HC/TN
HealthCareTN

Latest Innovative Technologies and Treatments in Diabetes Care

December 4, 2024

AGENDA

- **Welcome –** Phil Belcher, CEO, HealthCareTN
- **Innovative Technologies for Effective Blood Glucose Management**
  - David Hines, Executive Director, Benefits - Metro Nashville Public Schools (MNPS)
- **HCTN Diabetes Prevention and Management Pilot Opportunities**
  - Trinette Small, VP of Membership Engagement & Strategic Partnerships – HealthCareTN
- **Innovations in Diabetes – Past, Present, and Future**
  - Bobbi B Bentz, MHA, MPH, PhD, Associate Director, Health Outcomes and Medical Engagement - Eli Lilly and Company
- **Closing Comments -** HealthCareTN

Leveraging Innovative Technology in Diabetes Management

Harnessing Advances in Glucose Monitoring to Achieve Better Outcomes

David Hines, Executive Director of Benefits
Metro Nashville Public Schools

Challenges of Diabetes

Diabetes Prevalence Causes Substantial Health and Economic Burden[1,5]

In the United States, **over 38 million** people have diabetes[2,3]

The main types of diabetes are:

Type 1 diabetes, affecting

~2 million people[2]

Type 2 diabetes, affecting

~36 million people[2-4]

In addition, **1 in 3** Americans:

- Have prediabetes[2,3]
- Will develop diabetes sometime in their lifetime[6]

Diabetes is the most expensive chronic condition in the US:

$1 out of every $4

of US healthcare costs is spent on caring for people with diabetes[5,6]

Diabetes also costs **over $100 billion** in lost productivity per year*[,5-7]

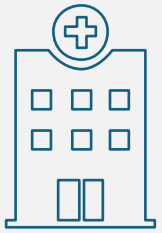
*Value adjusted for inflation in medical care cost from 2017 to 2024 based on database from the US Bureau of Labor Statistics.

References: 1. Koyama AK, et al. Trends in lifetime risk and years of potential life lost from diabetes in the United States, 1997–2018. *PLoS One*. 2022;17(5):e0268805. **2.** American Diabetes Association. Statistics About Diabetes. Accessed June 26, 2024. https://diabetes.org/about-us/statistics/about-diabetes. **3.** Centers for Disease Control and Prevention. National Diabetes Statistics Report. Accessed June 28, 2024. https://www.cdc.gov/diabetes/php/data-research/. **4.** Centers for Disease Control and Prevention. About Type 2 Diabetes. Accessed June 26, 2024. https://www.cdc.gov/diabetes/about/about-type-2-diabetes.html. **5.** American Diabetes Association. *Diabetes Care*. 2018;41(5):917-928. **6.** Centers for Disease Control and Prevention. Health and Economic Benefits of Diabetes Interventions. Accessed June 28, 2024. https://www.cdc.gov/nccdphp/priorities/diabetes-interventions.html. **7.** Federal Reserve Bank of Saint Louis. Research Consumer Price Index: Medical Care. Accessed June 28, 2024. https://fred.stlouisfed.org/series/CPIEMEDCARE.

Poorly Controlled Diabetes Can Lead to a Broad Range of Serious Complications[1,2]

ED Visits

~17 million visits reported with diabetes as a listed diagnosis[*,1]



Hospitalizations

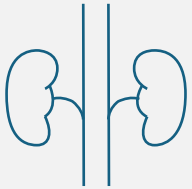
~8 million hospitalizations reported with diabetes as a listed diagnosis[1]

Cardiovascular Complications

Adults with diabetes are **2x** as likely to have heart disease or a stroke as those who do not have diabetes[2]

Kidney Disease

Diabetes is the **leading cause** of **end-stage kidney disease**[1]



Vision Disability

Diabetes is the **leading cause** of **new cases of blindness** in adults[1]

Gestational Diabetes

~50% of women who develop diabetes in pregnancy go on to develop type 2 diabetes[3]

Effective blood glucose management can reduce the risk of eye disease, kidney disease, and nerve disease by 40%[4]

*ED = emergency department.

References: 1. Centers for Disease Control and Prevention. National Diabetes Statistics Report. Accessed June 28, 2024. https://www.cdc.gov/diabetes/php/data-research/. **2.** Centers for Disease Control and Prevention. Your Heart and Diabetes. Accessed July 12, 2024. https://www.cdc.gov/diabetes/diabetes-complications/diabetes-and-your-heart.html. **3.** Centers for Disease Control and Prevention. About Gestational Diabetes. Accessed June 28, 2024. https://www.cdc.gov/diabetes/about/gestational-diabetes.html. **4.** Centers for Disease Control and Prevention. Health and Economic Benefits of Diabetes Interventions. Accessed June 28, 2024. https://www.cdc.gov/nccdphp/priorities/diabetes-interventions.html.

Managing Glucose Levels Is an Ongoing Challenge: Nearly Half of U.S. Adults With Diabetes Are Not at the A1C Goal of <7%[1]

42 Factors That Affect Blood Glucose[2]

"If you really look at it, having diabetes means you have an additional job to attend to every day."[3]

Aus Alzaid, MD. *Diabetes Technol Ther*. 2014;16(8):542–544.

Food
1. Carbohydrate quantity
2. Carbohydrate type
3. Fat
4. Protein
5. Caffeine
6. Alcohol
7. Meal timing
8. Dehydration
9. Personal microbiome

Medication
10. Medication dose
11. Medication timing
12. Medication interactions
13. Steroid administration
14. Niacin (Vitamin B3)

Biological
15. Insufficient sleep
16. Stress and illness
17. Recent hypoglycemia
18. During-sleep blood sugars
19. Dawn phenomenon
20. Infusion set issues
21. Scar tissue and lipodystrophy
22. Intramuscular insulin delivery
23. Allergies
24. A higher glucose level
25. Periods (menstruation)
26. Puberty
27. Celiac disease
28. Smoking

Activity
29. Light exercise
30. High-intensity and moderate exercise
31. Level of fitness/training
32. Time of day
33. Food and insulin timing

Environmental
34. Expired insulin
35. Inaccurate blood glucose reading
36. Outside temperature
37. Sunburn
38. Altitude

Behavioral & Decision-making
39. Frequency of glucose checks
40. Default options and choices
41. Decision-making biases
42. Family relationships and social pressures

References: 1. The CDC estimates that 47.4% of U.S. adults with diagnosed diabetes had an A1C value of 7.0% or higher. Centers for Disease Control and Prevention. National Diabetes Statistics Report. Accessed July 12, 2024. https://www.cdc.gov/diabetes/php/data-research/index.html. **2.** Brown A. Poster Now Available: 42 Factors That Affect Blood Glucose. Accessed June 28, 2024. https://diatribe.org/diabetes-management/poster-now-available-42-factors-affect-blood-glucose. **3.** Alzaid A. There is a missing ingredient in diabetes care today. *Diabetes Technol Ther.* 2014 Aug;16(8):542-544.

Diabetes Management at Metro Nashville Public Schools

METRO NASHVILLE PUBLIC SCHOOLS

41st largest district
(88,000 students)

Teacher's health plan
(9,200 active and retired teachers)

Support staff covered by Metro Nashville Government
(4,000 active employees)

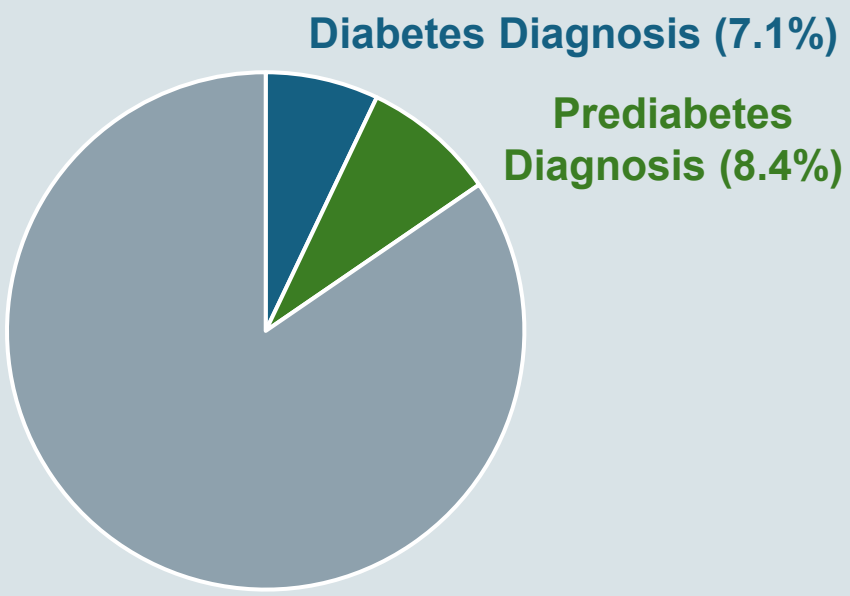
With a core belief that healthy employees are better employees

Source: Metro Nashville Public Schools

Diabetes Patients Are 7% of the MNPS Population With Average Costs >2.5 Times All Others

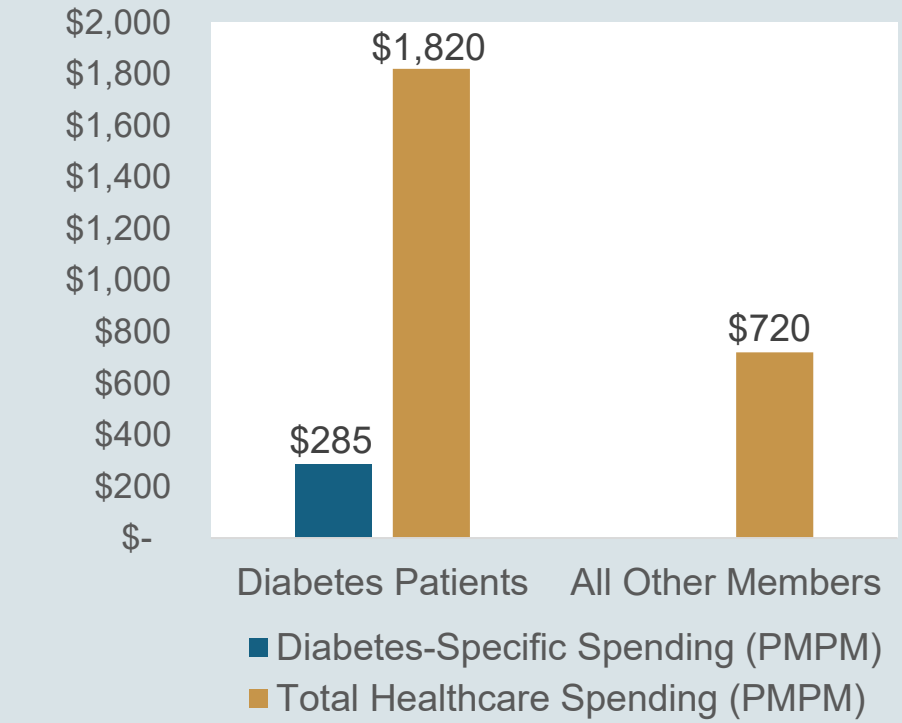
Share of the MNPS Population in 2023

Members Ages 18-64



Average Healthcare Spending in 2023

Members Ages 0-64

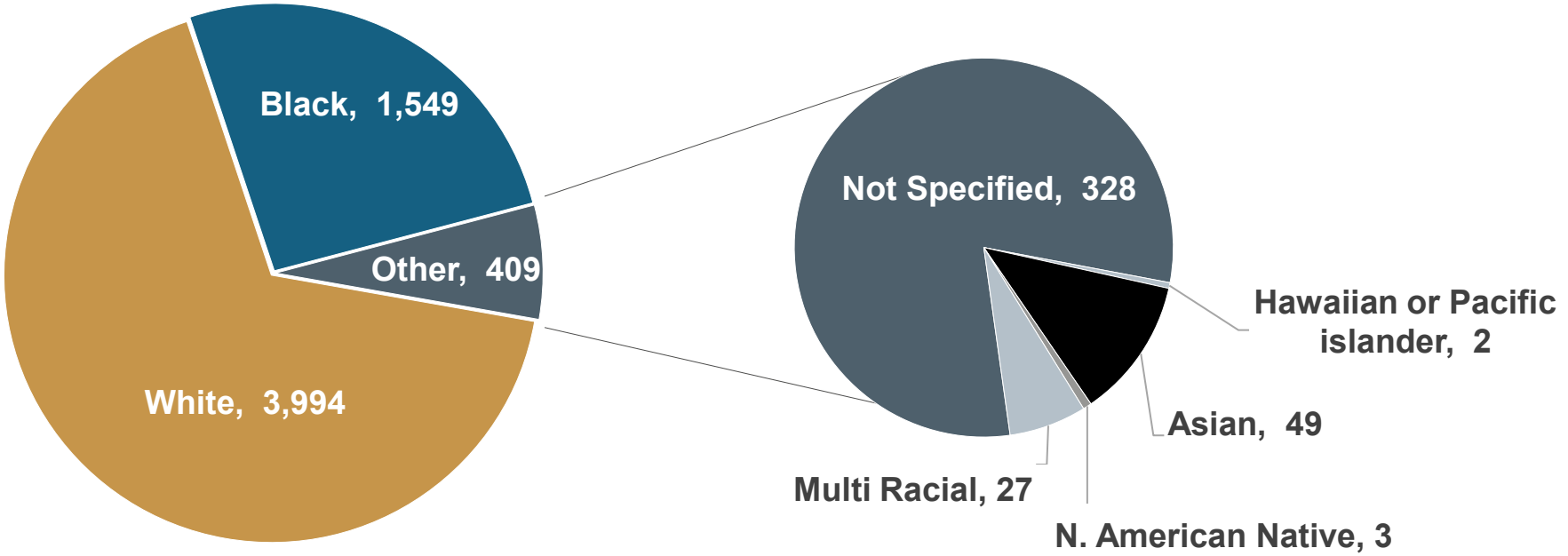


Source: Benegration (MNPS Data Warehouse) analysis, May 2024

MNPS Has Placed a Focus on Addressing Gaps in Care Related to Employee Demographics

