Mental Health Trajectories of Canadian Young Adults and Older Population Index: Evidence from the National Population Health Survey (1994-2011)

By
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Abstract

This study is primarily aimed to identify distinct subgroups of individuals following similar mental health conditions over a 16-year follow-up using the latent class growth modeling (LCGM). We also provided the description of characteristics of each trajectory group. Mental health trajectory analysis can show the long-term age-related developmental changes of young adults (18-29 at baseline) and older population's (60-75 at baseline) mental health condition.

The National Population Health Survey (NPHS), from 1994 to 2011 was used for this study. The results showed that the mental health conditions among the survey population during the follow-up period were not homogeneous, and there existed several common group patterns of mental health conditions at different age groups. The young adult group consisted of 2661 subjects, ranging from 18 to 45 years of age; while the senior group consisted of 2036 subjects, ranging from 60 to 91 years of age. Four trajectories were identified among the young adults' population, and two trajectories among the older population. Mental Health trajectory group memberships were related to numerous variables, including sex, social-economic status, lifestyle, as well as physical conditions. Through analyzing trajectories and attributes of different trajectories, this study might contribute to understanding the psychological conditions of the Canadian population.

General Summary

Our research's main purpose is to use statistical trajectory models to identify potential mental health subgroups among the Canadian population. Trajectory analysis allows us to observe the mental health's long-term development curve and distinguish different development patterns. This study focused on the trajectory of psychological distress in young people (baseline 18-29) and Alzheimer's disease trajectory in the elderly (baseline 60-75). We used data from the National Population Health Survey (NPHS), a 16-year longitudinal survey with more than 17,000 participants. We included 2661 young adults and 2036 elderly participants in our study. Analyzing different patterns of subgroup trajectories and characteristics of different subgroups, we can have a more comprehensive understanding of the Canadian population's mental health status.

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Candidate's Contribution to the Work

The candidate was responsible for the literature review and data analysis that was based on the National Population Health Survey. The candidate also drafted the first version of the manuscript and contributed to the presentation and results from this research. Dr. Yanqing Yi designed the study, and Dr. Yanying Yi and Dr.Zhoahi Fan offered advice on the research modeling and result interpretations.

Abbreviations

ALD	Accelerated longitudinal design
AvePP	Average Posterior Probability of Group Membership
BIC	Bayesian Information Criterion
CGM	Conventional Growth Modeling
CI	Confidence Interval
CS	Constant Smoker
DP-smoker	Decreased Probability of Being a Smoker
GMM	Growth Mixture Modeling
GMP	Group Membership Probability
HR	Hazard Ratio
LCGM	Latent Class Growth Modeling
NPHS	National Population Health Survey
PMP	Posterior Membership Probability
TVCs	Time-Varying Covariates
WHO	World Health Organizations

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Chapter 1 Introduction

This chapter mainly demonstrates the rationale of this study.

1.1 Background

According to the Canadian Mental Health Association, 1% of the Canadian population is impacted by schizophrenia, 5% of the population suffers from an anxiety disorder, and 8% of people experience major depression at some life stages [51].

There are various types of mental health illnesses, which have different symptoms and have different effects on people's lives. In this thesis, we focus on the psychological distress problem among young Canadian adults (18-29) and Alzheimer's disease and depression problems among the older population (older than 60).

The issue of mental health has brought a substantial financial burden to Canada. The mental health council reported that more than 6.7 million people, consisting of 19.8% of the total population in Canada, have mental illnesses [51]. The annual cost of mental health-related care services in 2011 exceeds $40 billion in Canada [44]. Mental health is just as crucial as our physical health; moreover, mental health problems can be lethal. Studies have shown that depression is significantly associated with suicidality [2].

According to psychologist Erik Homburger Erikson's theory on the psychological development of human beings, there are in total up to 8 stages of human development [102]. The first four cycles take place before age 11, and then the fifth, sxith, and seventh stages take place during adolescence, young adulthood, and middle life, respectively. The seventh stage takes place during middle life. The eighth and final stage takes place during old age [102]. In our study, young adulthood is defined as 18-29 based on previous literature, and the elderly is defined as people older than 60 [48, 3]. Studies have shown that young adulthood (18-29) and

the elderly (aged over 60) are two age groups of profound change and importance in terms of psychological development [30, 40, 113, 117]. Transition to adulthood is critical for the development of potential mental disorders [40]. Early adulthood is a time of constant change as people are exploring the possibilities of love, work, and worldview, and people are in the process of identity exploration [30, 117]. Young adults face the uncertainty of the future and many possibilities of life directions [117].

At each stage, individuals must confront a central crisis and psychological conflict before they can enter the next stage [77]. Each stage has a specific conflict because personal growth and social-cultural background work together to make the conflict attract personal attention in the individual's life stage [77]. Developmental transitions in young adulthood contribute to stress, which puts people aged 18-29 at greater risk of developing mental disorders. Through assessing young adults' psychological distress, we can gain more comprehensive knowledge about depression or anxiety so that people will have a more promising outlook to overcome these mental disorders' obstacles.

Besides the young adults' age group, the elderly age group is also facing potential mental health crises, like Alzheimer's disease (AD), which is an irreversible progressive brain disease that slowly destroys memory and thinking abilities, and ultimately destroys the ability to perform basic activities of daily living [113]. Worldwide, 3.9% of the population aged over 60 are living with dementia [3]. The AD significantly shortens life expectancy and is one of the main reasons for the physical disability, institutionalization, and substandard life quality of the elderly [3]. Since it is an age-related disease, senior people would have a larger risk of developing AD. By examining the Alzheimer's trajectory of the elderly, we can explore the potential trajectory patterns and gain more understanding about the developments of AD.

Since the young adults' group (18-29) and the elderly group (aged over 60) are the two pronounced age groups that prone to substandard mental health, the **objectives** of the study mainly focused on these two age groups.

1. Identify different psychological distress scale trajectory groups in young adults (18-29 at the baseline) and investigate how time-invariant and time-varying risk factors affect the psychological distress scale trajectories.
2. Identify different Alzheimer's disease trajectory groups in the elderly population (60 and higher), examine how time-invariant and time-varying covariates affect Alzheimer's trajectories.

Through the findings of my study, people can gain more insight of common mental health problems in the selected two age groups. If patients can identify the signs and symptoms and raise their awareness of psychological issues, they can seek professional help at an early stage.

1.1.1 Why Use Trajectory Analysis

Trajectory analysis is becoming more prevalent in epidemiology studies [89]. The trajectory can help us to understand better how an individual's mental health status develops naturally, which can aid in identifying the onset time of disease and taking up actions for early prevention. Trajectory modeling was initially developed in the field of criminology study to help criminologists to understand the development of delinquent behaviors and criminal activities [89]. It's also a prevalent method in the field of psychology and sociology. Nowadays, it's come into favor in the epidemiologic study. Researchers in epidemiology and other fields investigate the variable's trajectory shape and how potential covariates may affect the development trajectory.

Longitudinal data provides us more abundant data information to investigate the research objective than cross-sectional data. Cross-sectional studies capture the data at a single time point; thus, it cannot be used to examine behaviors over a long period. Another disadvantage is that the single point data may not be representative. Many of the existing studies regarding mental health studies are cross-sectional. Cross-sectional data provide little information about the influence of time on the current variable. Rather than using a cross-sectional study with a one-time measurement, longitudinal studies of mental health can show the change over time. Since the goal of our research is to investigate the mental health disease trajectories of young and older Canadians, only longitudinal data allow us to achieve our research goal. Longitudinal data repeatedly collect outcomes of the variable of interest for a period of time; thus, the longitudinal study is useful for examining the association between risk factors and the development of mental health illness. It allows us to know the degree and direction of change of mental status over time and give us enough power to investigate complex relationship over time.

1.1.2 Young Adults & Psychological Distress

It is well-known that people at different life stages have various concerns; thus, each life stages have age-specific risk factors leading to mental health problems. It is sensible to conduct mental health research on separate age groups instead of the whole population. This knowledge is backed up by current literature reviews where researchers do mental health research on different age groups (i.e., adults, seniors) [5,7,9,12,17,21,29,54]. In my study, I follow the previous literature's path and conduct a study on two separate age groups: young adult and senior age group.

People are increasing awareness of recognizing young adulthood as a special life stage [30]. Studies have shown that young adulthood tends to be the onset age of mental health

problems [40]. In the transition to adulthood, people are in the process of building their worldview and sense of worth, and they are also confronted with social identity challenges and crises; thus, mental health disorders show peak prevalence in early adulthood [30]; thus , the **first objective** of this thesis is to identify the psychological distress developmental trajectories of young adults aged 18-29 at the baseline and to examine risk factors influencing psychological distress trajectory. This can help us to identify the characteristics that each trajectory group holds.

The psychological distress scale is the scale we use to measure the mental health status of young adults. Studies showed that young adulthood is the most common onset age for mental health disorders, and these mental health orders ranging from depression to many other personality and behavior disorders. Compared with depression, psychological distress is a more broad term covering a border spectrum of mental health symptoms, but is mainly characterized as anxiety and depression [31,59]. Mirowsky's study stated that, "psychological distress is an unpleasant subjective state," which manifests as depression and anxiety. Nonspecific psychological distress is caused and indicated by a series of mental and physical premonitions; in other words, it is not just limited to any specific mental diseases but incorporates a series of mental disorders [52]. Drapeau et al. also stated that the term "psychological distress" is commonly referred to a large variety of mental health syndromes, and the spectrum includes depression, anxiety, personal traits, functional disabilities, and behavioral problems [20]. Common mental illnesses include major depression, generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress, and schizophrenia [52]. Anxiety disorder symptoms include fear and stress, having trouble falling into sleep, abnormal heartbeat, nausea, panic, difficulty maintaining calm, and etc. [75] Anxiety is often associated with depression symptoms. The symptoms of depression include repressed feelings, loss of interest or pleasure, reduced energy, guilt feelings or low self-

esteem, lack of sleep or loss of appetite, inattention [75]. Some people argue that psychological distress as an "unpleasant subjective state" is a path to depression in the absence of treatment [111].

We choose Kessler 6 psychological distress as the measurement for young adults because it is designed to cover more general mental diseases. NPHS used the short version of psychological distress, which is called the Kessler 6-items psychological distress scale. It is the tool to measure participants' mental health conditions in the National Population Health Survey.

1.1.3 Senior and Dementia/Alzheimer's disease

The WHO reckoned that 47.5 million people live with dementia worldwide, including AD [13]. It is estimated that by 2031, the total annual health care cost for Canadians with dementia will reach $16.6 billion, while the number was $8.3 billion in 2011 [13]. Dementia refers to a progressive decline of cognitive functions, and Alzheimer's disease is the most common cause of dementia. AD is an age-related neurodegenerative disease, and the pathophysiology of AD is still unclear. The patients with AD are mostly older than 60 years, and the number of patients is expected to double every 20 years until at least 2050 [3].

Modeling the trajectory development of AD can assist us in better knowledge about the characteristics of different subpopulations. It is more intuitive in depicting the onset time of the AD neurodegenerative disease. Early detection of the onset allows patients to prepare for coping with the disorder, and preventive interventions may improve the later life quality of patients; thus, the **second research** objective of the thesis is to identify Alzheimer's disease trajectories in the elderly population (60 and higher). NPHS gathered information on developing Alzheimer's disease/ dementia or not over 16 years of follow-up, which allowed us to investigate the development of the trajectory.

1.2 Trajectory Modeling Methods

It is unlikely that longitudinal mental health status is homogenous across different age groups. The numbers of longitudinal mental health trajectories of the sub-population and their structure are unknown. There are four statistical methods mainly used for examing trajectory analysis: growth mixture modeling (GMM), latent class growth model (LCGM), and conventional growth modeling (CGM).

The growth mixture model is the most general term, where LCGM and CGM can all be viewed as a particular case of GMM. LCGM and CGM can be obtained by constraining the GMM on the following three aspects (1) number of latent trajectories (2) parameterization of trajectory curve within each subgroup (3) source of variance [79]. LCGM and GMM modeling can identify multiple trajectories within the studied population, and the method for determining the optimal number of trajectories will be discussed in section 2.2, while the CGM method can only portray a single trajectory.

GMM models assume variances on the outcome measures coming from two aspects, which are (1) "individual time-specific variance in outcomes around the individual's trajectory" (first-source of variance) (2). "variances in the individual trajectory around his/her class average trajectory" (second-source of variance) [79].

Compared with CGM, in which all subjects are from the same population and modeled with common parameters, GMM holds the assumption that there exist different subgroups of individuals following similar trajectory curves. GMM allows different trajectories with different growth parameters and different trajectory means. Each trajectory groups (i.e., growth models) have its variance. GMM can address the potential heterogeneity in the population and assume different subpopulation groups possess different trajectory curves [80].

