the discomfort of an implanted device.
CGM systems are more expensive than conventional glucose monitoring, but they may enable better glucose control. U.S. Food and Drug Administration (FDA) approved CGM devices are available by prescription only. Although useful for those with problems controlling their diabetes, there are issues with current CGMs that hinder adoption. Issues such as - inaccuracy, false alarms, a lack of user-friendliness, a high cost, a lack of reimbursement and the fact they have to be frequently calibrated with SMBG. As a result, CGM is the smallest area of the diabetes device market, accounting for only 3% of its total value.

These devices provide real-time measurements of glucose levels, with glucose levels displayed at 5-minute or 1-minute intervals. Users can set alarms to alert them when glucose levels are too low or too high. Special software is available to download data from the devices to a computer for tracking and analysis of patterns and trends, and the systems can display trend graphs on the monitor screen. The next section presents a comparison of existing CGM product offerings.

### 2.2.1 Key product offerings

As one tries to analyze the various CGM offerings, in the US the 3 relevant players are: Medtronic, Dexcom and Abbott. Currently, Medtronic holds an estimated 85% to 90% of sales with its Guardian Real-Time CGM System. Dexcom’s Seven Plus has more than 10% of the market. In 2011 before Abbott’s FreeStyle Navigator discontinued their CGM systems in the US, they made up the rest of the market (Figure 2).

However in August 2011, Abbott Diabetes Care announced that it will permanently discontinue the FreeStyle Navigator CGM system in the US. This was due to a supply interruption affecting their ability to provide U.S. patients with new system kits or warranty replacement components. Therefore going forward the focus of the thesis will be primarily on Medtronic and Abbott.
The CGM patient kit comes with various components: receiver, software, carrying kit, cables, battery charger and sensors (or transmitters) that need to be replenished every few days. Some patients are prescribed an insulin pump as well. Medtronic is the only company in the US that has a pump integrated CGM system. Also to be noted is that it's the only company with the remote monitor. The remote monitor is a bed side tablet form factor that allows parents for example to watch over their sleeping diabetic children. Until Abbott suspended its offering it had the Freestyle Navigator and the accompanying Copilot personal therapy management software. Dexcom comes very close in offerings to Medtronic just lagging approval for their pump integrated CGM system – for which they have a joint development agreement with J&J’s Animas Corporation and separately with Tandem Diabetes. Animas filed an application for FDA approval for its Animas Vibe (insulin pump) device in April 2013, while the Dexcom G4 Platinum CGM system received their FDA approval in Oct, 2012.

Apart from CGM devices that are sold to patients, there is a professional version that is sold to physicians. Medtronic offers physicians a Professional CGM product called the iPro CGM and iPro2 Professional CGM. Physicians send patients home wearing the iPro recorder to capture glucose data, which is later uploaded in a physician's office to reveal glucose patterns and potential problems, including hyperglycemic and hypoglycemic episodes, which can lead to more informed treatment decisions.

The chart below depicts the most current offerings from each of the companies in the U.S.
Figure 3. Dexcom and Medtronic CGM product offering

Figure 3a. Medtronic (Guardian RT - top, Enlite - bottom) product images
2.2.2 Attribute comparison

It can be seen from the attribute comparison below (Figure 4) that although the Abbott product was pulled off the market it was the most accurate.

<table>
<thead>
<tr>
<th>CGM device</th>
<th>Accuracy (*MARD %)</th>
<th>Duration (days)</th>
<th>Calibration</th>
<th>Sensor Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Abbott Navigator</td>
<td>• 12.1</td>
<td>• 5</td>
<td>• 1, 2, 10, 24, 72 hr</td>
<td>• 6 mm</td>
</tr>
<tr>
<td>• Dexcom G4</td>
<td>• 13</td>
<td>• 7</td>
<td>• 2, every 12 hr</td>
<td>• 13 mm</td>
</tr>
<tr>
<td>• Dexcom Seven Plus</td>
<td>• 16</td>
<td>• 7</td>
<td>• 2, 8, every 12 hr</td>
<td>• 14 mm</td>
</tr>
<tr>
<td>• MDT Guardian</td>
<td>• 17.6</td>
<td>• 3</td>
<td></td>
<td>• 8.75 mm</td>
</tr>
<tr>
<td>• MDT Enlite</td>
<td>• 13.6</td>
<td>• 6</td>
<td></td>
<td>• 9 mm</td>
</tr>
</tbody>
</table>

Figure 4. CGM product attributes from leading suppliers (Accuracy values determined from recent study\(^4\))

*MARD is Mean Absolute Relative Difference = a standard of measure of accuracy for CGM devices. MARD is the average % difference between sensor glucose values (40 to 400mg/dL) and the patient reference values used for calibration. A lower MARD for a CGM device indicates closer accuracy to reference values.