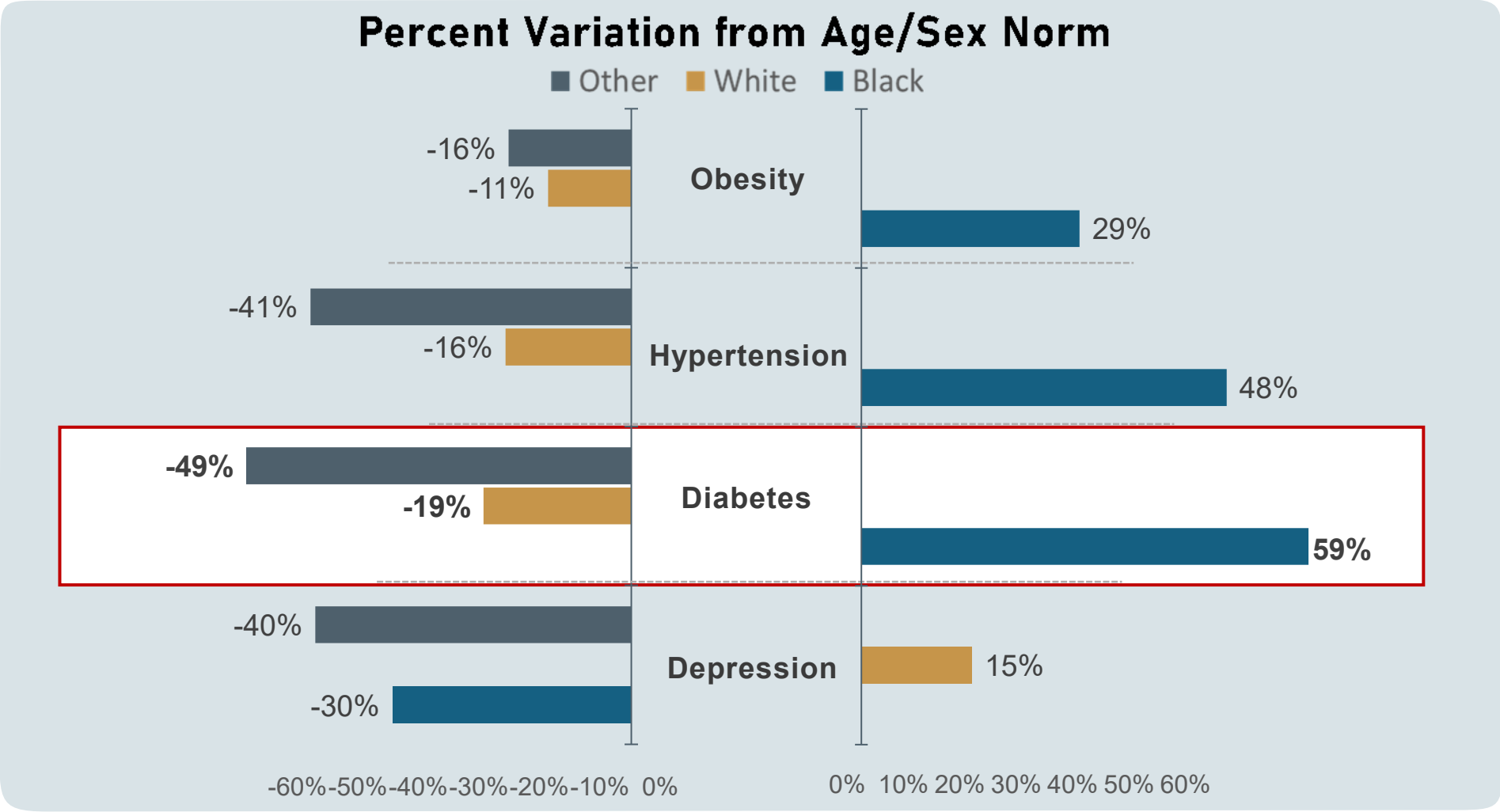
Subscribers by Race

2022 MNPS Active Certificated Employee Demographics



Source: Benegration (MNPS Data Warehouse), November 2022

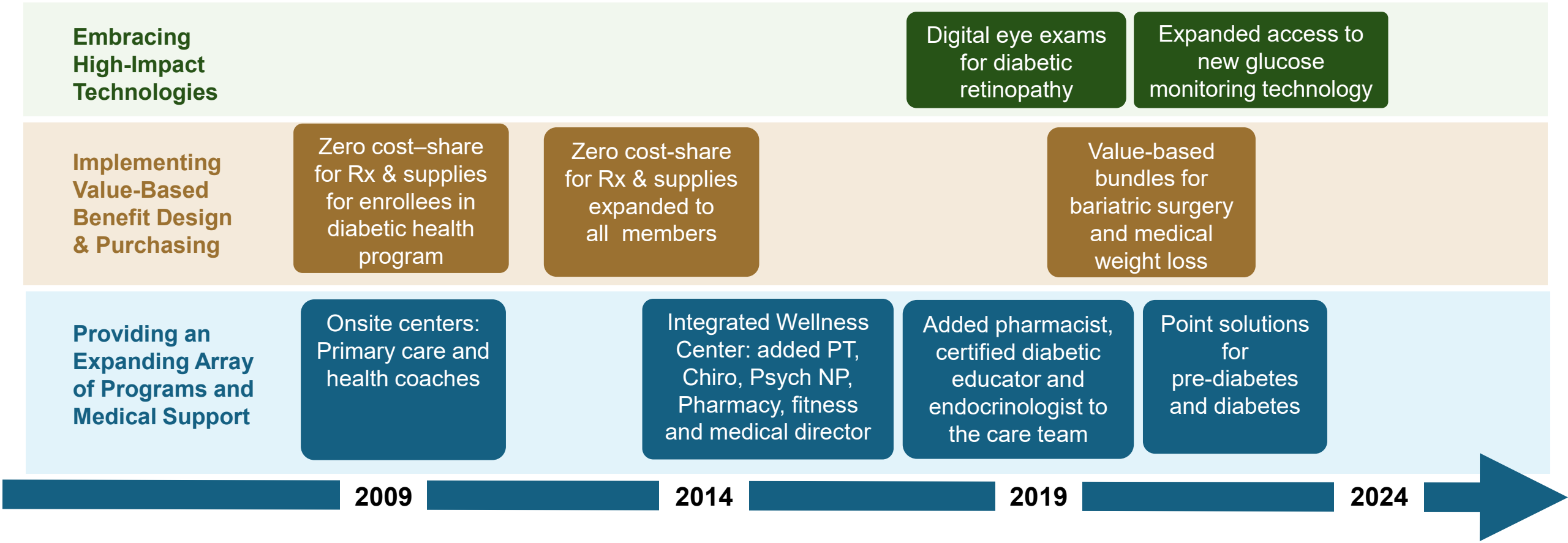
Employee Demographics Have an Impact on Diabetes and Its Common Comorbidities



Source: Benegration (MNPS Data Warehouse), November 2022

Over the Past 15 Years, MNPS Has Established Many Layers of Support for Members with Diabetes

Key Milestones of the MNPS Diabetes Strategy



Harnessing Advances in Glucose Monitoring

Continuous Glucose Monitoring (CGM) Provides a Step-Change Advance Over Conventional Measurement Devices

Conventional blood glucose measurement

- **Via painful, inconvenient fingersticks**
- Impractical, user error-prone, and not very discreet
- **Only snapshots** and no trends

Continuous glucose monitoring

- ✓ **Continuous, automatic** measurement via sensor
- ✓ **No painful fingersticks*** required for treatment decisions
- ✓ **Automatic transmission** of the glucose value to display device (phone or receiver)

*If your glucose alerts and readings from a CGM do not match symptoms or expectations, use a blood glucose meter to make diabetes treatment decisions.

Common Features of CGM Systems Enable More Effective Glucose Management

Discreet, easy-to-use wearable device *that simplifies the patient experience*

Works through a tiny sensor *inserted under the skin (in abdomen or arm)*

Transmits information wirelessly to a phone or monitor as often as every 5 minutes, 24/7 *to support decision-making in real time*

Translates readings into easy-to-follow data and insights *that promote healthier eating patterns and simplified diabetes management routines*

Automatic reporting and documentation of the glucose values *to enable tracking and analysis of trends over time*

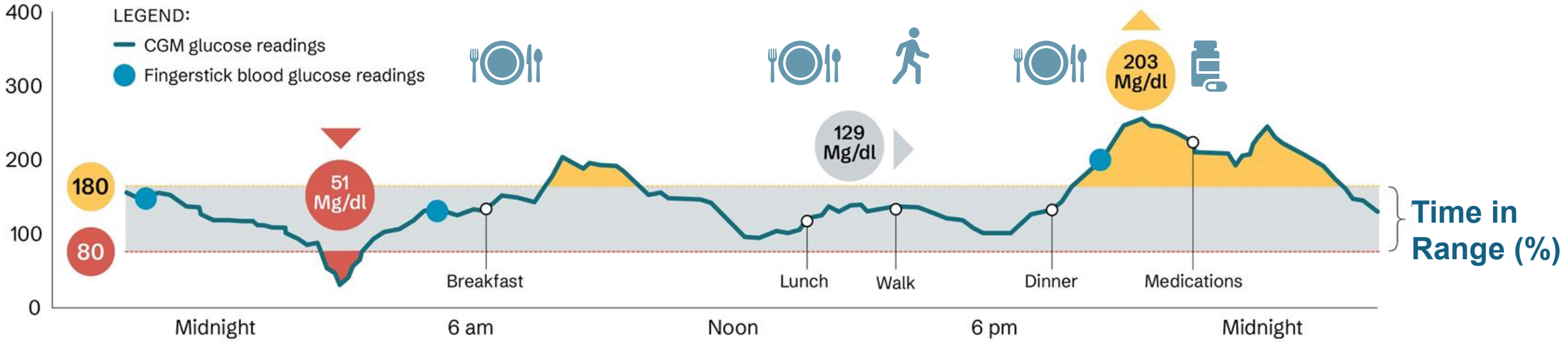
Alerts that can prompt immediate action *to help prevent periods of extremely high or extremely low blood glucose levels*

Ability to allow friends and family to view glucose information *and provide support to the patient*

Ability to share data with smart watches, insulin pumps and digital health apps *to further enhance glucose management*

Source: Dexcom G7 User Guide, 2024.

CGM Readings, Trend Information, Alarms and Other Feedback Help Patients Adjust Their Behaviors to Improve Time In Range[1]



References: 1. Dexcom T2D pilot study. Similar observations using Dexcom CGM have been published in: Vigersky RA, et al. Short- and long-term effects of real-time continuous glucose monitoring in patients with type 2 diabetes. *Diabetes Care.* 2012 Jan;35(1):32-38; Ehrhardt NM, et al. The effect of real-time continuous glucose monitoring on glycemic control in patients with type 2 diabetes mellitus. *J Diabetes Sci Technol.* 2011 May;5(3):668-75; Cox DJ, et al. Continuous glucose monitoring in the self-management of type 2 diabetes. *Diabetes Care.* 2016 May;39(5):71-73.

MNPS and Other Employers Have Identified Several Advantages of CGMs[1]

Better health outcomes including improved TIR and A1C levels[2]

No fingersticks can mean no need to step away from work to check glucose levels*

Increased patient engagement in diabetes management[3]

Better glucose control,[4,5] which can be helpful for workers in **safety-sensitive positions**

Healthcare cost savings through reduced ED visits and hospitalizations[6]

*If your glucose alerts and readings from a CGM do not match symptoms or expectations, use a blood glucose meter to make diabetes treatment decisions.

References: 1. Comments of employee health benefits decision-makers at large employers that attended Employer Advisory Board meetings hosted by Gallagher Employer Research & Insights, May 11, 17 and 23, 2023. 2. Karter AJ, et al. Association of real-time continuous glucose monitoring with glycemic control and acute metabolic events among patients with insulin-treated diabetes. *JAMA*. 2021 Jun 8;325(22):2273-2284. 3. Miller EM. Using continuous glucose monitoring in clinical practice. *Clin Diabetes*. 2020 Dec;38(5):429–438. 4. Visser MM, et al. Comparing real-time and intermittently scanned continuous glucose monitoring in adults with type 1 diabetes (ALERTT1): a 6-month, prospective, multicentre, randomised controlled trial. *Lancet.* 2021 Jun 12;397(10291):2275-2283. 5. Visser MM, et al. Effect of switching from intermittently scanned to real-time continuous glucose monitoring in adults with type 1 diabetes: 24-month results from the randomised ALERTT1 trial. *Lancet Diabetes Endocr*. 2023 Feb;11(2):96-108. 6. Isaacson B, et al. Demonstrating the clinical impact of continuous glucose monitoring within an integrated healthcare delivery system. *J Diabetes Sci Technol*. 2022 Mar;16(2):383-389.

MNPS Has Taken Action to Address Multiple Barriers to Appropriate Utilization of CGMs

Potential Barriers	Steps MNPS Has Taken to Address the Barriers
Cost	– **Provide CGMs at no charge** ~~to participants in employer-sponsored diabetes management programs~~ ✓ **Apply value-based benefit design approaches to CGMs (zero/~~low~~ member cost share)**
Coverage	✓ **Add pharmacy benefit coverage in addition to medical benefit (DME) coverage**
Criteria	✓ **Remove ~~or update~~ any prior authorization criteria that are overly restrictive**
Awareness	✓ **Integrate CGM data into diabetes health coaching protocols in worksite clinics, diabetes management programs, etc.** ✓ **Inform employees about CGM benefit design changes, etc.**

Results: MNPS Diabetes Patients Achieved Significant Improvements in Glucose Management with CGMs

Clinically Meaningful Improvements in A1C and Quality Measures[1]

Results for employees with Type 2 diabetes where MNPS has A1C data pre- and post-CGM use

more participants met the **ADA goal** of **A1C <7.0%**

more participants met the **HEDIS goal** of **A1C <8.0%**

- **T2D noninsulin** (n=57): **7.6%** → **6.8%***
- **T2D insulin** (n=84): **8.7%** → **7.9%***

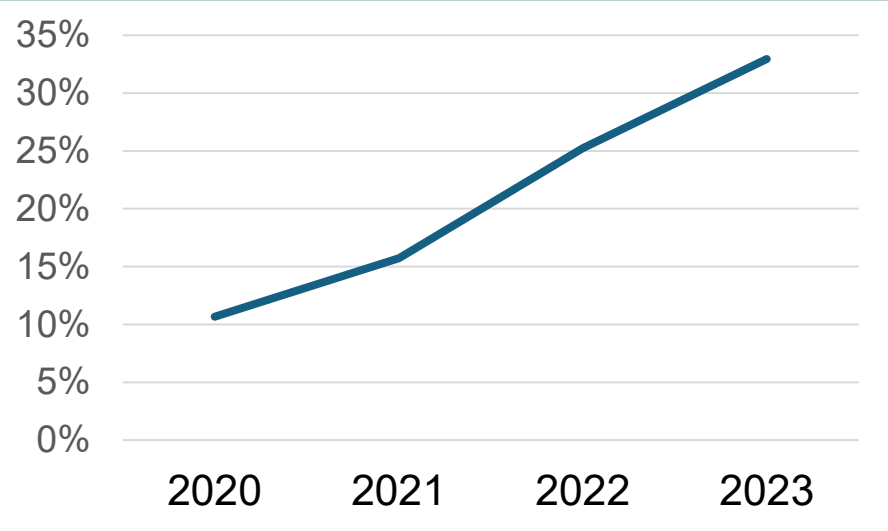
*P<.01

References: 1. Thomas R, et al. Improvements in glycemic control in people with diabetes in an employer health initiative offering continuous glucose monitors (CGMs) as a pharmacy benefit. Poster presented at: The Academy of Managed Care Pharmacy 2024 Annual Meeting; April 15-18, 2024; New Orleans, LA.

