Full Paper

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

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Introduction

Prediabetes is referred to an intermediate metabolic state characterized by elevated blood sugar levels that are higher than normal, but not yet reaching the diagnostic threshold for type II diabetes (American Diabetes Association, 2021). It has been recognized as a "high-risk state" by the American Diabetes Association (ADA), where majority of people may not experience clear symptoms, yet it is closely tied to metabolic syndrome and significantly has an increased susceptibility to developing not just diabetes but also other chronic conditions such as cardiovascular disease, stroke, cognitive dysfunction, and hypertension if left unmanaged. (Ambade, 2020; American Diabetes Association, 2021; Fox et al., 2008; Hashemi et al., 2022; Huebschmann et al., 2019; Lai et al., 2017; National Health Portal, 2016; Sattar et al., 2019). The estimated prevalence of prediabetes in 2021 was 9.1% worldwide, which has been projected to increase to 10.0% (638 million) in 2045 (Rooney et al., 2023). Based on a Nationally representative study done by the Indian Council of Medical Research (ICMR) on metabolic non communicable diseases, the weighted prevalence of prediabetes in 2021 in India alone was 15·3%, and predicted number of people with prediabetes were around 136 million (Anjana et al., 2023).

Among the various factors influencing the transition of prediabetes such as demographic characteristics, lifestyle behaviors, existing comorbidities, and family history; age and gender stand out as non-modifiable yet critical determinants, each associated with distinct patterns of risk. The risk of developing prediabetes has been shown to increase with advancing age (Hashemi et al., 2022; Ligthart et al., 2016). Ageing is associated not only with a higher incidence of prediabetes but also with a greater likelihood of its persistence and progression to type 2 diabetes (Bennasar-Veny et al., 2020). Additionally, gender-based differences in the incidence and prevalence of prediabetes have been documented; however, the extent and direction of these disparities vary

across studies. Some investigations have reported a higher prevalence among men (Andes et al., 2020; Breyer et al., 2020; *National Diabetes Statistics Report | Diabetes | CDC*, n.d.) , whereas others have found a greater prevalence among women (Hashemi et al., 2022; NARAYAN et al., 2022), and several studies have observed no statistically significant gender differences. Notably, this gender gap tends to narrow with advancing age (Herpt et al., 2020). In terms of age-specific trends, research has shown that the peak prevalence of prediabetes among men occurs between 55–64 years of age, while women exhibit a higher prevalence at 65 years and older (Anjana et al., 2011, 2017; Mohan V et al., 2016). Additionally, studies conducted in India have highlighted a higher prevalence of prediabetes in urban populations across most age groups, with the exception of those aged 65 years and above, where rural-urban differences tend to converge (Anjana et al., 2011, 2017; Mohan V et al., 2016).

Prediabetes is a complex condition characterized by varying trajectories, with some individuals progressing to type II diabetes while others remain stable or revert to normoglycemia. Despite its high prevalence particularly among older adult, the natural history of glycemic progression, especially the transition from normoglycemia to prediabetes or diabetes, remains incompletely understood (Rooney et al., 2021). The widespread occurrence of prediabetes represents a significant public health concern, given its substantially higher risk of progression to diabetes compared to normoglycemia (American Diabetes Association, 2021; Anjana et al., 2015; Bennasar-Veny et al., 2020; K. Narayan et al., 2021; K. M. V. Narayan & Kanaya, 2020; Pradeepa & Mohan, 2021; Rooney et al., 2021; Tabák et al., 2012). Estimates suggest that the annual rate of conversion from prediabetes to diabetes ranges between 5% and 10% (Bennasar-Veny et al., 2020; Tabák et al., 2012).

Conversely, numerous research investigations have explored the phenomenon of prediabetes reversal, particularly through targeted interventions like structured lifestyle modifications including increased physical activity and a 5–10% reduction in body weight—as well as certain pharmacologic agents, can reduce the risk of progression to diabetes by approximately 40–70% (Ramachandran et al., 2006; Rooney et al., 2021; Tabák et al., 2012; Tuso, 2014). As the earliest clinically identifiable stage of dysglycemia, prediabetes offers a critical window for prevention, wherein timely management of risk factors can significantly alter disease trajectory (Dagogo-Jack et al., 2022; Echouffo-Tcheugui et al., 2018; Galaviz et al., 2022; Glechner et al., 2018; Perreault

et al., 2012; Ramachandran et al., 2006; Rattey KT & Rosenthal M., 2014; Rooney et al., 2021; Tabák et al., 2012; Tuso, 2014).

Despite the growing global research focus on prediabetes, there remains a notable paucity of region-specific studies in India that comprehensively examine the transitions from normoglycemia to prediabetes, progression to diabetes, or potential reversal (Nazari et al., 2018). This gap is particularly concerning given India's high burden of diabetes and the recognized role of prediabetes as a critical, modifiable stage in its pathogenesis. Evidence indicates that the transition from prediabetes to diabetes is more rapid than from normoglycemia, underscoring the urgency of identifying population-specific risk patterns and trajectories. A deeper understanding of the unique characteristics and progression dynamics of prediabetes within the Indian context is essential for informing early detection efforts and designing targeted, culturally appropriate interventions to mitigate the growing diabetes epidemic. This study aims to estimate the incidence of diabetes among individuals with baseline normoglycemia and prediabetes, and to quantify the transition probabilities across glycemic states, with a particular focus on the progression from normoglycemia to prediabetes, prediabetic reversal and from prediabetes to diabetes as well.

Methods

Data

This study utilized electronic medical records of a retrospective cohort comprising 1,670 individuals, aged 30 years and above, who were beneficiaries of a health service scheme of a government hospital in Mumbai, India. This hospital exclusively serves the employees of a specific organization and their dependents free of cost and with uniform screening, forming a closed population.

All individuals included in the cohort were free of diabetes at baseline (January 2012), but further categorised as pre-diabetic and people with normoglycemia, which was based on the latest test results available from 2011[12]. These baseline statuses were considered valid for each individual as of January 1, 2012 (Day 1 of follow-up), who were followed for a period of ten years, till December 31, 2021, and the person-years at risk were calculated starting from January 1, 2012, to December

[1] To account for variability in testing dates, a 7-day window was applied; all blood tests conducted within this period were grouped together to minimize fluctuations in diagnostic status

[2] The study is a part of a broader research project and the methodology including the sample selection is published elsewhere (Sharma et al., 2024).

31, 2021, or until the last available follow-up test result, death, or onset of diabetes, whichever occurred first.