Dexcom has a leg up on Medtronic with the longer sensor life. Patients tend to use it beyond the 7 day period and seem to get reasonable accuracy and adhesion between 12-14 days. On the downside, Dexcom sensors are more expensive than Medtronic sensors, but the difference is not much when you consider how long the sensors last. In terms of data analysis, the Dexcom receiver does not generate any statistics for the user. Downloading the receiver to a PC (no Mac compatibility) can be rather slow. But the major drawback to the Dexcom system is that the display is not yet integrated into an insulin pump. With so many CGM users also being pump users, this is a significant shortcoming.

The major advantage to the Medtronic offering is the sensor augmented pump, being an all-in-one concept, avoiding the need to carry a receiver for the CGM since everything displays right on the pump screen. When viewing trend graphs on-screen, the user has the option of scrolling back in time to view specific data points. Advanced statistics, such as average, standard deviation, and “area under the

curve" can be generated right on the pump/receiver. Data from Medtronic Real-Time downloads through the internet to a website called "Carelink" which produces some excellent graphs, charts and statistical analyses. The download requires a simple USB plug & play device that works on Macs as well as PCs. When using a sensor-augmented pump, the CGM data is combined with pump data to create more comprehensive reports. Medtronic’s new (US pending) Enlite sensors have a shorter and much thinner introducer needle, and insert at a 90-degree angle to the skin. There is also extra tape on the sensor to help keep the transmitter firmly attached. Using the new Enlite insertion device, the new sensors are considerably easier to insert and would rank equal to Dexcom’s in terms of comfort and insertability.

2.2.4 Limitations of current CGM product offerings
CGM is effective in specific patient groups with regard to HbA1c lowering. First, and most evidently, poorly controlled type 1 diabetic patients seem to benefit from CGM when they use it frequently enough. This result reveals the first problem, because especially children and adolescents are noncompliant with CGM use, and its value in this patient group is therefore limited to only the most motivated patients⁵.

Secondly currently available CGM is not as accurate as most blood glucose monitors. The CGMS tends to be less accurate when the blood sugar is low (<70mg/dL or 3.9 mmol/L) and therefore may not be able to reliably indicate when you are low. Thus, most experts do not recommend continuous glucose monitoring alone for information about your blood glucose levels. It is important to do several finger sticks daily to calibrate the CGMS device and to verify that the sensor readings are accurate. In addition, the costs associated with continuous glucose monitors are much greater than those of traditional glucose monitors. Not all CGM and supplies are covered by commercial health insurance companies for all diabetic patients.

Another limitation maybe patient motivation, no matter how promising CGM is, it requires the patient to highly involved in managing their own health. For example, when the sensor needs to be replaced, when a glucose reading spikes to 300, when a low blood-sugar alarm sounds – all demand a response from the patient. Even on “good days,” you still have to check that the apparatus is working, that you’re responding correctly to the numbers, and that your glycemic levels are all in check. For some people with diabetes, the technology is daunting, and the investment in time and energy unreasonable especially if your insurer doesn’t cover it. And even if you are willing to make that commitment, will your healthcare provider download, graph, and interpret thousands of numbers? And if you’re using a pump, will your doctor cross-reference your insulin delivery patterns with your blood glucose readings to adjust your basal rates and insulin-to-carb ratios?

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3. Market Overview

3.1 Addressable US diabetic population
The American Diabetes Association lists that as of 2013, 25.8M Americans have diabetes. Only 18.8M of these cases are diagnosed, of which 1M have type 1, the majority 17M have type 2 and the remaining have other rare types. CGM systems currently are only reimbursable for type1 and on a case by case basis for type2. It is estimated that CGM has penetrated only 5-10% of the type 1 diabetic population\(^6\). That implies that most of the market is still not addressed. In fact in the US, more 90% of all type 1 patients with commercial insurance have access to CGM if they meet health plan criteria. All the more reason to question why more type 1’s are not using CMG. Do type 1 patients just don’t want to deal with the hassle of a new device that comes with new usage learning? Is it too complicated? Or is it the pricing that is too high for the perceived value as compared to current SMBG, i.e. finger pricks? Finger pricks multiple times a day and insulin injections as and when needed are not pleasing either. The only plausible explanation is that SMBG has been around for ages and patients have gotten used to it. Above all in spite of the inconvenience it is cheaper, is reimbursed and very simple to use – there are not screens, trends, graphs, buttons, customized alerts or recharging to worry about.