Results: MNPS Has Accelerated Adoption of CGMs While Successfully Bending the Cost Curve for Diabetes

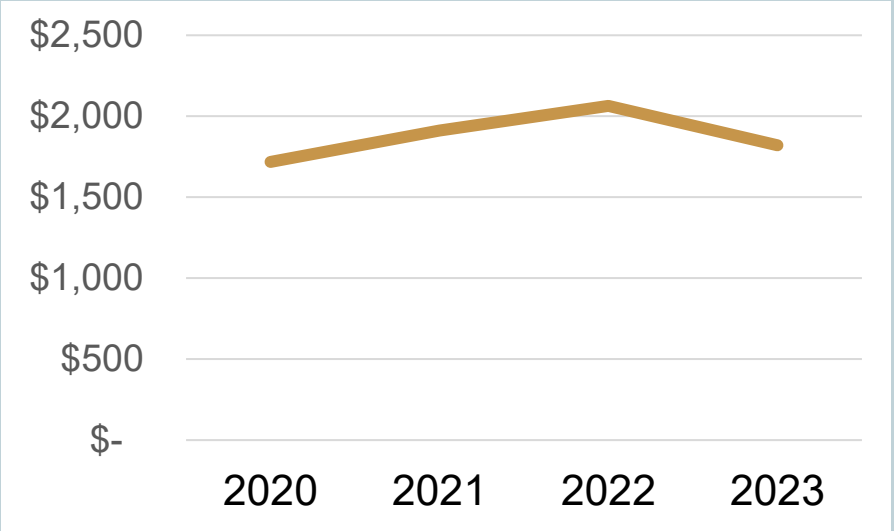
Increase in Appropriate Utilization of CGMs

Share of diabetes patients ages 18-64 in the MNPS population that are using CGMs



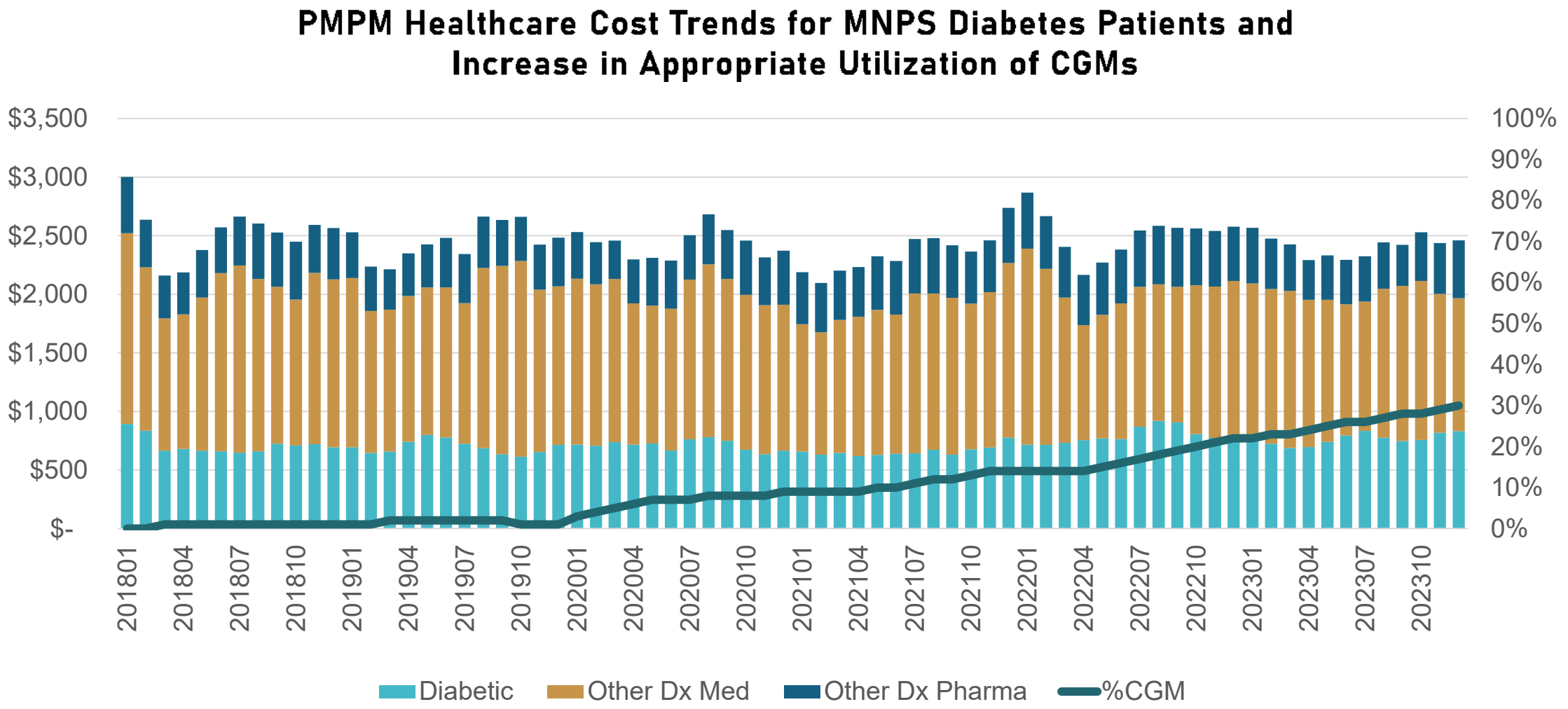
PMPM Healthcare Cost Trends for Diabetes Patients

Average annual healthcare costs for all diabetes patients in the MNPS population



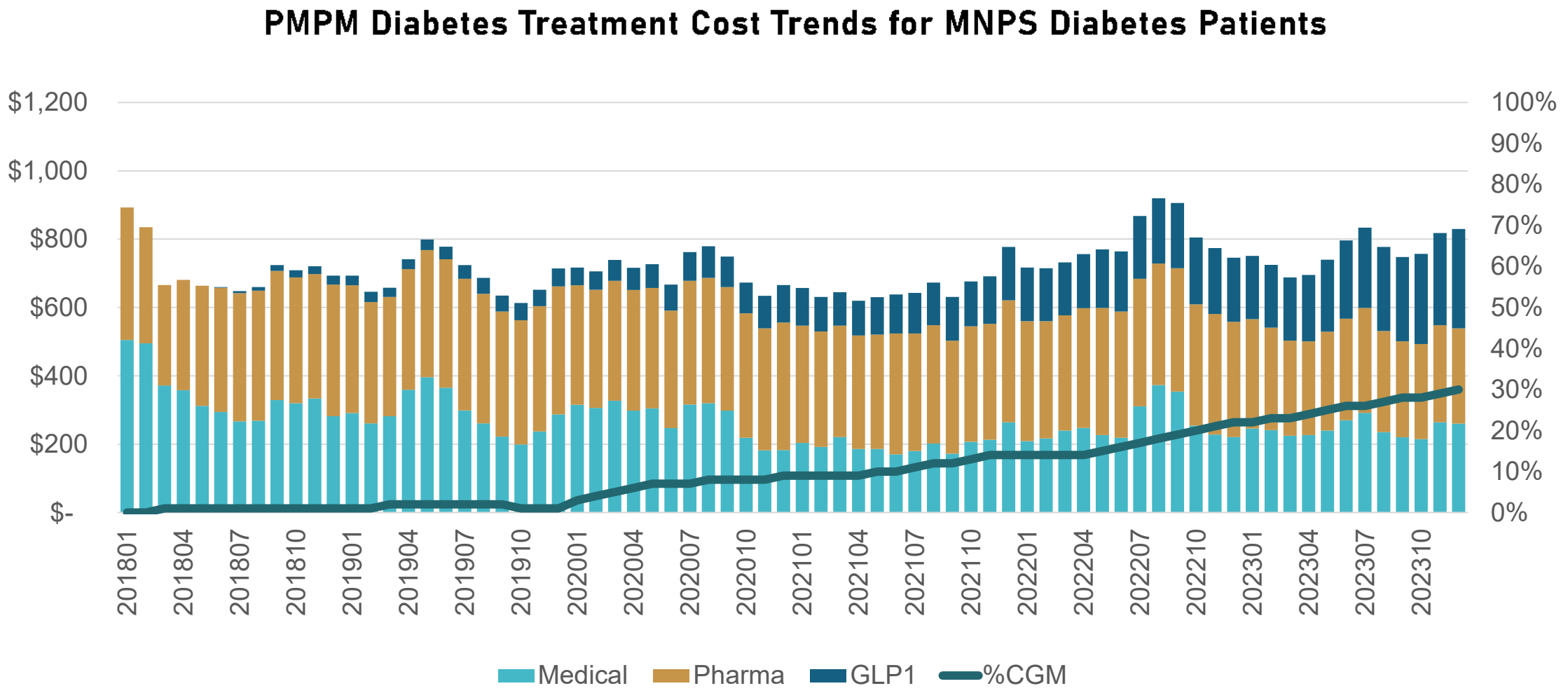
Source: Benegration (MNPS Data Warehouse) analysis, May 2024

Results: MNPS Has Accelerated Adoption of CGMs While Successfully Controlling Costs for Diabetes Patients



Source: Benegration (MNPS Data Warehouse) analysis, May 2024

Other than GLP-1 Medications, Per-Patient Costs of Diabetes Treatments Have Been Falling Over Time



Source: Benegration (MNPS Data Warehouse) analysis, May 2024

Opportunities for Action

Employers Have Multiple Opportunities to Improve Employee Access to CGMs

Review the organization's CGM benefit design and make any changes needed to:

Cost
- Reduce or eliminate out-of-pocket costs

Coverage
- Provide coverage through the pharmacy benefit

Criteria
- Remove or simplify prior authorization criteria

Integrate CGMs into employer-sponsored diabetes management programs:

Awareness
- Align CGM criteria and benefit design with the program offerings
- Incorporate CGM data into coaching guidance

For employers with onsite clinics:

Awareness
- Align the CGM criteria and benefit design with clinic-based offerings
- Educate clinic staff on CGMs

Questions?

Want to learn more about CGMs?

Scan this code:

Please join us at

Slido.com

and enter code: 31154

to answer 3 audience questions.

Which of the following was the most important key takeaway for you from the presentation?

ⓘ Start presenting to display the poll results on this slide.

Which key point from the presentation provided you with the most insight?

ⓘ Start presenting to display the poll results on this slide.

After hearing the presentation, which of the following next steps are you considering? (Select all that apply.)

ⓘ Start presenting to display the poll results on this slide.

Questions?

Want to learn more about CGMs?

Scan this code:

HCTN Pilot Opportunities

Trinette Small - HealthCareTN

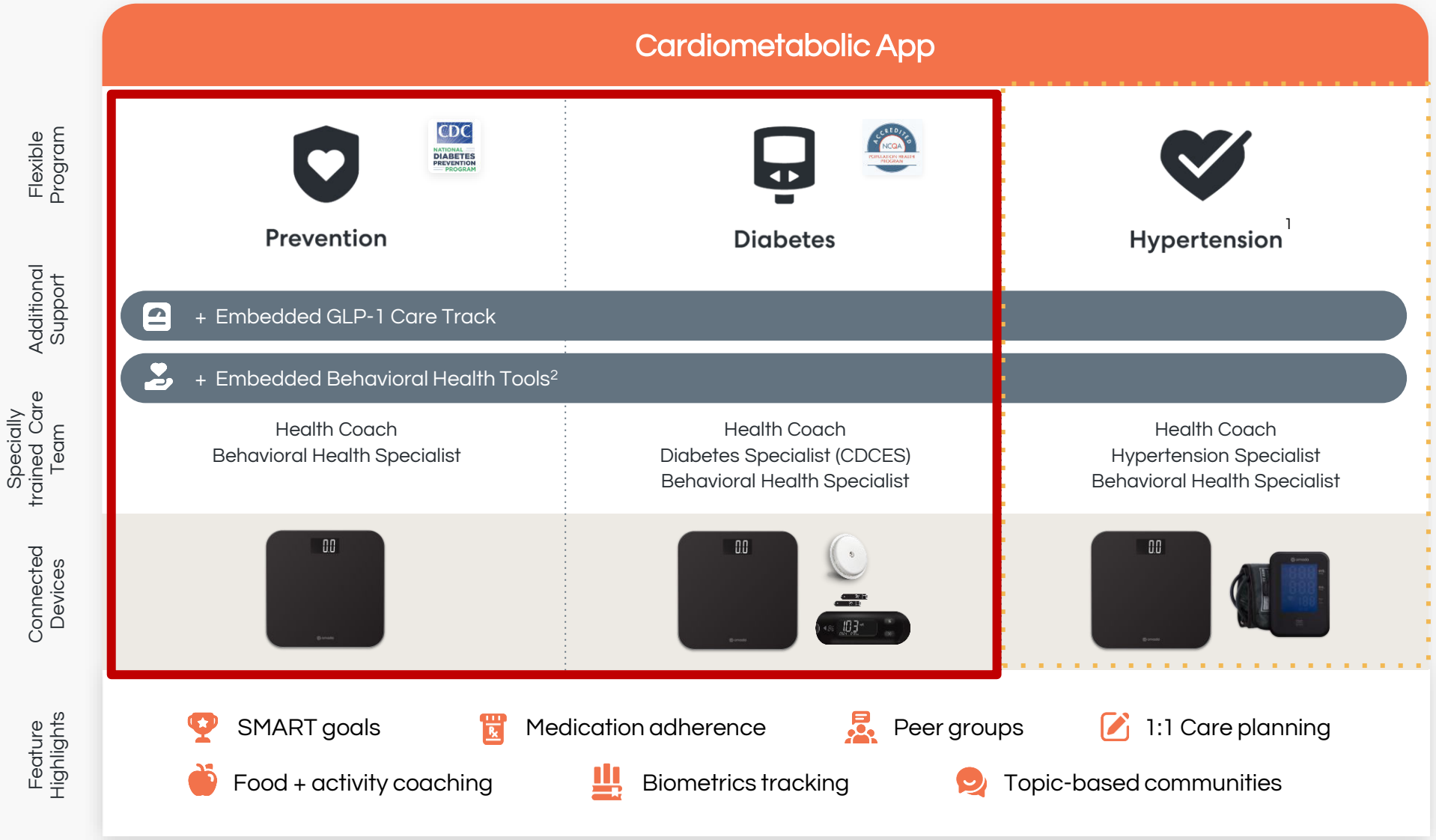
Omada & HCTN Pilots
A Partnership Continually Committed to Excellence

Free Pilots to TN organizations since April 2023

Enrolled Members

Available Pilots for 2025

The Omada Suite | Multi-condition platform for key member needs



1: NCQA population health accreditation for Diabetes + Hypertension program

2: Behavioral Health Specialists operate behind the scenes with other members of the care team and do not have a member-facing role

Members see improved outcomes across the cardiometabolic suite

	Clinical Outcomes
Prediabetes	**5.5%** 1yr Weight ↓ **58%** shifted to normal range A1C ↓
Type 2 Diabetes	**2%** A1C ↓ (base ≥ 8%) at 12 months
Hypertension	Stage 2: SBP ↓ by **10.3** mmHg DBP ↓ by **7.5** mmHg at 12 mo

Methodology and data from Omada BOB, or from Omada studies available at https://resourcecenter.omadahealth.com/peer-reviewed-studies

HCTN & Omada Health Pilot

HCTN & Omada celebrate pilot success as measured through Enrollment, Engagement & Outcomes trends.