The classification of individuals as diabetic or pre-diabetic in this study followed the diagnostic criteria outlined in the American Diabetes Association's Standards of care in Diabetes (Committee et al., 2025). A diagnosis of diabetes was made if any of the following criteria were met: the Fasting Plasma Glucose (FPG) ≥126 mg/dl (7.0 mmol/l), or Postprandial Glucose ≥200 mg/dl (11.1 mmol/l), or HbA1c ≥ 6.5 percent. In accordance with ADA recommendations, a diagnosis of diabetes was confirmed by repeat testing—either using a different test on the same day or the same test on a subsequent day, if initial results were inconclusive or only one criterion was met. An individual is considered to be pre-diabetic if he/she either has a glucose level between these cut-offs: Fasting Plasma Glucose: 100<= FPG <126 mg/dL, or Postprandial Glucose: 140<= PPG <200 mg/dL, or HbA1c: 5.7<= HbA1c < 6.5 percent.

The table below presents the detailed classification thresholds used for categorizing individuals based on these three diagnostic tests. Individuals not meeting any of the above criteria were classified as **normoglycemic** (normal glucose regulation) (Committee et al., 2025).

Table 1: Definition of diabetes and pre-diabetes as per the American Diabetes Association, 2021

Category	Fasting Plasma Glucose (FPG)	Postprandial Glucose (PPG)	HbA1c
Normoglycemia	FPG <100 mg/ dL	PPPG<140 mg/ dL	HbA1c<5.7%
Pre-diabetic	100<=FPG<126 mg/ dL	140<=PPPG<200 mg/ dL	5.7<=HbA1c<6.5%
Diabetic	FPG >= 126 mg/ dL	PPPG>=200 mg/ dL	HbA1c>=6.5%

***Note**: In the absence of unequivocal hyperglycemia, diagnosis requires two abnormal results from different tests which may be obtained at the same time (e.g., A1C and FPG), or the same test at two different time points.*

Further, it is important to note that the frequency of glycemic testing varied among beneficiaries, as tests were conducted during outpatient visits at the discretion of patients and clinicians. Consequently, not all individuals underwent all three diagnostic tests (FPG, PPG, and HbA1c) at each time point. For the classification of diabetes and pre-diabetes, available test results within a 7-day window were considered. When multiple tests were available within this period,

classification was based on the most conclusive result (if any of the two tests abnormal) according to ADA 2025 criteria. If only a single test was available, diabetes status was determined based solely on that test.

Sample Characteristics

Table 2 summarizes the age and sex distribution of the 1,670 beneficiaries who were free from diabetes at the baseline. Of the total sample, 748 (44.8%) were male and 922 (55.2%) were female, indicating a slightly higher representation of females in the cohort. The mean age of the overall cohort was 55.41 years, with males being older on average (58.55 years) than females (52.86 years). Further, a substantial proportion of the population i.e. 37% were aged 60 years and above, suggesting that the sample skews toward an older demographic. When stratified by sex**,** 44% of males (344 out of 748) and 29.5% of females (272 out of 922) fell within this older age bracket of 60 years and above. The 70+ age group alone accounted for 20.32% of males and 10.85% of females, indicating a higher representation of older males in the cohort.

Table 2: Characteristics of sampled beneficiaries who were free from diabetes at the baseline (N=1670)

	Overall		**Male**		**Female**	
Age Group (age as of 2012)	**Frequency (N)**	**Percentage (%)**	**Frequency (N)**	**Percentage (%)**	**Frequency (N)**	**Percentage (%)**
30-34	50	2.99	8	1.07	42	4.56
35-39	112	6.71	32	4.28	80	8.68
40-44	200	11.98	50	6.68	150	16.27
45-49	214	12.81	86	11.5	128	13.88
50-54	252	15.09	114	15.24	138	14.97
55-59	226	13.53	114	15.24	112	12.15
60-64	218	13.05	122	16.31	96	10.41
65-69	146	8.74	70	9.36	76	8.24
70+	252	15.09	152	20.32	100	10.85
Grand Total	**1670**	**100**	**748**	**100**	**922**	**100**
Mean age	**55.41**		**58.55**		**52.86**	
% total sampled				**44.8**		**55.2**

Statistical Analysis

Incident diabetes is defined as occurring if an individual is free from diabetes at the baseline (2012) and has been subsequently diagnosed with diabetes in the follow-up years. i.e. if there is a transition between the state normoglycemia or pre-diabetes to diabetes in any year between 1st January 2012 to 31st December 2021. The **incidence rate** is calculated as the total number of new cases of diabetes over the ten-year follow-up period divided by the total time that the sampled beneficiary population was under risk of developing diabetes (person years contributed) [3].

A multistate model was employed to estimate transition probabilities over time across three mutually exclusive glycemic states: normoglycemia, prediabetes, and diabetes. The model allowed for transitions from normoglycemia to prediabetes, normoglycemia to diabetes, prediabetes to normoglycemia, and prediabetes to diabetes. Transition probabilities were estimated using the Aalen–Johansen estimator, a non-parametric method that provides cumulative transition probabilities based on observed data without assuming a specific distribution for the time to transition. This estimator relies on the Nelson–Aalen approach for estimating cumulative hazards and incorporates competing risks through the cumulative incidence function, allowing for flexible and robust estimation of both transition probabilities and expected time spent in each state.

Statistical analyses were conducted using STATA version 16 and Python 3.x. Incidence rates and state-specific transition probabilities over time in each state were estimated and visualized to support interpretation.

Results

Incidence of Diabetes

The overall incidence of type II diabetes was calculated to be 20.94 cases per 1000 person years. Further, it is found that the incidence rate of diabetes among the beneficiaries with baseline pre-diabetes was 41.74 cases 1000 person-years (PYs), which was significantly higher compared to those who had normoglycemia (i.e. normal blood glucose levels) with only 15.89 cases per 1000 PYs. Furthermore, the incidence rate of diabetes was found to be higher among males compared to females with baseline pre-diabetes (44.60 cases per 1000 PYs in males and 39.75 cases per 1000

[3] The person-time of observation, or observation time, is determined by calculating the total time for which an individual was at risk. This is calculated as the time between the date of the event (i.e., diabetes diagnosis, censorship, death, or the end of follow-up), whichever occurred first, and 1st January, 2012. This time interval is then converted from days to months/years to facilitate data analysis.

PYs in females). Table 3 presents the number of new diabetes cases over a 10-year period, the total person-years contributed, and the corresponding incidence rates with 95% confidence intervals in both groups.