LCGM is a unique type of GMM [78]. LCGM holds the assumption that the variance and covariance estimates for the trajectory factor (i.e., dependent variable) within each potential subgroup (i.e., latent class) are zero. This assumption implies that the individuals within a subgroup are homogeneous, which means LCGM only has the first-source of variance. Since variances estimates in the "individual trajectory around his/her class average trajectory" are fixed to zero, this zero restriction can make the numerical estimation easier for the optimization procedure on the model parameters. Nagin et al. designed the LCGM model, and Jones et al. developed the Proc Traj package in SAS [81]. When addressing concerns about "heterogeneity in change of outcome variables," the latent class model is one of the ideal methods to use. It will show each individual's trajectory and also reveal the individual differences in each developmental trajectory curve over time. If we find a series of trajectory lines through LCGM, each trajectory line is modeled with different parameters (i.e., different intercepts and slopes). If we have a linear trajectory curve where the starting time point is treated as zero, the first parameter is the average intercept, which is a parameter illustrating the group's initial status. Its variance explains individual differences at the starting time point. The second parameter is the average slope, which is a parameter representing group growth rate and direction, and its variances show "individual difference in change over time" [80].

Conventional growth models (CGM) modeling the dependent variable as an averaged single growth trajectory of change, which holds a major assumption that the population is homogenous. The conventional growth model can be described as a multilevel, random-effects model [78]. According to this framework, intercept and slope vary across individuals, and this heterogeneity is captured by random effects (i.e., continuous latent variables). It also holds another assumption that individuals are affected by the risk factors in the same way. CGM showed average values of the dependent variable across all the measurement points, and this single trajectory is the trajectory growth for the entire population [78,82].

Conventional growth models can show the long-term change over time, but due to the nature of the single trajectory curve, some "change rate of the direction of change" cannot be seen via the single growth trajectory (piecewise) [82]. If we (1) limit the number of classes in GMM to one, (2) assume that the trajectory can be described by certain parameters, (3) allow both first-source variance and second-source variance, then we obtain the CGM model. In other words, using the CGM single trajectory curve to represent the whole population may overgeneralize the growth patterns of subgroups. It is a preferred trajectory analytical method if we can make sure that the studied population is homogeneous (i.e., all the subjects in the studied population have similar response patterns).

1.2.1 Why Choosing LCGM over Other Methods.

There is a growing interest in using LCGM technique to identify individuals' mental health trajectory response patterns. Mental health trajectory can describe the course of individuals' mental status over time. In our study, we used LCGM method to identify the potential trajectories for the psychological distress of young adults and the Alzheimer's disease trajectories of the elderly population. LCGM is a group-based trajectory modeling, which assumes that the whole population consists of several subgroups, and each subgroup has its own growth pattern.

GMM model and LCGM method all require the assumption that the population consists of distinctive subgroups, but the LCGM model requires the zero constrain assumption, which means there is no internal variance within each subgroup. With the assumption that the homogeneity within groups exists, LCGM offers more straightforward illustrations and LCGM can be easily implemented using the TRAJ package in SAS. The issue of GMM non-convergence and local solutions is often raised. The problem of local solutions (e.g., largest value, smallest value) occurs when the maximum or minimum value is

identified for only a given area of the curve estimation. In the mixture modeling, the nature of estimating parameters by the method of maximum likelihood (e.g., Expectation-maximization algorithm) is iterative, and the iteration should achieve successful convergence on the global maximum solution under ideal circumstances [80].

In summary, CGMs are only suited for a homogeneous population where all the subjects in the population have common response patterns. GMM and LCGM models both need the assumption that there is unobserved heterogeneity in the studied population, and there exist multiple latent subgroups. A practical limitation of GMM is that it may have a convergence issue due to the complex nature of the model.

1.3 Literature Review

This part mainly summarizes the previous studies on mental health trajectories, which have adopted the three previously-mentioned trajectory methods (i.e., conventional growth modeling (CGM), growth mixture modeling (GMM), and the latent class growth modeling(LCGM). This part also summarizes the covariates that are related to AD.

1.3.1 Literature about Mental Health Trajectory Using Different Growth Models (CGM/GMM/LCGM)

We found 19 papers about mental health trajectory that are related to my research topic. Four of them are Canada-based, and the trajectory levels of these literature ranging from 2 trajectory classes to 6 trajectory classes. Colman et al. showed two trajectory lines [16]. Liang et al. generated 6 trajectory lines [45].

All of these studies have been following the participants for longer than 5 years. However, not many of the 19 research focused on the 18-29 age group. The majority of these papers focused on children and older adults.

We found 4 papers on mental health trajectories Canada-wide that have included the young adulthood age period. The identified mental health trajectory groups are between 2-3. The methods used are mainly multilevel growth curve modeling and the LCGM model. Langlois et al. and Drapeau et al. both used the multilevel growth model, and they both built sex-specific psychological trajectories [21,43]. Langlois et al. specifically emphasized the impact of parental addiction [43]. The research showed that both men and women showed higher distress scores at age 18, and distress declined quicker among women with growing age; children who experienced parental addition, such as, parental alcoholism would persistently demonstrate high distress scores than people who had not. Drapeau et al. analyzed participants aged 18 and older from NPHS; their study showed that the average level of psychological distress is higher in women than in men in all age groups [21]. It also showed that the 18-29 age group had a higher psychological distress scale than the older adults age group.

Unlike Drapeau and Langlois's research method, Ferro et al. and Colman et al. both used latent class growth modeling [16, 25]. Ferro et al. examined the Center for Epidemiological Depression Scale (CES-D) among young Canadians [25]. This study used data from the National Longitudinal Survey of Children and youth. It is a 14-year follow-up survey that included 2825 Canadian youths between 10 to 25 years old. This research generated three parallel trajectories, which were minimal (CES-D <6), subclinical (9-13), and clinical (CES-D>18), respectively. Their result demonstrated that the female gender, lower self-concept, lower economic status, poorer interpersonal relationship, and chronic health condition are more likely to be associated with the subclinical and clinical group [25]. The 3 trajectories were similar; in other words, the graph showed the peaks and troughs of the three trajectory groups were consistent. The parallel nature of this graph indicated the development of depressive symptoms was a function of natural youth development after the risk group is

identified. Distress due to lower socioeconomic status and bad physical health tended to impose a more negative effect on the early life period of adults. Their study focused on a younger group compared with my study. However, variables like parental depression, family function, and anxiety were only included in the first three cycles; thus, these variables were not able to be treated as time-varying variables in the model due to the lack of information. These variables might be significant for the model building but were neglected due to data limitations.

Colman et al. identified 2 trajectories and found people who were daily smoker and had low mastery and history of depression, were more likely to be in the second trajectory group, which was people with repeated episodes of depression [16]. This study investigated the predictors for long-term depression. In their study, they only included 585 participants with depression in the NPHS survey. Furthermore, this study only used the measurement at the baseline (i.e., a point estimate) to test the association between smoking status and depression. People's smoking behavior may change over time, so in my study, we identified long-term trajectories of smoking behavior by allowing a person’s behavior change during the follow-up period using the LCGM. We used the identified smoking behavior trajectory groups for further analysis. The 4 studies mentioned above for the Canadian population have different research objectives or aiming at different groups of people. There were few common risk factors of mental health among these 4 domestic studies as a categorical variable to test the association between smoking status and depression.

Many of the Canadian mental health studies were cross-sectional rather than longitudinal. Moreover, among the Canadian-based trajectory research, most of the existing Canadian studies about mental health targeted some particular populations. For example, Statistics Canada conducted a trajectories analysis of the psychological distress of adults who had experienced parental addiction in childhood [25,43].

Canada-wide, a limited number of studies used the LCGM trajectory method to identify the mental health-related risk factors on the general population.

There were five international studies among young adults that related to our research [9,17,33,60,64]. These studies identified 3 to 4 trajectories in the population. Two of the studies found that financial difficulty/low social-economic status and unhealthy behaviors are associated with higher risk of mental health [17,33]. These two studies both used the LCGM method. The Australian study also reported other risk factors, such as poor physical health and weight/shape dissatisfaction, were related to mental health [33]. Two American studies using the LCGM method both found race was a risk factor regarding mental health performances [9,17]. One of them investigated people aged between 10-21 years old, and the other stduy focused on people aged 12 to 25 years old. [9,17]. A Finland study and a Switzerland study used growth mixture modeling, one of which found people with depressive symptoms had fewer success expectations and poorer environment adjustability. [60,64]

Some studies investigated the pattern of depression trajectories [18,42,45,50,84,100, 108]. An American study of people who are older than 50 years, identified 6 trajectories by using the LCGM method [45]. They found that peoples being an ethnic minority tend to show a higher level of depressive symptoms. Studies from the United States and France both identified 4 trajectories [42,50]. The study from United States used GMM method and found that having a higher education level, better health, more social resources, and being male are significantly associated with better mental health condition [42]. The French study conducted by Melchior included 12,650 employees from French national gas and electricity companies [50]. The age range of male participants was 40-50, while the age range of female participants was 35-50. They identified sex-specific depression trajectories for men and women, respectively. Their results showed four male-specific trajectories groups, which were no depression group (60.9%), decreasing depression group (13.4%), Intermittent depression

(21.1%), persistent depression group (4.6%). Four female-specific trajectory groups, which were no depression group (69.1%); increasing depression (4.2%); decreasing depression (20.4%); and persistent depression (6.3%). This French study suggested that depression is linked with the disadvantages of social-economic class.

A Korean study by Park et al. investigated the depression trajectories among women aged 65 years or older [108]. This study examined the differences in depressive symptoms by categorizing the population into two social-economic classes (i.e., poverty group, non-poverty group). The data is from a longitudinal survey (2006-2013), and 2435 subjects were included in this depression study. The researcher used the CGM method and depicted the mean depressive symptoms trajectories for the poverty group and the non-poverty group.

A study of 3,922 participants aged over 60 from Taiwan identified 4 different depressive trajectory curves during a 10-year follow-up, which were persistent-low group(41.8%), persistent-mild (46.8%), late-peak group (4.2%), and high-chronic (7.2%) via the LCGM method [100].

An American study of 3182 participants aged 52 to 81 years old from the National Longitudinal Survey of Mature Women showed that in comparison to White women, black women possess persistently higher level of depressive symptoms. The research study used the hierarchical linear model and plotted the trajectory curve for black women and white women, respectively. [84].

In summary, few of the existing studies covered the Canadian population, and most of the studies are American or European-based. For the limited number of Canadian studies, many of them are cross-sectional. Some of the longitudinal studies demonstrated the heterogeneity in mental health conditions in the Canadian population, but very few of them used the LCGM method to investigate the trajectory curves.

Studies conducted by research groups Langlois et al., Drapeau et al., Ferro et al., and Coleman et al. are all Canada-based [43,21, 25,16]. Langlois et al. and Drapeau et al. both built sex-specific trajectories using the multilevel growth model [43,21]. The four Canadian studies all included young adult participants. Drapeau et al. investigated age groups 18-29 and 60-69, respectively [21]. They identified two overall trajectories to describe the development of the two age groups using the multilevel growth model, which does not capture the heterogeneity nature of the development curve like GMM or LCGM. Langlois et al. studied the psychological distress among Canadian adults who experienced parental addiction in childhood, but it was not possible to determine if the addicted parent was a father, mother, or both. The age when the child was influenced by parental addiction and duration are unknown [43]. Ferro et al. studied the young population aged from 10-25 years old using LCGM, their study was limited due to the data attrition, and their study only treated self-concept as a time-variant variable. Other covariates like socioeconomic factors were all treated as time-invariant [25]. Coleman et al. used LCGM and investigated people over 16 years old. In their study, smoking status was treated as a time-invariant variable instead of a time-variant. They used the smoking status in the baseline as the covariate in the logistic regression [16].

Another three foreign studies also investigated the mental disorder trajectories among young adults, which are from Finland, Australia, and Switzerland [64,33,60]. The first two focus on people aged 18-23 years old using the GMM method, and participants aged18-29 years old using the LCGM method [33, 60], respectively. The Australian study relied on the self-reported data, which may have biases in the reporting data; while the Finnish study only included university students as participants and was not necessarily representative of all young adults. The Swiss study, conducted by Paksarian et al., examined the mental disorder trajectories on 591 young adults aged around 20 years old at baseline using the GMM

method; however, their study included a relatively small sample size and suffered a high attrition rate over the long follow-up might also affect the estimates [60].

For the older population group, the American study conducted by Liang et al. studied the heterogeneity of the depressive symptoms in the middle and older American population [17]. Since America is a multiracial society, their results might be improved by further differentiating subgroups of Blacks, Hispanics, and Whites; thus, factors like acculturation and age at immigration may have a significant impact on the depression in the middle and later life, which was not included in their study. Spence et al. explored the racial difference in depression trajectories among older women, but they used the hierarchical growth model, which only showed overall depressive trajectories for white and black women, respectively; while the LCGM model in our study can better capture the heterogeneity among the population [84]. The Taiwanese study by Huang and the Korean study by Park used the CGM, and they generated two sex-specific depressive trajectories for the older population, which cannot show the heterogeneous nature of the development of depression pattern among the older population [100,108]. The French study explored the depressive trajectories for middle-age women and men at the baseline, respectively, which used the same LCGM method as our study; however, in their study, all the recruited population were employed; thus, they might omit the population who were in lower social-economic status [50]

1.3.2 Literature Review on Alzheimer's Disease

Alzheimer's disease(AD) is a common and suffering chronic psychiatric disease among the elderly. Its symptoms manifest as memory loss and comprehension deterioration

[13]. Depression is a risk factor for Alzheimer's disease, but it is unknown whether this relationship is causal [16]. Depression sometimes coexists with Alzheimer's disease in the elderly. Since the symptoms of the cognitive prospect of the two conditions overlap, the diagnosis between Alzheimer's disease and depression might be difficult [109].

