PointClickCare®
Life Sciences

Are GLP-1s Treating Both Type 2 and Type 3 Diabetes?

How Using Longitudinal Data Can Support These Findings

Heather Hiscock, MSc.
Data Translator
PointClickCare

Type 2 Diabetes in Long-Term Care

The prevalence of diabetes mellitus, specifically type 2 diabetes (T2DM), is high among older adults and is estimated to impact the lives of more than 400 million people globally[1]. It is anticipated to increase by nearly 11% by 2045, impacting the lives of nearly 700 million people[2]. PointClickCare (PCC) Life Sciences data alone contains more than 3 million records for residents with T2DM. This data provides a longitudinal patient journey reflecting the documentation legally required to holistically care for individuals by capturing measurements and assessments including, regular blood sugar (BS) readings, complete cognitive and physical assessments, and monitoring all medication management.

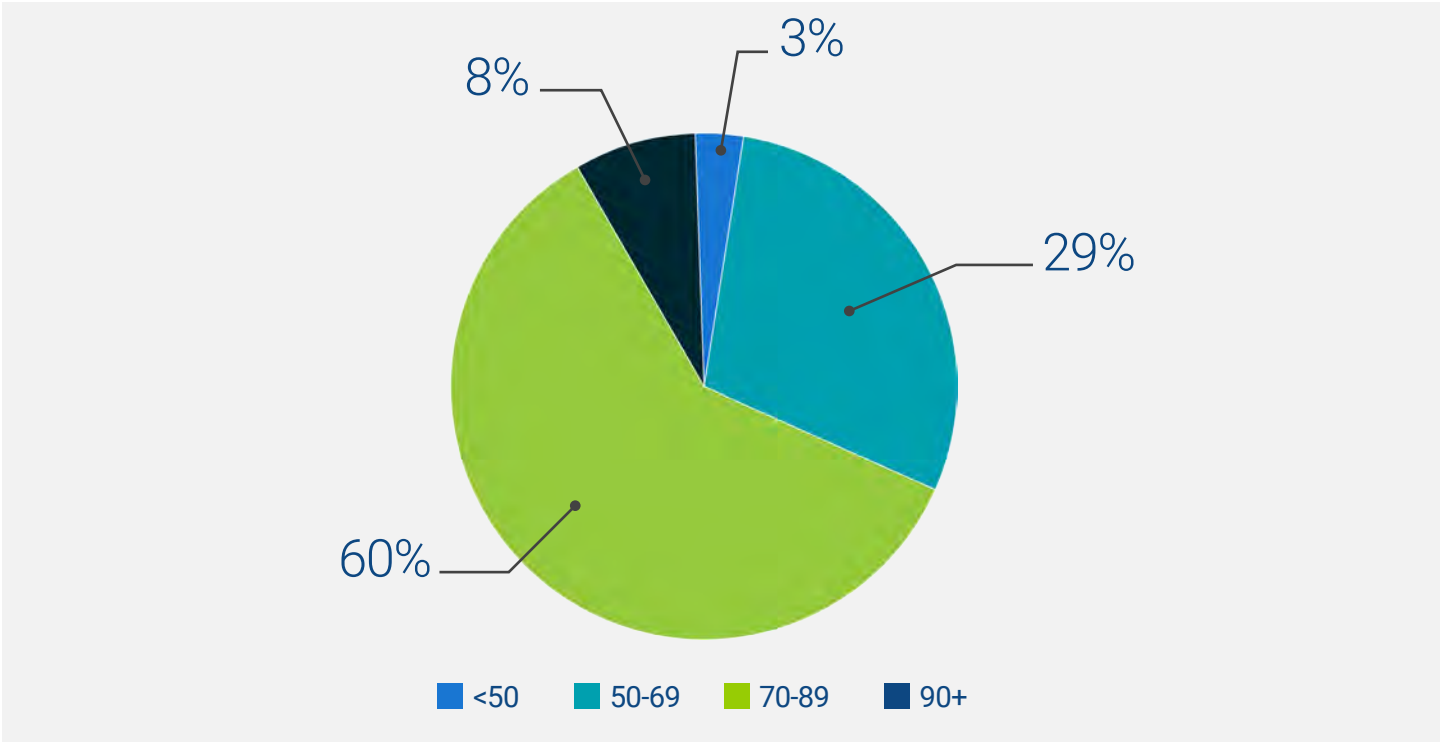

Figure 1. Ages of T2DM residents within PCC LTC facilities

PCC Life Sciences data suggests that within long-term care (LTC) facilities, a large proportion of the T2DM individuals fall in the age range of 70-89 years (Figure 1), an age group that has an **average of two comorbidities**[3]. Recent studies demonstrate that the high prevalence of diabetes within this population can be correlated to age-related physiological changes, leading to an increase in insulin resistance in peripheral tissues and relatively impaired pancreatic islet function[3]. The American Diabetes Association states that increasing insulin resistance among many other factors (obesity, family history, physically inactive, race/ethnicity) can raise the risk of T2DM diagnoses. Considering this subset of Electronic Health Records (EHR) population could offer researchers insight into the patient's journey, venturing back to a prediabetic diagnosis using **regularly captured measures** occurring in LTC facilities, **including vitals** (blood sugars, blood pressure, body weight fluctuations), **symptoms** (urinary incontinence, changes to eating regimes, numbness or tingling sensations, sores, and infections, as well as associated healing time frames), **and therapies** (titrations on/off, new associated diagnoses post therapy). Most PCC LTC residents arrive at the facilities previously diagnosed with T2DM (approximately 96%), however there is a small, yet significant ($p>0.0001$) proportion of residents who have developed T2DM whilst living in a facility (Table 1).

Table 1. Counts and percentage of residents from 2017 – early 2023** with a diagnosis of T2DM pre and post PCC LTC admission.