Table 3: Incidence of diabetes (per 1000 PYs) among beneficiaries with normoglycemia and beneficiaries with pre-diabetes over the period of ten years, 2012-2021 (baseline N= 1670)

	Status at the beginning of the follow-up	Person-years contributed	Newly diagnosed cases of diabetes	IR (95% CI) per 1000 PYs
	Total	13132.87	275	20.94 (18.46, 23.41)
Overall	**Normoglycemia**	10569.65	168	15.89 (13.49, 18.3)
	Pre-diabetes	2563.22	107	41.74 (33.83, 49.65)
Males	**Normoglycemia**	4713.80	72	15.27 (11.75, 18.80)
	Pre-diabetes	1053.79	47	44.60 (31.85, 57.35)
Females	**Normoglycemia**	5855.84	96	16.39 (13.11, 19.67)
	Pre-diabetes	1509.44	60	39.75 (29.69, 49.81)

Note: *The person years contributed for those who were didn't visit the hospital from 2012 onwards was taken to be 0, hence not impacted the results overall. IR: Incidence Rate, CI: Confidence Interval, PYs: Person years*

Transition Probabilities for each of the glycemic states

Figure 1 presented below shows the Aalen–Johansen estimates of transition probabilities between glycemic states over the 10-year follow-up period (120 months). The probability of transitioning from normoglycemia to prediabetes increased gradually, reaching approximately 25% by the end of the follow-up, indicating that one-fourth of the cohort developed prediabetes over the study period. Among individuals with baseline prediabetes, the probability of progressing to diabetes rose steadily and reached approximately 30% by the end of 120 months (10 years). In comparison, the probability of direct transition from normoglycemia to diabetes remained low throughout the follow-up, staying below 20%. Additionally, a substantial proportion of individuals with prediabetes reverted to normoglycemia during follow-up with the highest transition probability. The probability of reversion peaked early, approaching 60% within the first 24 to 36 months, and declined gradually thereafter to 40% by the end of the follow up period.

Figure 1: Transition probability for each of the glycemic states of the multistate model over the period of 10 years (120 months), 2012-2021

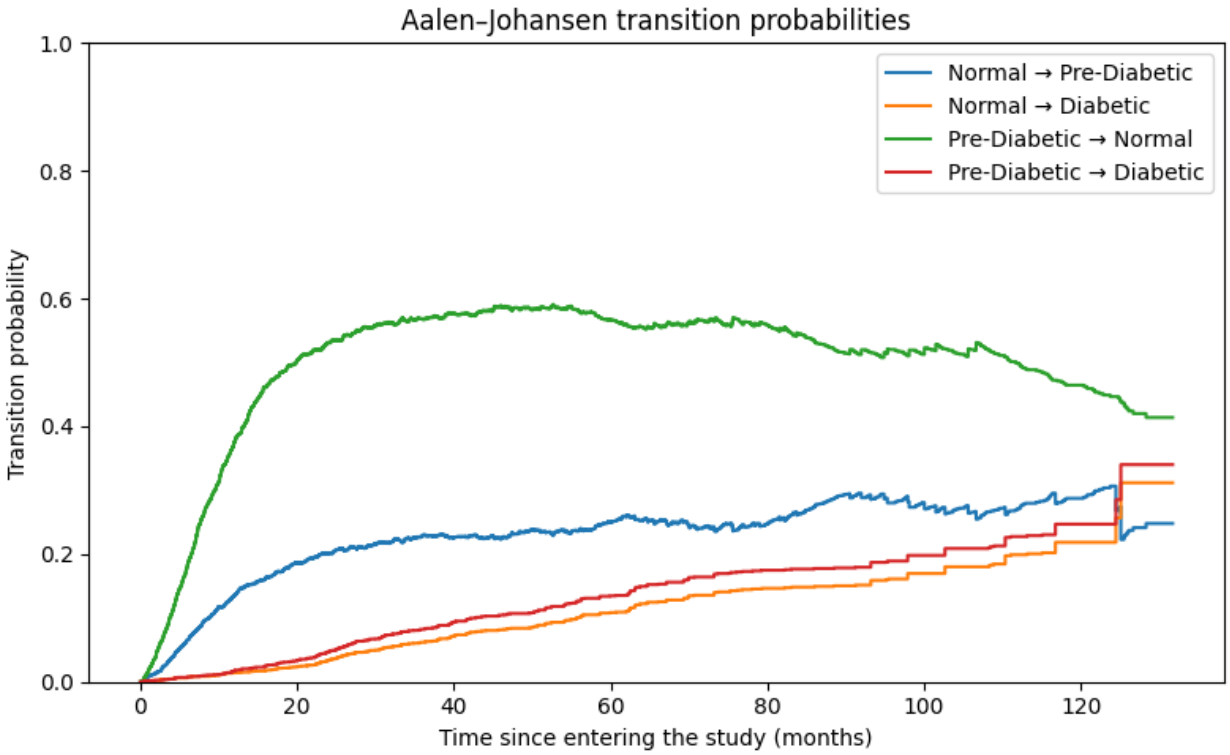
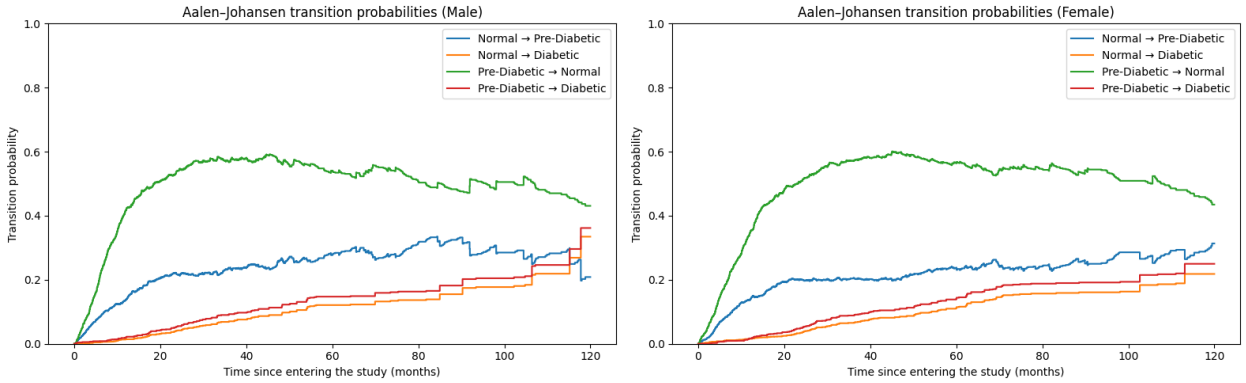


Figure 2 presents the Aalen–Johansen estimates of transition probabilities between glycemic states over a 10-year follow-up period, stratified by sex. Overall, the transition patterns were broadly similar between male and female beneficiaries. However, the probability of transitioning from normoglycemia to prediabetes was consistently higher and showed a steady increase over time among males. Also, the probability of a direct transition from normoglycemia to diabetes remained higher in males in comparison to females throughout the follow-up period.

