Changing Cost of Insulin Therapy in the U.S.
Irl B. Hirsch, MD
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The history of the cost of insulin is complex, but even going back to 1923 the manufacturing of insulin has always been a (very) profitable business. In innovations of initially purified animal insulins, progressing to human insulins, and eventually insulin analogues have come at a cost. Still, in the US, for the vast majority of patients insulin has been affordable and in fact as recently as the 1980s and early 1990s one of the marketing messages was insulin, even with home blood glucose monitoring, was cheaper than tablets. Have times changed!

“Average Whole Prices” of insulin, similar to list prices, are not what is paid by most patients. Still, for traditional third party insurances, the dramatic cost increases of AWP pricing in the past decade in most cases has resulted in much higher co-pays, to the point many can’t afford the insulin at all. The statistics are staggering. In the past 13 years, a vial of glargine has risen 593% while a box of five insulin lispro pens has increased 522%. This compares to a total inflation of 8.3%, and overall medical inflation of 46% in this same time period.

The US (but not many countries) has been willing to pay for small incremental benefits in insulin, recently related to improvements of hypoglycemia, especially overnight. The world-wide insulin market in 2013 was $21 billion (clearly higher now) but 52% of that came from North America, even though we only account for 7% of world-wide insulin users. It is concerning that the price increases from one insulin is matched within 24 hours by the competition, and this has happened 13 times in the past decade.

While most of the attention with the rising prices of insulin have focused on the manufacturers, it is actually the pharmacy benefit manger (PBM) responsible for much of the problem (for commercial insurances) since they are the ones directly dealing with the insulin companies. The PBM receives a rebate and the health plan and co-pay from the patient pays for the drug. But how much profit does the PBM make? In 2013 CVS Caremark had revenues of $123 billion while ExpressScripts was at $94 billion, with annual returns to investors at 15.5% and 24.6% respectively. Meanwhile, for Medicare patients in the “donut hole”, retail insulin prices are unaffordable, as for those patients who have no insurance despite the ACA. The retail prices of analogue insulin are also not affordable for those with high-deductible insurance plans. Many of these patients are new to insurance and did not realize they would first have to spend over $6,000 as a deductible.

Although no specific data are available, we know of more DKA and patients rationing their insulin. Many with type 2 diabetes simply have had to stop.

In the short term, movement to human insulin (Walmart brand) and the use of programs from each company for those below certain income levels need to be better implemented. It is doubtful biosimilar insulins will have much of an impact on insulin costs.
Changing Costs of Insulin Therapy in the U.S.

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Disclosures

- Research/Grants:
- Consultant: Abbott, Roche, BD, Bigfoot

The Cost of Diabetes Therapy

To understand where we are one needs to know how this all started…

What is the Real Increase in Insulin Costs in the past 55 Years?

- Data obtained from a variety of on-line sources
- Only showing regular (animal and human) and rapid-acting analogues
- Cost/vial not a good metric: early vials U-40 and U-80 so for 1960 and 1975 used U-40 insulin and calculated “cents/unit of insulin”
- Used Tom’s inflation calculator (halfhill.com/inflation.is.html) for medical inflation (NOT consumer price index or US price inflation)

Sources for insulin costs:

Von Wartberg, L: Diabetes Health, May 23. 2007
Altman LK: NY Times, Oct 30, 1982
mendosa.com/insulin_cost.htm assessed January 31, 2016
GoodRx.com, assessed May 17, 2015
Price of Insulin:
1960-2015 US-per unit (Regular and Rapid-Acting Analogue)

By 2005 more than US $7.3 billion was spent globally on the purchase of insulin products.

Thought due to increased prevalence/need, increase cost, increased use of analogues.

No one could have predicted what would happen over the next decade.

Average Wholesale Price (AWP)

- AWP: “list prices” reported by manufacturers
- The prices I will be quoting came from drugstore.com and more recently goodrx.com but are not AWP (AKA, “Aint What’s Paid”)
- AWP has often been compared to the “list price” or “sticker price”, meaning it is an elevated drug price that is rarely what is actually paid
- AWP is not a government-regulated figure, does not include discounts or rebates often involved in prescription sales, and is subject to fraudulent manipulation by manufacturers or even wholesalers. As such, the AWP, while used throughout the industry, is a controversial pricing benchmark


Sticker Shock

- January, 2016 (after deductibles)
  - Co-pay for insulin aspart: $150/vial (the “preferred insulin” for a physician in NY City) $190 on GoodRx.com
  - Co-pay for a box of 5 insulin glargine pens: $185 (for a college professor in Everett, WA) $381 on Goodrx.com
  - Co-pay for a vial of NPH insulin, $40 (student in Eugene, OR) $135 on GoodRx.com

Accessed May 24, 2015

The Rising Cost of Insulin in the Past Decade (20.9% cumulative inflation rate)

While 30 name brand drugs have doubled in price in the past 5 years, 3 of the top 6 drugs were insulin.