3.2 Global diabetic market
Although this thesis is focused on the US market, it is beneficial to understand the US market with respect to the global market. The growth in the global market for diabetes products from 2010 to 2018 is illustrated by major geographic area below:

![Figure5. Global diabetes market by region, 2010 & 2018](image)

The U.S. is contributing the maximum in terms of the total revenue earned from CGMs. The European market is still in a nascent stage and contributes a small amount to the total revenue. The Asia-Pacific region and Brazil also contribute very little to the global revenues. The CGM systems markets in the U.S

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\(^6\) Closer Look Memorandum, Medtronic MiniMed 530G threshold suspend insulin pump, Enlite sensor secure FDA approval; launch in next several weeks - September 27, 2013”

\(^7\) MedMarket Diligence, LLC; Report #D510
and Europe are growing at a fast pace and estimated to reach to a three digit (in USD million) market size globally at a CAGR of double digits. The rapid increase in the number of diabetes patients is the major driving force for the estimated growth. The most important driver for the CGM market in Europe is the need for a convenient, affordable, and patient-friendly device that facilitates superior therapy management for diabetes and this need can be fulfilled by CGM devices. In the present scenario, the slow growth rate of the market in the Asian region is due to the late launch of CGM systems and a slow acceptance of these systems in low and middle income nations such as China and India due to the unaffordable price. In Japan and Australia, various regulatory approvals are a hindrance for the growth of the market.

In general the overall growth in the device market is due to the following factors:

- **Increasing diabetes prevalence**: with the numbers of diabetes patients rising significantly, there is increasing demand for all types of diabetes care devices globally. The Centers for Disease Control (CDC) estimates 1.5 million newly diagnosed diabetes patients in 2007 in the United States and a total U.S. diabetes population of 23.6 million. The growth of the diabetes population is driven, in turn, by the obesity epidemic in the United States, overall world population growth, and aging of the population in many developed countries (in which type 2 diabetes is more likely to occur).

- **Continued revenue streams**: all types of diabetes care devices require the use of disposable products. Lancets and test strips for SMBG; implanted sensors for CGM; pen needles for insulin pens; syringe for other manual injection products; infusion sets for durable insulin delivery pumps; and the disposable pump itself for patch pumps. Therefore, all diabetes devices manufacturers generate a continued revenue stream after the sale of the initial hardware.

- **New technology**: innovation is continuing in every sector of the diabetes device market. Advances in SMBG testing technology that make it easier and more convenient to perform testing. The use of smartphone applications (“apps”) has been shown to be a useful method for accurately logging and managing SMBG results. A study revealed that using SMBG data stored in and/or shared through a PDA (personal data assistant) along with consistent feedback from a health care provider (HCP), enhanced glycemic improvements and reduced hospitalizations. While CGMs that work with insulin pumps to realize artificial pancreas in concept are driving demand in both of these sectors. Another salient innovation in CGM is the prediction and earlier detection of hypo & hyperglycemic events. In addition, smaller pumps without tubing are becoming increasingly popular and there is strong demand for insulin pens that include functions to help users remember when they last took their insulin. These newer products can command a higher selling price and so demand for these products is leading to market growth.

Currently, the strongest growth in the diabetes care market is coming from the two smaller segments in terms of patient numbers: CGM and insulin pumps. Growth is coming from the fact that both markets are under-penetrated and there is increasing clinical evidence as to the product effectiveness in stabilizing blood glucose levels, particularly when they are used in combination.

### 3.3 Dexcom and Medtronic

Specifically for the US, it makes sense to understand market penetration for Medtronic and Dexcom. For both companies, their US sales are graphed for a 5 year period from 2009 to 2013 from respective annual reports, as seen below. The US CGM market is valued at roughly $250M. For Dexcom, the total

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product revenue was used because CGM is their primary product in the US. Along with the ambulatory CGM system for patients, they have acquired CE mark for an in-hospital glucose monitoring platform, called GlucoClear. But no information could be found for what percent of the total sales is contributed by GlucoClear, therefore it was assumed that a majority of the sales were from the CGM systems.

Medtronic on the other hand has multiple businesses and diabetes has roughly been 9% of the entire business. Their diabetes (MDT Diabetes in the chart below) business though covers insulin pumps, related consumables as well as CGM systems. Therefore revenue was identified for CGM alone and only in the US market. Numbers for CGM sales as a percentage of total diabetes sales were not available for more recently in 2011, 2012 and 2013. CGM was approximately 14% of 2010 diabetes revenue, so the same assumption was used for 2011-2013. The insulin pump forms a majority of the diabetes business as it was a commercial product since 1983 pioneered by Minimed, which was later acquired by Medtronic in 2001.

It can be seen that Dexcom has made surprising growth in the past 5 years given they received FDA approval only in 2006. They have slowly been penetrating the CGM market from taking Medtronic’s monopoly status to a duopoly. Specifically in CGM Medtronic and Dexcom currently own comparable market share.

