

## **Estimating Transition Probabilities and Duration of Pre-Diabetes: A Retrospective Multistate Analysis**

*Palak Sharma, Dilip TR, Vikas Sharma, Anjali Kulkarni*

### **Introduction**

Pre-diabetes is a medical condition characterized by elevated blood sugar levels that are higher than normal but not yet reaching the diagnostic threshold for type II diabetes. It represents an intermediate stage between normoglycemia (normal blood sugar levels) and the development of diabetes ( $100 \leq \text{FPG} < 126$  mg/ dL, or  $140 \leq \text{PPG} < 200$  mg/dL, or  $5.7 \leq \text{HbA1c} < 6.5$  percent). Limited research conducted in India has specifically focused on pre-diabetes despite its significance as a high-risk state for the development of diabetes and associated complications. The increasing prevalence of pre-diabetes and its associated risks has underscored the need for extensive research in this area in recent decades (American Diabetes Association, 2021a).

Studies have revealed that the progression from pre-diabetes to diabetes occurs more rapidly compared to the transition from normoglycemia to diabetes. Consequently, this chapter aims to investigate the risk of prediabetes and the role of pre-diabetes in the progression to diabetes among non-diabetic beneficiaries. Understanding the specific characteristics and dynamics of pre-diabetes can provide valuable insights into the pathogenesis and early detection of diabetes, allowing for timely interventions and targeted strategies for individuals at high risk.

### **Objective**

The study aims at first calculating the incidence rate of diabetes among beneficiaries with normoglycemia and pre-diabetes. Further it estimates the transition probability to the state of diabetes and the duration of stay in prediabetic state among the cohort which is initially free from diabetes, retrospectively.

### **Data and Methods**

the Contributory Health Service Scheme in Mumbai. The dataset comprised 1,669 beneficiaries aged 30 years and above, who were non-diabetic during 2011–2012. It tracked their medical center visits and corresponding laboratory test results over a ten-year period, from January 2012 to December 2021. A multistate model was employed to estimate the transition probabilities between normoglycemia, prediabetes, and diabetes, as well as the duration of time spent in each state before progressing to diabetes.

## Results

***Incidence of Diabetes:*** Among the 1,669 beneficiaries initially free from diabetes, individuals were classified as either normoglycemic or prediabetic. In 2012, 873 beneficiaries (52%) were already in the prediabetic state, representing a higher-risk group. The incidence rate of diabetes among prediabetic individuals was 67.9 cases per 1,000 person-years (PYs), significantly higher than that observed in normoglycemic individuals. Additionally, the incidence rate was higher in prediabetic males (71.3 cases per 1,000 PYs) compared to prediabetic females (65.2 cases per 1,000 PYs). The table below provides detailed information on the number of new diabetes cases over ten years, including incidence rates in both the prediabetic and normoglycemic groups.

***Prediabetic Reversal:*** Of the 873 prediabetic beneficiaries in 2012, 373 (43%) progressed to diabetes over the ten-year follow-up period. The remaining 500 individuals exhibited fluctuating blood glucose levels during the follow-up. By the end of the study, 309 (35%) had reverted to normoglycemia, with a higher proportion of females (37%) compared to males (34%) showing improvement. Additionally, 191 individuals (22%) were lost to follow-up.

***The Multistate model:*** Of the initial 780 normoglycemic beneficiaries, 154 were lost to follow-up, leaving 626 for further analysis. Among these, 584 transitioned to a prediabetic state, while 42 progressed directly to diabetes. Of the beneficiaries who moved from normoglycemia to prediabetes, 447 were followed until the study's end, remaining prediabetic or lost to follow-up. During this period, 137 individuals progressed from prediabetes to diabetes.

Over ten years, the probability of transitioning from normoglycemia to prediabetes was approximately 42%, stabilizing after seven years. Males exhibited a higher probability of transitioning to a prediabetic state than females. The direct transition from normoglycemia to diabetes without passing through a prediabetic state was rare, occurring in only 6% of cases. The probability of transitioning from prediabetes to diabetes was significantly higher than remaining in the normoglycemic state.

Age-related differences in transition probabilities were observed. Beneficiaries aged 30-34 years had a lower probability of progressing to diabetes, while those aged 30-39 years had a higher likelihood of developing prediabetes. Individuals aged 65-69 years had the lowest probability of transitioning to a prediabetic state but the highest likelihood of progressing to diabetes. These findings highlight age-related variations in the progression from normoglycemia to prediabetes and diabetes.

The sojourn time, or average duration in the prediabetic state before progressing to diabetes, was approximately 48 months (~four years), indicating a high transition rate to diabetes in this population. The median time spent in the prediabetic state was longer in females (50 months) compared to males (46 months), suggesting that females experience a slower progression to diabetes. These insights provide valuable information on the time spent in various states before progressing from normoglycemia to prediabetes and from prediabetes to diabetes.

***Conclusion:*** This study underscores the critical need to address prediabetes as a key public health issue. Intervening during the 48-month prediabetic period and targeting the increasing transition probabilities can significantly impact diabetes prevention and improve population health.