Enrollment

- **Total Enrollments: 220**
  - Diabetes Prevention (NDPP): 35
  - Diabetes Management (DSMES): 12
  - Hypertension: 141

Engagement & Outcomes

- **94% early program engagement,** highlighted by Connected Scale and Blood Pressure Monitor utilization rates
- **1,100 pounds lost and counting,** with 32% of participants reporting at least 5% weight loss at Month 12
- Significant blood pressure reduction, including **9 mmHg reduction in Systolic Blood Pressure (SBP)** and **4 mmHg reduction in Diastolic Blood Pressure (DBP)** for Stage 2 Hypertension participants.

Want to learn more?

Connect with HCTN & Omada:

- Become an HCTN Member today
- Request a business case
- Schedule a demo
- Take advantage of one of the two additional pilot opportunities available for 2025

Innovation in Diabetes: Past, Present, and Future

HealthCareTN, December 4, 2024

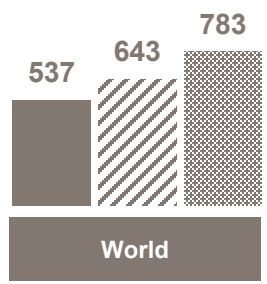
Bobbi Bentz, MHA, MPH, PhD
Health Outcomes Liaison, Eli Lilly

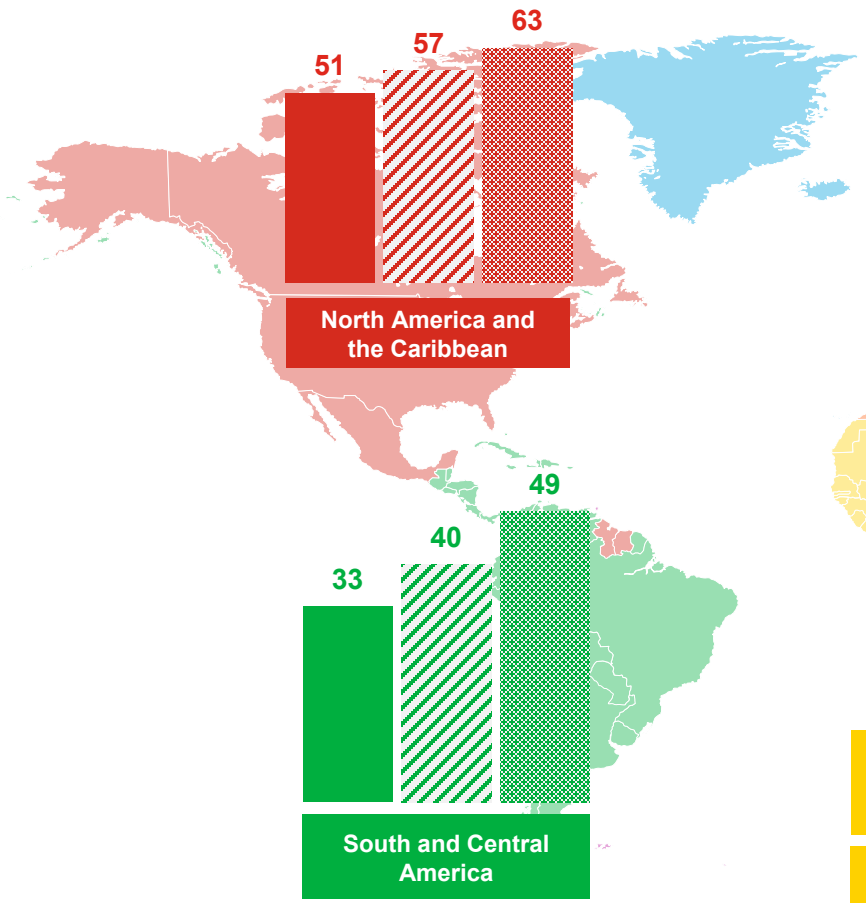
Purpose of Presentation/Disclaimers

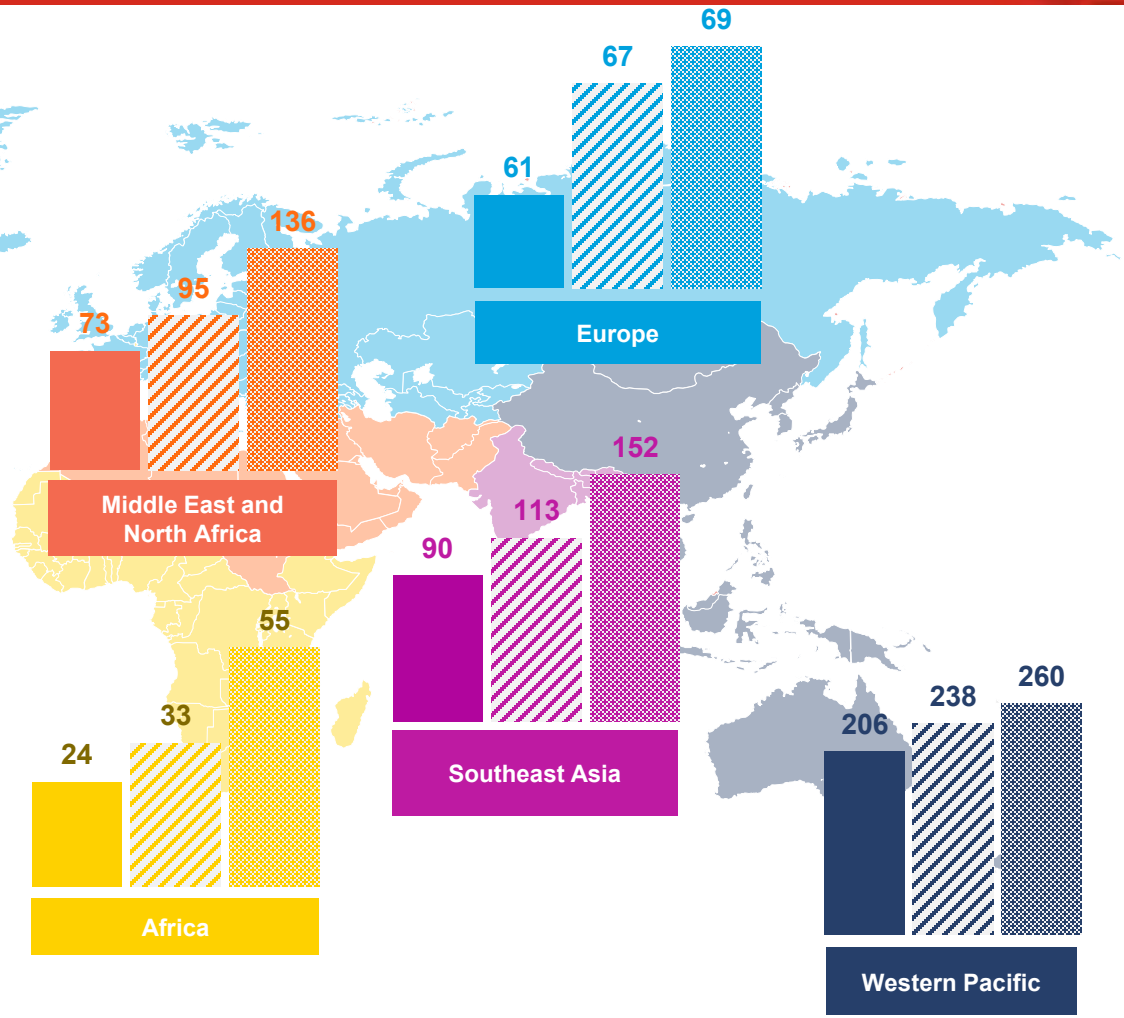
- Lilly Medical has developed this presentation in response to your unsolicited request for information about our pipeline.
- The purpose of this presentation is to provide Population Health Decision Makers (PHDM), upon request, with information on Lilly's development pipeline for the purpose of helping PHDMs plan and budget for future coverage and/or reimbursement decisions.
- This presentation is not intended to promote these molecules in any way. We are not providing the following pipeline information in an attempt to influence you to include these products on your formulary or preferred drug list, in the event that these drugs are approved.
- The molecules contained in this deck are under investigation and neither the safety nor effectiveness has been established. Some of the following products are not approved by the FDA and may never be approved. In the event they are approved, we do not know the specific content of the eventual package labeling, or the actual approved indication.
- The contents of this presentation are limited to the indications being sought as it is understood by Lilly at the time of presentation. All information included in this presentation has been published or presented previously.

Global Diabetes Prevalence Is Increasing

IDF regions and global projections of the number of people with diabetes (20-79 years old), 2021, 2030 and 2045





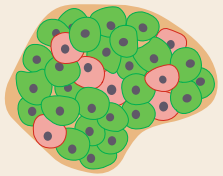


IDF=International Diabetes Federation.
Data from International Diabetes Federation. *IDF Diabetes Atlas, 10th ed*. 2021.

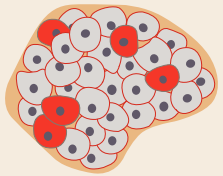
Charts depict people in millions: 2021 2030 2045

Multisystem Contributors Are Associated With Hyperglycemia and the Progression of T2D[1,2]

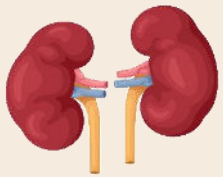
Pancreatic β-cells
▼ Insulin
▼ Incretin effect
▼ β-cell mass



Pancreatic α-cells
▲ Glucagon



Kidney
▲ Glucose reabsorption

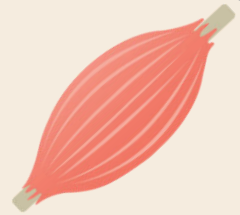


Adipose
▲ Lipolysis

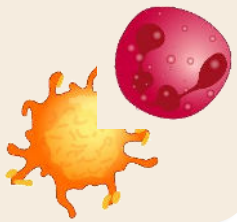
Stomach/ small intestine
▲ Rate of glucose absorption

HYPERGLYCEMIA

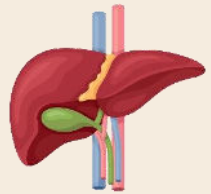
Muscle
▼ Peripheral muscle uptake of glucose due to insulin resistance



Immune system
Dysregulation/ inflammation



Liver
▼ Glucose production
▲ Hepatic insulin resistance



Colon/biome
Abnormal microbiota; possible decreased GLP-1 secretion

Neurotransmitter dysfunction
▲ Appetite
▲ Food intake

GLP-1=Glucagon-Like Peptide-1.

1. Schwartz SS, et al. *Diabetes Care*. 2016;39(2):179-186. 2. DeFronzo RA. *Diabetes*. 2009;58(4):773-795.

Common Comorbidities Affect People With Diabetes

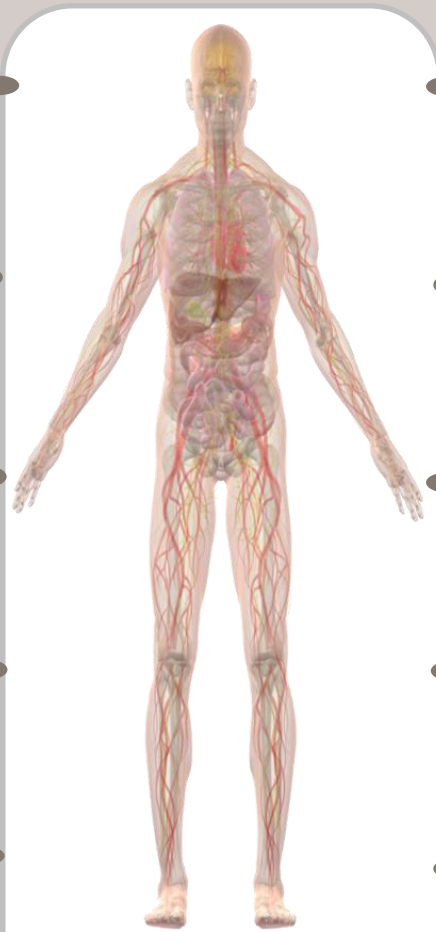
Cancer[1]
T2D is associated with increased risk of cancer of the liver, pancreas, endometrium, colon/rectum, breast and bladder

Cognitive impairment[1]
In people with T2D, both hyper- and hypoglycaemia are associated with cognitive impairment

Pancreatitis[1]
People with diabetes are at ~2-fold higher risk of developing acute pancreatitis

Hearing impairment[1]
Hearing impairment was about twice as prevalent in people with diabetes

Obstructive sleep apnea[1]
Obstructive sleep apnea occurs in up to 1 in 4 people with T2D



Fractures[1]
People with T2D have a higher risk of hip fracture

NAFLD[1,2]
NAFLD is associated with ~70% higher overall mortality in people with T2D as that in the general population[2]

HCV Infection[1]
HCV Infection is associated with a higher prevalence of T2D. Up to 1/3rd of individuals with chronic HCV infection have T2D

Periodontal disease[1]
Periodontal disease is more severe and more prevalent in people with diabetes

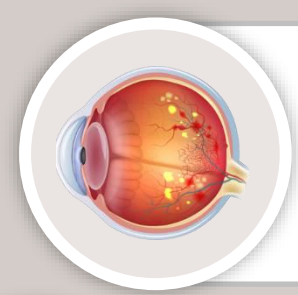
Low testosterone in men[1]
Mean levels of testosterone are lower in men with diabetes

HCV=Hepatitis C Virus; NAFLD=Nonalcoholic Fatty Liver Disease; T2D=Type 2 Diabetes.

1. Data from American Diabetes Association. *Diabetes Care*. 2022;45(Suppl. 1):S46-S59. 2. Data from Tai FW, et al. *Diabet Med*. 2015;32(9):1121-1133.

