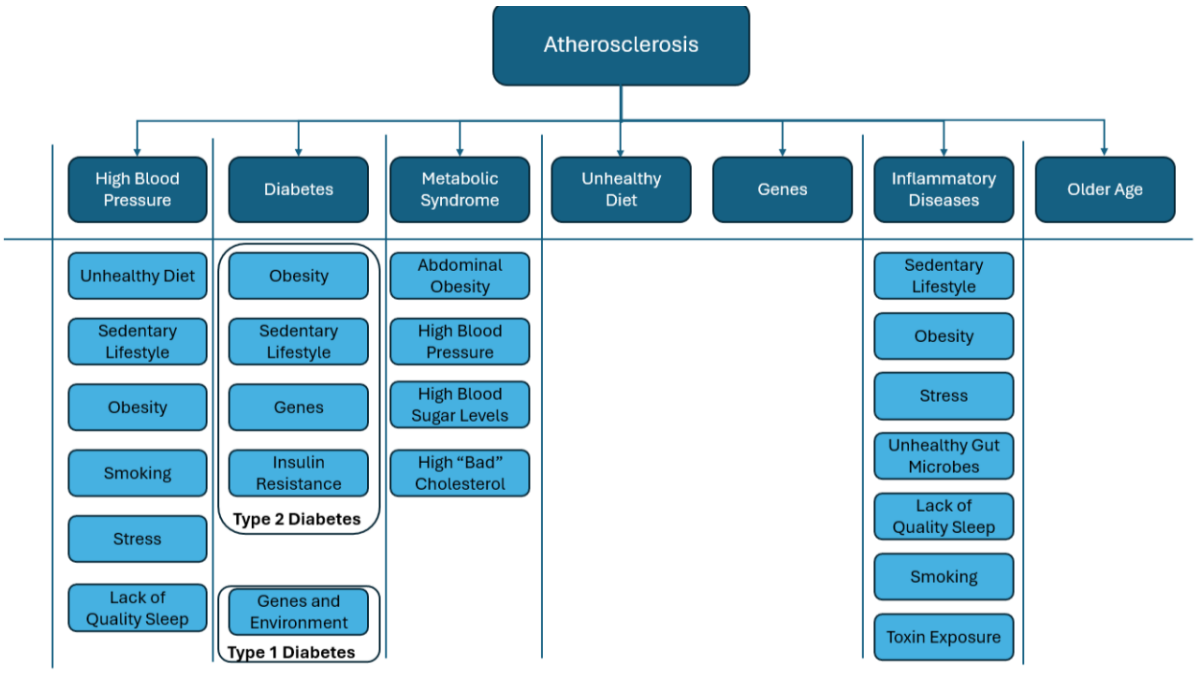


Sumptuous Lifestyle, Sweet Cravings and Heart

By Tamoghna Sengupta • Published Aug 29, 2024

https://www.linkedin.com/pulse/sumptuous-lifestyle-sweet-cravings-heart-tamoghna-sengupta-jl54c/

Note: The article below is a collection of my understanding of the businesses of prominent healthcare companies worldwide. Please do not consider any of the below opinions as expert advice. Please consider it as a friendly fireside chat.

Which form of disease is affecting the maximum population?

As per World Health Organization's 2021 data, the leading causes of death globally are below (Listed in descending order of number of people affected):

1. Ischemic heart disease (~9 million: 16% Deaths)
2. COVID 19 (~8.8 million)
3. Stroke (~6.5 million)
4. Chronic Obstructive Pulmonary Disease (~3.2 million)
5. Lower respiratory Infections (~2.4 million)
6. Trachea Bronchus Lung Cancers (~1.9 million)
7. Alzheimer's disease and other dementias (~1.7 million)
8. Diabetes mellitus (~1.6 million)
9. Kidney disease (~1.5 million)
10. Tuberculosis (~1.5 million)

As per more recent 2023 provisional data published by the CDC (Center for Disease Control and Prevention), Heart disease is the highest cause of death followed by diabetes at number #6.