2005 2015

264% 389% 348% 364% 508%
Insulin Financial Primer

- In 2013, insulin was a $21 billion global market with compound annual growth rate of 15% for the previous 5 years
- Secular volume growth: 6-7%/year 2008-2013
- Value growth much higher due to “US healthcare system willingness to pay for modest differentiation and its acceptance of repeated price increases”

Gal A: Novo Nordisk, an insulin primer; where is the market headed? Bernstein Research September 24, 2013

Insulin Financial Primer

- Revenue = unit SALES + unit PRICE
- For all 3 companies, the reliance on the US is problematic: role of biosimilars?
- These may attenuate growth, yet both Sanofi and Eli Lilly will be in the biosimilar market

Gal A: Novo Nordisk, an insulin primer; where is the market headed? Bernstein Research September 24, 2013

Diabetes Prevalence, % Insuln-Rx'ed Patients, Share of Sales

- On May 30, 2014 the price of insulin glargine was increased by 16.1% by Sanofi
- The next day, Novo Nordisk increased the price of insulin detemir by 16.1%
- The pattern repeated itself 6 months later and this has actually happened 13 times for these two products with total sales of $11 billion US.

Langreth R: Hot drugs show sharp price hikes in shadow market. Bloomberg Business May 6, 2015

Price Increases

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How Drug Company Revenue is Driven by Price Increases

- Growth Trends for 30 Top-Selling Drugs
- Average growth in revenue for top-selling prescription drugs in the U.S. far outstripped demand growth from 2010 through 2014

C. Canipe and J. Walker, WSLI Oct 5, 2015
What About Insulin Revenue?

Top 30 revenue drugs, 2010-2014

Lantus: #2 ($5.61B) +168% +98% +23%
Humalog: #18 ($1.63 B) +33% +33% +103%

Top 30 revenue drugs, 2010-2014

C. Canipe and J. Walker, WSJ, Oct 5, 2015

Comparing Prices of Insulin Around the World (Feb, 2016)

Cost/vial of insulin

Case 1

- 61 year-old right-handed woman with T1D and right arm sarcoma. Medicaid only allows vial/syringe. Is not able to draw up insulin with cancer. Arm amputation occurred September 2014. Letters and phone calls not effective and request for pens denied due to cost. Bipolar daughter not home enough to give all of her shots.
- After weeks of pleading with "peer-to-peer" consults, pen insulin was "approved" yet this will require a yearly repeat approval

Case 2 (but I see often)

- Patients with T1D using regular insulin in pump as can’t afford analogue co-pay
- More common in 2016: mixing analog insulin with regular insulin in pump

Case 3-4-5

- Insurance only allows 1 vial dispensed at a time (based on # units on ‘script). The next vial can only be picked up within 48 hours of running out of insulin, even if traveling!
- Another insurance: allows one PEN at a time! Patients are allowed 24 hour window prior to running out of insulin to retrieve their “liquid gold”.
- Seen every day: patients acknowledged limiting their carbohydrate intake so they would not need to take additional insulin; anecdotally more DKA in the US over the past 18 months but data not yet available

Case 6

- 18 year-old college freshman receives insulin with a $25 co-pay through her father’s individual plan
- She turns 19, and the co-pay goes up to $125 per box of pens
- After several months, she is deemed eligible for a patient assistance program
- Important: her parents had no idea the insulin would increase in price when she turned 19
Still Not Convinced?

- Medicaid patients who receive their insulin for minimum if any charge sell their insulin to Medicare patients in the donut hole. This has been on-going for years but has escalated over the past few years.

Let’s Be Clear: This Isn’t ALL Due to the Greed of the Insulin Companies

By far, the most common comment to me after my June 2015 ADA talk: “You are much braver than me.”

Perception: the insulin companies are doing this on their own. NOT TRUE

If this topic is of interest and you want more details: https://www.cbo.gov/publication/18275 which was written by the US Congressional Budget Office (2007).

