

Metabolic Disease and Malignancy: Investigating Breast Cancer Risk in Diabetes Using the NIH All of Us Database



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Introduction

- Breast cancer is the most common cancer worldwide and is becoming the leading cause of death in women in the United States.¹
- Type 2 diabetes (T2DM) affects about one in ten Americans and has been linked to many types of cancer through metabolic changes. A key example is the Warburg effect where tumors adapt to favor glucose-driven glycolysis within the harsh tumor microenvironment. This shift in metabolism supports many aspects of malignancy including proliferation, metastasis, drug resistance and immune evasion.²
- Glucose is the fuel for the process of glycolysis. Hemoglobin A1c is a widely used laboratory test that reflects average blood sugar (glucose) over three months. It is used in the diagnosis and surveillance of diabetes and often a part of health maintenance screenings as well as a determinate of diabetic treatment.

Methods

- With the metabolic characteristics of tumor cells in mind, this study uses data from the NIH All of Us program to determine how common uncontrolled blood glucose is in self-enrolled women with breast cancer within the database.
- Using de-identified patient data, average A1c was calculated six and twelve months prior to initial diagnosis of breast cancer to determine the prevalence of elevated baseline blood sugar as a possible predictor of malignancy in women enrolled in the database over the age of 18 years old.

A1c Distribution in Breast Cancer Patients 6 Months Prior to Diagnosis

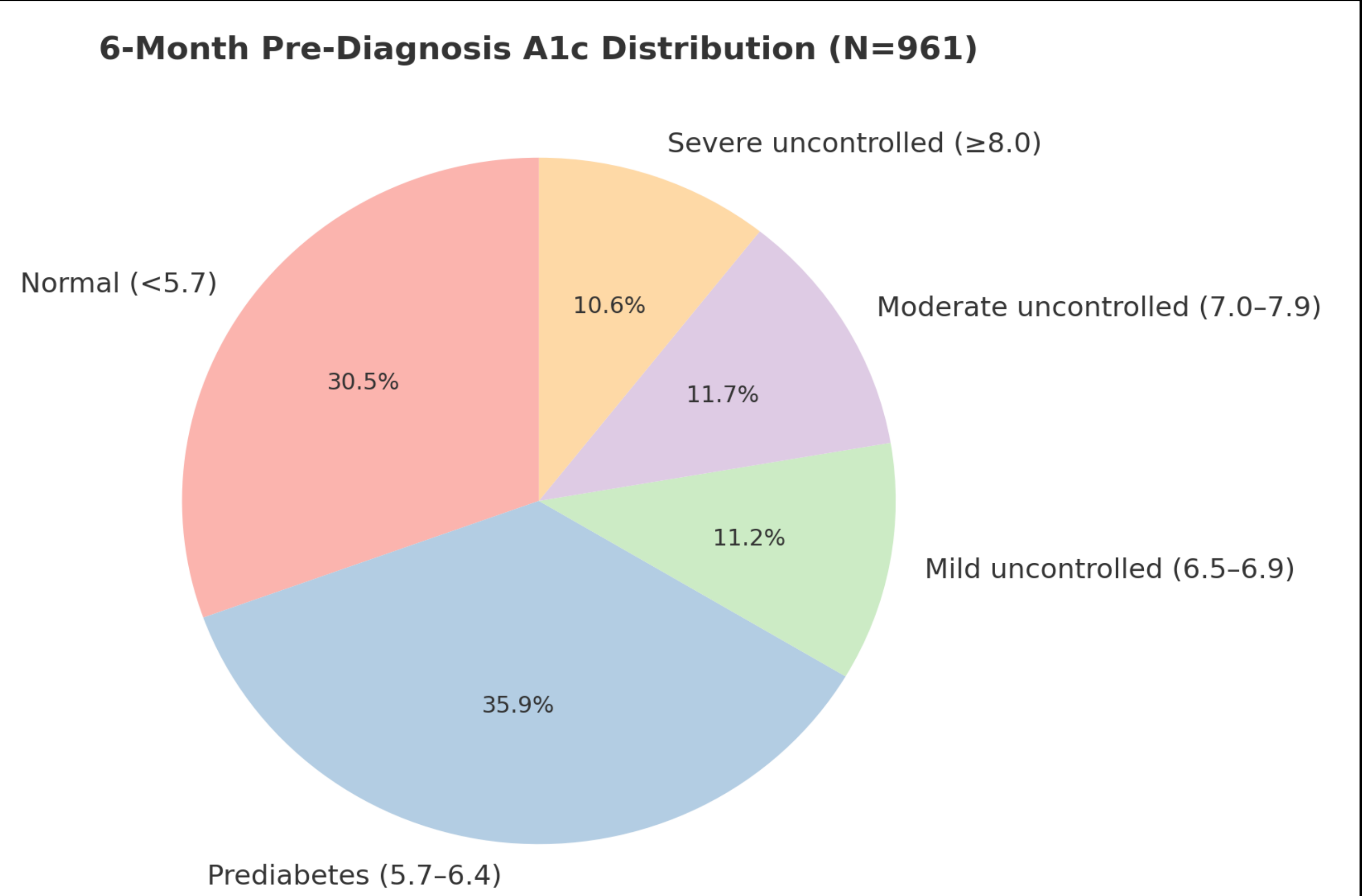


Figure 1: Among 961 patients with A1c measurements 6 months prior to diagnosis, most had normal or prediabetic average A1c while approximately one third had mild to severely uncontrolled glucose levels, suggesting baseline glucose dysregulation may be common in this group.