What is ischemic heart disease?

What is Ischemia?

Ischemia is a combination of three factors:

a.) Drop in oxygen

b.) Drop in nutrient delivery

c.) Drop in waste removal

The combination of the above three factors causes a decrease in blood flow to the myocardium (heart muscle) – which is ischemia.

What causes Ischemia?

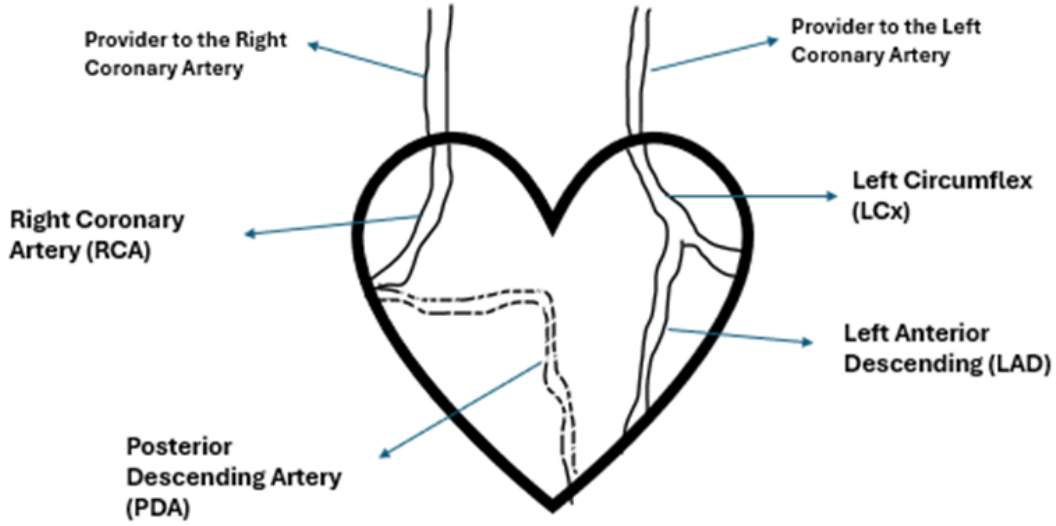
The biggest cause of Ischemia is –

Atherosclerosis. (>90% of the ischemic heart disease is attributed to this cause)

As a non-expert in the field of medicine, how can we best interpret atherosclerosis?

There are numerous blood vessels supplying blood to the heart muscle. These blood vessels are coronary arteries, and the heart muscle is myocardium.

If we try to visualize how these coronary arteries are making its way into the myocardium, it would be something like below (pardon my drawing)

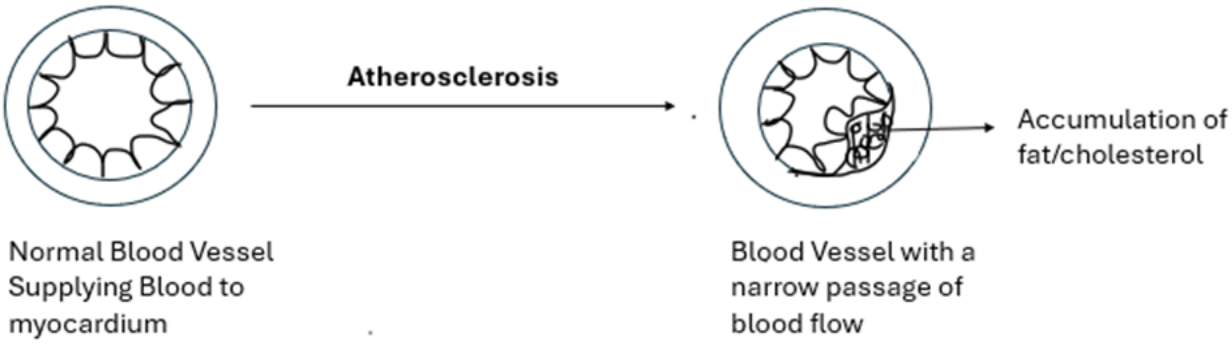


——— Supplying to the front muscles

- - - - Supplying to the back muscles

Now, these coronary arteries are epicardium – which means they sit on the surface layer of the heart.