Dexcom is also following suite by diversifying their product offering to capitalize on high-growth market opportunities. Dexcom’s G4 Sensor in Europe is part of the milestone Animas Vibe Insulin Pump System, developed in partnership with Animas Corp., a Johnson & Johnson company. The product is the first offering from the Animas/Dexcom collaboration and features an insulin pump that incorporates CGM technology. A similar development and commercialization agreement was put in place between Dexcom and Tandem Diabetes Care, Inc. (Tandem) to enhance Dexcom’s capabilities of current products. In spite of Dexcom’s late start in the market, they have shown respectable year on year growth rates. In 2009 their product revenue was a meagre $18M and by 2013 the revenue grew to $141M, which amounts to 68% average growth in that period.
3.4 Product segment
There was once little cross-segment participation, but we are now seeing large competitors diversify their product offerings to capitalize on high-growth opportunities in the market. Medtronic has successfully leveraged its dominant position in insulin pumps (Figure 7) to effectively market and distribute its CGM product. In 2013, this market share has grown to an estimated 74%\(^9\). It is estimated that anywhere from 300,000 to 400,000 Type 1 patients rely on pumps to regularly deliver insulin. Having an already established user base with insulin pump, CGM manufacturers such as Medtronic can successfully onboard existing insulin users to CGM since it is complementary and very beneficial to these patients. Besides these patients already have an attachment to Medtronic as a brand with the pump and will hence be willing to try other products from the same company. As a result, Medtronic’s 3 pronged approach to diabetes management: insulin therapy, glucose monitoring and therapy adjustment, provides patients with an integrated therapy option.

Another interesting find is that patients can use Medtronic pumps with Dexcom CGM sensors. It’s not convenient in that you have to carry an extra device and calibrate the CGM manually but even to learn that combined products from competitors is allowed is crucial. There was not readily available data on how many patients do this or prefer it even. Medtronic generated roughly $700M from their pump division in 2013. It would be very beneficial for them to analyze these numbers and develop a competitive bundled pricing strategy for the pump and their CGM system. The question though is if Medtronic should lead this pricing strategy or wait for Dexcom to enter the US and then make a change. This could potential lead to informal price wars eroding margin for both players.

From reading patient blogs it seems there are patients combining Dexcom G4 CGM with a MiniMed (Medtronic) Paradigm Revel pump. In spite of the hassle of not having everything integrated perfectly, some patients don’t mind this due to the increased accuracy Dexcom provides. This is an eminent threat to Medtronic – as soon as Dexcom’s partnership with J&J or Tandem receives FDA approval it can be expected that many patients will switch from using the Medtronic pump.

Because of the effects of this cross market segmentation between the CGM sensors and insulin pumps, it warrants a closer look at the trends in CGM market by product categories as well, shown below:

\(^9\) Medtech Insight: The Artificial Pancreas: A race to the finish, Oct 2013
\(^10\) Insulin pump world market briefing, MTB Europe, August 2010
The global market for CGM devices was worth $165.8M in 2010 and $183.7M in 2011. This market is projected to reach $356.5M by 2016, with a five-year compound annual growth rate (CAGR) of 14.2% from 2011 through 2016. The market for transmitters and receivers was $83.4M in 2011 and is expected to increase to $159.3M by 2016, at a CAGR of 13.8%. The market for glucose sensors was $76M in 2011 and is expected to increase to $140.9M by 2016, at a CAGR of 13.1%. The market for insulin pumps was $22M in 2011 and is expected to grow to $58M by 2016, at a CAGR of 7.2%.

4. Market Drivers
The ease of use and convenience of CGM devices compared with conventional glucose monitoring such as glucose meters that provide one-time snapshots of a person’s blood glucose level, is fueling demand for CGM systems. Aside from that, global awareness of such products, the ability to detect hypo and hyperglycemic events early as well as the rise in incidences of diabetes worldwide is contributing to the market growth. The following subsections will detail primary factors for market penetration.

4.1 First movers advantage
The chart below shows Medtronic has been the leader to get FDA approvals for the CGM system, the integrated CGM-pump system as well as opening up use of the CGM for children. Another recent milestone Medtronic took the lead on was a first generation artificial pancreas system (APS) with their MiniMed 530G. Dexcom tailgates Medtronic on average 6-7 years later and Abbott still later.