Wilkosz et al. investigated 201 Caucasian subjects with possible AD, whose age range at baseline was from 48 to 87 [121]. They followed their cognitive and psychotic symptoms measurements for up to 13.5 years. Their results showed that six trajectories with different paths and cognitive decline rates were identified among the 201 participants with AD using the latent class trajectory model. Subjects with higher initial cognitive scores tend to fall into the slower decline trajectory group, while subjects with lower initial scores are more likely to fall into a faster decline trajectory group. Subjects with psychosis were more likely to fall into a trajectory with a more rapid decline, after adjusting for age and initial cognitive group [121].

A Sweden study conducted by Small and Backman identified longitudinal trajectories of cognitive development in preclinical Alzheimer's disease using the growth mixture modeling [15]. Their study followed 528 participants for 7 years, and they found that a 2-class quadratic model provided the best statistical fit of the development of the cognitive performance during the preclinical period of AD. Trajectory 1 showed a relatively little decline in cognitive performance score, and trajectory 2 showed a relatively steep decline after the third year of the follow-up.

Many studies assumed that depression serves as one of the independent risk factors for developing AD. A meta-analysis by Ownby et al. showed that the risk of developing AD was two times higher for people with lifetime depressive episodes [106].

Geerlings et al. conducted a study investigating the relationship between depression and the risk of cognitive decline and Alzheimer's disease based on two surveys from Netherland [35].

Their data about Alzheimer's disease was provided by the Amsterdam Study of the Elderly. The research included 3,147 participants who were followed for an average of 3.2 years. The logistic regression analysis indicated that the association between depression and Alzheimer's disease was influenced by education. The odds ratio of developing depression was 5.31 for participants with more than 8 years of education compared with participants whose education was less than 8 years.

Some studies have shown that people with depression history are more prone to Alzheimer's diseases. A case-control study by Kokmen et al. investigated 415 people, and their results showed that episodic depression and personality disorder are two significant risk factors for Alzheimer's disease [92]. They also concluded that depression might be an early manifestation of Alzheimer's. Their results regarding the association between depression and AD are in line with Bore et al. [93].

Apart from cross-sectional studies, there are also studies investigating the relationship between depression and AD based on longitudinal studies. A Spanish study conducted by Modergo and Ferrandez investigated whether depression may increase the risk of developing Alzheimer's disease by following 14 patients with amnestic mild cognitive impairment,who were aged between 61-84, for an average period of 3 years [32]. The study found that patients with mild cognitive impairment and depression are more than twice as likely to develop Alzheimer's disease as those without depression (RR 2.6 95% CI 1.8-3.6). The survival analysis also showed that the onset age of Alzheimer's disease was earlier for the depressed population than the nondepressed. However, the research by Garre-Olmo et al. contradicts Modergo and Ferrandez's findings. Garre-Olmo et al. aimed to investigate whether clinical cognitive impairment and sociodemographic variables are associated with major depression [36]. They studied a sample of 150 people and showed that the presence of depressive symptoms had no significant impact on the course of cognitive impairment.

The longitudinal population-based Spanish study of 3,864 people aged over 55 conducted by Garcia- García et al. found that the incidence of AD was significantly higher in subjects with severe major depression compared with nondepressed individuals (incidence ratio: 3.59 [95% CI: 1.30-9.94]) [110]. In the multinominal logistic model, there was a significant association between severe depression and AD events at baseline (hazard ratio: 4.30 [95% CI: 1.39-13.33]) [110].

The studies conducted by Green et al. and Wilson et al. were exhibiting similar results that there is a significant association between depression and AD [98, 106]. Green et al. indicated that depression is significantly associated with Alzheimer's. Their report investigated 4,046 individuals, the odds ratio for individuals with depression to develop AD was 4.57 (95% CI 2,.87-7.31), compared to individuals without depression [98].
Wilson et al. investigated 648 subjects with an average age of 80.6 [106]. Their results indicated that the risk of developing clinical AD in patients with a high distress proneness was approximately 2.7 times higher compared with people who had low distress proneness. Since the clinical diagnosis of Alzheimer's disease can be difficult, Wilson et al. also examined the association between distress and cognitive decline, which is the major symptom of Alzheimer's disease.

Almeida investigated whether Alzheimer's disease-related to depression decreases with the use of antidepressants [24]. They examined a 14-year longitudinal survey among men aged 71-89. Their result showed that compared to men with no depressive symptoms, the sub-hazards ratios for men with severe depression to develop Alzheimer's disease were 2.1 (95%CI 1.4-3.2). It was demonstrated that the association between Alzheimer's disease and depression was only significant in the first 5 years of follow-up; the association between past/current depression and Alzheimer's disease was not significant in the time duration of 5-10 years and > 10 years of the follow-up period.

1.3.3 Potential Risk Factors

Risk Factors: We considered many potential risk factors, including sex, race, income, financial stress, years of education, BMI, smoking, drinking, physical activity, chronic condition, overall health and etc. The above factors were considered based on previous research findings.

Race and Ethnicity

Our research is interested in investigating the disparities in psychological distress/ depression across racial and ethnic boundaries. Studies show racial and ethnic minorities showed a higher incidence of getting depression. A study by Duran et al investigated a sample of patients from Indian Health Service Clinics aged from 18 to 45, and they found that nearly 20% of the population was in mood disorder for the past 12 months [22]. Using the National Longitudinal Study of Adolescent Health, Costello et al. found that Black and Asians are more likely to be in the depression group, either in the minor depression group or the severe depression group, as compared to the non-black/non-Asian people [17]. A study of mental health used the data from the Health and retirement study and showed that black people and Hispanics had a higher chance of developing depression [45].

Health Canada reported that indigenous women's suicide rate is five times as high as the rate in non-indigenous Canadian women [14]. MacMillan et al. studied the indigenous women's health from an Ontario Survey; their study found that the indigenous women's risk of suffering from depression is twice as much as non-indigenous Canadian women [47].

Education

Education is important to every individual as it facilities us to achieve self-improvement. A study about New York residents aged 18-65 also showed people whose educational attainment is lower than college would have a higher chance of developing depression in the unadjusted model [4]. Wang et al. included 9,589 participants from 18- 80 years old, using the NPHS and performed a logistic regression model to test the relationship between socioeconomic factors with depression [72]. The result showed that low education level is a disadvantage factor in this relationship. Among people who were employed, the odds of depression among people who were educated less than 13 years are 1.86 times higher than people with high education (people with more than 13 years of education). Based on Stoolmillers et al.'s study, lower education was related to the serious depression trajectories [68]

Gender

A sizable amount of mental health research targeting the gender differences found that women have higher possibilities of mental health issues, such as depression and anxiety. Women tend to manifest signs of mood and anxiety, while men are more susceptible to addictive or antisocial problems [1,37]. According to the World Health Organization (WHO), depression presents more than twice as often in females than males [76]. Beard et al. conducted a study investigating the trajectory of depression of New York Adult citizens from 18- 65 years old and found that compared to men, the probability of women developing depression is 1.53 times greater [4]. Another study conducted by Verger et al. in 2009 among 6 French universities has shown that the incidence of psychological distress among female students was 33%, which is higher than the incidence rate of 15.7% among male students [70]. Drapeau et al. used the growth curve method to analyze factors related to higher psychological stress among 9,067 women and 7877 men from the NPHS. Particiapnts were

aged over 18, and they devided all participants into 7 age groups, which were 18-29, 30-39, 40-49, 50-59, 60-69, 70- 79 and over 80. They found women showed higher psychological distress for all age groups compared with men [21]. Mental health issues appear in different ways between men and women. McDonough and Strohschein's research used the data of the first cycle of the NPHS survey. The participants were divided into 6 age groups, which are 20-29, 30-44, 45-54, 55-64, 65-74, and people who are above 75, and they found women in all age groups showed higher distress levels than men [49].

Financial and Socioeconomic Status

The disparity in socioeconomic status is a crucial factor impacting public health. Social disadvantage usually leads to lower overall health status, even disability, and mortality [72]. A large body of research has demonstrated that debt demonstrated a strong association between anxiety and mental disorder. In the U.S., the average amount of student loans was around $23,000 for each student borrower [11]. The cross-sectional study conducted by Walsemann and her colleagues used multivariate linear regression to test the relationship between student loan owned by each student and the psychological functioning of that individual and they also concluded that student loan is linked with worse mental functioning [71]. Research investigating residents of New York City showed that people with household income lower than $50,000 are more likely to develop depression compared to people with a household income greater than $50,000 [4]. Some cross-sectional studies have also illustrated the link between insufficient financial earnings and the symptoms of depression [29]. Lower-income was also related to depression development in the adults and senior adult's population, stated by Stoolmiller et al. [68]

Lifestyle

Lifestyle is another crucial factor related to mental health. Young adults can make more independent choices than before, but some choices, including diet, physical activity and alcohol consumption, may deteriorate their mental health [2,41]. The amount of physical exercise is negatively associated with the chance of developing depression and anxiety [70]. Young adults with depression have a promising probability of alleviating their condition by increasing the amount of exercise. Drinking is another problem for university students, and has been associated with many negative consequences. A large number of university students treat drinking as an inevitable and integral part of university life [61]. Studies have demonstrated that students are susceptible to a steep increase in alcohol consumption during the transition from high school to university, even at universities where the first-year university students are on a separate campus from the senior students. Studies have also shown college students' alcohol abuse is more common than their peers who are not in school [61,63]. The university environment forms a specific social context that tends to promote excessive alcohol consumption [61]. The Tertiary Health Research Intervention study showed that 48% of students who are between 17-24 years old topped the benchmark for acute harm related to excessive alcohol consumption. Sizable research has shown that excessive alcohol drinking cannot only jeopardizing people's physical health, such as memory loss, vomiting, risky sexual behavior, and car accidents, but can also lead to mental health problems such as depression, anxiety [10,19,67]. But Melchior showed alcohol is associated with lower symptoms in the adult group. Moreover, some researchers showed there is no association between alcohol consumption and the risk of developing depression [50,55].

Khaled et al. adopted multinomial logistic regression and proportional hazard models to test potential risk factors for major depression [38]. They found that compared with people who are former heavy smokers, the unadjusted hazard ratio for the current heavy smokers of developing major depression is 4.3 with $p<0.001$. After controlling age, sex, and stress, the

adjusted odds ratio between current heavy smoker and former heavy smoker in terms of developing major depression is 3.1, which is still significant. Byers et al. and Montagnier et al. found that smoking is associated with older women and men, respectively [12,53]. Colman et al. conducted research, which included 585 people who were above 16 years of age, using a growth trajectory model, and found that smoking was a significant predictor of depression episodes [16]. Other lifestyle issues, such as problematic social media use, were also shown to be related to depression symptoms [65].

Exercise can provide many mental health benefits. Paluska and Schwenk stated that increased aerobic exercise and strength training could significantly reduce depressive symptoms [83]. Research from Calgary university used data from NPHS and showed that major depression was linked with health utility index, and appropriate recreational physical activity can improve the health utility index, which makes physical activity a potential factor for depression [58]. Moses et al. studied 109 sendentary-lifestyle adults' psychological status who were randomly assigned to high-intensity exercise, moderate-intensity exercise, attention-placebo, or waiting list, and they found that people with moderate-intensity exercise showed improved psychological response after 10 weeks of training [91].

However, King et al. studied 120 people who performed a 6-month regular exercise, and it shows that although the perceived fitness and satisfaction on body image increased, there is no significant reduction in a depressed mood [99].

Obesity

Obesity has been defined as a chronic disease by WHO, and it is interrelated with mental health. Gariepy et al. conducted research using Cox proportional hazard regression model in terms of investigating the association between obesity and depression [28]. They divided obesity into two levels, normal/overweight (BMI 18.5-29.9) and obese (BMI >30),

and tested the risk of depression based on two obese statuses separately (normal/overweight BMI 18.5-29.9; obese BMI >30). After controlling for social demographics, health, and lifestyle factors, the study found that men who are normal/overweight had a lower hazard ratio (0.71) of developing depression compared with the obese population. However, in Patten et al.' study, obesity was not related to the major depressive episode under the proportional hazards model [57].