	T2DM cohort	Onset recorded during Facility admission	Onset after >30* days of admission
Residents N	3,081,962	2,954,009	87,541
Resident %	100%	95.84%	2.84%

*Post admission was captured after 30 days within the facility to remove potential error due to capturing/ reporting during first assessment. We also account for disease progression (prediabetes to type 2 diabetes) as studies indicate that T2DM develops slowly, even those with prediabetes tend to receive a diagnosis within ~ 5 years**.

** Although PCC data goes back to 2010, we only used data captured between January 2017 to April 2023 (spanning >5 years) to represent diabetic progression based on previous literature

Type 3 Diabetes in Long-Term Care

Individuals between 65 and 80 years of age are predisposed to neurodegenerative disorders such as Alzheimer's disease (AD), dementia, Parkinson's disease, peripheral, and autonomic neuropathy[5,6,7]. In recent years, with accumulating evidence from scientific literature, certain diagnoses of Alzheimer's disease may, in fact, be a **new brain specific form of diabetes which is now being termed type 3 diabetes** throughout the scientific community[6,7,8]. There is rising evidence validating the correlation between type 2 diabetes and Alzheimer's disease[7,8]. Studies have shown that type 2 diabetes and Alzheimer's disease share many common pathophysiological mechanisms associated with insulin resistance, such as oxidative stress, insulin signaling disorders, mitochondrial dysfunction, neuroinflammation, advanced glycosylation end products, and metabolic syndrome [7, 8, 10].

The association between AD and T2DM of slow progressing brain damage is still being investigated, however it is of great concern to researchers and healthcare professionals. LTC residents are the ideal candidates to study and monitor the implications of these diagnoses, as they are most impacted physically and mentally. Researchers should also consider and evaluate resident assessments (cognitive and physical), vitals, and medications, as they are highly regulated and regularly assessed by staff. PCC Life Science data shows that more than 1.8M diabetic residents have an average of 380 high blood sugar readings, exponentially higher than the amount of normal blood sugar readings. High blood sugar (hyperglycemia) can be extremely dangerous for this population, and it is important that there is a strong effort in preventing these events. The quantity of measures taken can be directly tied to staff's daily interactions with residents, capturing their data in a structured way (ex. PCC EHR) by documenting their vitals and symptoms in real time. This data can be used to provide research insights that have been previously unavailable.