<table>
<thead>
<tr>
<th>FDA Approval Timeline</th>
<th>Medtronic</th>
<th>DexCom</th>
<th>Abbott</th>
</tr>
</thead>
<tbody>
<tr>
<td>• CGM</td>
<td>• 1999</td>
<td>• 2006</td>
<td>• 2008</td>
</tr>
<tr>
<td>• CGM+Pump</td>
<td>• 2006</td>
<td>• Applied in 2013</td>
<td>• n/a</td>
</tr>
<tr>
<td>• CGM for children</td>
<td>• 2007</td>
<td>• 2014</td>
<td>• n/a</td>
</tr>
<tr>
<td>• iPro</td>
<td>• 2008</td>
<td>• PMA for G4 applied</td>
<td>• n/a</td>
</tr>
</tbody>
</table>

Figure 9. FDA approval timeline across Medtronic, Dexcom, Abbott

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With the lead Medtronic has established in the diabetes management market, one would think it might have a strong position in creating a brand loyalty. As a monopoly offering, it is obvious patients had no other choice. But the true brand loyalty comes into test when new companies emerge and how easily they can capture market. Dexcom and Abbott entered market in 2006 and 2008 respectively. Since then Dexcom has slowly been gaining market share. Patients were not as attached to Medtronic as expected. For one, being the first in the market, Medtronic released CGM products that still had room for improvement. Dexcom designed to incrementally improve market offering – in simplifying user experience, extending sensor life and improving accuracy. Unlike biopharmaceuticals, where the life cycle to developed a new drug is 10+ years costing close to $1B, medical device life cycles are shorter. This comes into play especially when the device is non-implantable, so not requiring surgeon acceptance and lengthy clinical trials. Therefore both Medtronic and Dexcom have been releasing product revisions to enhance features frequently in the last 10 years (Figure 10). During 2005 and 2011 Medtronic was actively innovating with the insulin pump Paradigm platform.

This does not include innovation in the software for patients, professional use devices, in insulin pumps, the CGM system components (transmitter from wired to wireless, receiver user design etc.) or remote monitoring and still the last 8 years have seen a cluttered product launch from both companies. It is exactly this cycle of continuous improvement that allows entrants to test products, incorporate patient feedback and redesign to launch an improved product. Patients are not supporting any one company but rather products that meet their needs.

Another off-shoot of frequent launches is that the product names are not sticky. The diabetic community is more attached to the company name unlike in pharmaceuticals where the drug name is what takes off and manufacturer’s names are hardly remembered. For example in the case of Prosac and Zoloft, no one ever talks about Eli Lily or Pfizer as the manufacturers respectively.

![Figure 10. Medtronic & Dexcom International CGM innovation timeline](image-url)
Another point to note is that Dexcom enjoys second mover advantage here. Medtronic for a few years enjoyed huge margins because of monopoly status but it also paved the way for CGM and wetted the product with patients, payors, and physicians. Because of the level of technology advancements still required, later entrant Dexcom has been able to leverage the already established acceptance - particularly the cost to lobby and get reimbursement codes for physician time and durable medical equipment for patient copays. Additionally the switching cost is non-existent. One year a patient can try the Medtronic products and another year they can switch to Dexcom if they want. The cost is slightly more in the case of type 2 patients where coverage is spotty for CGM and also depends on various payor policies. Simultaneously patients are much more aware of their health and are far more educated than they used to be. They are rationally evaluating devices purely based on what is important to them - accuracy, automatic insertion so you don’t see the needle, comfort, cost etc. The mushrooming of online patient community blogs, device comparison reports by patients and physicians, together with video content dispersion has allowed pros and cons on various products to drive product loyalty.

4.2 Pricing
CGM is a promising technology and has been around for years now, so why are not more diabetics using it? With only 5-10% penetration in the type 1 patients and a majority of the 17M type 2s not on board, there is a huge market to address. There is a small subset of the type 2s that do use CGM but that is because they can afford it. In most cases insurance has denied coverage stating there is not the clinical evidence to show efficacy in their case. So if medical suppliers were then to assume that insurance and Medicare will not provide coverage in the short run, is there a potential to lower CGM pricing to capture more market? Obviously without pricing too low because they will not be able to increase pricing once coverage improves. So is there a better price than today’s which will account for coverage in the near term (H.R. 3710: Medicare CGM Coverage Act) and account for economies of scale.

Currently for type 2 patients the cost for CGM is on average about $4200 annually compared to $500 on SMBG (Figure 11a, 11b). It should be noted that pricing the SMBG treatment for types 2 can vary quite a bit based on how often they test and whether they are on oral anti-diabetics versus insulin. Nonetheless, this is a huge price gap especially when patients are paying out of pocket. The $500 is covered for. So essentially its $4200 versus a free treatment, then why would a patient pay to opt for CGM? Might be that they are willing to pay for the convenience and its hard metric to put a $ value to. For example, wanting to sleep peacefully knowing they can rely on their CGM to monitor night basal rate. And this happens to be the population that is also educated and most motivated to manage their disease - taking control of life style (diet, exercise, doctor visits, diabetes education), to keep their glucose in control. They realize the consequences of chronic diabetes progressing into other complicated disorders and the cost of that is far worse than paying for CGM. The most common long-term effect of type 2 diabetes is damage to blood vessels. Because of this, people with diabetes are up to five times more likely to develop heart disease or have a stroke. In a sense, these patients consider it their insurance against such cardiovascular disorders.
### Pricing from 2008