Research conducted in three German cities studied over 9,000 seniors aged 65 and older on the association between BMI-class and symptoms of depression [105]. Center for Epidemiologic Studies Depression Scale (CES-D Scale) was used as the tool for measuring senior's depression degree. The research used logistic regression to analyze the cross-sectional data, which is a snapshot in the fifth year of the original longitudinal data. After controlling age, education, marital status, smoking, and several other variables, the study found that the odds of having depression were higher in women with obesity classes II (35≤BMI<40) with OR 1.63(95% CI 1.13 to 2.35) compared with normal weight . The researchers also conducted a longitudinal analysis of the original data set. The result showed that the odds of depression for women at the baseline with obesity classes II (35≤BMI<40) and III (BMI≥40) is 1.67 times higher than the normal-weight women. The research also found that overweight men are less likely to have depression compared with normal-weight men. Poor general health, weight/shape dissatisfaction are demonstrated to be linked with poor mental health [33]. The German study seems contradict this belief. The anthor explained that one reason for this result is the prevelance of the overwight condition in elderly men;, thus overweight could have been considered as heathier condtion for men.

Marital Status

People's relationship with family members can affect their psychological distress level. Ehsan Latif's cross-sectional study found that people who are married have lower possibilities of developing depression compared with people who are divorced and widowed [44]. This finding is congruous with Helliwell and Blanchfolower's research that married people tend to be more delightful than singles [8,31].

Chronic Condition

Physical condition and mental health conditions are interrelated. Studies showed that people with arthritis are susceptible to depression. Fuller-Thomson et al. demonstrated that adults who reported high chronic pain need more time to relieve depression [26]. Wang found that the odds ratio of depression, between people who had chronic stress and no chronic stress, was 1.6 with a 95% confidence level (1.13, 2.27) [73].

Childhood experience

Childhood experience can impose a long-lasting influence on an individual's life. Research conducted by Fuller-Thomson et al. showed that childhood physical abuse and parental addiction are linked with depression remission [27]. Fuller-Thomson et al. included 1,128 adults in the study from 1994 to 2006 cycle year of NPHS and investigated potential factors that may impact the remission from depression. Based on the Cox proportional hazards model, they found that the child abuse history was the only statistically significant variable when the rest variables, such as social support and education, are controlled [27]. They found the probability that people who have experienced child abuse are more difficult to remit from depression with a hazard ratio of 0.85(95% CI 0.73, 0.99). Wang and Schmitz's research demonstrated that people who have experienced childhood traumatic events were more likely to develop major depression [73]. According to the report of Statistics Canada,

adults who had experienced parental addiction, such as drug or alcohol abuse, are more likely to have high psychological distress scores than those who had not [43]. Benjet stated that youth who experienced hardship in childhood, such as war-related violence, showed a higher possibility of developing a psychological disorder [5].

1.4 Data

The NPHS data set is a longitudinal dataset that consists of 17,276 people in the first cycle in 1994/1995, and the same individuals were interviewed every two years [23]. There were a total of nine cycles, and this survey ended in 2010/2011.The response rates for the nine cycles were 83.6% (cycle 1,1994/1995) , 92.8% (cycle 2, 1996/1997), 88.3% (cycle 3,1998/1999), 84.9% (cycle 4 , 2000/2001), 80.8% (cycle 5, 2002/2003), 77.6%(cycle 6, 2004/2005) , 77%(cycle 7, 2006/2007) , 70.7(cycle 8, 2008/2009) and 69.7%(cycle 9, 2010/2011) respectively.

The attrition rate compared with prior cycles were 9.3% (cycle 2, 1996/1997), 6.6% (cycle 3,1998/1999), 7.1% (cycle 4 , 2000/2001), 7.6% (cycle 5, 2002/2003), 7.5% (cycle 6, 2004/2005) , 5.4% (cycle 7, 2006/2007) , 9.2% (cycle 8, 2008/2009) and 6.9% (cycle 9, 2010/2011) respectively.

The cumulative attrition rate after 9 cycles was 46.2%. This survey only included people above 12 years old and also excluded people residing on Indian Reserves and Crown lands, residents of health institutions, and full-time members of the Canadian Forces Bases, as well as a few rural areas in Ontario and Quebec. The survey captured a representative sample of the Canadian population. In the NPHS survey, a two-stage stratified sampling method was used in the sample selection, and samples of dwellings within the clusters based on the geographic and socioeconomic status of provinces were selected.

In our study for the young adults (aged 18-29), we included sex (female/male), race (white/ non-white) as time-invariant variables. Other risk factors are time-varying, including income, years of education, BMI, smoking, drinking, physical activity, chronic condition, marital status, as well as overall health. For the time-varying factors, we used the LCGM method to recategorize the levels of factors, so we can know how the development of risk factors influenced the psychological scale. For the elderly population (aged above 60), we included sex (female/male) as the time-invariant variable. We also introduced time-varying variables like depression, social support, marital status, smoking and physical activity into the LCGM method. The selection of covariates were based on previous literature reviews and the availability of the data in the NPHS survey.

In our study, people in the young adulthood group (aged 18-29) were included if they have completed at least three cycles of the survey based on the records of psychological distress score. This selection criterion is backed up by Lowe's study, where they collected three records on psychological distress to investigated mental health trajectories among low-income, female survivors of Hurricane Katrina [46]. People in the elderly (age over 60) group were included if they have completed at least two cycles of the survey based on the records of Alzheimer's disease. This selection criterion is based on Xie's study of identifying trajectories of cognitive change in older persons with mild cognitive impairment, where they only included participants with at least two records and excluded participants with only one record [69].

This research aims to understand the mental health developmental trajectory of the Canadian sub-populations. My study consists mainly of two parts. The first part focuses on the psychological distress scale trajectories in young adults; the second part focuses on the Alzheimer's disease trajectories in the elderly population.

The remaining of the thesis is organized as follows.

Chapter 2 is the findings of the young adults' population, which is in line with our first research objective. Chapter 3 is the findings of the elderly population, which is following our second objective. Chapter 4 is a summary of our research findings and discussions of limitations of our research.

Chapter 2

Psychological Distress Scale Trajectories among Young Adults (18-29 at baseline) and Related Covariates

2.1 Introduction

Nonspecific psychological distress incorporates a series of mental health problems or illness [52]. Psychological distress is a more comprehensive term covering a border spectrum of mental health symptoms, but it is mainly characterized as anxiety and depression [31,52]. Depression is feeling sad, lonely, hopeless, or worthless, having insomnia, crying, feeling everything is an effort, and unable to get going. Anxiety is being tense, restless, worried, fractious, having difficulty maintaining calm and afraid [52]. Canadian Mental Health Association showed that nearly 20% of the Canadian population would experience a mental health problem or illness at some stage of their lives [51]. The measurement tools designed to assess psychological distress, depression, and general anxiety disorders, in fact, have several things in common. Thus, while psychological distress and these mental disorders are not the same, they are, to some extent, depending on each other [52]. Some people argue that psychological distress as an "unpleasant subjective state" is a path to depression in the absence of treatment [111].

High psychological distress indicates possessing severe mental health illness, which can severely affect individuals and their families. Major mental illnesses may even lead to suicide. Besides the impact on individuals and families, there is a high cost from mental health problems and diseases to the Canadian economy. The study by the MHCC indicated that the economic loss to Canada is at least $50 billion per year [112]. Studies have shown that young adulthood tends to be the onset age of mental health problems, and the current

depression rate among young adults with a 12 month of duration of the episode is the highest in history. Young adults tend to have a higher level of depression and anxiety related to social identity challenges and crisis; thus, mental health disorders show a peak prevalence in early adulthood [30]. The transition of becoming an adult is an important period, both physical and mental, in personal development. So, in this chapter, we focused on the young adults' psychological distress trajectory development.

Psychological distress scale trajectory can capture the participants' mental status over time. By identifying the underlying subgroups, we can better understand the development of psychological distress trajectory curves. Although a large body of literature has studied the factors affecting mental health, few studies are Canadian-based or used the LCGM method. Some of the studies used the CGM or multilevel growth methods, such as Langlois et al. and Drapeau et al., which does not allow them to recognize the heterogeneity of the whole population [21,43]. Moreover, few studies focus on the 18-29 age group, and many existing works of literature focused on children or older adults. Some trajectory analyses on young adult mental health are not Canadian-based [9, 33, 64].

The existing studies have shown numerous factors impacting young adults psychological distress scale, such as race and ethnicity, education, social-economic status, lifestyle, gender and etc. [4,11,29,55,65,75]. Among the sizable research investigating the psychological distress scale- related risk factors, most of them are cross-sectional studies.

Despite the heterogeneity of the psychological distress development curve among the young adults population, there are no studies investigating the developmental trajectory of psychological distress in a large population of young Canadian adults. Therefore, the first purpose of the present study was to perform an analysis using the NPHS data to examine different psychological distress trajectories in young adults. The second purpose is to identify the characteristics that each trajectory group holds. This epidemiological study provides a

comprehensive analysis of the current mental health condition of young Candian adults, which may offer more insight for mental health workers and policymakers on how to address mental health-related social equities.

2.2 Methods

The NPHS dataset is a longitudinal dataset that consisted of 17,276 people in the first cycle in 1994/1995, and individuals were interviewed every two years [23]. There were a total of nine cycles, and this survey ended in 2010/2011. In our study for the young adults population, we included participants aged between 18-29 at the baseline cycle, and they must have completed at least three cycles of the survey based on the records of psychological distress. We included 2,661 participants that met our criteria. Statistics Canada used Kessler 6-items psychological distress scale as the tool to measure participants' mental health conditions in the National Population Health Survey. The total score range of k6 is between 0 and 24, and the cutoff point is at 13. The widely-used K6 is a non-specific distress scale screens for severe mental illness. Respondents who scored over 13 are defined to have severe mental problems [7]. An American study identified K6≥5 as the optimal lower threshold cut-point for moderate mental distress [86].

The LCGM is used to identify subgroup trajectories of psycholological distress (i.e., dependent variable in our study), where trajectories are a series of polynomial functions [88,89]. Trajectories are determined through the general quasi-Newton maximum likelihood estimation [88, 89,90]. We conducted the statistical analysis in SAS version 9.4 (SAS Institute Inc., USA), and used the PROC TRAJ implemented in SAS to conduct the LCGM.

LCGM model can identify distinct mental health developmental patterns belonging to each subgroup, which allows us to investigate the characteristics that each subgroup holds. In

this chapter, we apply the LCGM to identify the existing but not yet manifest subgroups for young adults(18-29 at baseline), and participants must have at least completed three cycles of the survey. We will examine factors contributing to serious psychological distress scale.

The LCGM is used for the trajectory analysis, and it is known as semi-parametric group-based trajectory modeling. This model requires a major assumption that a whole population is composed of several sub-groups following similar patterns [55]. For the purpose of building a suitable model for the study population, we need to take 3 major criteria into account, which are group membership probability, Bayesian Information Criterion (BIC), and average posterior probability. The Bayesian Information Criterion (BIC) value is calculated for every model established and is a value designed for selecting the best model, which is used to compare two models with distinct numbers of trajectories or trajectories of different shapes(i.e., linear, quadratic, or cubic). For a given model, BIC is calculated as :

$$BIC=log\ (L)-0.5*log(N)*(K)$$

Where

L: value of the model's maximized likelihood.

K: number of parameters

N: sample size

Determination of Optimal Number of Trajectories

The determination of optimal number of trajectories is based on three major criteria, which are BIC value, group membership probability(GMP) , and average posterior membership probability (AvPMP).

Models with different numbers of parameters will have different BIC values. Using the BIC value of the more complex model to subtract the BIC value of the simpler model, we can get the difference in the BIC values for the two competing models and is denoted by ΔBIC. Log Bayes factor is approximately equivalent to 2*(ΔBIC). If the Log Bayes factor is between 0 to 2, it is treated as weak evidence for the more complex model (i.e., models with more parameters). Log Bayes factor between 2 to 6 is treated as moderate evidence. Log Bayes factor greater than 6 is the sign of demonstrating the more complex model is the ideal model when comparing two models [81,90].

Group membership probability shows the percentage of the population of each trajectory group(i.e., class). Ideally, the percentage of each trajectory should be at least five percent [81,90]. Based on the characteristics of individuals, we can calculate the probability that each individual belongs to each trajectory group. The Posterior Membership Probability (PMP) is used to the assigned individual to the trajectory group with the largest PMP. The average posterior probability (AvePP) is calculated by averaging the PMP, and the average posterior probability of each group should be higher than 70% to indicate that individuals with different developmental changes are appropriately classified into different groups, and people who are classified into the same group possess similar trajectory patterns.

The model building usually starts with 2 quadratic trajectories, and more groups will be added if the added model shows a better fit. In the beginning, the linear, quadratic, and cubic forms will be tested for each trajectory, so we get different combinations of parameters of intercept and slope for each trajectory. In the selection process, we keep significant non-linear terms and the linear terms, no matter if it is significant or not. Different combinations of parameters of intercept and slope are estimated for each trajectory [6].

As previously stated in section 2.2.1, the number of trajectories was determined based on the Bayes factor, group membership probability, average posterior probability, and the

significance of the model parameters (polynomial terms only). Since BIC value is always negative, the model with the at least negative Bayesian information criterion (BIC) value was selected as the best-fitting one; in other words, we select the one with the smallest absolute value [85]. Group membership probability (GMP) is the proportion of the population included in each group. This GMP is ideally larger than 5% to make the subgroup classification meaningful. Posterior probability refers to each subject's probability of belonging to each trajectory group. Subjects were divided into different groups of psychological distress trajectories based on the highest posterior probabilities that belonged to each subgroup. "Individuals do not belong to trajectory groups; rather, they are assigned a probability of group membership."[104]. After identifying the optimal number of trajectories, we then used the multinominal logistic regression to test the factors associated with different trajectory group membership.