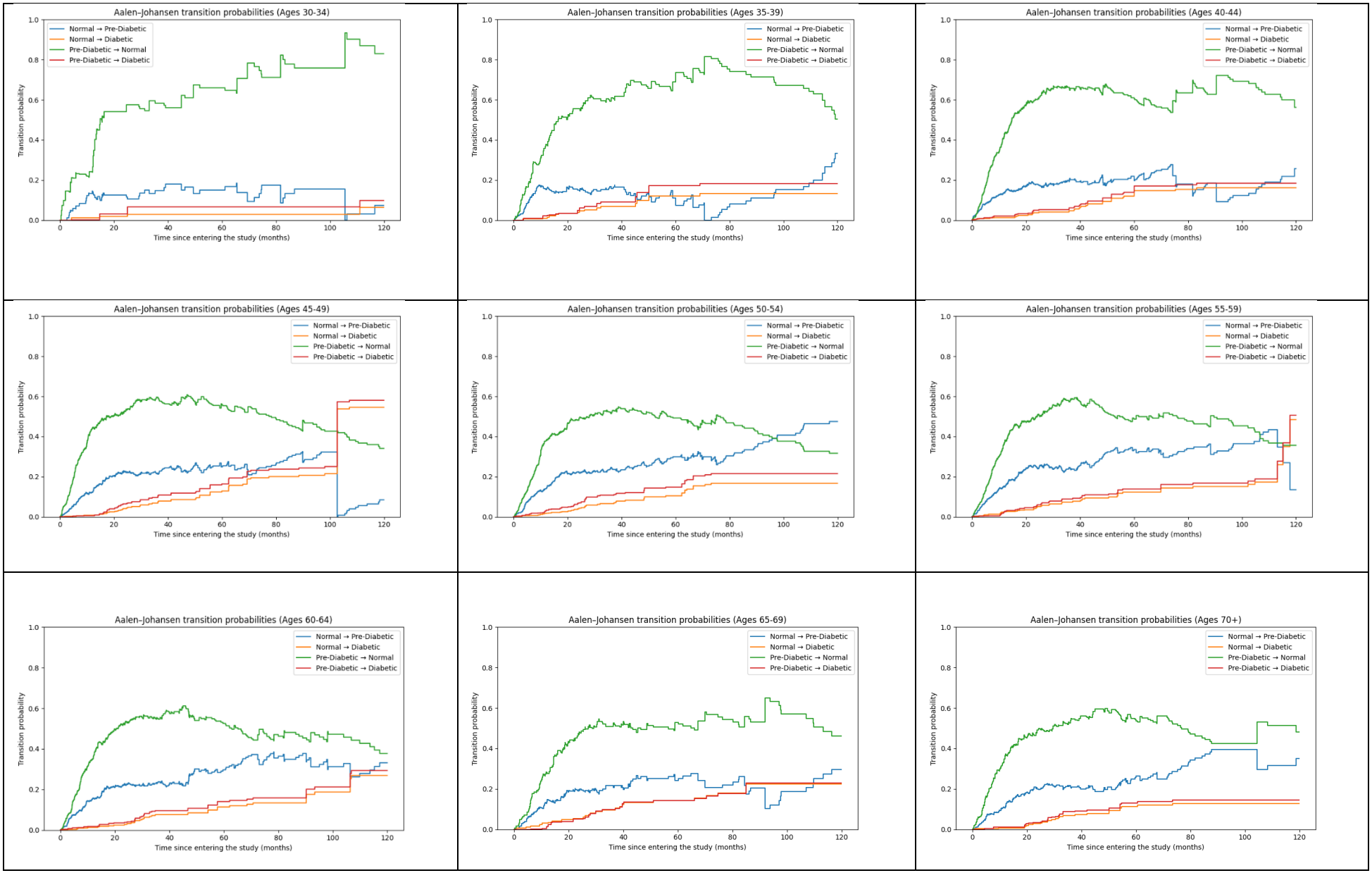
Among individuals with prediabetes, the probability of progression to diabetes was notably higher in males (~35%a) compared to females (~21%) at the end of the 120 months of timespan, with an increasingly upward trend among in males. The findings show that the probability of reverting from prediabetes to normoglycemia peaked early during the follow-up (within the first 24–36 months) for both sexes—approaching 60%—and declined gradually thereafter. However the prediabetic reversal transition was observed higher among females, but no substantial sex differences could be seen in the overall pattern.

Figure 2: Estimates of transition probability for each glycemic state estimated stratified by sex for each of the states of the multistate model



The **figure 3** below illustrates age-related differences in transition probabilities across various glycemic states. The probability of transitioning from normoglycemia to pre-diabetes increases with age. The lowest probability is observed among individuals aged 30–34 years, remaining close to 10% by the end of the follow-up period. In contrast, the highest transition probability approximately 50% was observed in the 50–54 age group. Conversely, the probability of reversal from pre-diabetes to normoglycemia over the 10-year period is highest among younger individuals, particularly those in their early thirties, and shows a steady decline with advancing age. This suggests that younger age groups are more likely to revert to normoglycemia, while older individuals are at greater risk of progression to pre-diabetes.

Figure 3: Transition probability for each glycemic state estimated separately from the state of normoglycemia to pre-diabetes and diabetes for each of the age groups[4]



[4] Age is considered as of 2012 i.e. the start of the follow-up

Discussion

Prediabetes represents a critical transitional state in the glycemic continuum, where early metabolic dysregulation often occurs silently but carries a markedly increased risk for progression to type II diabetes. As the burden of diabetes continues to rise in India, understanding the trajectory from normal glucose levels to prediabetes and how prediabetes affects the transition to developing type II diabetes is essential for timely intervention and prevention strategies. Despite the high prevalence of prediabetes, there remains a scarcity of longitudinal studies in India that explore these transitions using clinical data. Addressing this gap, the present study estimated the incidence of type II diabetes over a 10-year follow-up period in a closed cohort of individuals initially classified as normoglycemic or prediabetic. Further the study also quantified the transition probabilities associated with progression from normoglycemia to prediabetes, its reversal i.e. prediabetes to normoglycemia and from prediabetes to diabetes, which contributes to a deeper understanding of natural history of glycemic progression within an Indian population and provides valuable insights for targeted screening, risk stratification, and public health planning.

The findings of this study indicate a substantially higher incidence of type II diabetes among individuals with prediabetes at baseline compared to those with normoglycemia. Specifically, the incidence rate among those with baseline prediabetes was found to be 41.74 cases per 1,000 person-years, more than double the rate observed among normoglycemic beneficiaries, which was 15.89 cases per 1,000 person-years. These results are consistent with earlier evidence from a population-based study in Chennai, which reported an even higher incidence of 78.9 per 1,000 person-years among individuals with prediabetes (Anjana et al., 2015). Similarly, another Indian study reported diabetes conversion rates of 58.9% among individuals with prediabetes and 19.4% among those with normal blood glucose levels at baseline (Pradeepa & Mohan, 2021). The findings from the Strong Heart Study (SHS) conducted among American Indians, revealed that the diabetes incidence among those with baseline prediabetes was 66.1 cases per 1,000 person-years compared to 23.4 cases per 1,000 person-years in normoglycemic individuals over a median follow-up of 7.8 years (Wang et al., 2010). Further, a significant and steady transition from prediabetes to diabetes was observed in the cohort, with the cumulative risk reaching approximately 30% over ten years. This persistent, moderate progression risk highlights the importance of prediabetes as a critical window for intervention to prevent or delay diabetes onset. Our findings are consistent with prior studies; for instance, a study (Bennasar-Veny et al., 2020) reported a 23% progression rate to

diabetes among prediabetic workers over a shorter follow-up period. Similarly, another study (Tabák et al., 2012) has estimated that 5–10% of individuals with prediabetes progress to diabetes annually, emphasizing the substantial risk within this group.