When lipid/cholesterol accumulates under the linings of the above blood vessels, it creates a plaque as the below diagram shows:



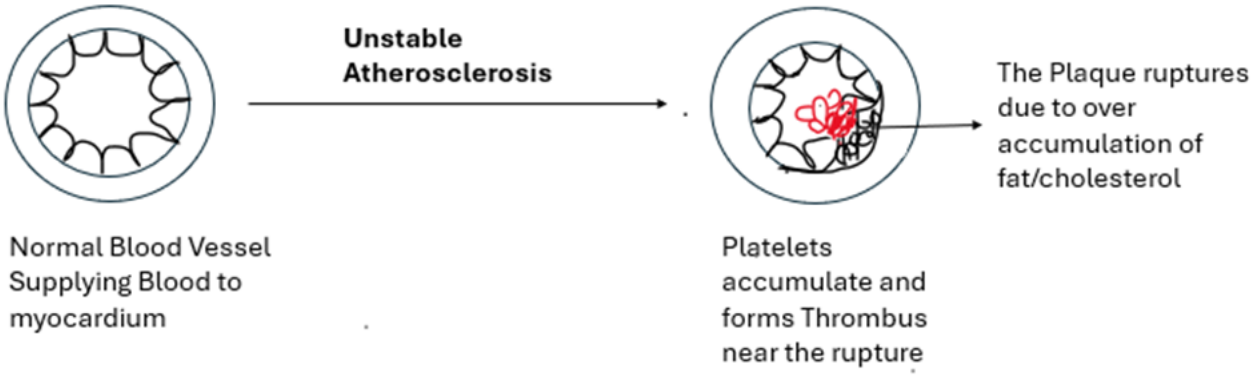
Even though the above diagram looks scary, believe it or not, it is called stable atherosclerosis . This means that this state will not cause any problems while you are resting.

However, it can result in chest pain when the demand for oxygen in the heart (due to exercise, running, stress (emotional/physical), etc.) increases and surpasses the possible

supply.

Thus, even though stable atherosclerosis is an alarming signal, it’s not all that bad yet. The situation can still improve through lifestyle changes and medications (if doctors feel it’s required).