2.2.1 Accelerated Longitudinal Design (ALD)

In this study, we adopted the accelerated longitudinal design (ALD) in our model. ALD can span the age of interest in a shorter follow-up period since participants entered the survey at different initial ages. Because each participant joined the study at a different initial age, the age range of participants is expanded compared to recruiting participants with the same initial age. The ALD study is less impacted by the dropout concern [87].

The primary disadvantages of the ALD study are the age or time cohort effect. Since the ALD method "splicing" trajectories from different age groups, the representativeness of the age range may be compromised due to the age cohort effects. A single cohort longitudinal

study consists of only one age group, and it will produce an unbiased estimate of the internal changes to the set of objects [88]. We included participants age 18-29 at the baseline cycle(1994/1995). The NPHS survey total lasts 16 years. Due to the adoption of the ALD design, the entire age range of our study is 18-45.

2.2.2 Factors Associated with Psychological Distress

Noted that I also performed dtrajectory analysis on time-varying risk factors and used trajectory groups of risk factors as covariates. Since all the risk factors are longitudinal data, and most of the risk factors are changing over time(except sex and race); for example, people's lifestyle or overall health status might change dramatically during the 16 years of the follow-up study. To better capture the developmental nature of the risk factors, we did trajectories analysis on all risk factors instead of using a "point measurement" of the risk factors. All risk factors are finally classified based on their trajectory groups. Using trajectory groups of risk factors as covariates in the logistic regression can better grasp the development of all these risk factors, compared with using the measurement of the risk factors at a single time point.

Then the Chi-squared method is used to test the independence between the trajectory groups of risk factors and trajectory groups of psychological distress. The null hypothesis is that there are no relationships between the risk factors with the trajectory groups (i.e., independence is assumed) at significance level a=0.2. Factors with probability bigger than 0.2 will not be included in the multinominal logistic model.

In the multinomial logistic test, we adopted the backward elimination method. We tested what characteristics each trajectory group holds. We tested how sex, gender, smoking status, physical activity, drinking, income, overall health condition, marital status, chronic condition, body mass index, education, and financial stress might influence the psychological

distress trajectory of group memberships. We also tested the potential interactions between sex and smooking status. The model with the interaction term of sex and smoking status attempts to describe how the effect of a predictor variable (sex) depends on the level of another predictor variable (smoking status). If the interaction term of sex * smoking status is significant, we can no longer talk about the effect of sex, holding all other variables at a certain value, since it does not make sense to fix smoking status and sex*smoking status at a certain value and still allow sex change from 0 to 1. In other words, when the interaction term exists, the odds ratio of smoking status is always influenced by the level of sex and vice versa; thus, there is no single odds ratio for sex or smoking status.

The standard multinomial model generates j-1 sets of parameter estimates, comparing different levels of the dependent variable to a base level, where 'j' is the number of categories of the dependent variable. In our study, we had four psychological distress group memberships (i.e., j=4). In the multinomial logistic analysis, the distress-free group was set as the reference group for all comparisons among four psychological distress groups.

Trajectory variable: Nonspecific Psychological Distress. The psychological distress scale is the dependent variable in our study. Statistics Canada used Kessler 6-items psychological distress scale as the tool to measure participants' mental health conditions in the National Population Health Survey. The total score range of k6 is between 0 and 24, and higher score indicates higher stress [7]. This variable is a derived variable in the NPHS. Participants were included if they had at least completed three cycles of the survey.

Covariates (Time-invariant and Time-varying) : sex (female / male), race (white/ non-white) are time-invariant variables. Other risk factors are time-varying, including income, years of education, BMI, smoking, drinking, physical activity, chronic condition, marital

status, financial stress, as well as overall health. The above factors were included based on previous research findings. The NPHS survey covered many variables, and it also contains derived variables based on the collected data. In our study, risk factors, including physical activity, smoking status, drinking status, household income, years of education were analyzed based on derived variables. For the time-varying risk factors, we used the LCGM method to recategorize the levels of factors, so we can know how the development of risk factors influenced the psychological distress scale.

Smoking Status:

The derived variable of smoking status consists of 6 categories in the NPHS dataset, which are daily smoker, occasional smoker, always an occasional smoker, former daily smoker, former occasional smoker, and never smoked. We defined the first three categories as current smoker, which were assigned with value "1", and the rest of the categories as non-current smokers who were assigned with value "0". Then we used the LCGM method to examine an individual's long-term smoking status.

Physical Activity:

In the NPHS, physical Activity level was derived based on survey questions like "Have you done any of the following in the past 3 months? - Walking for exercise" "Have you done any of the following in the past 3 months? - Gardening or yard work" "Have you done any of the following in the past 3 months? - Exercise class or aerobics."

NPHS defined the derived physical activity into three levels, which are active, moderate, and inactive. We assigned a dummy value "1" for individuals who were active or moderately active and assigned a value "0" for individuals who were not active at all. Then we used the LCGM method to examine an individual's long-term physical activity status.

Alchol Consumption

Type of alcohol drinker is a variable derived based on multiple survey questions, such as "During the past 12 months, how often did you drink alcoholic beverages?" "How often in the past 12 months have you had 5 or more drinks on one occasion?" "Have you ever had a drink?"

NPHS has four derived types of drinker, which are regular drinker, occasional drinker, former drinker, and abstainer. In our coding in SAS, regular drinkers and occasional drinkers were defined as having an active drinking status, which was assigned with value "1"; while former drinkers and abstainers were defined as the non-drinker, which was assigned with "0". Then we used the LCGM method to examine an individual's long-term alcohol consumption status.

Income:

This variable is derived based on total household income from all sources. Participants answered income-related survey questions, such as "What is your best estimate of the total income, before taxes and deductions, of all household members from all sources in the past 12 months? Was the total household income: - less than $20,000 or $20,000 or more?" The derived variable of income is divided into 4 categories by NPHS, which are low-income quartile, lower-middle-income quartile, upper-middle-income quartile, highest income.

We grouped low and low middle income together, and they are considered as a low-income group, which was assigned with dummy value "0"; while the upper middle and highest income are considered as a high-income group, which was assigned with dummy value "1". Then we used the LCGM method to examine an individual's long-term income status.

Overall Health:

In the survey, participants were asked " How do you describe your overall health condition" There were four categories of the self-rated overall health defined by NPHS, which are excellent, good, fair, and poor. We grouped people who self-rated as excellent and good together and defined them as "good overall health"; while people who self-rated as fair and poor are defined as "poor overall health." In our coding in SAS, individuals with good overall health were assigned with value "1", and individuals with poor overall health were assigned with value "0". Then we used the LCGM method to examine an individual's long-term overall health status.

Marital Status:

In this survey, participants were asked, "what is your current marital status?". There were 7 categories, which were married, common-law, had a partner, single, widowed, separated, and divorced. In our study, we defined people who were married, common law, has a partner as the reference group, and they were defined as "married". People who were single, widowed, separated, and divorced are defined as "not married". Then we used the LCGM method to examine an individual's long-term marital status.

Chronic Condition:

This variable was derived based on multiple survey questions. These questions include but are not limited to "Do you have food allergies diagnosed by a health professional?" "Do you have high blood pressure diagnosed by a health professional?" "Do you have migraine headaches diagnosed by a health professional?" Derived chronic conditions definition in NPHS has two

categories: Yes or No. Then we used the LCGM method to examine an individual's long-term chronic condition status.

Body Mass Index:

The NPHS survey followed the international standard on measures of obesity using the body mass index. People are categorized as underweight (=<18.5), normal weight (18.5-24.9), overweight (25-30), obese I (30-35), obese II (35-40), obese III (40-45). In our study, the first three categories are assigned with value "0", and the rest are assigned with value "1". Then we used the LCGM method to examine an individual's long-term body mass index status.

Years of Education:

If an individual received a high school diploma in the first cycle, these individuals' "years of education" is documented as 12. If individuals advance themselves in education, we add the corresponding time to these individuals' "years of education." For example, if the individual received a university degree in one of the future cycles, 4 years will be added to the initial 12 years of education. We calculate each person's total years of education in this way. Then we used the LCGM method to examine an individual's long-term years of education status.

Financial Stress:

Participants were asked whether they experienced financial stress in the past 12 months. NPHS defined the response categories as MIN=0 and Max=1; a higher value indicates having experienced financial stress in the past 12 months. Then we used the LCGM method to examine an individual's long-term financial stress status.

2.3 Results

2.3.1 Charateristics at Baseline Cycle (1994)

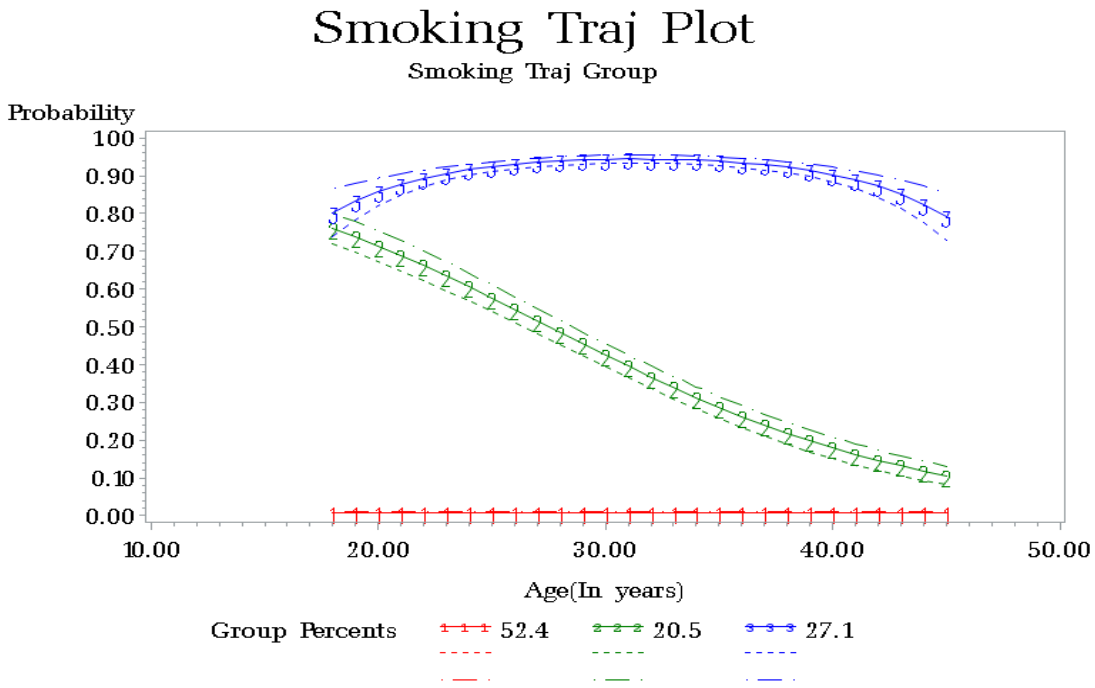
Table 2.1 shows the characteristics of studies subjects in the baseline. In the first cycle of the survey (1994), the average age of the participants was 23.6. Around 23.2% of the participants were married, and the Caucasian race is dominated in our study (88.66%). The majority of the population's education is above high school, and most of the people experienced low financial stress level (73.32%).

Table 2.1 Characteristics of Studied Participants at Baseline (1994)

Characteristics	Sample Size
	No.(%)
Average Age	23.64
Marriage Status	
Married	618 (23.22)
Not-married	2043 (76.78)
Sex	
Males	1357 (51.03)
Females	1303 (48.97)
Race	
White	2359 (88.66)
Non-white	302 (11.34)
Education	
High School graduate or less	243 (9.12)
Above high school	1466 (55.11)
University and above	952 (35.76)
Financial Stress	
Low financial stress	1951(73.32)
High financial stress	710 (26.68)

2.3.2 Results of Trajectories of Risk Factors and Psychological Distress Scale

Smoking Status: We identified three trajectory groups through the LCGM method. Around 52.4% of the subjects never smoked; 20.5% of the subjects had a decreasing probability of smoking over time, while 27.1% of the population had a consistently high probability of smoking. The average posterior probabilities for the three trajectory memberships are 0.97,0.89 and 0.92, respectively.