<table>
<thead>
<tr>
<th>Component</th>
<th>MDT Guardian</th>
<th>Dexcom G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kit: receiver, battery charger,</td>
<td>$940</td>
<td>$800</td>
</tr>
<tr>
<td>cables, software</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensor/transmitter</td>
<td>$35/sensor</td>
<td>$60/sensor</td>
</tr>
<tr>
<td>Monthly consumable</td>
<td>$280</td>
<td>$240</td>
</tr>
<tr>
<td>Yearly consumable</td>
<td>$3360</td>
<td>$2880</td>
</tr>
<tr>
<td>Calibration glucose strips</td>
<td>$120</td>
<td>$120</td>
</tr>
<tr>
<td><strong>Total cost</strong></td>
<td>$4420</td>
<td>$3800</td>
</tr>
</tbody>
</table>

Figure 11a. Price comparison for CGM offering across Medtronic and Dexcom

<table>
<thead>
<tr>
<th>Average SMBG Pricing</th>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test strips</td>
<td>$772</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>$2078</td>
<td></td>
</tr>
<tr>
<td><strong>Total cost</strong></td>
<td>$2850</td>
<td>$55013</td>
</tr>
</tbody>
</table>

Figure 11b. SMBG price comparison for type 1 and type 2 patients

### 4.3 Doctor preference

CGM systems require prescription for use. Specifically endocrinologists, physicians and diabetes educators educate and influence patient adoption of CGM. In interviewing Dr. Robert Vigersky, Director of the Diabetes Institute at the Walter Reed National Military Medical Center, it was gathered that physicians prefer Dexcom for product accuracy. Another feature doctors hear patients place emphasis on is the procedure to insert the pump and CGM in a single site which currently is only offered in Europe. Doctors prefer the Dexcom sensor but rank the Medtronic software portal and data analysis capabilities much higher than that of Dexcom.

Both patients and doctors really appreciate the clean design of the Omnipod. Omnipod is Insulet Corporation’s insulin pump. It is a revolutionary tubeless pump that is discrete and easy to use. It offers water proof capability and patients enjoy the fact that they can swim and shower with it. It is a 3 day disposable pump that is controlled via a wireless device. Doctors note that children particularly love it. More on Omnipod will be covered later in the emerging technologies section.

When a patient visits with his or her doctor, they discuss pros and cons of the various choices and select a CGM system that is appropriate for them. Hospitals, clinics and doctor’s offices do not order or store any CGM systems. Patients order the device through the vendor and work with their insurance coverage. Doctors only order the professional 3 day CGM versions based on whatever their preference is. Primarily it has been Medtronic, since they are the market leaders in professional CGM.

### 4.4 Patient communities

Patient interviews conducted as part of this thesis, have shown that CGM is appreciated more by patients who have trouble keeping a structured lifestyle, e.g. professionals who need to travel a lot for work, or get called into ad-hoc meetings, they often don’t know what they are going to have access to when – they feel more comfortable in those situations – there’s a piece of mind. CGM also gives patients

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living alone a sense of security, especially at night. Still a very small percentage of the addressable market is using CGM. Apart from pricing and other complexities involved with CGM as discussed above, patient education is a key component to be analyzed — especially since diabetes is a disease where treatment is patient-empowered. Dexcom CEO Terry Greg, said “Each day, a patient with diabetes must measure their glucose levels and administer insulin or another anti-diabetes injected or oral medication to help regulate their glucose levels. They don’t get a shot a month from a doctor or nurse; it is daily and patients must do this every day.”

In 2009, Medtronic announced a strategic marketing collaboration with Eli Lilly. The alliance reached with Lilly provided for marketing and sales operations in the U.S. to improve the delivery of diabetes education for insulin-taking patients and their caregivers. This included the development of new educational resources and classes around the initiation and intensive management of insulin, insulin pump therapy and CMG — as a result increasing future product acceptance and customer preference. Net sales for external insulin pump and related consumable was 5% higher when compared to the prior fiscal year. The increase in net sales resulted from demand for the MiniMed Paradigm that integrates CGM and insulin pump functionality and related consumables. Net sales of CGM systems and other accessories increased 56% when compared to the prior fiscal year. Therefore the role of educating patients is critical when driving increased market penetration.

Apart from the push from manufacturer salesforce in educating the providers and staff in promoting their product, a force playing in favor for the manufacturers is that the diabetic population is very well educated about the way treatment is evolving. Peer-to-peer communication, especially online, is spreading the word about the benefits of CGM. Typically patients often walk into their doctor’s office and request the technology they have researched online. After a doctor prescribes the technology to the patient, the system is ultimately sent directly to the user. Patients are trained on how to use the device at their physician’s office and later receive supplemental training via the company’s website. This makes it very imperative for future advancements in device to be focused on user friendliness.