The real problem occurs in the below scenario –



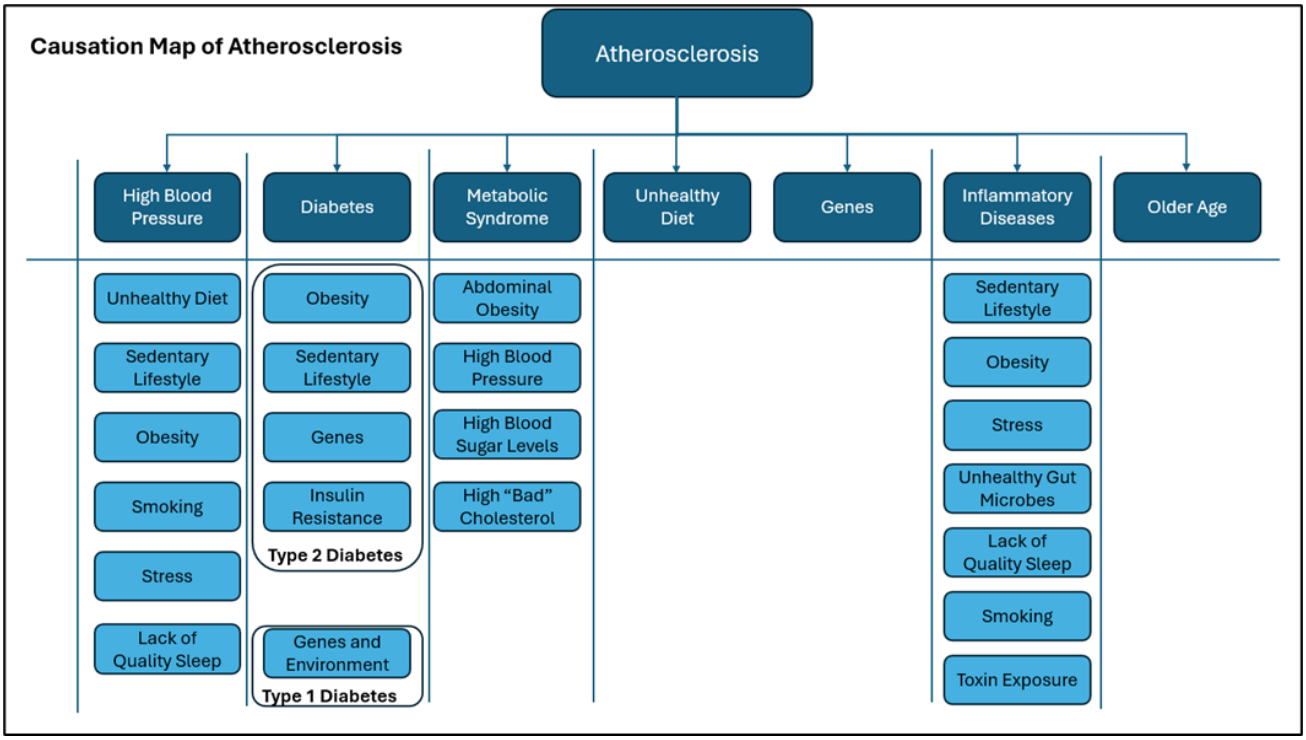
The above scenario is Unstable Atherosclerosis. This can cause an acute coronary syndrome, which can result in either – a.) Unstable Angina or b.) Myocardial Infraction (MI)

Unstable Angina is the onset of the rupture, which causes severe chest pain. If it lasts too long, it can cause an infarction – which is the death of the tissue.

The other two significant causes are 2.) Vasospasm and 3.) Microvascular Dysfunction. I am not delving much deeper into either of these two causes, because together they contribute to less than 10% of the total ischemic heart disease occurrences compared to Atherosclerosis which contributes to approximately 90% of the total occurrences.

Let us look at ‘Whys’

If we draw a causation map of Atherosclerosis, it will appear as below:



Information Source for the above Map:

https://www.nhlbi.nih.gov/health/atherosclerosis/causes

Therefore, we can conclude from the map above that the root causes of ischemic heart disease are closely linked to common diseases that we frequently encounter. Interestingly, diabetes, which is one of the main underlying causes, ranks among the top 10 major diseases globally. Even more intriguing is the observation that the underlying causes of most of these diseases (aside from genetic factors and old age, which are often unavoidable) are predominantly related to lifestyle:

- Unhealthy Diet
- Obesity
- Sedentary Lifestyle
- Abdominal Obesity
- Stress
- Lack of Quality Sleep

For example, if we just cherry pick diabetes - the number of adults above 18 years age affected by diabetes globally has been increasing (Information Source: CDC – Centers for Disease Control and Prevention):

Time Period	Diagnosed diabetes Percentage (95% CI)	Undiagnosed diabetes Percentage (95% CI)	Total diabetes Percentage (95% CI)
2001–2004	7.1 (6.5–7.8)	3.2 (2.7–3.8)	10.3 (9.4–11.3)
2003–2006	7.4 (6.7–8.1)	2.8 (2.2–3.6)	10.2 (9.3–11.2)
2005–2008	7.7 (6.9–8.5)	2.9 (2.4–3.6)	10.6 (9.6–11.6)
2007–2010	7.9 (7.1–8.7)	3.2 (2.7–3.7)	11.1 (10.1–12.2)
2009–2012	8.1 (7.4–8.9)	3.2 (2.6–3.8)	11.3 (10.3–12.3)
2011–2014	8.7 (8.1–9.4)	2.7 (2.3–3.3)	11.5 (10.7–12.3)
2013–2016	9.4 (8.6–10.2)	2.6 (2.2–3.1)	12.0 (11.1–12.9)
2015–2018	9.8 (9.0–10.7)	2.9 (2.4–3.4)	12.7 (11.6–13.8)
2017–2020	10.1 (9.2–10.9)	3.1 (2.6–3.8)	13.2 (12.1–14.4)