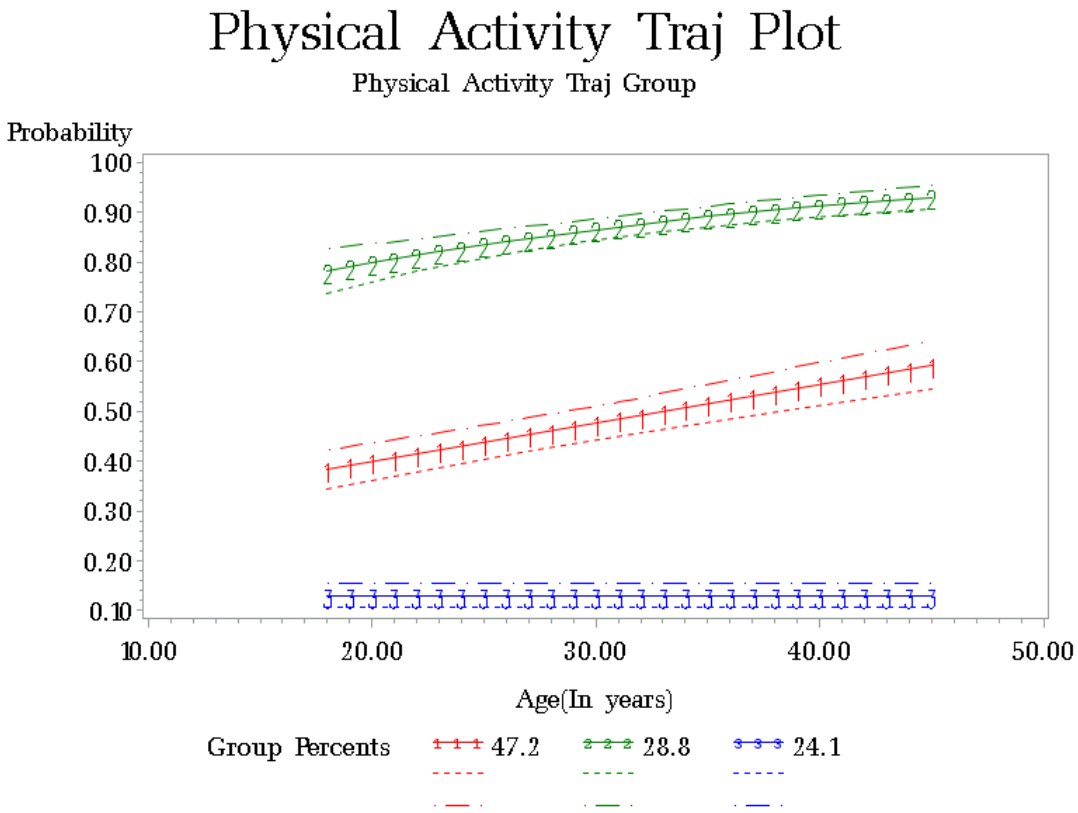


*Trajectory 1: Non-Smoker
*Trajectory 2: Decreased Probability of Being a Smoker (DP-Smoker)
*Trajectory 3: Constant-Smoker

Figure 2.1 The trajectories of the probability of being a smoker for young adults (18-45 years), with 95% confidence intervals (three-group model, no covariates included), NPHS, 1994-2011

Physical Activity: Through the LCGM method, we identified three trajectory groups. It is shown that 24.1% of the population are not physically active at all; 47.2% of the studied population showed an increasing tendency of exercising; 28.8% of the population are highly

active. The average posterior probabilities for the three trajectory memberships are 0.79,0.83 and 0.79, respectively.

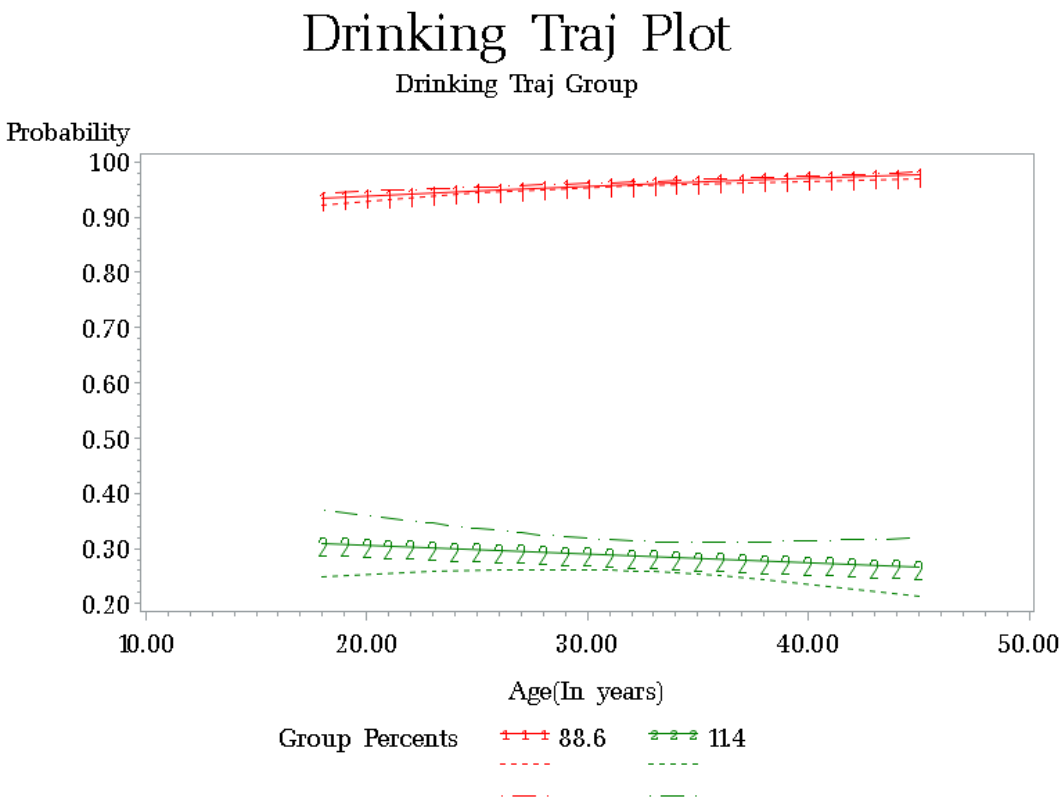


*Trajectory 1: Increasing-Active
*Trajectory 2: Constant-Active
*Trajectory 3: Not-Active

Figure 2.2 The trajectories of the probability of being physically active for young adults (18-45 years), with 95% confidence intervals (three group model, no covariates included), NPHS, 1994-2011.

Alcohol Consumption:

Two drinking trajectory membership groups were identified through the LCGM method. It is shown that 11.4% of the sample have consistant low probability of alcohol consumption, and 88.6% of the population are constant drinkers. The average posterior probabilities for the two trajectory memberships are both greater than 0.75.

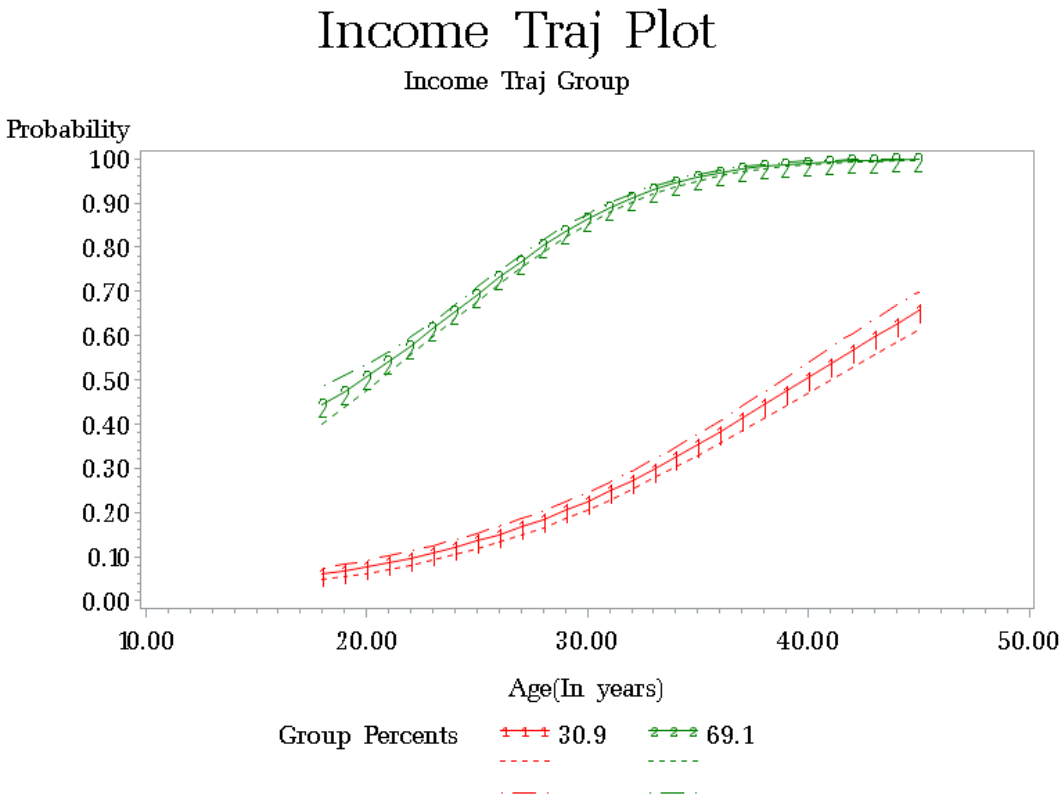


*Trajectory 1: Constant-Drinker
*Trajectory 2: Low-Probability

Figure 2.3 The trajectories of the probability of being a drinker for young adults (18-45 years), with 95% confidence intervals (two-group model, no covariates included), NPHS, 1994-2011.

Income:

We identified 2 income trajectory membership groups. 30.9% of the population had a relatively low household income, while 69.1% of the population had a relatively high household income. The average posterior probability of group 1 and group 2 are 0.915 and 0.957, respectively.

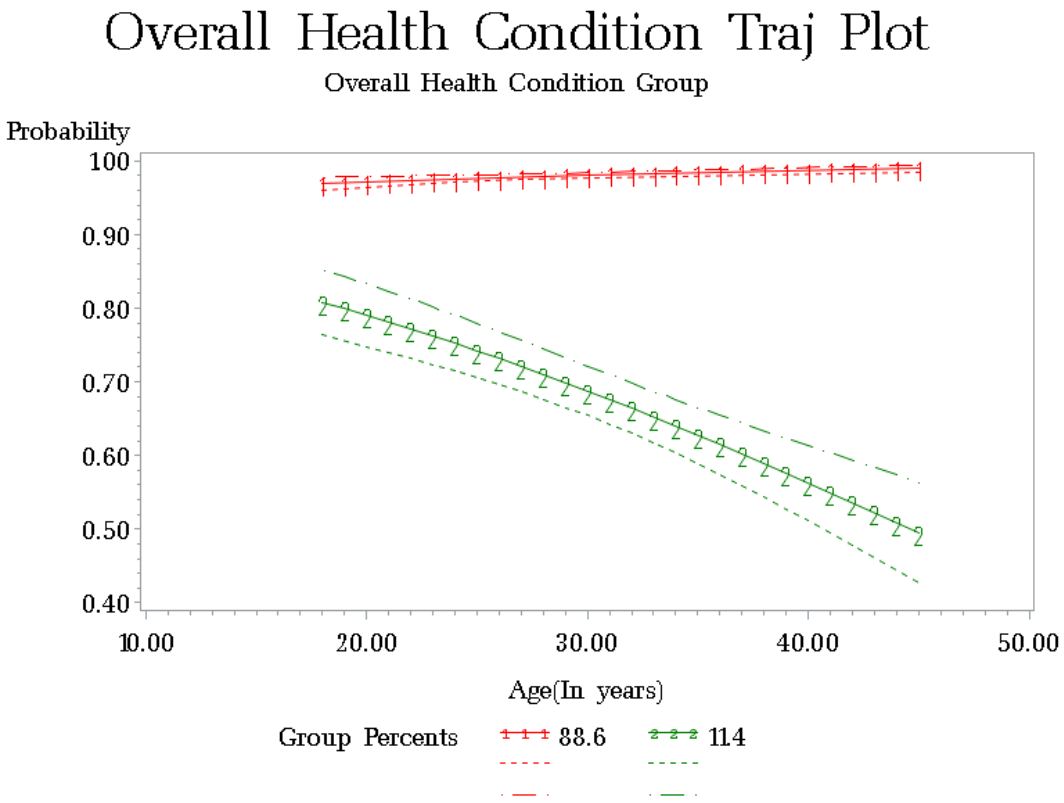


*Trajectory 1 : Low-Increasing
*Trajectory 2: High-Increasing

Figure 2.4 The trajectories of the probability of having a high level of income for young adults (18-45 years), with 95% confidence intervals (two-group model, no covariates included), NPHS, 1994-2011

Overall Health:

Around 88.6% of the population had consistently good overall health, while the psychical condition of the rest population was decreasing over time. The average posterior probability of group 1 and group 2 are 0.96 and 0.878, respectively.