The incidence of diabetes among individuals with baseline prediabetes in our study is comparable with some previous studies and the overall direction of the findings also remains consistent. This difference can largely be attributed to methodological and design-related variations. Our study followed a retrospective cohort design with a 10-year follow-up period, during which individuals underwent repeated testing at multiple, though irregular, time points. This allowed for continuous monitoring and more precise identification of transitions based on dynamic changes in glycemic status. We applied the American Diabetes Association (ADA) 2025 criteria (Committee et al., 2025) and required confirmatory evidence from at least two diagnostic tests within a defined window to classify individuals as diabetic or prediabetic. In contrast, many previous studies were cross-sectional or used only two time points over an average interval of 8–10 years (Anjana et al., 2015; Deepa et al., 2003; Ghorpade et al., 2013; Vijayakumar et al., 2019), with broader diagnostic criteria or reliance on a single test, which may have led to higher and less temporally precise estimates of diabetes incidence. Previous studies have observed huge differences in the progression rates from pre-diabetes to diabetes based on definitional differences (Bennasar-Veny et al., 2020; Davidson et al., 2021; Nazari et al., 2018), and due to heterogeneous nature of definition of pre-diabetes as well (Wang et al., 2010).

The study also found that probability of transitioning from normoglycemia to prediabetes increased gradually to approximately 25% by the end of follow-up, reflecting the slow metabolic decline associated with older age-sex, urbanization driven lifestyle changes, and even obesity, which are some of the socio-demographic characteristics of the studied cohort. In contrast, the direct transition from normoglycemia to diabetes remained around 20%, confirming that while bypassing prediabetes is possible, it is uncommon. This supports the conceptualization of prediabetes as a critical, intermediate, and clinically actionable phase preceding diabetes onset. Our findings align with previous studies; for example, a study reported a 16% ten-year transition probability and a 8.7% five-year transition probability from normal glycemia to diabetes (Nazari et al., 2018).

The present study revealed notable differences in the incidence rates of diabetes and transition probabilities across age groups and between sexes. While age and sex are non-modifiable risk factors, the progression from prediabetes to diabetes and the potential for reversion to normoglycemia appear to be influenced by these demographic characteristics. Among individuals with prediabetes, males exhibited a higher incidence rate of diabetes (44.60 cases per 1,000 person-years) compared to females (39.75 cases per 1,000 person-years). This finding aligns with some studies reporting a higher incidence among men (Engberg et al., 2009; Magliano et al., 2008; Sharma et al., 2024; Vega et al., 2015), though others have observed a greater incidence among women (Van Dieren et al., 2010; Wang et al., 2010). For instance, in contrast to our findings, a cohort study with an 8-year follow-up reported lower diabetes incidence among prediabetic men compared to women (57.6 vs. 72.4 cases per 1,000 person-years, respectively) (Wang et al., 2010). However, a few studies have also reported that differences in the incidence of males and females have not been statistical (Hyun et al., 2022; Urrutia et al., 2021). A particular observation from the present study was the markedly higher cumulative probability of progression from prediabetes to diabetes among males (~35%) compared to females (~21%) over the 10-year period. This difference suggests that once prediabetes is established, males may be at a significantly greater risk of progressing to overt diabetes. These sex-based differences may reflect underlying physiological and behavioral factors, including hormonal influences, fat distribution, and healthcare-seeking behaviors, underscoring the need for targeted strategies that account for sex-specific risks in diabetes prevention and management. Additionally, the age was also found to be a prominent factor influencing transition dynamics. The Aalen–Johansen estimates indicated that the probability of transitioning from normoglycemia to prediabetes increased progressively with age. Conversely, the likelihood of reversing from prediabetes to normoglycemia was highest among younger individuals, peaking within the first few years of follow-up, and declined steadily with advancing age. These patterns underscore the dynamic nature of prediabetes, particularly in younger adults, and highlight the importance of early identification and intervention to maximize the chances of glycemic recovery.

A key finding of the study was the substantial probability of reversal from prediabetes to normoglycemia, particularly early in the follow-up period. The estimated probability of reversion peaked at approximately 60% within the first 2–3 years and declined to around 40% by the end of

the 10-year follow-up. This high early reversion rate underscores the significant metabolic flexibility during the prediabetic stage and suggests that reversals are most likely to occur soon after prediabetes is detected. Such reversibility may be influenced by behavioral changes following diagnosis, natural glycemic fluctuations (including regression to the mean), or timing-related variation in testing. Notably, few Indian cohort studies have explored glycemic reversibility in depth, making these findings particularly relevant for population-level diabetes prevention strategies. The inverse association observed between age and the likelihood of prediabetic reversal further emphasizes the importance of early detection and timely intervention especially among younger individuals, where the physiological potential for normalization appears to be greater. In contrast, older adults may require more intensive or sustained efforts to prevent progression due to accumulated metabolic risk and reduced plasticity. Our findings are supported by international evidence. For instance, a workplace cohort study from Spain reported that approximately 36% of individuals with prediabetes reverted to normoglycemia within five years (Bennasar-Veny et al., 2020). Similarly, the Atherosclerosis Risk in Communities (ARIC) study found that 13% of prediabetic adults aged 45–64 years transitioned back to normal glucose regulation over a 6-year period (Rooney et al., 2021). A Chinese cohort study (Yang et al., 2024) reported that 570 of 2,655 participants (21%) reverted to normoglycemia over a four-year follow-up. Estimates of reversion rates have varied considerably in the literature, ranging from 9% to over 36% depending on population characteristics and diagnostic criteria (Hu et al., 2025). In addition to age and sex, there are several modifiable factors, identified in previous studies as facilitators of glycemic reversal, including younger age, favorable metabolic profiles, higher levels of 25-hydroxyvitamin D and free thyroxine (Chen et al., 2024), reduced remnant cholesterol, increased HDL cholesterol, and engagement in moderate physical activity (Hu et al., 2025; Jeon et al., 2007). However, due to limitations in the available data—particularly on biochemical parameters, BMI, and physical activity—our study was unable to directly assess the role of these predictors.

Nevertheless, the high probability of reversal observed in our cohort provides strong support for the notion that prediabetes is a modifiable condition. This reinforces the need for systematic screening and early, targeted lifestyle interventions. Evidence from landmark trials such as the Diabetes Prevention Program (DPP) and the Indian Diabetes Prevention Programme (IDPP) has already demonstrated that weight loss, dietary changes, and increased physical activity can significantly reduce diabetes incidence and even restore normoglycemia in high-risk individuals

(Dagogo-Jack et al., 2022; Galaviz et al., 2022; Glechner et al., 2018; Perreault et al., 2012; Ramachandran et al., 2006; Tuso, 2014). Therefore, integrating strategies to identify and reverse prediabetes—particularly in younger, high-risk adults—should remain a public health priority.