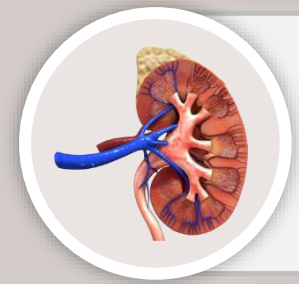
Suboptimal Glycaemic Control Can Lead to Long-term Complications

Microvascular Complications[1-3]
(unique to people with diabetes[2,3])



Diabetic retinopathy[1-5]

Leading cause of blindness in working-age adults

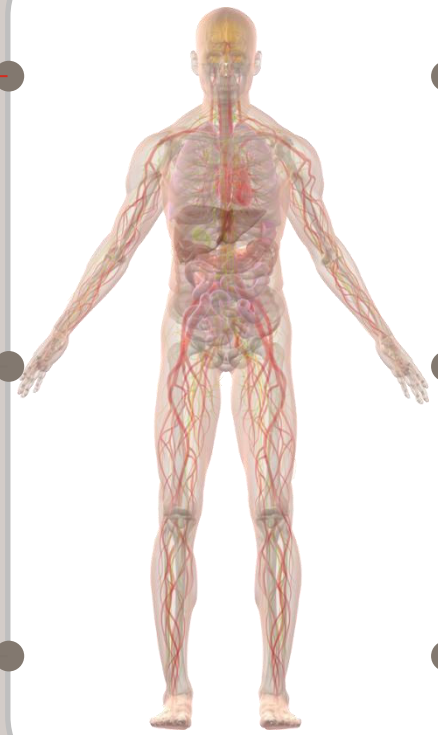


Diabetic nephropathy[1,6]

Leading cause of end-stage renal disease (kidney failure)

Diabetic neuropathy[1,5,7]

Leading cause of nontraumatic lower-limb amputations



Macrovascular Complications[1,2]
(common in people with diabetes[2])

Stroke[1]

Increased stroke risk (150%-400%) and increased cerebrovascular mortality

Heart disease[8]

Responsible for 50%-80% of diabetes-related deaths

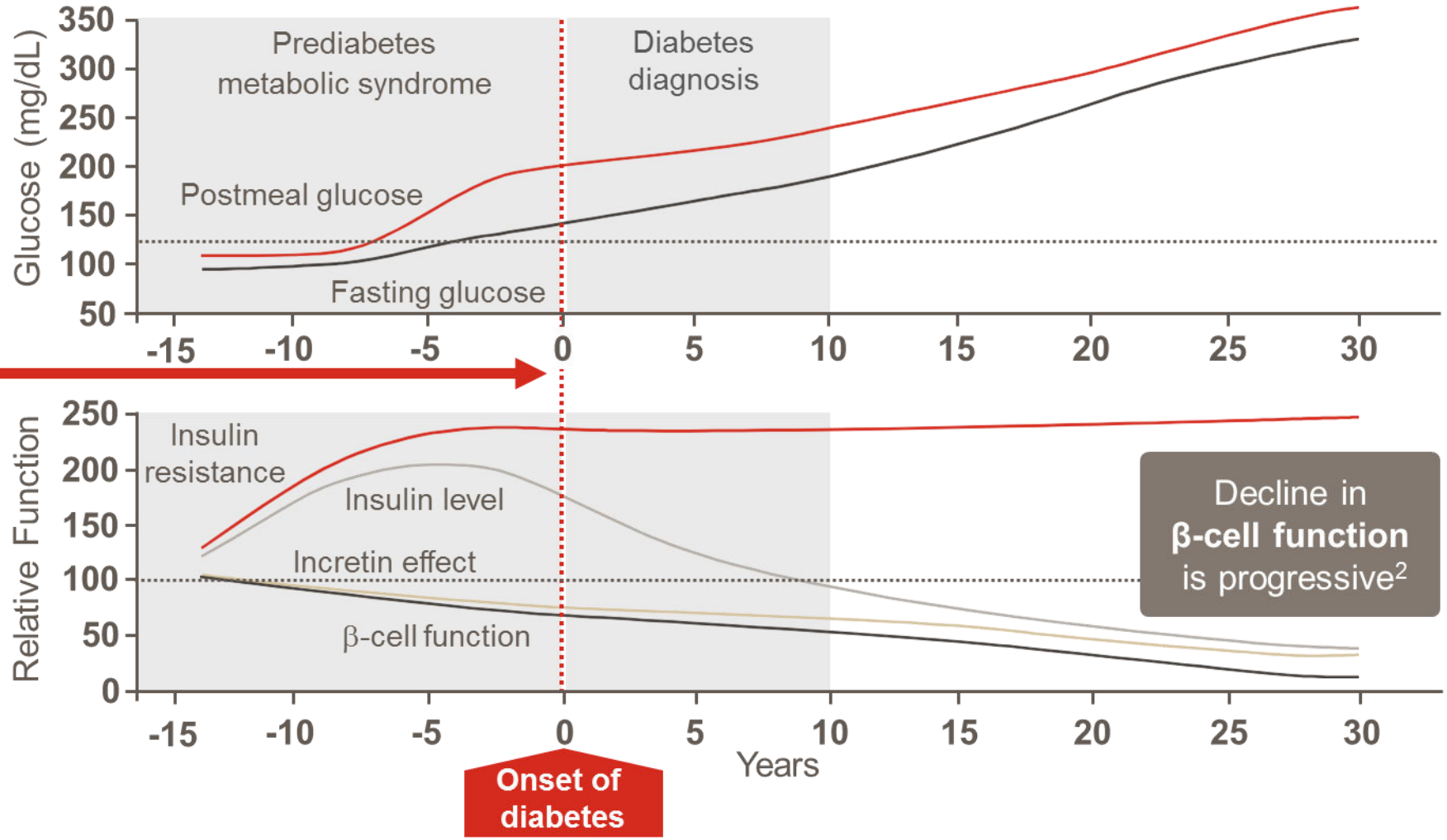
Peripheral arterial disease[1,5,9]

Atherosclerosis in the lower extremities, leading to pain and amputation

1. Data from Fowler MJ. *Clin Diabetes*. 2008;26(2):77-82. 2. Data from Graves LE, Donaghue KC. *Front Endocrinol (Lausanne)*. 2020;11:370. 3. Data from Vithian K, Hurel S. *Clin Med (Lond)*. 2010;10(5):505-509. 4. Data from https://nei.nih.gov/health/diabetic/retinopathy (Accessed June 7, 2022).
5. Data from American Diabetes Association. *Diabetes Care*. 2022;45(Suppl. 1):S185-S194. 6. American Diabetes Association. *Diabetes Care*. 2022;45(Suppl. 1):S175-S184 (updated 2022;45(3):758;45(9):2182-2184).
7. Data from https://professional.diabetes.org/content/fast-facts-data-and-statistics-about-diabetes (Accessed June 7, 2022). 8. Data from Tabish SA. *Int J Health Sci (Qassim)*. 2007;1(2):5-8. 9. Data from American Diabetes Association. *Diabetes Care*. 2003;26(12):3333-3341.

T2D Is a Progressive Disease[1,2]

50%
reduction
in β-cell function at the time of diagnosis of T2D[2]



T2D = type 2 diabetes.

1. Kendall DM, et al. *Am J Med.* 2009;122(suppl 6):S37-S50. 2. DeWitt DE, et al. *JAMA.* 2003;289(17):2254-2264.

ADA 2024 Recommendations for Hyperglycemia in Adults with T2D

Healthy lifestyle behaviors; diabetes self-management education and support; social determinants of health

To avoid therapeutic inertia, re-assess and modify treatment regularly (3-6 months)

Goal

To reduce cardiorenal risk in high-risk people with T2D (in addition to comprehensive CV risk management)[a]

+ASCVD[b]

CVOTs included participants with established CVD (eg, MI, stroke, or any revascularization procedure), but the definition of ASCVD differed between them. Variably included were TIA, unstable angina, amputation, symptomatic or asymptomatic CAD.

+High-risk indicators

Definition of ASCVD may vary across CVOTs; however, most patients are ≥55 years of age with ≥2 additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+ASCVD/High-risk indicators

GLP-1 RA[c] with proven CVD benefit

Either/ Or

SGLT-2i[d] with proven CVD benefit

If HbA1c above target levels

- Consider the addition of SGLT-2i with proven CVD benefit or vice versa in people using GLP-1 RA
- TZD[e]

+HF

HF symptoms, currently or earlier, with documented HFrEF or HFpEF

+HF

SGLT-2i[d] with proven HF benefit

+CKD

eGFR <60 mL/min/1.73 m^2 or albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may differ over time, needing a repeat measure to document CKD

+CKD (on MTD of ACEi/ARB)

SGLT-2i[d] with primary evidence of reducing CKD progression

Use SGLT-2i in people with eGFR ≥20 mL/min/1.73 m^2; once initiated, continue until initiation of dialysis or transplantation

Or

GLP-1 RA with proven CVD benefit if SGLT-2i not tolerated or contraindicated

If HbA1c above target levels, for people on SGLT-2i, consider including a GLP-1 RA or vice versa

Goal

To achieve and maintain glycemic and weight management goals

Managing glycemia: Choose approaches that provide the efficacy to achieve goals:

Metformin **or** medicines including **combination** treatment that provide adequate **efficacy** to achieve and maintain treatment goals

In high-risk individuals, consider avoidance of hypoglycemia a priority

Generally, higher efficacy approaches have increased the possibility to achieve glycemic goals

Efficacy for lowering glucose levels

Very High

Dulaglutide (high dose), semaglutide, tirzepatide

Insulin

Combination oral, combination injectable (GLP-1 RA/insulin)

High

GLP-1 RA (not listed above), metformin, SGLT-2i, sulfonylurea, TZD

Intermediate

DPP-4i

Achieving and maintaining weight management goals:

Setting individualized weight management goals

Lifestyle advice: MNT/ healthy eating patterns/ physical activity

Intensive evidence-based structured weight management programme

Weight-loss medication to be considered

Metabolic surgery to be considered

When choosing antihyperglycemic medications: Consider regimen with high-to-very-high dual glucose and weight efficacies

Efficacy for weight loss

Very High

Semaglutide, tirzepatide

High

Dulaglutide, liraglutide

Intermediate

GLP-1RA (not listed above), SGLT-2i

Neutral

DPP-4i, metformin

If additional reduction of cardiorenal risk or lowering of glycemia required

If HbA1c above target levels

Identify barriers:

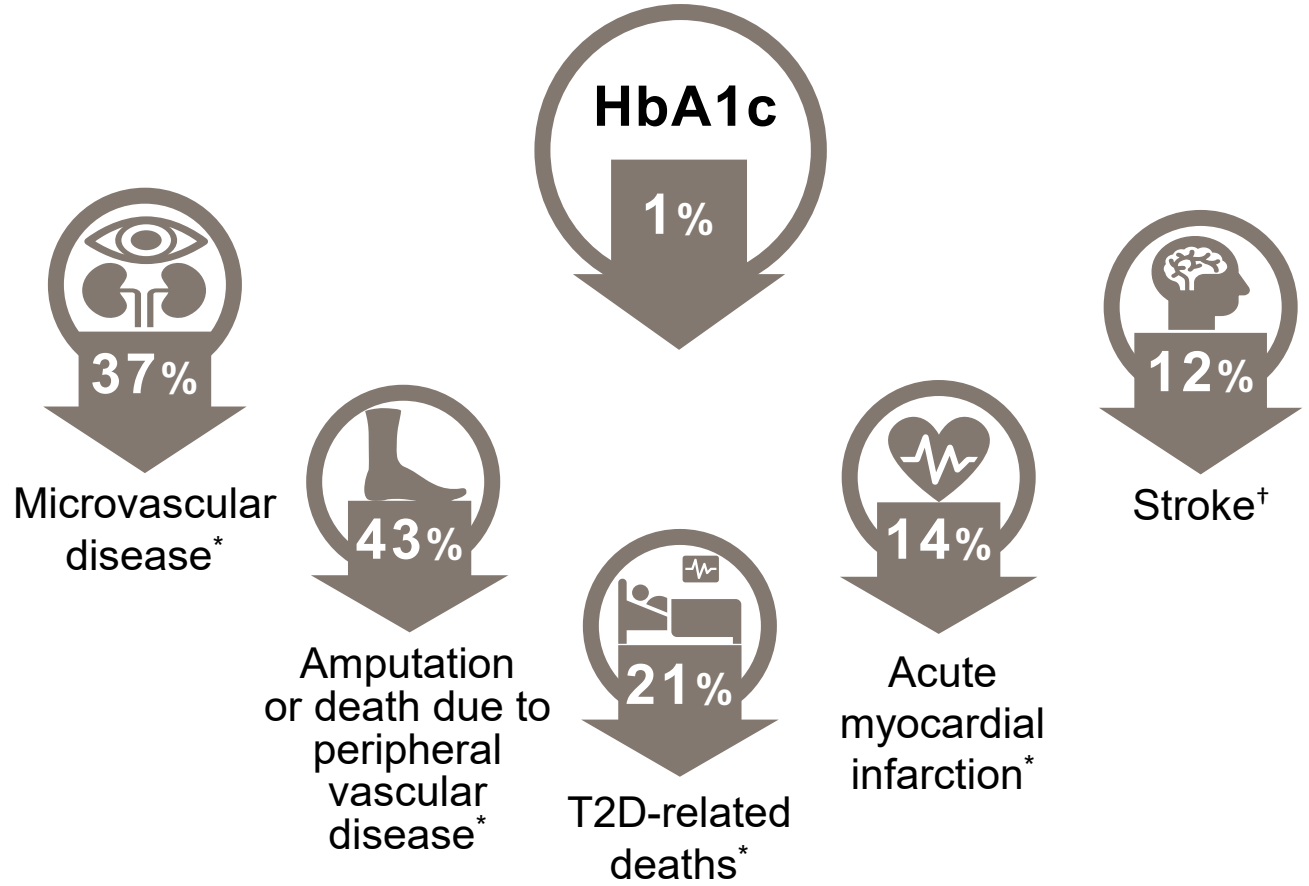
- Consider DSMES referral to support self-efficacy in goal achievement
- Identify and address social determinants of health that affect goal achievement
- Consider technology (eg, diagnostic CGM) to identify therapeutic lacuna and individualize therapy

Note: Explanation for footnote indicators and abbreviations are available in the speaker notes. This slide is reproduced from ADA guideline content and is not intended to make comparative conclusions and the drug products included

American Diabetes Association Professional Practice Committee. *Diabetes Care* 2024;47(Supplement_1):S158–S178.

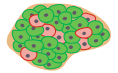
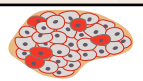
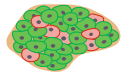
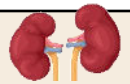
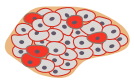
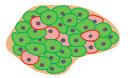
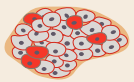
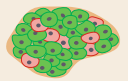
Stringent Glycaemic Control Can Reduce Complications[a]

Epidemiological extrapolation shows the benefits of a 1% reduction in mean HbA1c levels



[a]In newly diagnosed people with T2D; *P=.035; †P<.0001.
HbA1c=Glycated Haemoglobin; T2D=Type 2 Diabetes.
Data from Stratton IM, et al. *BMJ.* 2000;321(7258):405-412.

Available Medications Can Treat Multiple Metabolic Mechanisms That Drive T2D Progression[1-3]

Class[2,3]	Direct Primary Physiological Action(s)[2,3]	Core Defects[1-3]
Biguanides	↓ Hepatic glucose production	 Liver
SUs	↑ Insulin secretion	 Pancreatic β-cell
TZDs	↑ Insulin sensitivity	 Whole body
DPP-4 inhibitors	↑ Insulin secretion[a] ↓ Glucagon secretion[a]	 Pancreatic α-cell  Pancreatic β-cell
SGLT2 inhibitors	✕ Block glucose reabsorption by the kidney, increasing glucosuria	 Kidney
GLP-1 RAs	↑ Insulin secretion[a] ↓ Glucagon secretion[a] ↓ Delay gastric emptying ↓ Weight	 Pancreatic α-cell  Pancreatic β-cell  GI tract  Brain
GIP/GLP-1 Ras	↑ Insulin secretion[a] ↑ Insulin sensitivity ↓ Glucagon secretion[a] ↓ Delay gastric emptying ↓ Weight	 Pancreatic α-cell  Pancreatic β-cell  GI tract  Brain  Whole body (from pre-clinical data)

Schematic is intended to provide an overview of T2D drugs and is not specific to only one product within each class listed. It is not limited to make any express or implied comparison among products. Classes shown are from the ADA guidelines and do not represent all T2D classes available to treat hyperglycemia.

[a]Glucose-Dependent.