Payers

1. Includes both PBMs and health plans
   - Health plans may choose to partner with a PBM for Rx benefits
2. Negotiate discounts/rebates with manufacturers on behalf of plans/employers
   - Goal is to increase revenue (Rebate Per Unit + Admin Fees) and decrease total member costs
3. Rebates typically based on formulary access

Drug Channel Companies

- PBMs, chain pharmacies, wholesalers
- Drug channel companies have higher revenues than pharmaceutical manufacturers, so they rank higher on the Fortune 500. This results from quadruple-counting of prescription revenues.
  - When these profits are measured by Return on Assets, channel company profitability is about half that of pharmaceutical manufacturers.
Fein AJ: Drug Company Channels, June 2013

How Can This Be?
Insulin Price Shock
David Sell, Philly.com, Jan 4, 2016

Express Scripts’ chief medical officer, Steve Miller, said its clients spend more on diabetes than any other category. He said the historical “social contract” under which American healthcare providers priced their products reasonably had “broken down” because of “extravagant” year-over-year price increases by drug companies.

“If not for Express Scripts using market forces to fight this, it would be worse,” Miller said.

But Let’s Be Clear: We Can Point Our Fingers At Everyone

“The company reported the fourth-quarter revenue increase Thursday, with sales of Humalog insulin leading the company’s U.S. pharmaceutical revenues with a 20% increase. That growth was ‘driven by higher realized prices, and, to a lesser extent, increased volume,’ the company said.”

What We See in Our Clinics and Offices

• Patients with high deductibles (over $6K), not understanding the implications with the ACA
• “Donut hole patients”, early in the year
• Young patients off of their parent’s insurance for the first time who don’t now how to navigate the system
• Patients who simply can’t afford the high co-pays

Medicare Primer: Understanding the Difference Between a Donut Hole and a Loophole

• Medicare medications: “part D” (includes insulin)
• Durable Medical Equipment (DME): “part B”
• So not all drug coverage is included in the “part D” program. Medicare pays 80% AND if you have secondary coverage or Medicare Advantage, the insulin can be 100% covered with insulin pump therapy.

Short of putting a patient on an insulin pump, what can we do to help?
**My Take**

- For the typical patient with type 2 diabetes, while I prefer analogues due to decreased hypoglycemia risks, most do well with human insulin
  - NPH (2009 Cochrane Review): no difference from analogues with HbA1c, there was no difference in severe hypoglycemia although increased risk of symptomatic and nocturnal hypoglycemia*
  - Regular insulin-no difference in glycemic control and no increased risk of hypoglycemia compared to rapid-acting analogues (in T2D) **
  - Analogues should always be used as much as possible with T1D

*Cochrane Database Syst Rev. 2007;(2): CD005613
**Diabetes Obesity Metab 2009;11:53-59

However…

- Younger physicians without experience with NPH and Regular require training-simply switching insulins without understanding the caveats could result in poor outcomes
- Training for the use of human insulin for both post-graduate physicians, fellows, residents, and students should be a priority
- Shouldn’t this be the role of our professional and advocacy societies (ADA, Endocrine Society, and AACE)?


**So Are We Using More Human Insulin?**

- Between 2011 and 2015 human Regular insulin sales have decreased from 5.8% to 3.9% and all NPH insulin has decreased from 6.2% to 4.5% (pre-mix human insulin has decreased from 6.2% to 4.5%)
- WHY (one reason)?
  - In 2015 promotional detailing for human Regular and NPH were 0.5% and 0.3% of all calls respectively; long-acting analog is 34% with rapid-acting analog 24% of detailing (pre-mix analogues > 30% for both companies)

Warburg Pharma Rx January, 2016

Why Did This Happen?

- Costs from developing current insulins were paid years (decades) ago; can we attribute the slope of the increase in price all to R&D of new insulins?
- Does the benefit of a 10, 20, or 30% reduction of mild hypoglycemia justify even greater costs?
- The actual cost of insulin manufacturing is extremely cheap; is it ethical to charge such a price for a medication *required for survival* by some?
- The emerging role of biosimilar insulins
- "Supply and Demand" economics is not at work
- Insulin is not alone in its cost increase
Possible Solutions?

For the record, I don’t particularly like any of them

- Develop diabetes (insulin) guidelines that incorporate cost/benefit analysis
- “Value-based pricing”-physician panels to recommend target prices based on magnitude of benefit
  - But panels doing these two need to be all inclusive, including an economist and endocrinologist
- Allow importation of drugs from abroad for personal use
  - Unlikely to be allowed

Take Home Points

- We have never had such challenges with insulin costs in the US as it has become unaffordable for many
- Primary care physicians in particular are asking for education about how to use human insulins
  - For many with type 2 diabetes, given the cost this seems reasonable
- We don’t know where the cost rise will end and biosimilar insulins are unlikely to make a large change in the costs of insulin
- There will likely need to be changes to ensure all patients have access to appropriate insulin products-the roles of government, patient advocacy groups, and non-profit foundations are unclear