This study provides robust evidence on the incidence of diabetes among people with normoglycemic and prediabetes, revealing a substantial risk of progression over time. By employing a multistate model, we quantified the transition probabilities between glycemic states, offering a detailed view of the dynamic and the natural history of glycemic deterioration and emphasize a critical window during which early identification and intervention can be most effective. The observed transition patterns underscore the importance of prediabetes as a key target for risk stratification and preventative strategies. Addressing this stage with timely and targeted public health interventions holds significant promise for curbing the growing burden of type II diabetes and improving long-term population health outcomes.

References

Ambade, M. (2020). *Economic Burden of Diabetes and Cardio-Vascular Diseases on Households in India Prof. Balram Paswan*. International Institute for Population Sciences.

American Diabetes Association. (2021). Classification and diagnosis of diabetes: Standards of medical care in diabetes-2021. *Diabetes Care*, *44*, S15–S33. https://doi.org/10.2337/dc21-S002

Andes, L. J., Cheng, Y. J., Rolka, D. B., Gregg, E. W., & Imperatore, G. (2020). Prevalence of Prediabetes Among Adolescents and Young Adults in the United States, 2005-2016. *JAMA Pediatrics*, *174*(2), e194498–e194498. https://doi.org/10.1001/JAMAPEDIATRICS.2019.4498

Anjana, R. M., Deepa, M., Pradeepa, R., Mahanta, J., Narain, K., Das, H. K., Adhikari, P., Rao, P. V., Saboo, B., Kumar, A., Bhansali, A., John, M., Luaia, R., Reang, T., Ningombam, S., Jampa, L., Budnah, R. O., Elangovan, N., Subashini, R., … Yajnik, C. S. (2017). Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR–INDIAB population-based cross-sectional study. *The Lancet Diabetes and Endocrinology*, *5*(8), 585–596. https://doi.org/10.1016/S2213-8587(17)30174-2

Anjana, R. M., Pradeepa, R., Deepa, M., Datta, M., Sudha, V., Unnikrishnan, R., Bhansali, A., Joshi, S. R., Joshi, P. P., Yajnik, C. S., Dhandhania, V. K., Nath, L. M., Das, A. K., Rao, P. v., Madhu, S. v., Shukla, D. K., Kaur, T., Priya, M., Nirmal, E., … Mohan, V. (2011). Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase i results of the Indian Council of Medical Research-INdia DIABetes (ICMR-INDIAB) study. *Diabetologia*, *54*(12), 3022–3027. https://doi.org/10.1007/S00125-011-2291-5/FIGURES/1

Anjana, R. M., Rani, C. S. S., Deepa, M., Pradeepa, R., Sudha, V., Nair, H. D., Lakshmipriya, N., Subhashini, S., Binu, V. S., Unnikrishnan, R., & Mohan, V. (2015). Incidence of diabetes and prediabetes and

predictors of progression among Asian Indians: 10-year follow-up of the Chennai urban rural epidemiology study (CURES). *Diabetes Care*, *38*(8), 1441–1448. https://doi.org/10.2337/dc14-2814

Anjana, R. M., Unnikrishnan, R., Deepa, M., Pradeepa, R., Tandon, N., Das, A. K., Joshi, S., Bajaj, S., Jabbar, P. K., Das, H. K., Kumar, A., Dhandhania, V. K., Bhansali, A., Rao, P. V., Desai, A., Kalra, S., Gupta, A., Lakshmy, R., Madhu, S. V., … Ghosh, S. (2023). Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). *The Lancet Diabetes & Endocrinology*. https://doi.org/10.1016/S2213-8587(23)00119-5

Bennasar-Veny, M., Fresneda, S., López-González, A., Busquets-Cortés, C., Aguiló, A., & Yañez, A. M. (2020). Lifestyle and progression to type 2 diabetes in a cohort of workers with prediabetes. *Nutrients*, *12*(5). https://doi.org/10.3390/nu12051538

Breyer, M. K., Ofenheimer, A., Altziebler, J., Hartl, S., Burghuber, O. C., Studnicka, M., Purin, D., Heinzle, C., Drexel, H., Franssen, F. M. E., Wouters, E. F. M., Harreiter, J., Kautzky-Willer, A., & Breyer-Kohansal, R. (2020). Marked differences in prediabetes- and diabetes-associated comorbidities between men and women—Epidemiological results from a general population-based cohort aged 6-80 years—The LEAD (Lung, hEart, sociAl, boDy) study. *European Journal of Clinical Investigation*, *50*(3), e13207. https://doi.org/10.1111/ECI.13207

Chen, W., Hu, H., Cao, C., Liu, D., & Han, Y. (2024). Link between remnant cholesterol and the reversion to normoglycemia in Chinese adults with prediabetes: a 5-year cohort study. *Scientific Reports 2024 14:1*, *14*(1), 1–14. https://doi.org/10.1038/s41598-024-69169-x

Committee, A. D. A. P. P., ElSayed, N. A., McCoy, R. G., Aleppo, G., Balapattabi, K., Beverly, E. A., Briggs Early, K., Bruemmer, D., Ebekozien, O., Echouffo-Tcheugui, J. B., Ekhlaspour, L., Gaglia, J. L., Garg, R., Khunti, K., Lal, R., Lingvay, I., Matfin, G., Pandya, N., Pekas, E. J., … Bannuru, R. R. (2025). 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. *Diabetes Care*, *48*(Supplement_1), S27–S49. https://doi.org/10.2337/DC25-S002

Dagogo-Jack, S., Umekwe, N., Brewer, A. A., Owei, I., Mupparaju, V., Rosenthal, R., & Wan, J. (2022). Outcome of lifestyle intervention in relation to duration of pre-diabetes: The Pathobiology and Reversibility of Prediabetes in a Biracial Cohort (PROP-ABC) study. *BMJ Open Diabetes Research and Care*, *10*(2). https://doi.org/10.1136/bmjdrc-2021-002748

Davidson, K. W., Barry, M. J., Mangione, C. M., Cabana, M., Caughey, A. B., Davis, E. M., Donahue, K. E., Doubeni, C. A., Krist, A. H., Kubik, M., Li, L., Ogedegbe, G., Owens, D. K., Pbert, L., Silverstein, M., Stevermer, J., Tseng, C. W., & Wong, J. B. (2021). Screening for Prediabetes and Type 2 Diabetes: US Preventive Services Task Force Recommendation Statement. *JAMA - Journal of the American Medical Association*, *326*(8), 736–743. https://doi.org/10.1001/jama.2021.12531

Deepa, M., Pradeepa, R., Rema, M., Mohan, A., Deepa, R., Shanthirani, S., & Mohan, V. (2003). The Chennai Urban Rural Epidemiology Study (CURES)-Study Design And Methodology (Urban Component) (CURES-1). In *Original Article* (Vol. 51).