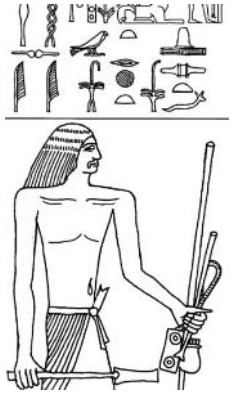
ADA=American Diabetes Association; DDP-4=Dipeptidyl Peptidase-4;GI=Gastrointestinal; GIP=Glucose-Dependent Insulinotropic Polypeptide; GLP-1=Glucagon-Like Peptide-1; RA=Receptor Agonist; SGLT2=Sodium-Glucose Cotransporter 2; SU=Sulfonylurea; T2D=Type 2 Diabetes; TZD=Thiazolidinedione.

1. DeFronzo RA. *Diabetes*. 2009;58(4):773-795. 2. Inzucchi SE, et al. *Diabetes Care*. 2015(1);38:140-149. 3. Mounjaro (tirzepatide once weekly Prescribing Information. 2023. Eli Lilly and Company.

Historic Milestones of Insulin and Diabetes Care

Historic Milestones

BCE = Before Common Era



Hesy-Ra

1552 BCE

On a 3rd Dynasty Egyptian papyrus, physician Hesy-Ra mentioned frequent urination as a symptom. This is the earliest known record of diabetes.[1]

1500 BCE

In Ancient India, ants are attracted to the urine of people with a mysterious emaciating disease.[2]

250 BCE

Apollonius of Memphis coined the term “Diabetes” (Greek for siphon) for a disease that drains patients of more fluid than they can consume.[3]

1. Gearing, M. (2015). From 1552 BC to 2015: How Science Made Diabetes Treatable. Science in the News. http://sitn.hms.harvard.edu/wp-content/uploads/2015/04/Diabetes_final.pdf.
2. Diabetes History. (2014, January 16). Defeat Diabetes Foundation. http://www.defeatdiabetes.org/diabetes-history/.
3. The History of Diabetes. (2019, December 26). The Diabetes Council. https://www.thediabetescouncil.com/the-history-of-diabetes/.

Historic Milestones

CE = Common Era

164 CE

Galen of Pergamum (present-day Bergama, Izmir Province of Turkey) diagnosed diabetes as a kidney ailment[1]

1675

- London physician Dr. Thomas Willis sampled urine of patients with diabetes.[2]
- If the urine tasted sweet, patients were diagnosed with "honeyed" diabetes.
- "Mellitus" (Latin for honey) was added to the term "diabetes."

1776

English physician Matthew Dobson observed that diabetes was fatal in less than five weeks in some people, whereas it was a chronic condition in others. This is the first modern distinction between type 1 and type 2 diabetes.[3]

1850

French physician Dr. Pierre Priory advised patients with diabetes to eat large quantities of sugar to treat their disease.[4]

1. Christopoulou-Aletra, H., Papavramidou, N. (2008, March 26). 'Diabetes' as described by Byzantine writers from the fourth to the ninth century AD: the Graeco-Roman influence. Diabetologia. https://doi.org/10.1007/s00125-008-0981-4.
2. Rlyaz-i-Qadeer, A. (2015). The History of Diabetes Mellitus. Fighting Diabetes. http://www.arqdiabetes.com/History.php
3. Weatherspoon, D. (2020, June 17). Diabetes: Past treatments, new discoveries. Medical News Today. https://www.medicalnewstoday.com/articles/317484.
4. Bliss, M. (1982). The Discovery of Insulin. University of Chicago Press.

Historic Milestones

1869

Paul Langerhans, a medical student from Berlin, discovered a distinct collection of islands of cells within the pancreas, but was unable to determine their function.[1]

1909

Jean De Mayer introduced the term “insuline” (derived from the Latin word “insula” meaning island).[3]

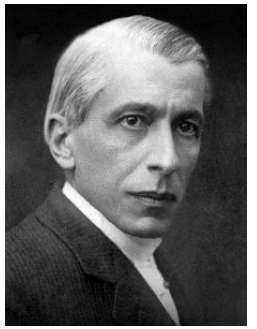
1916

Dr. Elliot Joslin published the first edition of his textbook “The Treatment of Diabetes Mellitus.”[4]

1893

Gustave-Édouard Laguesse named the islet cells as “islets of Langerhans.”[2]

- He suggested a role for the islets separate from being involved with digestion.

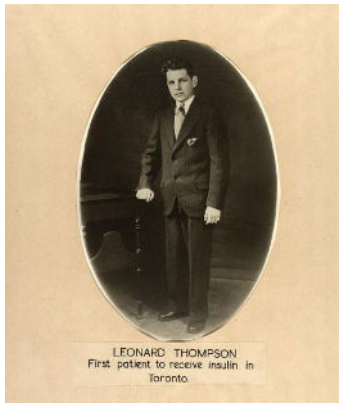


1916

- Romanian professor Nicolae Paulescu developed an extract of the pancreas and showed that it lowered blood sugar in diabetic dogs.[5]
- World War I prevented experiments from continuing. Paulescu published evidence of his experiments in 1921.

1. Jolles, S. (2002, April). Paul Langerhans. Journal of Clinical Pathology. https://dx.doi.org/10.1136%2Fjcp.55.4.243.
2. Hoet, J. (1953, July). Gustave Edouard Laguesse: His Demonstration of the Significance of the Islands of Langerhans. Diabetes. https://doi.org/10.2337/diab.2.4.322
3. Vecchio, I., Tornali, C., Bragazzi, N., and Martini, M. (2018, October 23). The Discovery of Insulin: An Important Milestone in the History of Medicine. Frontiers in Endocrinology. https://dx.doi.org/10.3389%2Ffendo.2018.00613.
4. Mazur, A. (2011, March 11). Why were "starvation diets" promoted for diabetes in the pre-insulin period? Nutrition Journal. https://dx.doi.org/10.1186%2F1475-2891-10-23.
5. Nicolae Paulescu. (2019, January 15). Diabetes.co.uk. https://www.diabetes.co.uk/pioneers/nicolae-paulescu.html.

Clinical Proof-of-Concept: The First Patient



December 1921

At 14 years old, **Leonard Thompson** was admitted to Toronto General Hospital weighing 65 pounds and near death from diabetes.[1]

January 1922

Banting and Best decided that they could safely begin testing their pancreatic extracts on human subjects.[1]

January 11, 1922

Thompson was the first patient to receive Banting and Best's pancreatic extract, which lowered blood glucose by 25% and urine glucose, but not ketones.[2]

- Unfortunately, Thompson had an allergic reaction to impurities present in the initial extract. [1]

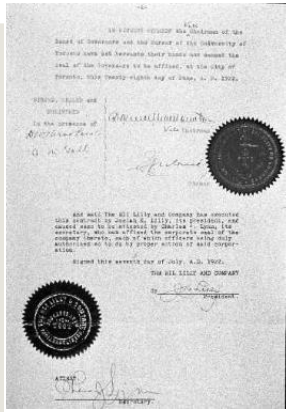
January 11-23, 1922

James Collip developed an improved extraction process that removed contaminants from Banting and Best's extract.[1]

- Repeat treatment with Collip's bovine extract eliminated urinary glucose and ketones.[2]
- The first patient in the U.S. to receive this treatment was Jim Havens in May 1922.[3]

1. Bliss, M. (2018, November 8). *The Discovery of Insulin*. The Canadian Encyclopedia
2. Espinal, J. (2011). *Understanding Insulin Action Principles and Molecular Mechanisms*. Springer Verlag.
3. Discovery of Insulin at University of Toronto. Heritage U of T.

A Collaboration Paves the Path to Large-scale Production of Insulin



May 30, 1922

An agreement was made between the Governors of University of Toronto and Eli Lilly and Company to collaborate on the mass production of insulin in the U.S.[1]

The official contract between University of Toronto and Eli Lilly and Company to commercially produce insulin

August 1922

Eli Lilly and Company ships the first commercial insulin to Toronto.[3]

1923

Full-scale production of insulin was perfected by Eli Lilly and Company

In October of 1923, the first commercial insulin product Iletin® was launched, available in U-10, U-20, and U-40 concentrations.[2]

By the end of 1923, Eli Lilly and Company had shipped 60 million units and benefited millions of patients. [2]

April 3, 1922

On behalf of Eli Lilly and Company, **Dr. Clowes made a formal offer to University of Toronto to collaborate** in preparing insulin commercially.[1]

Spring - Summer 1922

Eli Lilly and Company research chemist George Walden was instrumental in the development of processes for the mass production of insulin.[2]

Walden's use of isoelectric precipitation of insulin from crude pancreatic extract revolutionized the amount, purity, and stability of the final product, which was an essential step toward mass production of insulin.[2]

January - March 1923

By March 1923, Eli Lilly and Company had produced over 80,000 units of insulin. [4]

1. Discovery of Insulin at University of Toronto. Heritage U of T.
2. McCormick, G. (2005). The Discovery and Manufacture of Insulin. Eli Lilly and Company Archives.
3. Hegele, R. (2020, October 29). Insulin's centenary: the birth of an idea. The Lancet.
4. Clowes AW. The doc and the duchess. Bloomigton, Indiana. Indiana University Press 2016; pp 85

Impact on Patients - Early Examples

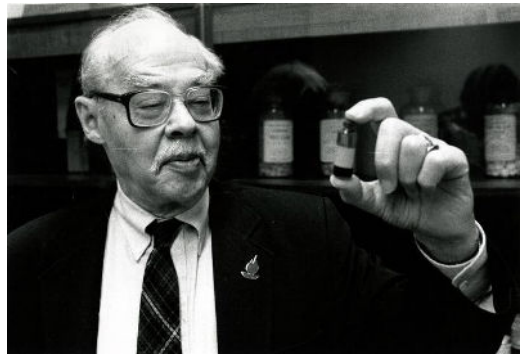
Ted Ryder

July 10, 1922

Weighed just 27 lbs at the age of 6 years before insulin treatment.[1]

January 16, 1923

Weighed 40 lbs after insulin treatment. [1]



1990

Visited Eli Lilly and Company.[2]

JL

December 7, 1922

Weighed just 15 lbs (6.8 kg) at the age of 3 years.[3]

February 26, 1923

Weighed 30 lbs (13.6 kg) following treatment with insulin.[3]

1. Delle Palme, R. (2018, September 27). The Long Life of One of Banting's First Patients. Banting House National Historic Site
2. Eli Lilly and Company Archives.
3. Major, R. (1923, June 2). The treatment of diabetes mellitus with insulin. JAMA.

Early Efforts to Extend Insulin Time Action Through Formulations

1936

According to Hans Hagedorn and B. Norman Jensen, addition of protamine obtained from the "milt" or semen of river trout could prolong the effects of injected insulin.[1]

1937

The introduction of **protamine insulin** in 1936 and PZI by researchers at Connaught Laboratories enabled Eli Lilly and Company to produce **PZI insulin**.[2]

1946

Novo Nordisk developed an intermediate-acting insulin by **forming crystals of protamine and insulin,** which was marketed as **NPH insulin** in 1950.[1] NPH insulin can be mixed with a fast-onset insulin to complement its long-lasting action. These mixed solutions came to be known as "premixed" insulin.[1]

1950

Lilly introduced **NPH animal-source insulin.**[3]

1953

Novo Nordisk introduced Lente insulins (semilente, lente, and ultralente), which are longer-lasting insulin suspensions.[4]

Lente insulin has its own degree of prolonged action, achieved through a chemical combination of insulin and zinc, thus enabling doctors to prescribe a dosage regimen suited to the needs of an individual. [4]

1954

Eli Lilly and Company marketed **Lente insulin.**[3]

1957

Eli Lilly and Company marketed Semilente® and Ultralente® insulins.[3]

1973

Eli Lilly and Company introduced U-100 concentration NPH insulin.[3]

1. Payne, S. (2017). NPH Insulin. The Info List. http://www.theinfolist.com/php/SummaryGet.php?FindGo=NPH insulin.
2. White, J. (2014, May). A Brief History of the Development of Diabetes Medications. *Diabetes Spectrum*.
3. Hughey, J. (2001, April 16). When insulin was marketed. Insulin-Pumpers.org.
4. Novo Nordisk. (2011). Novo Nordisk History. https://www.novonordisk.com/content/dam/Denmark/HQ/aboutus/documents/HistoryBook_UK.pdf

Early Insulin

Pig and cow pancreata for insulin production

From 1922 up until the 1980s, piles of pig and cow pancreata were brought to Indianapolis from the surrounding farms in trains.[1]

Pigs and cows were the predominant sources of insulin (porcine and bovine insulins) due to the availability of these animals' pancreata and the similarity of their protein structure to that of humans.[1]

1. Gebel, E. (2013, July). Making Insulin. Diabetes Forecast. http://www.diabetesforecast.org/2013/jul/making-insulin.html.

Insulins Analogs Provide More Rapid and Longer Time Action

1996

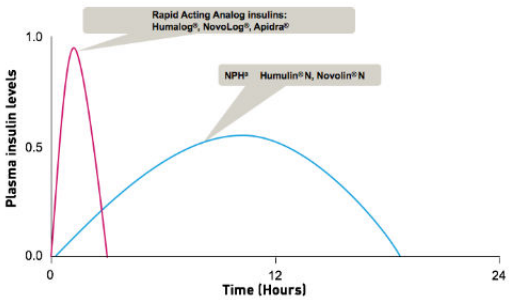
Eli Lilly and Company marketed **insulin lispro, which was approved as the first, rapid-acting insulin analog** under the trade name Humalog®.[1]

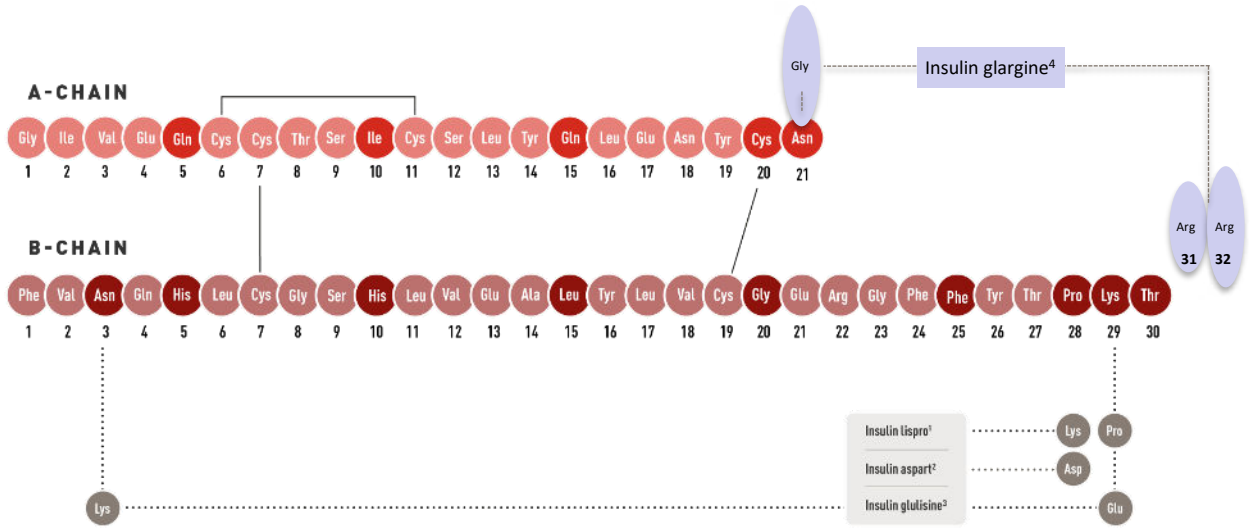
2000 Novo Nordisk's **insulin aspart** received FDA approval [2]
2008 Sanofi's **insulin glulysine** received FDA approval [3]

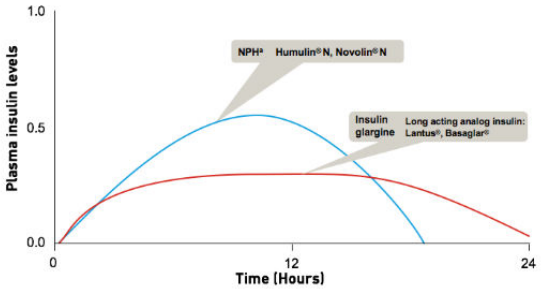
2000

Sanofi (Aventis in 2000) received approval for the **first long-acting basal insulin analog, insulin glargine,** under the trade name Lantus®.[4]

2005 Novo Nordisk's **insulin detimir** received FDA approval
2015 Novo Nordisk's **insulin degludec** received FDA approval
2015 Eli Lilly's **"follow on biologic" insulin glargine** received FDA approval







1. *Humalog® Full Prescribing Information. (2019, November). Eli Lilly and Company.*
2. *NovoLog® Full Prescribing Information. (2019, November) Novo Nordisk.*
3. *Apidra® Product Monograph. (2019, November 26). Sanofi.*
4. *Lantus® Product Monograph. (2019, December 6). Sanofi.*

CELEBRATING 100 YEARS OF INSULIN

The Progression of Insulin Development*

**Not all products are commercially available in all geographies; placement indicates first availability in market.*

1921 Insulin discovery[1]

1923 First purified animal insulin[1]
The first insulins sold contained approximately 3 U/mL. These often varied in purity and strength.