4.5 Reimbursement landscape
The FDA has approved CGMs as tools for managing glucose levels through trending and tracking, but the agency does not officially recognize the devices as a proven technology for detecting hyperglycemia or hypoglycemia. This distinction presents a hurdle for anyone involved in the development of a closed-loop system that utilizes CGMs, a standard part of all major research in this area today.

Reimbursement has three components: coverage, coding and payment as seen in the figure\textsuperscript{14} below.

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\textsuperscript{14} Medtronic 2013 Professional CGM Reimbursement Guide
The Current Procedural Terminology (CPT) codes provide a uniform language for healthcare professionals to bill their services to payers. There are two CPT codes specific for CGM:

- **95250**: Ambulatory continuous glucose monitoring of interstitial tissue fluid via a subcutaneous sensor for a minimum of 72 hours; sensor placement, hook-up, calibration of monitor, patient training, removal of sensor, and printout of recording.
- **95251**: Ambulatory continuous glucose monitoring of interstitial fluid via a subcutaneous sensor for a minimum of 72 hours; interpretation and report.

As medical device companies, reimbursement from Medicare and private third-party healthcare payors is an important element of market success. Although the Centers for Medicare and Medicaid ("CMS") released 2008 Alpha-Numeric Healthcare Common Procedure Coding System ("HCPCS") codes applicable to the CGM systems, to date, approved products are not reimbursed by virtue of a national coverage decision by Medicare. It is not known when, if ever, Medicare will adopt a national coverage decision with respect to CGM devices. Until any such coverage decision is adopted by Medicare, reimbursement of CGM products will generally be limited to those patients covered by third-party payors that have adopted coverage policies for CGM devices.

CGM is considered "durable medical equipment" (DME) and is subject to the same deductibles and copays as other types of DME. Specifically the transmitter is covered under DME and the supplies including the sensors are covered under drug benefit.

As of February 2013, the seven largest private third-party payors, in terms of the number of covered lives, have issued coverage policies for the category of CGM devices. These include:

- Blue Cross/Blue Shield
- Aetna
- Cigna
- Humana
- United Healthcare
- Kaiser Permanente
- Wellpoint

Many of these coverage policies are restrictive in nature and require the policy holder to comply with extensive documentation and other requirements to demonstrate medical necessity under the policy.
People with Type-1 (insulin-dependent) diabetes often qualify for insurance coverage, particularly if the following criteria are met:

- A history of hypoglycemia, documented in the physician’s chart/records
- Presence of hypoglycemia unawareness (lack of symptoms during the early phases of hypoglycemia)
- Erratic blood glucose levels
- Suboptimal HbA1c
- Frequent blood glucose monitoring
- Having completed diabetes self-management education

In some cases, people with Type-2 diabetes, whether or not insulin is used, can obtain coverage if many of these same conditions exist.

In addition, people with diabetes who are insured by payors that do not offer coverage for CGM devices will have to bear the financial cost of the products. Every CGM company (i.e. Medtronic, Dexcom) has a team of specialists dedicated to helping patients obtain maximum coverage. Most plans require the CGM to be prescribed by an endocrinologist. Many people who are initially denied are approved for coverage after the second, third, and even fourth round of appeals. External appeals play a big role in getting coverage. An external appeal requires the health insurer to pay a physician who is not employed by their company to review patient’s case in detail. An external appeal will usually cause the health insurance company to overturn their decision and begin CGM coverage. It should be noted that coverage varies state by state for the same payor.

5. Emerging technologies

The market is overcoming challenges towards the commercialization of closed loop CGMs with significant focus on technological innovation. This is expected to take the concept of CGM to a next level from research to mass adoption. But scientists envision the ultimate goal is to create an artificial pancreas that mimics the functionality of a real pancreas. Many companies are trying to build an artificial pancreas. Medtronic has taken a step toward that direction with its MiniMed 530G and the Enlite sensor that the FDA approved in September 2013. The system is able to suspend the delivery of insulin when the sensor detects that a pre-determined low glucose threshold has been reached in a patient’s body. This avoids the patient slipping into hyperglycemia, a problem that can commonly occur when diabetics sleep. The MiniMed 530G is the first system approved under the FDA’s newly created product classification, OZO: Artificial Pancreas device System, Threshold Suspend. It is currently indicated for use in patients 16 years and older.