Echouffo-Tcheugui, J. B., Niiranen, T. J., McCabe, E. L., Jain, M., Vasan, R. S., Larson, M. G., & Cheng, S. (2018). Lifetime prevalence and prognosis of prediabetes without progression to diabetes. In *Diabetes Care* (Vol. 41, Issue 7, pp. 117–118). American Diabetes Association Inc. https://doi.org/10.2337/dc18-0524

Engberg, S., Vlstisen, D., Lau, C., Glümer, C., Joørgensen, T., Pedersen, O., & Borch-Johnsen, K. (2009). Progression to impaired glucose regulation and diabetes in the population-based inter99 study. *Diabetes Care*, *32*(4), 606–611. https://doi.org/10.2337/DC08-1869,

Fox, C. S., Pencina, M. J., Wilson, P. W. F., Paynter, N. P., Vasan, R. S., & D'agostino, R. B. (2008). Lifetime Risk of Cardiovascular Disease Among Individuals With and Without Diabetes Stratified by Obesity Status in the Framingham Heart Study org/licenses/by-nc-nd/3.0/ for details. *DIABETES CARE*, *31*(8). https://doi.org/10.2337/dc08

Galaviz, K. I., Weber, M. B., Suvada, K., Gujral, U. P., Wei, J., Merchant, R., Dharanendra, S., Haw, J. S., Narayan, K. M. V., & Ali, M. K. (2022). Interventions for Reversing Prediabetes: A Systematic Review and Meta-Analysis. *American Journal of Preventive Medicine*, *62*(4), 614–625. https://doi.org/10.1016/j.amepre.2021.10.020

Ghorpade, A. G., Majgi, S. M., Sarkar, S., Sekhar Kar, S., Roy, G., Ananthanarayanan, P., & Das, A. (2013). Diabetes in rural Pondicherry, India: a population-based study of the incidence and risk factors. *WHO South-East Asia Journal of Public Health*, *2*(1), 6. https://doi.org/10.4103/2224-3151.115828

Glechner, A., Keuchel, L., Affengruber, L., Titscher, V., Sommer, I., Matyas, N., Wagner, G., Kien, C., Klerings, I., & Gartlehner, G. (2018). Effects of lifestyle changes on adults with prediabetes: A systematic review and meta-analysis. *Primary Care Diabetes*, *12*(5), 393–408. https://doi.org/10.1016/j.pcd.2018.07.003

Hashemi, S. J., Karandish, M., Cheraghian, B., & Azhdari, M. (2022). Prevalence of prediabetes and associated factors in southwest iran: results from Hoveyzeh cohort study. *BMC Endocrine Disorders*, *22*(1). https://doi.org/10.1186/s12902-022-00990-z

Herpt, T. T. W. van, Ligthart, S., Leening, M. J. G., Van Hoek, M., Lieverse, A. G., Ikram, M. A., Sijbrands, E. J. G., Dehghan, A., & Kavousi, M. (2020). Lifetime risk to progress from pre-diabetes to type 2 diabetes among women and men: Comparison between American Diabetes Association and World Health Organization diagnostic criteria. *BMJ Open Diabetes Research and Care*, *8*(2). https://doi.org/10.1136/bmjdrc-2020-001529

Hu, S., Ji, W., Zhang, Y., Zhu, W., Sun, H., & Sun, Y. (2025). Risk factors for progression to type 2 diabetes in prediabetes: a systematic review and meta-analysis. *BMC Public Health*, *25*(1), 1220. https://doi.org/10.1186/S12889-025-21404-4

Huebschmann, A. G., Huxley, R. R., Kohrt, W. M., Zeitler, P., Regensteiner, J. G., & Reusch, J. E. B. (2019). Sex differences in the burden of type 2 diabetes and cardiovascular risk across the life course. In

Diabetologia (Vol. 62, Issue 10, pp. 1761–1772). Springer Verlag. https://doi.org/10.1007/s00125-019-4939-5

Hyun, M. K., Park, J. H., Kim, K. H., Ahn, S. K., & Ji, S. M. (2022). Incidence and risk factors for progression to diabetes mellitus: A retrospective cohort study. *International Journal of Environmental Research and Public Health*, *19*(1). https://doi.org/10.3390/ijerph19010123

Jeon, C. Y., Lokken, R. P., Hu, F. B., & Van Dam, R. M. (2007). Physical Activity of Moderate Intensity and Risk of Type 2 DiabetesA systematic review. *Diabetes Care*, *30*(3), 744–752. https://doi.org/10.2337/DC06-1842

Lai, Y. J., Hu, H. Y., Lee, Y. L., Ku, P. W., Yen, Y. F., & Chu, D. (2017). A retrospective cohort study on the risk of stroke in relation to a priori health knowledge level among people with type 2 diabetes mellitus in Taiwan. *BMC Cardiovascular Disorders*, *17*(1), 1–8. https://doi.org/10.1186/s12872-017-0568-4

Ligthart, S., van Herpt, T. T. W., Leening, M. J. G., Kavousi, M., Hofman, A., Stricker, B. H. C., van Hoek, M., Sijbrands, E. J. G., Franco, O. H., & Dehghan, A. (2016). Lifetime risk of developing impaired glucose metabolism and eventual progression from prediabetes to type 2 diabetes: A prospective cohort study. *The Lancet Diabetes and Endocrinology*, *4*(1), 44–51. https://doi.org/10.1016/S2213-8587(15)00362-9

Magliano, D. J., Barr, E. L. M., Zimmet, P. Z., Cameron, A. J., Dunstan, D. W., Colagiuri, S., Jolley, D., Owen, N., Phillips, P., Tapp, R. J., Welborn, T. A., & Shaw, J. E. (2008). Glucose indices, health behaviors, and incidence of diabetes in Australia: The Australian diabetes, obesity and lifestyle study. *Diabetes Care*, *31*(2), 267–272. https://doi.org/10.2337/DC07-0912,

Mohan V, Kaur Tanvir, Anjana R.M, & Pradeepa R Guha. (2016). *ICMR-INdia DIABetes Phase I Report*. https://main.icmr.nic.in/sites/default/files/reports/ICMR_INDIAB_PHASE_I_FINAL_REPORT.pdf

Narayan, K., Kondal, D., Kobes, S., Staimez, L. R., Mohan, D., Gujral, U. P., Patel, S. A., Anjana, R. M., Shivashankar, R., Ali, M. K., Chang, H. H., Kadir, M., Prabhakaran, D., Daya, N., Selvin, E., Tandon, N., Hanson, R., & Mohan, V. (2021). Incidence of diabetes in South Asian young adults compared to Pima Indians. *BMJ Open Diabetes Research and Care*, *9*(1). https://doi.org/10.1136/bmjdrc-2020-001988