1923 Iletin insulin 10 U/mL, 20 U/mL, 40 U/mL, 80 U/mL[1]

1950 Discovery of intermediate-acting insulins[1]

1952 Animal insulin 500 U/mL[1]

1973 Standardization to insulin 100 U/mL[1]

1977 Elimination of 40 U/mL, 80 U/mL[2]

1982 First human insulins by recombinant DNA 100 U/mL[1]

1996 First "Analog" rapid-acting insulin lispro 100 U/mL[1,3]

1997 Human insulin 500 U/mL[1,4]

2000 Insulin aspart 100 U/mL[5]

2000 First analog long-acting (basal) insulin glargine 100 U/mL[6]

2004 Insulin glulisine 100 U/mL[7]

2005 Insulin detemir 100 U/mL[8]

2015 Insulin lispro 200 U/mL[3]

2015 Insulin glargine 300 U/mL[9]

2015 First "follow on biologic" long-acting insulin analog glargine 100 U/mL[10]

2015 Insulin degludec 100 U/mL, 200 U/mL[11]

2017 Fast-acting insulin aspart 100 U/mL[12]

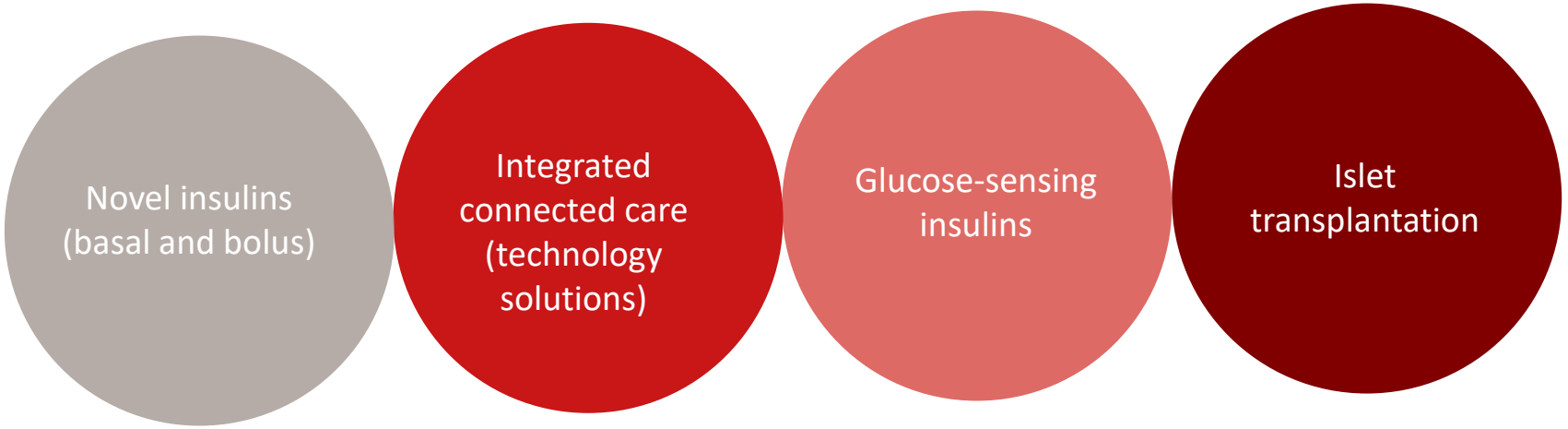
2020 Fast-acting insulin lispro 100 U/ml, 200 U/ml.[13]

1. Hirsch, I., Juneja, R., Beals, J., et al. (2020, October 5). The Evolution of Insulin and How it Informs Therapy and Treatment Choices. Endocrine Reviews. https://doi.org/10.1210/endrev/bnaa015.
2. Moss, J., Galloway, J. U-100 Insulin A Progress Report. JAMA. https://doi.org/10.1001/jama.1977.03280180027018.
3. Humalog® Full Prescribing Information. (2019, November). Eli Lilly and Company. http://pi.lilly.com/us/humalog-pen-pi.pdf.
4. Humulin® R Full Prescribing Information. (2019, November). Eli Lilly and Company. http://pi.lilly.com/us/humulin-r-pi.pdf.
5. NovoLog® Full Prescribing Information. (2019, November). Novo Nordisk. http://www.novo-pi.com/novolog.pdf.
6. Lantus® Full Prescribing Information. (2019, November). Sanofi. http://products.sanofi.us/lantus/lantus.pdf.
7. Apidra® Full Prescribing Information. (2019, November). Sanofi. http://products.sanofi.us/Apidra/apidra.pdf.
8. Levemir® Full Prescribing Information. (2020, March). Novo Nordisk. http://www.novo-pi.com/levemir.pdf.
9. Toujeo® Full Prescribing Information. (2019, November). Sanofi. http://products.sanofi.us/toujeo/toujeo.pdf.
10. Basaglar® Full Prescribing Information. (2019, November). Eli Lilly and Company. http://pi.lilly.com/us/basaglar-uspi.pdf.
11. Tresiba® Full Prescribing Information. (2019, November). Novo Nordisk. https://www.novo-pi.com/tresiba.pdf.
12. Fiasp® Full Prescribing Information. (2019, December). Novo Nordisk. http://www.novo-pi.com/fiasp.pdf.
13. Lyumjev® Full Prescribing Information. (2020, June). Eli Lilly and Company. http://pi.lilly.com/us/lyumjev-uspi.pdf.

Diabetes Innovation

Areas of Insulin Innovation

CURRENT RESEARCH EFFORTS INCLUDE:



The global prevalence of diabetes and advances in health technology necessitate further innovation in insulin formulation and diabetes treatment.

By understanding how insulin acts and how it is absorbed, distributed, metabolized, and excreted, we can engineer proteins to modulate time-action and biologic profiles.

Novel Weekly Basal Insulins in Development

Once-weekly basal insulins are in development to help reduce the number of injections needed by people living with diabetes.

ICODEC[1]

A once-weekly insulin receptor analog developed by modifying three amino acids in the human insulin molecule to reduce enzymatic degradation and adding a C20 fatty diacyl side chain to allow for increased binding to albumin.

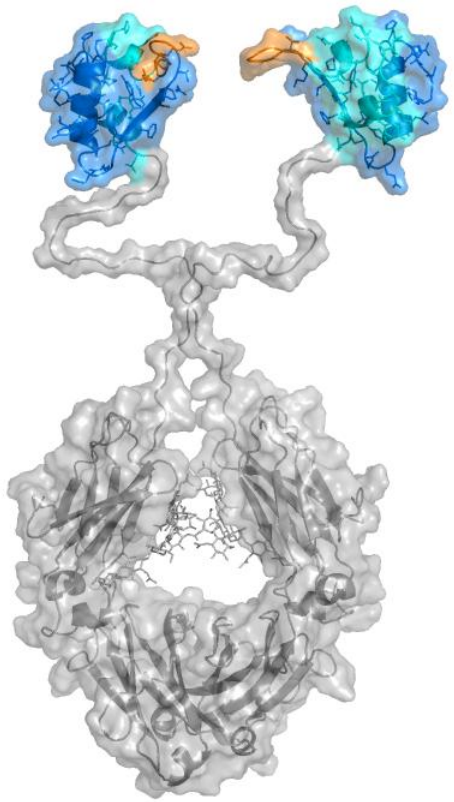
INSULIN EFSITORA ALFA[2]

A once-weekly insulin receptor agonist developed by fusing a single-chain insulin to an Fc domain from an antibody to prolong its time-action profile.

1. Rosenstock, J. Bajaj, H.S., Janež, A., et al. (2020, November 26). *Once-Weekly Insulin for Type 2 Diabetes without Previous Insulin Treatment*. The New England Journal of Medicine. https://www.nejm.org/doi/10.1056/NEJMoa2022474.
2. Eli Lilly and Company. (2020, March 17). *A Study of LY3209590 in Participants With Type 2 Diabetes Mellitus*. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03736785.

Basal Insulin-Fc: ‘BIF’
Novel Basal Insulins in Clinical Development

Weekly Basal Insulin Fc (BIF) is a fusion protein that combines a novel single-chain variant of insulin with a human IgG Fc domain. It is designed for once weekly subcutaneous administration.



Attributes

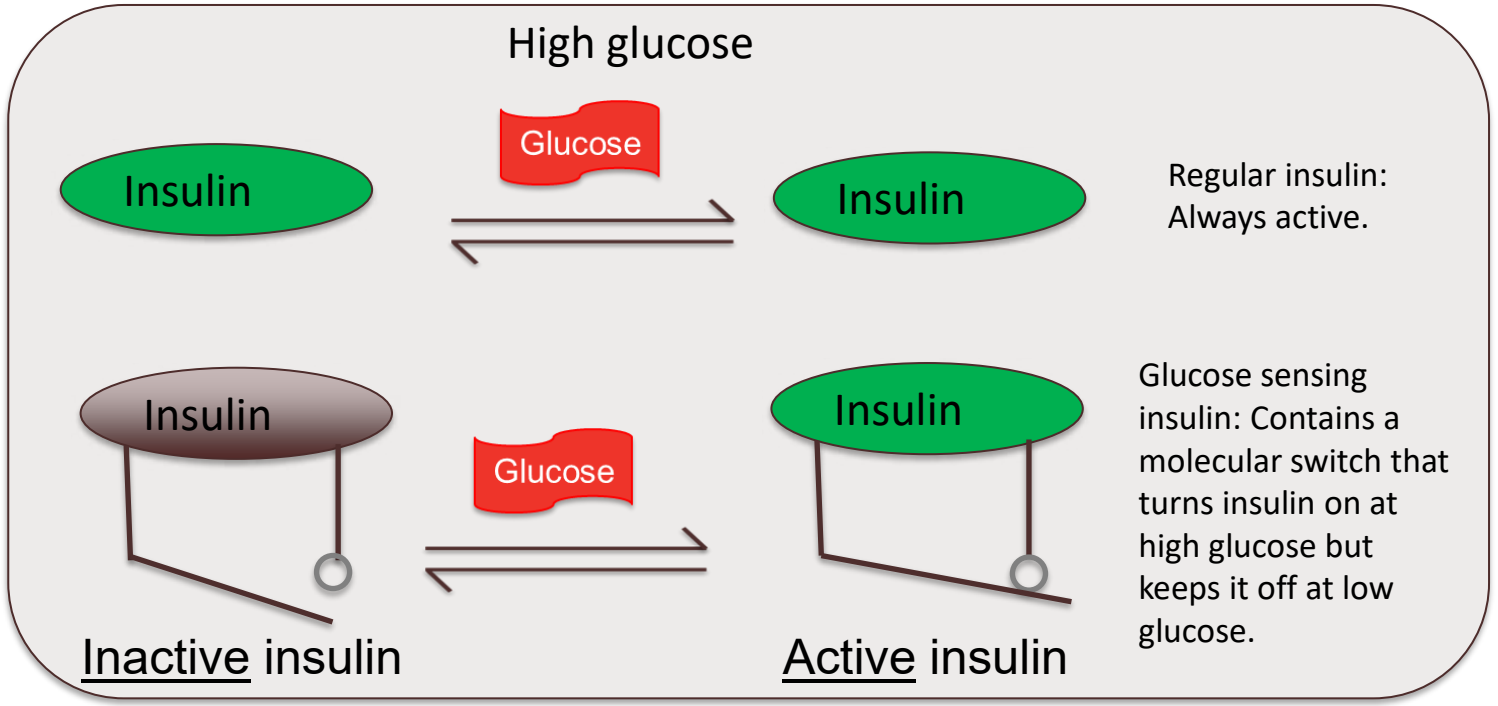
Selective insulin receptor agonist

- >1000x selectivity versus IGF-1 receptor
- Low mitogenicity potential

Could be co-formulated with other weekly compounds, e.g. incretins

Low immunogenicity risk

Glucose-Sensing Insulins



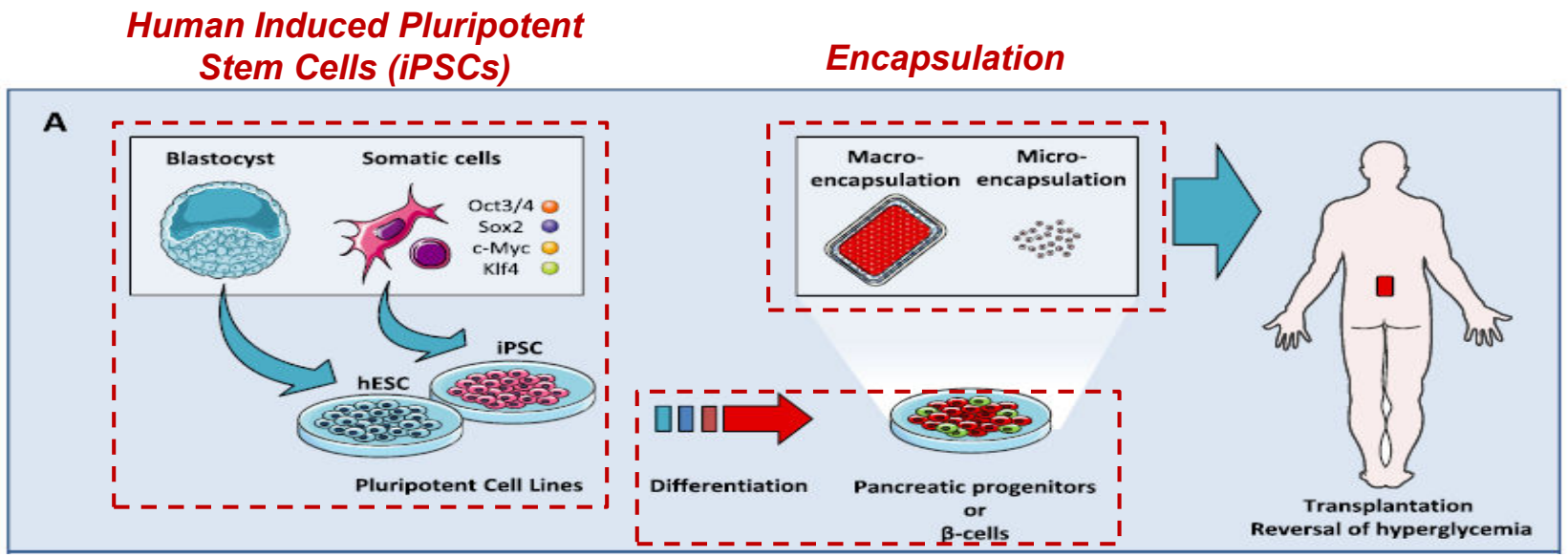
Designing molecular switches that can be built into an insulin molecule.