GLP-1 Therapeutics in Long-Term Care

New glucagon-like peptide 1 (GLP-1) therapeutics developed by **Novo Nordisk (Ozempic)** and **Eli Lilly (Trulicity)** are key in addressing this ongoing epidemic. GLP-1 therapies are gaining traction for the further investigation of neuro cell death. GLP-1 expression occurs in the brain and is demonstrated primarily through a large output of neurons[7]. Its physiology and functionality within the brain is what allows for potential cognitive improvement[7]. Similarly, it has been studied to reduce the occurrence of hypoglycemic episodes and improve weight for those struggling with T2DM[1].

GLP-1 agonists, including exenatide, liraglutide, and more recently lixisenatide, may be advantageous regarding cognition and insulin resistance, as they do not increase hypoglycemic risk, unless associated with sulfonylureas[1,7]. A recent pooled analysis of 6 randomized trials indicated that liraglutide is effective and well tolerated in persons older than 65[14]. However, liraglutide dosage needs to be adjusted according to kidney function[1]. Those with comorbidities that have any implications on the kidneys need to be considered. These therapies require a period of 2-4 weeks for dose titration to reach their maximal effect and therefore require a long-term study to understand their outcomes[14]. Similarly, studies need to consider susceptibility, further titration periods for other relating and conflicting therapies, GLP-1 adoption, and cognitive assessments long term. Based on research conclusions, the above should be considered when addressing questions regarding the risk of the older population, especially those investigating both T2DM and T3DM.

Currently, the use of GLP-1s within PCC LTC facilities is significantly lower ($p<0.05$) than other diabetic therapies such as insulin (**Sanofi's Lantus, Eli Lilly's Humalog**), sulfonylureas (**Pfizer's Glucotrol, Aventis Pharmaceutical's Amaryl**), MR antagonists (**Bayer's Kerendia**), and biguanides (**metformin**). Strong therapeutics such as DPP4i (**Merck's Januvia, Astra Zeneca's Onglyza**) are displaying equal advantageous results for the LTC population. As GLP-1 researchers continue to outline the advantages of the use of therapy on the older population, it will be interesting to see in the upcoming months their potential to reach and retain individuals in LTC.

Similarly, will companies developing therapeutics for AD and dementia such as **Biogen, Eisai, Pfizer, Novartis, Abbvie, Otsuka, and Merck**, consider the LTC T3DM population as a population of interest as the data continues to support the association between the two chronic conditions?