Controlled vs Uncontrolled A1c Levels Before Breast Cancer Diagnosis

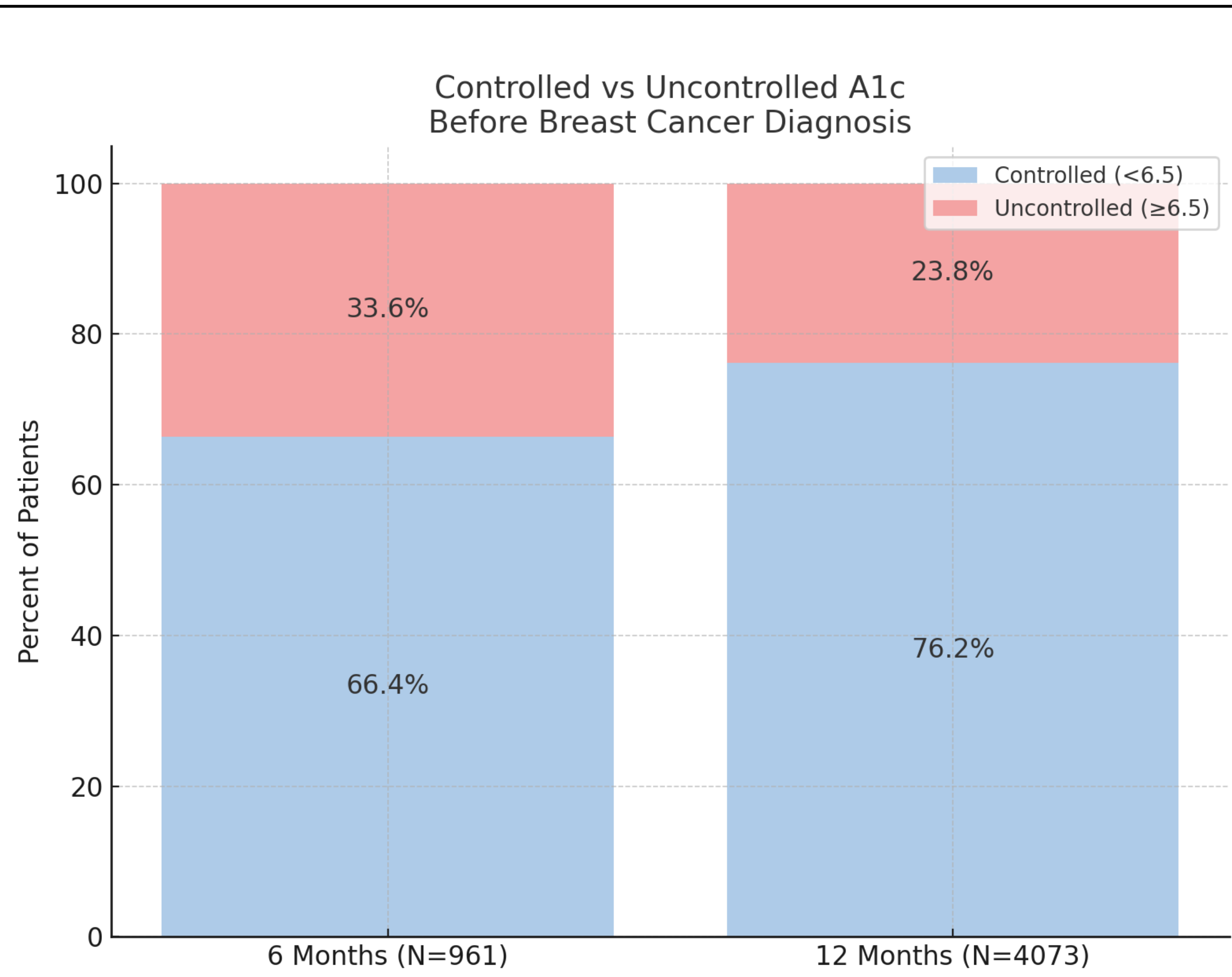


Figure 2: Among 4073 patients with A1c measurements 12 months prior to diagnosis, better glucose control was observed in the larger cohort farther from diagnosis.

Results

- A total of 961 patients had A1c measurements available six months prior to diagnosis, while 4073 patients had measurements at 12 months.
- At six months, 33.6% had uncontrolled A1c (≥6.5) compared to 23.8% at twelve months, indicating a higher burden of poor glucose control closer to diagnosis.
- The most common A1c category was prediabetes (5.7-6.4) followed by normal A1c (<5.7). About one third had some degree of elevated glucose suggesting baseline blood glucose dysregulation in those patients.
- A higher rate of average elevated blood glucose was noted closer to diagnosis, suggesting potential metabolic shifts and/or worsening glycemic control as patients approached breast cancer diagnosis.

Conclusion

- Uncontrolled glucose levels were more prevalent closer to the time of breast cancer diagnosis which could suggest a potential association between blood glucose levels and tumor development or progression.
- These findings underscore the importance of routine metabolic screening, particularly in patients with prediabetes or diabetes. In the primary care setting, this supports the dual emphasis on regular mammography alongside glycemic monitoring, especially in high-risk populations.
- Future studies within these cohorts could explore the potential protective effects of diabetes medications – including oral agents, injectables, and insulin – on breast cancer development. Improved glycemic control may play a role in reducing cancer risk or progression.

1. Centers for Disease Control and Prevention. "Type 2 Diabetes." *Diabetes*, 15 May 2024, www.cdc.gov/diabetes/about/about-type-2-diabetes.html.
2. Liu, Shaojun, et al. "Correlation between the Warburg Effect and Progression of Triple-Negative Breast Cancer." *Frontiers in Oncology*, vol. 12, 27 Jan. 2023, www.ncbi.nlm.nih.gov/pmc/articles/PMC9913723/#:~:text=Evidence%20suggests%20that%20the%20Warburg,https://doi.org/10.3389/fonc.2022.1060495. Accessed 6 Oct. 2023.