Insulin can be turned on and off in response to changes in the circulating glucose concentration through these switches.

Islet Cell Therapy

Collaboration between Lilly and Sigilon Therapeutics

Goal: Normalize glucose control with no hypoglycemia and freedom from exogenously administered diabetes treatments or devices



Sigilon materials allow functional islet implantation with no observed fibrosis (monkey data)

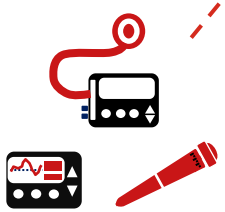
Adapted from Quiskamp N et al. 2015 *Best Pract Res Clin Endocrinol Metab* 29: 833

Focus on Developing Insulin Management Solutions for Patients

DATA ANALYTICS ENGINE

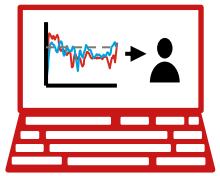
Medication

- Insulin products
- Glucagon treatment of severe hypoglycemia



Connected Devices

- Insulin delivery: pen, pump
- Glucose monitoring: meter monitors (BGM), continuous glucose monitors (CGM), and flash glucose monitors (FGM)

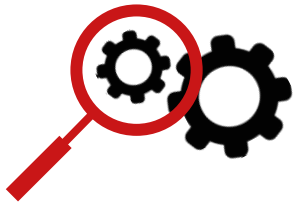


Individualized Analysis & Dosing Guidance

- Cloud-based data storage
- Dosing calculations
- Data visualization and sharing capability

Educational Tools & Training Resources

- Comprehensive education and training (virtual or in-person)
- Resources available 24/7 in various formats
- Integration of supplemental tools & apps



Customer Support

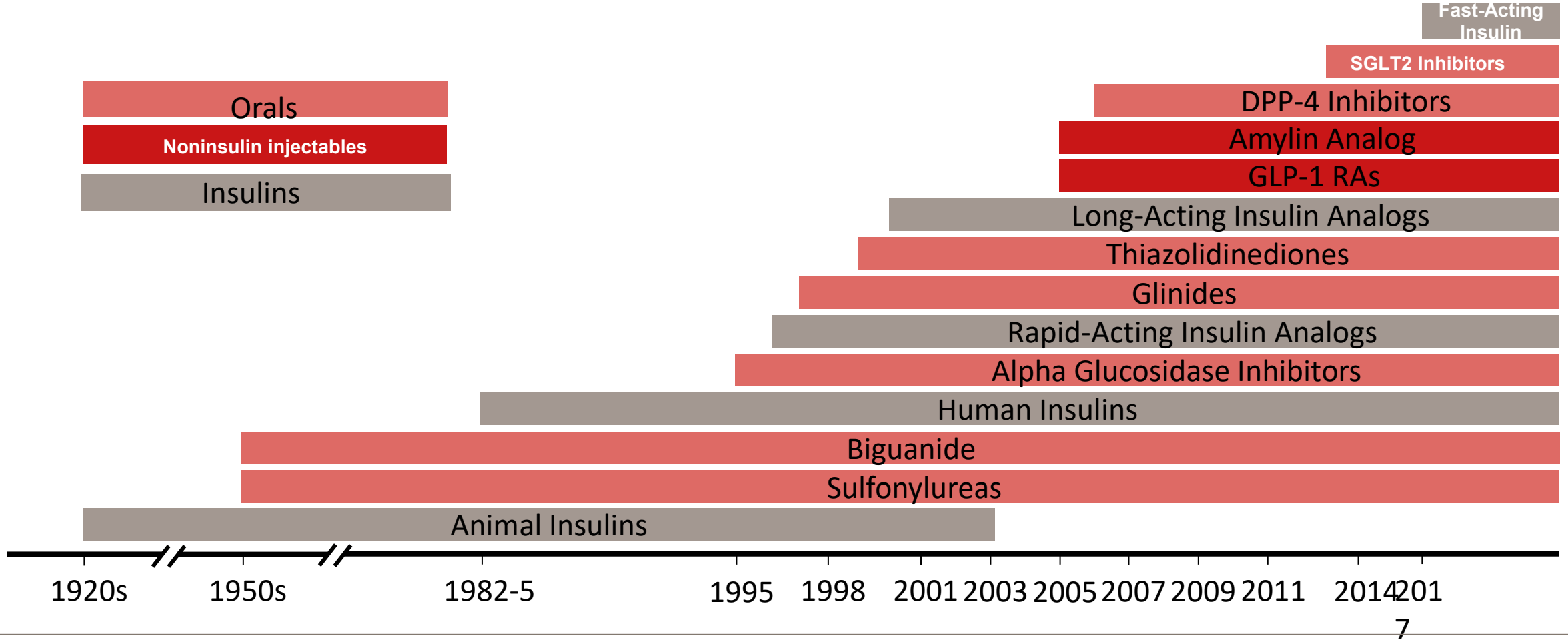
- Troubleshooting (hardware, software)
- Supply logistics
- 3rd-party management
- System-wide communication

The Next Frontier

Can we prevent the development of type 1 diabetes?

Can we prevent the progression of type 2 diabetes to insulin therapy?

Glucose-Lowering Therapy: Multiple Classes

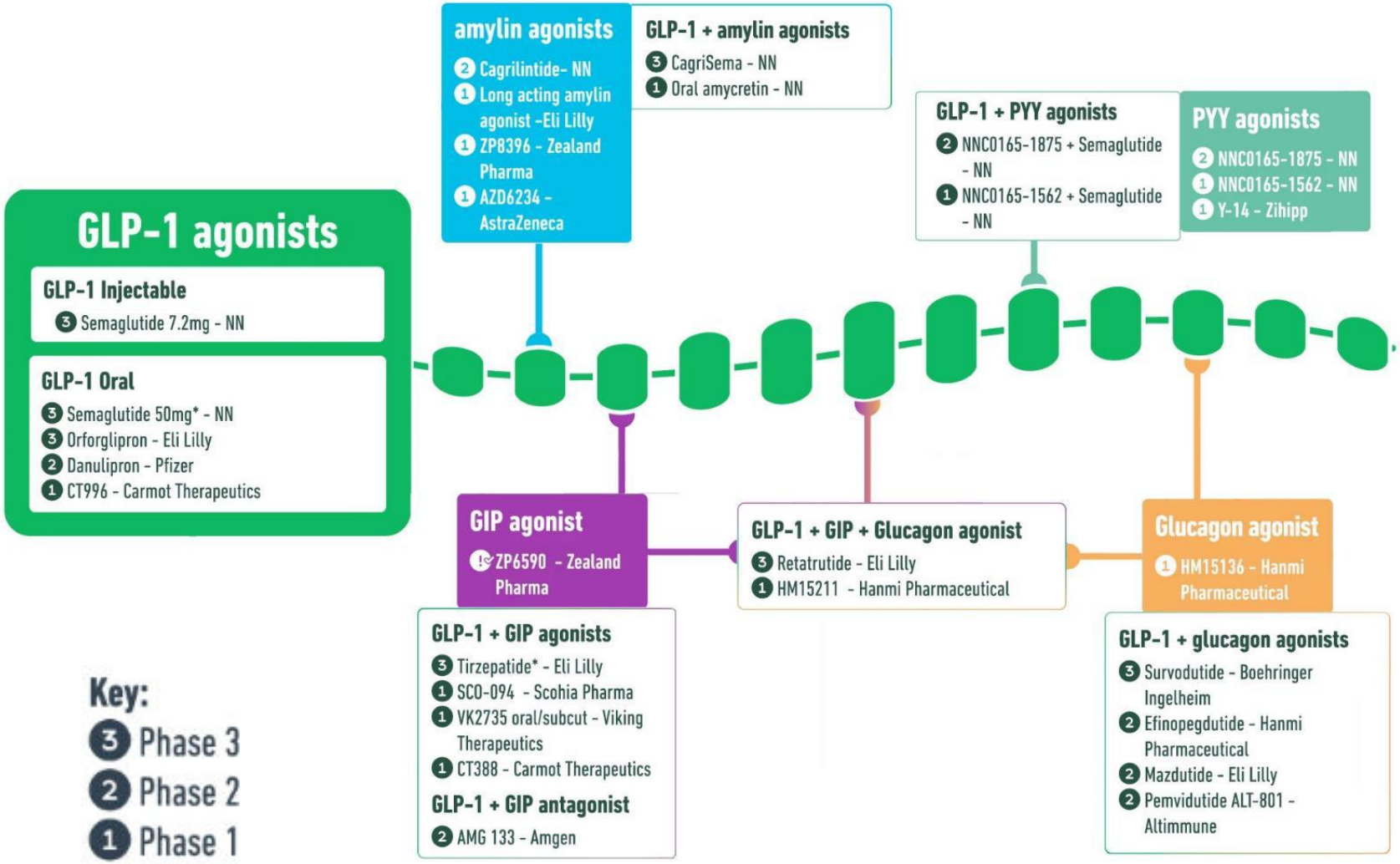


Approved Incretins

Generic	Brand	Company	Indications					
			T2D*			CWM^		
			Adult	Peds	CV RR	Adult	Peds	CV RR
Dulaglutide	Trulicity	Lilly	√	10+	1°/2°			
Exenatide	Byetta/Bydureon#	Amylin	√	10+#				
Liraglutide	Victoza*/Saxenda^	Novo Nordisk	√	10+	2°	√	12+	
Lixisenatide	Adlyxin	Sanofi	√					
Semaglutide	Ozempic*/Wegovy^	Novo Nordisk	√		2°	√	12+	2°
Semaglutide	Rybelsus (po)	Novo Nordisk	√	10+				
Tirzepatide	Mounjaro*/Zepbound^	Lilly	√		2°	√		1°/2°

T2D=Type 2 Diabetes Mellitus; CWM = Chronic Weight Management; CV RR = Cardiovascular Risk Reduction; Under investigation

GLP is the Backbone of Incretin Pipeline



GLP-1 glucagon like peptide-1,
GIP glucose-dependent insulinotropic polypeptide,
PYY peptide YY,
NN: novo nordisk,
*completed phase 3 trials for obesity.

Graphic adapted from Melson E. Int J Obes. 2024 Feb 1 Epub ahead of print.

Obesity Pipeline

- There are over 80 assets in clinical development for obesity from Phase 1 – approval
- Phase III Assets Include:

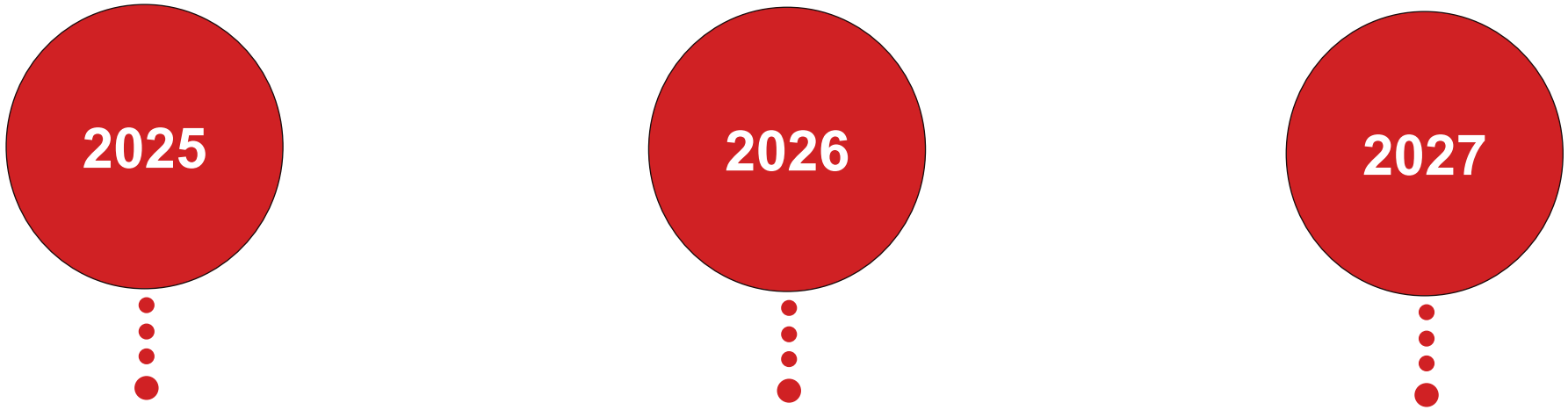
Asset	Company	Mechanism	Dosing	Potential Reg Decision^
Oral Sem high dose	Novo Nordisk	GLP-1 agonist	PO QD	Late 2024
Cagrisema*	Novo Nordisk	GLP agonist/Amylin Analogue	SQ QW	2026
SQ Sem high dose	Novo Nordisk	GLP-1 agonist	SQ QW	2026
Orforglipron*	Lilly	GLP-1 agonist	PO QD	2026
Survodutide	BI/Zealand	Glucagon/GLP agonist	SQ QW	2027
Retatrutide*	Lilly	GLP/GIP/Glucagon agonist	SQ QW	2027

*Also has Phase III studies in Diabetes population

^Assets have not yet been submitted to FDA; Dates are estimates and subject to change

Late-Phase Obesity Assets

POTENTIAL Regulatory Decision Timeline



GLP | GLP/GIP | GLP/ Amylin | GIP/ Glucagon | GLP/GIP/ Glucagon

Assets have not been submitted to FDA; Timing is estimated and is subject to change

Thank you!

Upcoming HealthCareTN Events

- Women's Health Webinar
  - "Empowering Change: Advancing Women's Health in the Workplace"
    - December 17, 2024
    - 10:00 am – 11:30 am EST

THANK YOU