Subsequently when we peek into the causes of type 2 diabetes (as per WHO, type 2 is the most common type of diabetes), the same lifestyle factors pop up:

· Overweight

· Obesity

· Physical Inactivity

· Insulin resistance (which is in turn caused by Obesity)

· Genes and family history

Source of information - https://www.niddk.nih.gov/health-information/diabetes/overview/symptoms-causes#type

R&D Spendings of Major Pharma companies globally

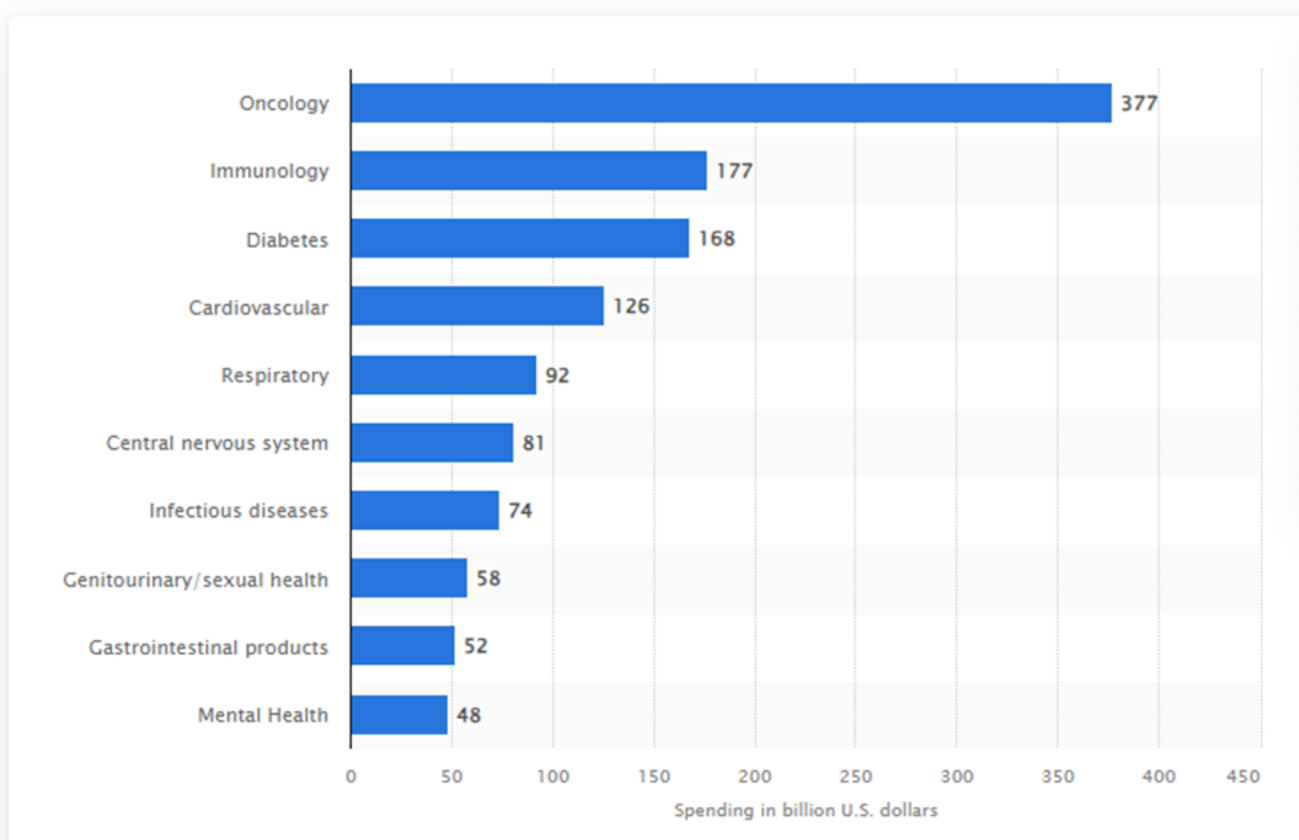
Below is a snapshot of the R&D Spending focus of the two most valuable healthcare companies globally:

		2024	2023	2022	2021	2020	2019	Median Growth
Company 1	Revenue	258,003	232,261	176,954	140,800	126,946	122,021	
	R&D Expense	36,246	31,029	23,287	17,199	15,462	14,220	
	Growth	17%	33%	35%	11%	9%		17%
	% of Revenue	14%	13%	13%	12%	12%		13%
	Diabetes and Obesity Care	215,098	156,412	121,597				
	% Revenue	93%	88%	86%				88%
	Rare Disease	17,163	20,542	19,203				
	% Revenue	7%	12%	14%				12%

		2024	2023	2022	2021	2020	2019	Median Growth
Company 2	Revenue	38,923	34,124	28,541	28,318	24,540	22,320	
	R&D Expense	10,206	9,313	7,191	6,931	5,976	5,595	
	Growth	10%	30%	4%	16%	7%		10%
	% of Revenue	26%	27%	25%	24%	24%		25%
	Diabetes and Obesity Care	19,668	14,465	13,188				
	% Revenue	58%	51%	47%				51%
	Oncology	6,658	5,666	5,741				
	% Revenue	20%	20%	20%				20%
	Immunology	3,798	3,345	3,361				
	% Revenue	11%	12%	12%				12%
	Neuroscience	2,879	1,546	3,361				
	% Revenue	8%	5%	12%				8%

So, as you can see, most of the research and development budget for the biggest pharma companies are focused on the therapeutic area – “Diabetes and Obesity Care”.

As per Statistica, the Diabetes and Cardiovascular diseases appear at #3 and #4 in the list of projected top therapy area spending worldwide by 2027:



Diabetes Drug Market and Drug Classes

As per fortune business insights – “The global diabetes drugs market size was valued at USD 79.25 billion in 2023 and is projected to grow from USD 89.39 billion in 2024 to USD 153.98 billion by 2032, exhibiting a CAGR of 7.0% during the forecast period (2024-2032).”. And as per the same research – “The growing prevalence of diabetes ,

especially type 2 diabetes , and the increasing demand for effective drug therapies for treating the disease are some factors anticipated to upsurge the market growth during the forecast period.”.

Thus, far we have observed, one of the biggest fallouts of the sumptuous and sedentary lifestyle is cardiovascular disease and diabetes. And diabetes being one of the root causes of cardiovascular disease, curing diabetes globally is a critical component of R&D expenditure for the global healthcare sector.

There are primarily four major drug classes used to attack Diabetes, which are:

a.) Insulin

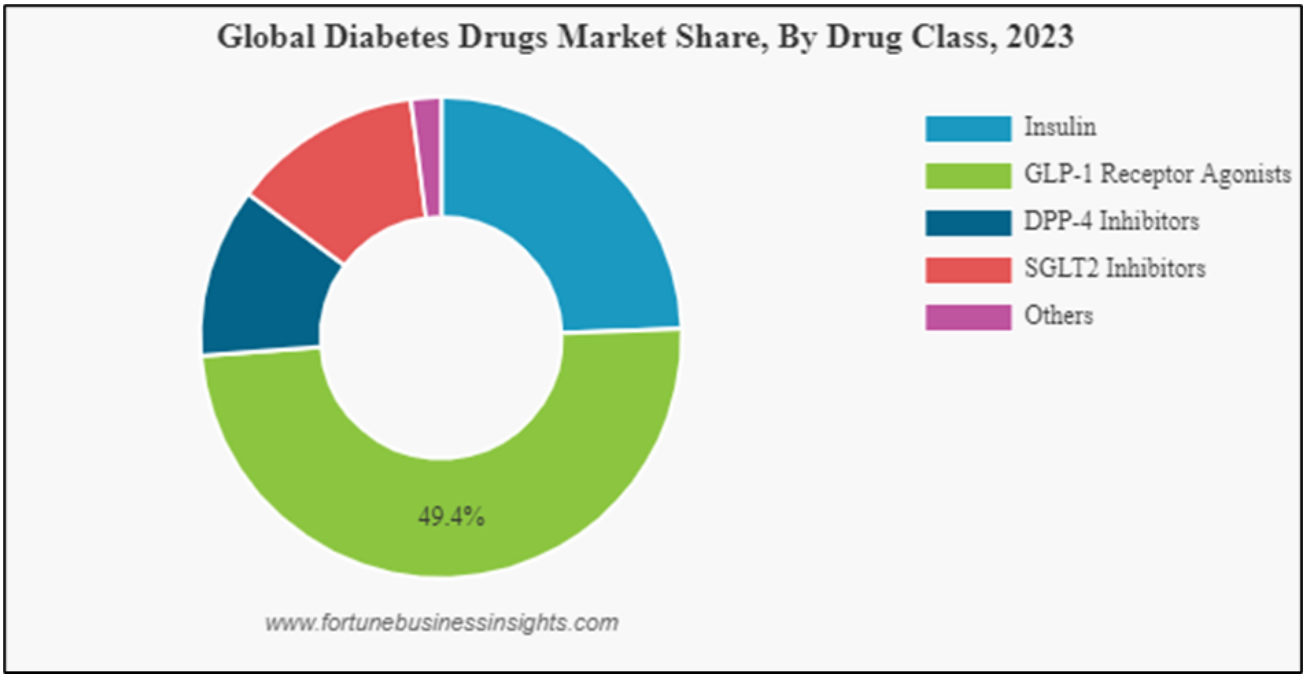
b.) GLP-1 Receptor Agonists

c.) DPP-4 Inhibitors

d.) SGLT2 Inhibitors

e.) Others

We are very used to seeing our parents and uncles taking insulin shots directly in the stomach. But the trend started to reverse over the past few years. Currently, as of 2023, it is not insulin, but GLP-1 Receptor Agonists drug class holds the dominant market share.



Currently GLP-1 Receptor Agonists Market is valued at USD 49.3 billion. It is expected to grow at a CAGR of 11% during the period from 2024-2035.

What is GLP-1 Receptor Agonists and How does it work?

GLP Stands for Glucagon-Like Peptide .

Glucagon-like Peptides are proteins produced in the Intestine and act on Pancreas.

GLP-1 Agonists are drug classes that mimic GLP.

When Pancreas receives Glucagon like Peptide, it performs the following –

Increases insulin secretion Decreases glucagon production.

Glucagon is responsible for the breakdown of Glycogen in liver and production of Glucose, thus reduction in glucagon production reduces glycogen breakdown activity in liver.

Reduces Gluconeogenesis.

This is the process of production of glucose from amino acids and fatty acids.

The above 3 functionalities are performed by the traditional Insulin drug class too. But GLP-1 Receptor Agonist additionally has the following effects too:

Affects the hypothalamus directly causing appetite suppression. Affects Gut, by delaying Gastric emptying.

Since Gastric emptying is delayed it reduces secretion of Ghrelin hormone, which causes a reduced feeling of hunger. Basically, when Ghrelin hormone is produced, we feel hungry.

It also increases Leptin hormone, which increases the feeling of satiation

Thus overall, GLP-1 Agonists act in reducing obesity and, the need to satisfy constant hunger and blood glucose levels.

I also asked ChatGPT – “Can you please explain like I am 5-year-old - How does GLP-1 Receptor works?”. Below was the response, and I feel, this is a more helpful response 😊

> “Imagine you have a tiny superhero inside your body called GLP-1. This superhero has a special way of talking to your body. When you eat food, GLP-1 comes out and tells your body, “Hey, it’s time to slow down!”