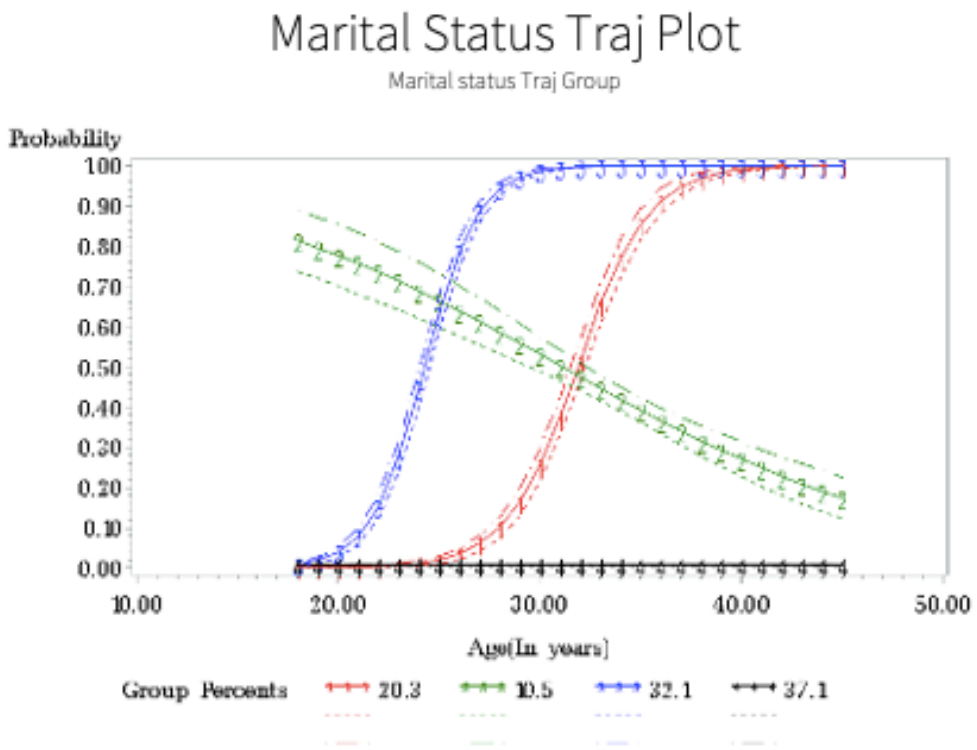


*Trajectory 1: Constant-Good Overall Health
*Trajectory 2: Decreasing-Overall Health

Figure 2.5 The trajectories of the probability of having good overall health for young adults (18-45 years), with 95% confidence intervals (two-group model, no covariates included), NPHS, 1994-2011.

Marital Status:

Based on the NPHS data, we identified four marital status trajectory groups through the LCGM method. Trajectory 3 shows that 32.1 % of the population got married around the early 20s, and trajectory 2 shows that 20.3 % of the population got married around the early 30s. Trajectory 4 shows that 37.3% of the population were not married, and trajectory 2 shows that 10.5% of the population showed a decreased probability of being married, which means people who got married early have a higher divorce rate. The average posterior probability each group is 0.91, 0.92, 0.94, and 0.90, respectively.



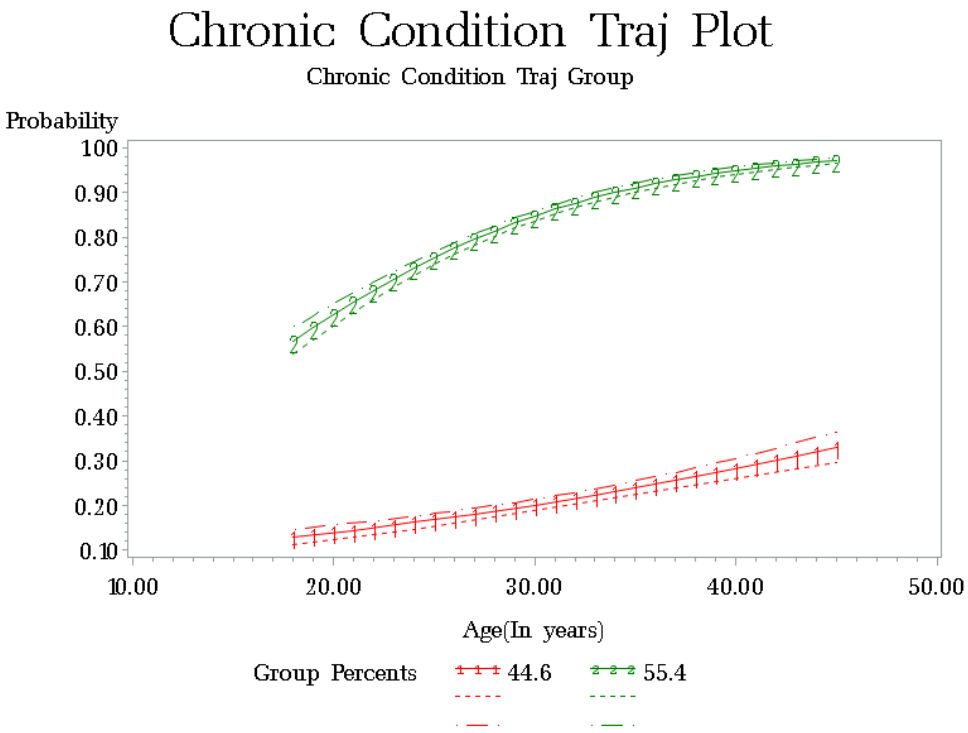
*Trajectory 1: Married at Early 30s
*Trajectory 2: Decreasing Probability of Being Married.
*Trajectory 3: Married at Early 20s
*Trajectory 4: Not-Married

Figure 2.6 The trajectories of the probability of being married for young adults (18-45 years), with 95% confidence intervals (four-group model, no covariates included), NPHS, 1994-2011.

Chronic Condition:

Based on the data from NPHS, two trajectory groups were identified through the LCGM method. Around 44.6% of the population has a low probability of having any chronic disease, while 55.4% of the population had a high and increasing chance of developing chronic

disease. The average posterior probability for the two groups is 0.952 and 0.956, respectively.

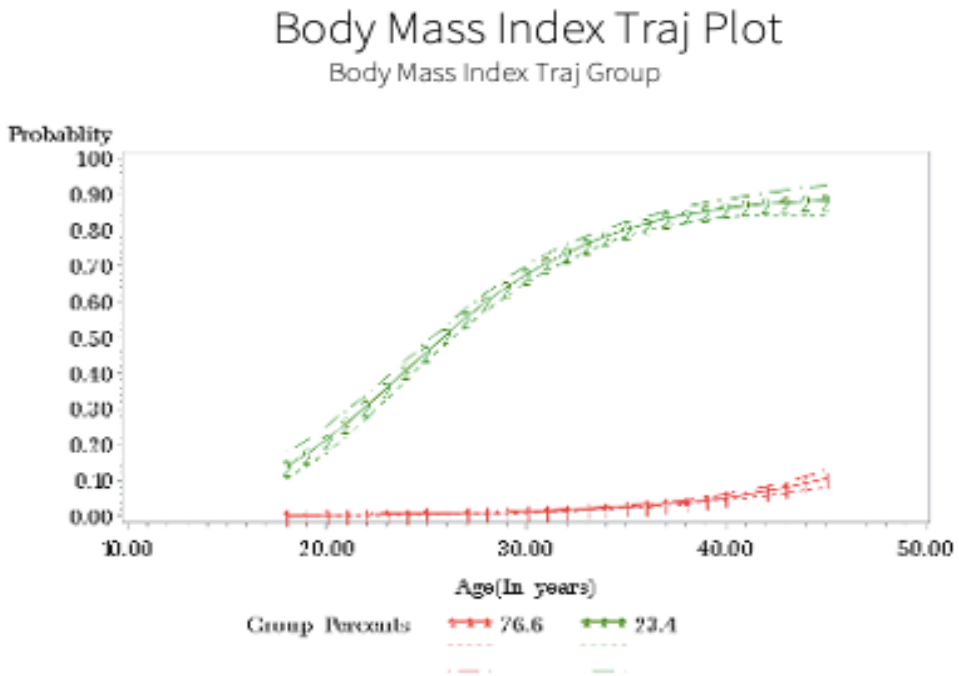


*Trajectory 1: Low Probability of Having Chronic Condition
*Trajectory 2: High Probabiltiy of Having Chronic Condition

Figure 2.7 The trajectories of the probability of having at least one chronic disease for young adults (18-45 years), with 95% confidence intervals (two-group model, no covariates included), NPHS, 1994-2011

Body Mass Index:

We identified 2 trajectory groups. 76.6% of the population had normal weight, while 23.4% of the population had an increasing probability of being obese or weights over time. The average posterior probabilities of the two groups are 0.985 and 0.969.

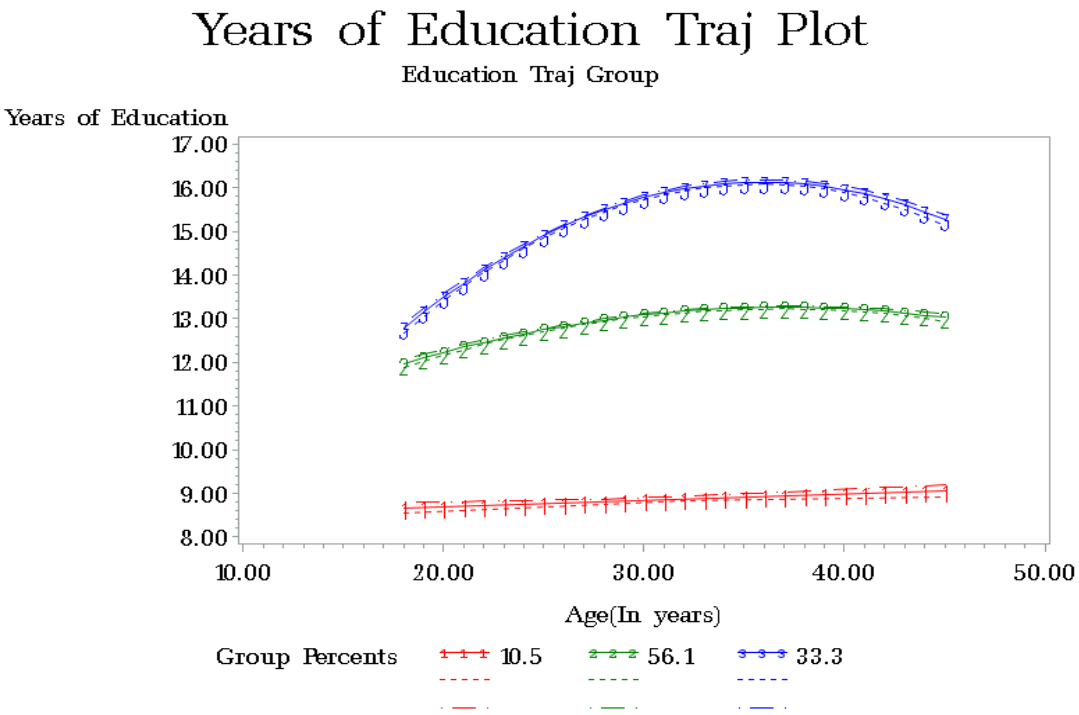


*Trajectory 1: Constant Normal Weight
*Trajectory 2: Increasing Probability of Being Obese or Overweight

Figure 2.8 The trajectories of the probability of having a high level of body mass index for young adults (18-45 years), with 95% confidence intervals (two-group model, no covariates included), NPHS, 1994-2011

Years of Education:

We identify three trajectory groups thourgh the LCGM method based on the records of education. It is shown than 10.5% of the population received less than 10 years of education; 56.1% of the population received about 12 years of education, and 33.3% of the population received higher education, which is around 15 years. The average posterior probabilities of these three groups are all greater than 0.75.