One of the main challenges CGM companies face is onboarding the larger type 2 patient community onto CGM. CGM systems need to show a benefit from continuous monitoring in lowering hemoglobin A1c levels (used to measure long-term glucose control) compared with traditional finger-stick testing. New CGM systems also need to demonstrate effectiveness in understanding trends in glycemic variation and help patients detect and avoid hypoglycemic and hyperglycemic events. However, the under commercialization is presenting opportunities as innovative products will easily take the advantage of lower product presence.

One such hot area of research in CGM is around non-invasive CGM (NICGM). Companies and researchers are exploring various technologies to detect glucose levels without using blood. A few prominent ones will be highlighted below:
Switzerland-based Solianis AG is involved in developing a NICGM device based on a multi-sensor concept to address the perturbing effects such as sweat, changes in skin hydration, variations in microvascular perfusion, body temperature, thickness variations of different skin layers, or movement artefacts. The multi-sensor employs impedance spectroscopy as the principal component, to measure the dielectric effects of glucose variations in skin and underlying tissue in the frequencies between 100 kHz to 100 MHz, including 1 and 2 GHz. The underlying concept is that when an electromagnetic field is applied to the skin, it penetrates through the skin and based on changes in glucose levels, a change in the dielectric characteristics is observed. This change is influenced by the effect of the glucose transport and the resulting changes in the electrical characteristics of blood and cutaneous tissue.

GlySens Inc. is working on a device that could improve the use of a closed-loop system. Their goal is to develop a long-term, implantable sensor. Their website states that the system will be comprised of two elements: the fully implanted sensor (demonstrated up to 18 months in preclinical studies) and an external receiver with a monitor. The technology is described as a system based on utilizing two sensors within a single implantable device. The first sensor is a glucose sensor, in which a selective chemical reaction involving glucose and oxygen is monitored by an electrochemical oxygen detector. The second sensor, an oxygen reference sensor, detects tissue oxygen. The device’s electronic circuitry determines the difference between the two sensors' signals and utilizes the information to determine glucose levels. Part of the function is to ensure glucose measurements are not compromised by secondary factors such as temperature, blood flow in surrounding tissue, and long-term changes due to the body's immune system response to the implanted device. This system will require no needle insertion, or through-the-skin/skin-adhered components.

Echo's lead program in analyte monitoring is focused on glucose and utilizes the Symphony CGM System, a non-invasive (needle-free), wireless, continuous glucose monitoring system designed to provide accurate, real-time blood glucose data conveniently and continuously. Symphony incorporates Prelude, Echo’s proprietary skin permeation device, a transdermal sensor, wireless transceiver and data display technologies.

Integrity Applications, an Israeli company, has developed the GlucoTrack - another non-invasive method to measure glucose levels in the blood and has received the European CE Mark for it. The user clips a sensor to their earlobe, and then waits a minute or so until the result is displayed on the device’s display which is also spoken out. The readings are stored in the device as well, so it can calculate the average glucose level over the course of many months. The device itself is about the size and weight of a smartphone. It uses three independent technologies: ultrasonic, electromagnetic and thermal, to painlessly obtain blood glucose levels.

Insulet Corp. with its innovative pump technology, Omnipod, is not to be missed. They are only playing the pump field without dealing with the issues of glucose monitoring. Until Insulet's OmniPod came on the market at the end of 2005, all insulin pumps consisted of a controller and insulin reservoir attached to the injection site by a long flexible tube. The OmniPod design eliminates the tubing, consolidating the insulin reservoir and a self-inserting cannula into a single pod. In an effort to enlarge its presence in the larger diabetes market, Insulet purchased Neighborhood Diabetes, a specialty distributor of diabetes supplies and equipment, in 2011. Strategically the combination makes sense - increasing Insulet's breadth of products and services for the diabetic patient, but diabetic supplies are lower-margin and new competitive bidding measures have resulted in price pressure. Insulet reached operating profitability in late 2013 and continues to work at gaining enough economies of scale to bring down
manufacturing and operating costs. They are a potential acquisition target by a large rival like J&J or Abbott.

6. Conclusion
The incidence of diabetes is growing with an alarmingly large prevalence in the US at over 25M diabetics. Tight control of blood glucose levels is crucial in preventing life-threatening complications related to diabetes. Continuous advances in the field of glucose monitoring during the last four decades have led to the development of highly evolved blood glucose meters. CGM systems have led to tremendous improvements in diabetic management, as shown by the significant lowering of glycated hemoglobin (HbA1c) in adults with type I diabetes. But more studies are required to show the same effect for type 2 diabetics. The main limitation in increasing CGM usage is their extremely high cost, which is beyond the reach of most diabetics given the current reimbursement landscape. Other challenges include development of NICGM techniques for precise and specific glucose detection, with significant reduction of calibration. As these developments are achieved CGM has the potential to grow to approximately $910M in the global market by 2019\(^\text{15}\).