Here’s what it does:

Talks to Your Stomach: It tells your stomach, “Let’s keep the food here a little longer,” so you feel full and don’t get hungry too quickly. Talks to Your Pancreas: It says, “Let’s make some insulin!” Insulin is like a key that helps sugar from your food get into your cells, where it’s used for energy. Tells Your Brain: It also sends a message to your brain, “You’re not hungry anymore,” so you don’t eat too much.

So, GLP-1 is like a helpful superhero that keeps everything in balance after you eat!

> “

A Quick look at DPP-4 Inhibitors and SGLT2-Inhibitors

DPP-4 inhibitors

DPP-4 inhibitors, or dipeptidyl peptidase-4 inhibitors restrict or as the name suggests – inhibit DPP-4 enzyme.

What is the function of DPP-4 enzyme? Well, in very simple terms, DPP-4 enzyme restricts GLP-1’s action. Thus, by restricting DPP-4 enzyme’s action DPP-4 inhibitors in turn facilitate more GLP-1 secretion.

However, as far as I have understood, DPP-4 inhibitors would work the best way if blood sugar level were the biggest concern and weight loss is not a big concern.

As per NCBI research, the following conclusion is derived from a study of DPP-4 inhibitors vs GLP-1 Agonist Receptors – “GLP-1RAs provide superior glycemic control and weight

loss vs. DPP-4 inhibitors in patients with T2D. DPP-4 inhibitors may sometimes be preferred to a GLP-1RA if weight is not a concern, oral administration is a desirable feature or when a GLP-1RA cannot be tolerated."

SGLT2-Inhibitors

SGLT2 or Sodium-Glucose Cotransporter-2 inhibitors inhibit a special protein in the kidney called SGLT-2 (Sodium Glucose Co-Transporter -2). SGLT2 helps kidney reabsorb the sugar (glucose) back into the blood after it is filtered out by kidneys.

Thus, by inhibiting SGLT2, reabsorption of glucose in kidney is reduced using SGLT2 inhibitors, and excess glucose is flushed out via urine.

As per goodrx.com – "GLP-1 agonists, such as Ozempic (semaglutide), promote greater weight loss and blood glucose reduction. SGLT2 inhibitors, such as Jardiance (empagliflozin), may be a better option if you also have heart failure or chronic kidney disease."

My Observations and Inferences

When I tie all the loose ends together, I do see a trend driven by – a.) Obesity b.) Unhealthy Diet c.) Sedentary Lifestyle d.) Lack of Quality Sleep, which manifests in the form of high occurrences of Cardiovascular disease, Diabetes, and Stroke in turn results in high R&D Expenditure in the field of Diabetes and Obesity Care and a Spike in the uptake of GLP-1 Receptor Agonist kind of Drug classes.

Why do I think this assortment of occurrences is occurring?

According to me, health and lifestyle are closely correlated to a long-term mindset. Normally I have observed that people who create a 10–15-year vision ahead of them are not only good in terms of financial planning, but they also adopt a better lifestyle. If we try to piece together – these people think – "If I have to achieve a certain financial/professional/academic goal 10-15 years from now, I need to not only enjoy the journey but also enjoy the fruits of the journey 10-15 years hence"

But today's world is designed in such a way that it is extremely difficult to resist those instant gratifications. The temptations to be instantly swarmed with likes and loves on Facebook, the pleasure of anonymously supporting or abusing a successful celebrity in X sets into action a lifestyle that also craves the sweet pastry lying in the refrigerator and a plate of chicken nuggets little later, just to neutralize the palate.

The waterfall model has converted to agile, now sprints are getting shorter too. And we are thinking – "Let us first outlive this project and save my job, then we will look beyond", and thus end up binging on food and Netflix to escape the stress.

If you are thinking, what suggestions do I have – I do not have any. As I am not an expert.