Narayan, K. M. V., & Kanaya, A. M. (2020). Why are South Asians prone to type 2 diabetes? A hypothesis based on underexplored pathways. In *Diabetologia* (Vol. 63, Issue 6, pp. 1103–1109). Springer. https://doi.org/10.1007/s00125-020-05132-5

NARAYAN, K. M. V., KONDAL, D., STAIMEZ, L. R., ANJANA, R. M., GUJRAL, U., DEEPA, M., PATEL, S. A., ALI, M. K., PRABHAKARAN, D., CHANG, H. H., TANDON, N., & MOHAN, V. (2022). 1194-P: Gender Differences in Incidence of Prediabetes and Diabetes in South Asians. *Diabetes*, *71*(Supplement_1). https://doi.org/10.2337/DB22-1194-P

National Diabetes Statistics Report | Diabetes | CDC. (n.d.). Retrieved April 29, 2025, from https://www.cdc.gov/diabetes/php/data-research/index.html#cdc_report_pub_study_section_5-prevalence-of-prediabetes-among-adults

National Health Portal. (2016). *Overview of Diabetes Burden | National Health Portal of India*. https://www.nhp.gov.in/overview-of-diabetes-burden_mtl

Nazari, M., Hashemi Nazari, S., Zayeri, F., Gholampour Dehaki, M., & Akbarzadeh Baghban, A. (2018). Estimating transition probability of different states of type 2 diabetes and its associated factors using Markov model. *Primary Care Diabetes*, *12*(3), 245–253. https://doi.org/10.1016/j.pcd.2018.01.004

Perreault, L., Pan, Q., Mather, K. J., Watson, K. E., Hamman, R. F., & Kahn, S. E. (2012). Effect of regression from prediabetes to normal glucose regulation on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. *The Lancet*, *379*(9833), 2243–2251. https://doi.org/10.1016/S0140-6736(12)60525-X

Pradeepa, R., & Mohan, V. (2021). Epidemiology of type 2 diabetes in India. In *Indian journal of ophthalmology* (Vol. 69, Issue 11, pp. 2932–2938). NLM (Medline). https://doi.org/10.4103/ijo.IJO_1627_21

Ramachandran, A., Snehalatha, C., Mary, S., Mukesh, B., Bhaskar, A. D., & Vijay, V. (2006). The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia*, *49*(2), 289–297. https://doi.org/10.1007/S00125-005-0097-Z/TABLES/8

Rattey KT, & Rosenthal M. (2014). Reversing the diabetes epidemic: a role for primary care in identifying pre-diabetes and referral to an evidence based program. *Delaware Medical Journal*, 307–313.

Rooney, M. R., Fang, M., Ogurtsova, K., Ozkan, B., Echouffo-Tcheugui, J. B., Boyko, E. J., Magliano, D. J., & Selvin, E. (2023). Global Prevalence of Prediabetes. *Diabetes Care*, *46*(7), 1388. https://doi.org/10.2337/DC22-2376

Rooney, M. R., Rawlings, A. M., Pankow, J. S., Echouffo Tcheugui, J. B., Coresh, J., Sharrett, A. R., & Selvin, E. (2021). Risk of Progression to Diabetes among Older Adults with Prediabetes. *JAMA Internal Medicine*, *181*(4), 511–519. https://doi.org/10.1001/jamainternmed.2020.8774

Sattar, N., Rawshani, A., Franzén, S., Rawshani, A., Svensson, A. M., Rosengren, A., Mcguire, D. K., Eliasson, B., & Gudbjörnsdottir, S. (2019). Age at Diagnosis of Type 2 Diabetes Mellitus and Associations With Cardiovascular and Mortality Risks: Findings From the Swedish National Diabetes Registry. *Circulation*, *139*(19), 2228–2237. https://doi.org/10.1161/CIRCULATIONAHA.118.037885/FORMAT/EPUB

Sharma, P., Dilip, T. R., Kulkarni, A., & Bhandarkar, P. (2024). Age and sex dynamics in the incidence of diabetes in Contributory Health Services Scheme beneficiaries: A retrospective cohort study in

Mumbai. *International Journal of Noncommunicable Diseases*, *9*(1), 13–20. https://doi.org/10.4103/JNCD.JNCD_33_23

Tabák, A. G., Herder, C., Rathmann, W., Brunner, E. J., & Kivimäki, M. (2012). Prediabetes: A high-risk state for diabetes development. In *The Lancet* (Vol. 379, Issue 9833, pp. 2279–2290). Elsevier B.V. https://doi.org/10.1016/S0140-6736(12)60283-9

Tuso, P. (2014). Prediabetes and lifestyle modification: time to prevent a preventable disease. *The Permanente Journal*, *18*(3), 88–93. https://doi.org/10.7812/TPP/14-002

Urrutia, I., Martín-Nieto, A., Martínez, R., Casanovas-Marsal, J. O., Aguayo, A., del Olmo, J., Arana, E., Fernandez-Rubio, E., Castaño, L., Gaztambide, S., García-Castaño, A., Gómez-Conde, S., Larrauri, S., Martínez de LaPiscina, I., Saso, L., & Velasco, O. (2021). Incidence of diabetes mellitus and associated risk factors in the adult population of the Basque country, Spain. *Scientific Reports*, *11*(1). https://doi.org/10.1038/s41598-021-82548-y

Van Dieren, S., Beulens, J. W. J., Van Der Schouw, Y. T., Grobbee, D. E., & Neal, B. (2010). The global burden of diabetes and its complications: An emerging pandemic. *European Journal of Cardiovascular Prevention and Rehabilitation*, *17*(SUPPL. 1). https://doi.org/10.1097/01.hjr.0000368191.86614.5a

Vega, T., Gil, M., & Lozano, J. (2015). Age and sex differences in the incidence of diabetes mellitus in a population-based Spanish cohort. *Journal of Diabetes*, *7*(3), 411–417. https://doi.org/10.1111/1753-0407.12183

Vijayakumar, G., Manghat, S., Vijayakumar, R., Simon, L., Scaria, L. M., Vijayakumar, A., Sreehari, G. K., Kutty, V. R., Rachana, A., & Jaleel, A. (2019). Incidence of type 2 diabetes mellitus and prediabetes in Kerala, India: Results from a 10-year prospective cohort. *BMC Public Health*, *19*(1). https://doi.org/10.1186/s12889-019-6445-6

Wang, H., Shara, N. M., Calhoun, D., Umans, J. G., Lee, E. T., & Howard, B. V. (2010). Incidence Rates and Predictors of Diabetes in Those with Prediabetes: The Strong Heart Study. *Diabetes/Metabolism Research and Reviews*, *26*(5), 378. https://doi.org/10.1002/DMRR.1089

Yang, H., Liu, Y., Huang, Z., & Deng, G. (2024). Achieving prediabetes reversal in China: a nationwide longitudinal study on the role of blood glucose and lipid management in middle-aged and elderly adults. *Frontiers in Endocrinology*, *15*, 1463650. https://doi.org/10.3389/FENDO.2024.1463650/BIBTEX