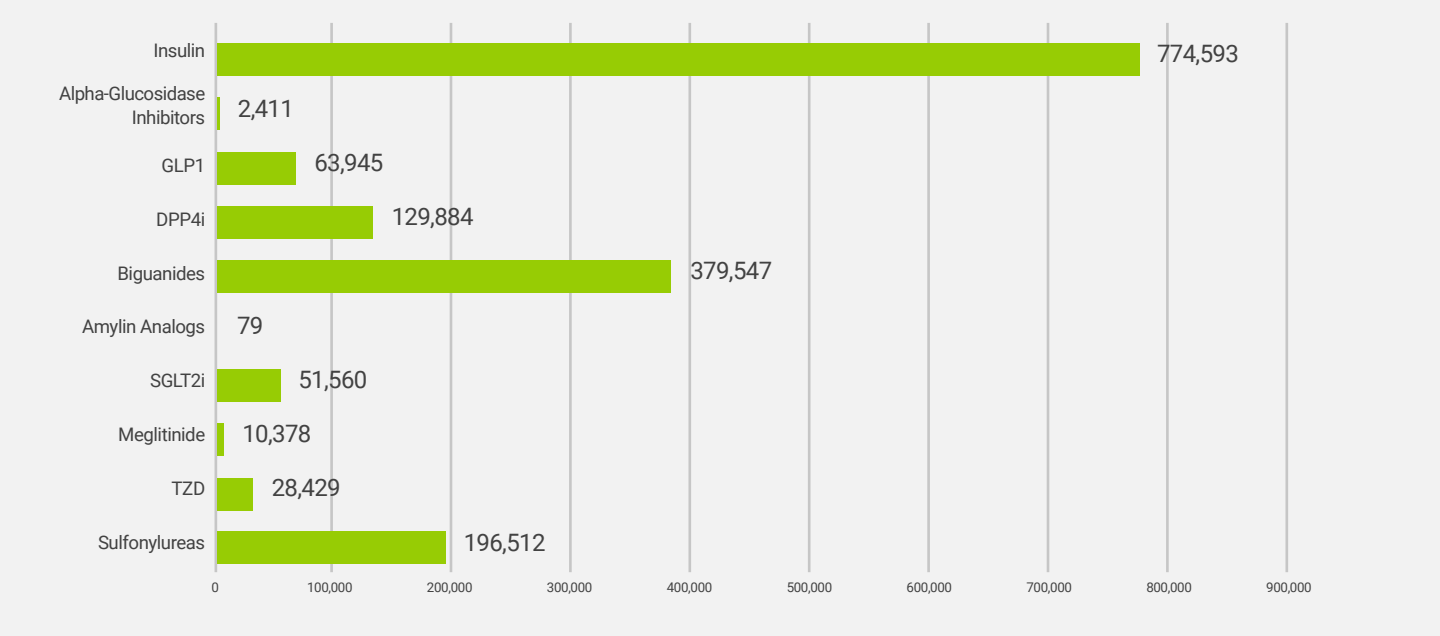

Figure 2. PointClickCare residents on different T2DM therapies. Data was pulled from medication orders from the PointClickCare T2DM population (approx. 3 million residents).

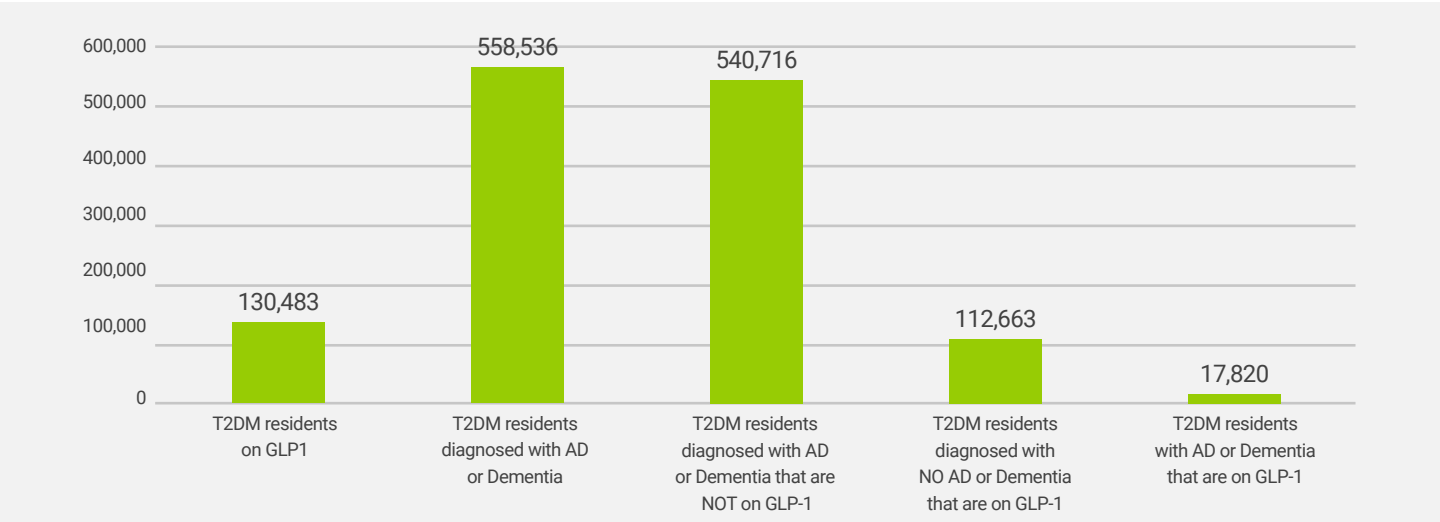

Figure 3. The distribution of GLP-1 administration for T2DM residents (~3 million total residents) and T2DM residents with AD or dementia who are residing in PointClickCare facilities. Figure demonstrates that there is a small proportion of the population who have both T2DM and AD or dementia who are using GLP-1s.

PointClickCare does not prescribe drugs nor does it reflect the position of any medical professionals. Readers should consult a medical professional for any medical treatments, including any drugs mentioned.

References

1. Steinberg, J., & Carlson, L. (2019). Type 2 diabetes Therapies: a STEPS approach. *American family physician*, 99(4), 237-243.
2. Ioannidis, I. (2014). Diabetes treatment in patients with renal disease: Is the landscape clear enough? *World journal of diabetes*, 5(5), 651.
3. Chentli, F., Azzoug, S., & Mahgoun, S. (2015). Diabetes mellitus in elderly. *Indian journal of endocrinology and metabolism*, 19(6), 744.
4. Robertson, D. A., & Home, P. D. (1993). Problems and pitfalls of sulphonylurea therapy in older patients. *Drugs & Aging*, 3(6), 510-524.
5. Munshi, M. N., Florez, H., Huang, E. S., Kalyani, R. R., Mupanomunda, M., Pandya, N., ... & Haas, L. B. (2016). Management of diabetes in long-term care and skilled nursing facilities: a position statement of the American Diabetes Association. *Diabetes care*, 39(2), 308-318.
6. Clemens, K. K., O'Regan, N., & Rhee, J. J. (2019). Diabetes management in older adults with chronic kidney disease. *Current diabetes reports*, 19, 1-11.
7. Duarte, A. I., Candeias, E., Correia, S. C., Santos, R. X., Carvalho, C., Cardoso, S., ... & Moreira, P. I. (2013). Crosstalk between diabetes and brain: glucagon-like peptide-1 mimetics as a promising therapy against neurodegeneration. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, 1832(4), 527-541.
8. Idrees, T., Castro-Revoredo, I. A., Migdal, A. L., Moreno, E. M., & Umpierrez, G. E. (2022). Update on the management of diabetes in long-term care facilities. *BMJ Open Diabetes Research and Care*, 10(4), e002705.
9. Kandimalla, R., Thirumala, V., & Reddy, P. H. (2017). Is Alzheimer's disease a type 3 diabetes? A critical appraisal. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease*, 1863(5), 1078-1089.
10. Nguyen, T. T., Ta, Q. T. H., Nguyen, T. K. O., Nguyen, T. T. D., & Van Giau, V. (2020). Type 3 diabetes and its role implications in Alzheimer's disease. *International journal of molecular sciences*, 21(9), 3165.
11. Janoutová, J., Machaczka, O., Zatloukalová, A., & Janout, V. (2022). Is Alzheimer's disease a type 3 diabetes? A review. *Cent. Eur. J. Public Health*, 30, 139-143.
12. Mishra, M. M. (2023). *Finding Common Involution Between Type 2 Diabetes And Alzheimer's Disease (Type 3 Diabetes) And The Recent Advancement In Their Therapeutic Regime Using Computational Approach* (Doctoral dissertation).
13. González, A., Camila, C., & Maccioni, R. B. (2021). Alzheimer's disease: A potential diabetes type 3. *Alzheimer's & Dementia*, 17, e058533.
14. Scheen, A. J., & Bonnet, F. (2023). Efficacy and safety profile of SGLT2 inhibitors in the elderly: how is the benefit/risk balance?. *Diabetes & Metabolism*, 101419.