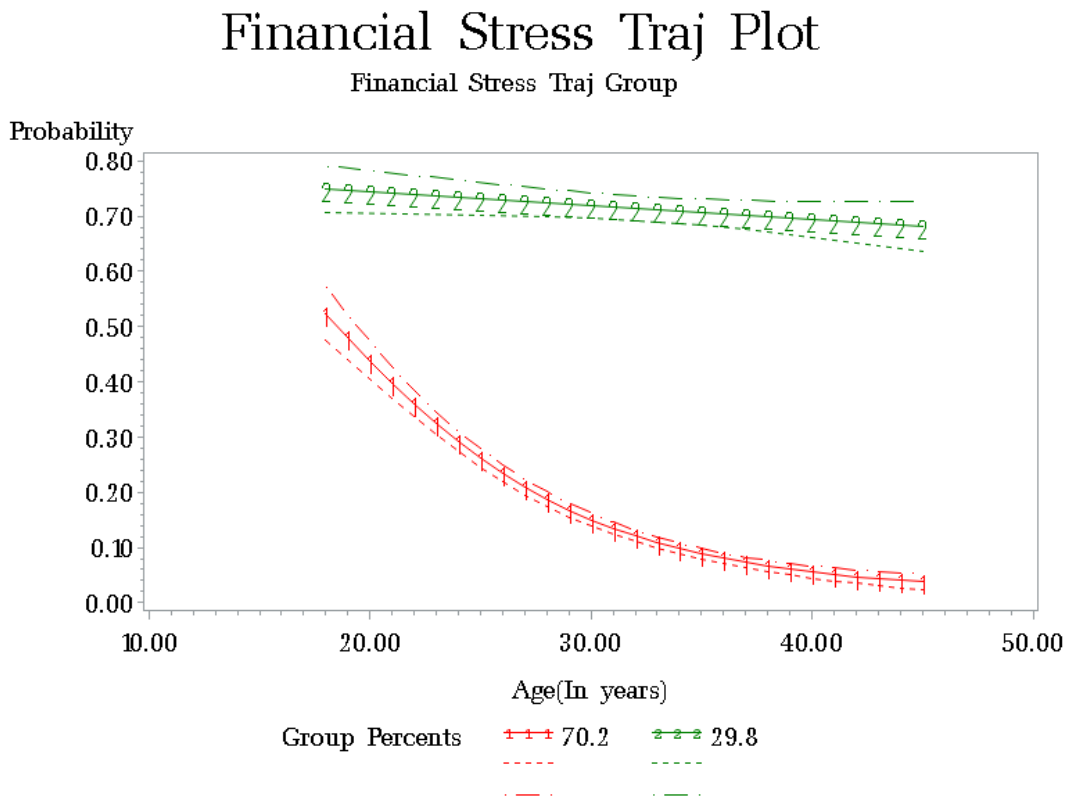


*Trajectory 1: Lower education (less than 10 years)
*Trajectroy:2: Average dducation years (10-12 years)
* Trajectory3: Higher education (above 12 years)

Figure 2.9 The trajectories of years of education for young adults (18-45 years), with 95% confidence intervals (three-group model, no covariates included), NPHS, 1994-2011

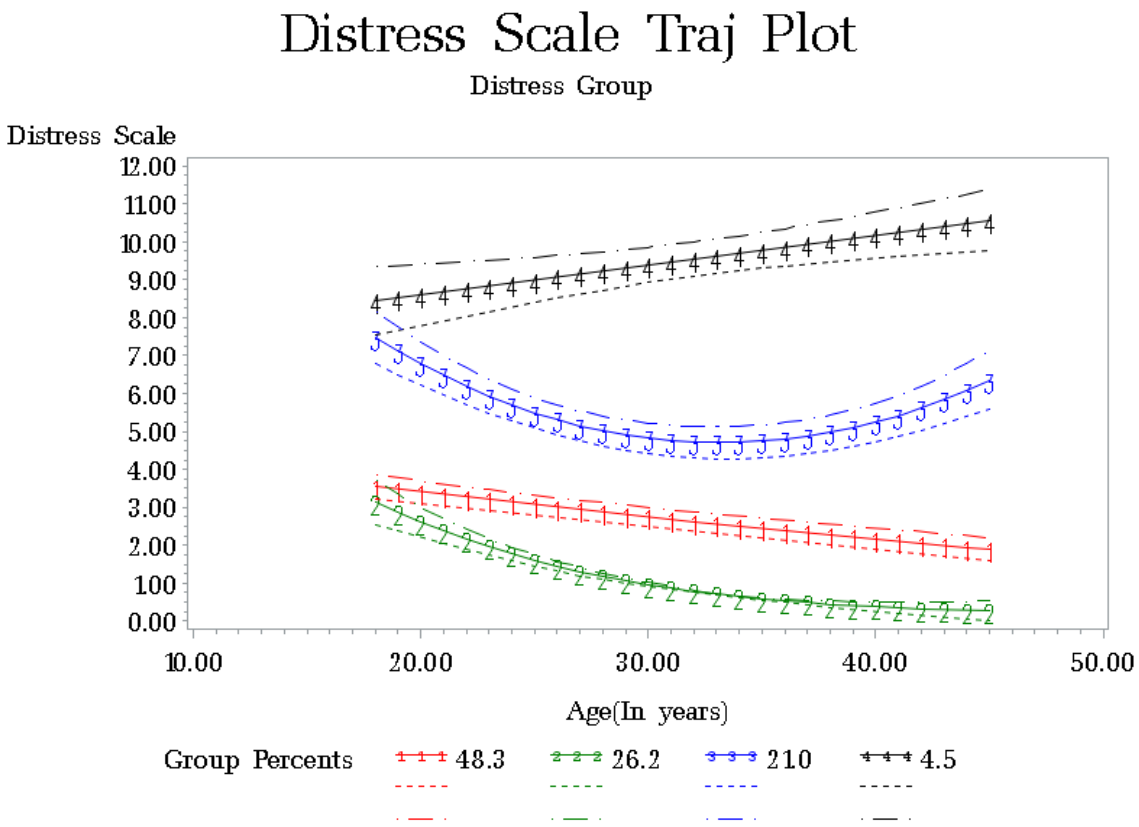
Financial Stress:

We identify two financial stress trajectory groups based on the data from NPHS. It is shown that 29.8% of the population experienced consistent high financial stress overtime, while 70.2% of the population had a relatively high probability of feeling stress from the financial aspect, but the probability decreased gradually. The average posterior probabilities of the two groups are 0.985 and 0.969.



*Trajectory 1: Decreasing Financial Stress
*Trajectory 2: Constant High Financial Stress.

Figure 2.10 The trajectories of the probability of having a high level of financial stress for young adults (18-45 years), with 95% confidence intervals (two-group model, no covariates included), NPHS, 1994-2011.



*Trajectory 1: Low-Distress

*Trajectory 2: Distress-Free

*Trajectory 3: Moderate-Distress

*Trajectory 4: High-Distress

Figure 2.11 Psychological Distress Trajectories (18-45), with 95% confidence intervals(four-group model, no covariates included), NPHS (1994-2011)

Table 2.2 Parameters of Psychological Distress Trajectories (18-45), with 95% confidence intervals(four-group model, no covariates included), NPHS (1994-2011)

Trajectory Groups of Psychological Distress	Intercept at Age 18	Linear Coefficients(s.e)	Quadratic Coefficients (s.e)	GMP	AvePP
Distress-Free	10.472(1.413)	-0.508(0.095)	0.0045(0.00158)	26.20%	0.798
Low-Distress	4.74(0.229)	0.0045(0.0015)	.	48.30%	0.811
Moderate-Distress	18.35(1.578)	-0.829(0.100)	0.0125(0.00157)	21.02%	0.82
High-Distress	7.015(0.877)	0.079(0.026)	.	4.47%	0.889

As shown in Figure 2.11, we identified 4 psychological distress trajectories using the LCGM method. The first trajectory group is the Distress-Free group. People in this group have extremely low or no risk of having psychological distress. This group consists of 26.3% of the total population. In the first cycle, the initial psychological score for this group is around 3; then, the score decreased to 1 in the next 20 years. In the plot, this group is colored in green. The second group is the Low-Distress group, which means people in this group have a low risk of experiencing psychological distress. The initial average psychological score in 1994 is slightly below 4; then, the score decreased gradually and dropped to 2 in 2011. This group consists of 48.3% of the total population, and it is in red in the plot.

The third group is the Moderate-Distress risk group, which means people in this group showed a relatively higher psychological distress score. The starting psychological score was around 7; then, the number decreased to 5 around age thirty. The score gradually increased to 7 again at age 45. This group consists of 21 percent of the total population. In the plot, this trajectory is in blue.

The fourth group is the High-Distress group, which showed a consistently high and increasing tendency. The initial number started at 8, and by age 45, the number reached 11. In the plot, this trajectory is in black. This curve consists of 4.5 percent of the total population. The group membership probabilities and average posterior probabilities are 0.798, 0.811, 0.820, and 0.889, respectively.

2.3.3 Univariate Analysis

The results of the Chi-sqaured test are shown in the following table 2.3.
Since the probability of race, type of drinker in the Chi-squared test are all greater than 0.2, they would not be further considered as potential risk factors.

Table 2.3 Univaraite Analysis

Characteristic	Distress-Free	Low Distress	Moderate Distress	High Distress	P-value
	No.(%)	No.(%)	No.(%)	No.(%)	
Sex					<.0001
male	372(62.00)	752(52.40)	189(37.43)	44(36.67)	
female	228(38.00)	683(47.60)	316(62.57)	76(63.33)	
Race					0.7936
white	523(87.90)	1261(88.55)	455(90.46)	105(88.23)	
non-white	72(22.10)	166 (21.45)	48 (9.54)	14 (11.77)	
Financial Stress					<0.0001
low	491(82.24)	1119(78.25)	325(64.61)	67(55.37)	
high	106(17.76)	311(21.75)	178(35.39)	54(44.63)	
Smoking Habit					<0.0001
non-smoker	376(62.66)	809(56.38)	216(42.86)	34(28.10)	
dp-smoker*	112(18.67)	270(18.81)	123(24.40)	15(12.40)	
smoker	112(18.67)	356(24.81)	165(32.74)	72(59.50)	
Drinking Status					0.2143
low	54(9.00)	1280(89.20)	441(87.33)	99(82.5)	
high	546(91.00)	155(10.80)	64 (12.67)	21(17.5)	
Physical Activity					<.003
non-active	106(17.67)	332(23.14)	145(28.71)	39(32.23)	
medium	275(45.83)	702(48.92)	241(47.72)	51(42.15)	
active	219(36.50)	401(27.94)	119(23.56)	31(25.62)	
Chronic Disease					<0.0001
low	337(56.45)	625(43.71)	171(33.93)	24(2.00)	
high	260(43.55)	805(56.29)	333(66.07)	96(98.00)	
Overall Condition					<0.0001
decreasing	13(2.18)	91(6.36)	72(14.29)	68(67.33)	
high	583(97.82)	1339(93.64)	432(85.71)	53(32.67)	

Education					<0.0001
low	44(7.38)	123(8.60)	56(11.11)	19(15.70)	
medium	336(56.38)	764(53.43)	285(56.54)	76(62.81)	
high	216(36.24)	543(37.97)	163(32.34)	26(21.49)	
Marital Status					0.0003
married at early 20	444(31.03)	225(37.69)	131(26.00)	13(10.83)	
married at early 30	224(15.65)	109(18.26)	72(14.29)	23(19.17)	
dp-married**	145(10.13)	48(8.04)	40(7.94）	15(12.5）	
not-married	618(43.19)	215(36.01)	261(51.76)	69(57.5)	
BMI					0.0062
low	492(82.69)	1134(79.58)	400(79.52)	77(46.17)	
high	103(17.31)	291(20.42)	103(20.48)	43(53.83)	
* dp-smoker: decreased probablity of being a smoker					
**dp-married: decreased probability of being married					

2.3.4 Multinomial Logistic Analysis on Associated Factors of Psychological Disress

As shown in table 2.4, in the multinomial logistic analysis, the distress-free group was set as the reference group for all comparisons among four psychological distress groups. Compared with people without financial stress, people with financial stress had higher odds of being in the low–distress group(OR = 1.69 (95%CI: 1.301,2.194), moderate-distress group (OR= 2.763(95%CI 2.035,3.753)), and the high-distress group (OR=5.776 (95%CI: 3.473,9.608)), relative to distress-free; with simultaneous adjustment for all other variables.

Concerning the physical health aspect, compared with people without chronic conditions, people with chronic disease had higher odds of being in the low-distress(OR=1.69(95%CI 1.18, 2.011), moderate-distress(OR=2.041(95%1.456, 2.861), and

high-distress (OR=2.608(95% CI 1.304)), relative to distress-free after controlling for other variables.

The overall health variables showed that the odds of having Low-Distress was higher for people who had decreasing overall well-being over time compared with stable high-quality overall well-being(OR=2.013 95%CI 1.216,3.637). The odds ratio for moderate-distress vs. distress-free and high-distress vs. distress-free, OR is 4.505 (95%CI 2.548,7.967) and 10.529 (95%CI 5.346,20.738), respectively.

There were some differences regarding the impact of marital status on different trajectory groups. By treating people who got married in the early 20s as the reference group, the multinomial logistic regression showed that the other two groups, people who got married later than 20 or people who were never married, did not pose a significant impact on determining people's distress trajectory memberships. But it is shown that for people who were never married relative to people who were married in the early 20s, the odds ratio for having high distress over distress-free is 3.97 (95%CI 2.136, 7.381); the odds ratio for having moderate-distress over distress-free is 2.204 (95%CI 1.624, 2.991); the odds ratio for having low-distress over distress- free is 1.709 (95%CI 1.352, 2,16), given all other predictors in the model are held constant. In other words, people who were never married are more likely to have high distress.

The variable sex and smoking status are both significant with type-3 analysis p-value less than 0.05, which are p-value< 0.0005 and p-value<0.0001, respectively.

Since the results showed that the interaction term of the sex*smoking status is significant (p-value <0.0006), the odds ratio of different level of sex (male/female) of having higher psychological distress scale is changing with the level of smoking status (non-smoker, constant smoker, decreasing probability of being a smoker), and vice versa. That’s why we do not have odds ratio values for sex and smoking in the table.

Although the interaction between smoking status and sex is statistically significant, this significance only showed among the females who had a decreasing probability of being a smoker in the high-distress group. In terms of the odds ratio, it is shown that among female participants, the odds ratio of having high distress in the DP-smoker group over the constant smoker group is 2.507 (95%CI 1.1138,5.6467), withholding other covariates constant. This means that women who quit smoking are more likely to fall into high-risk groups as they age.

Table 2.4 Covariates Influencing Psychological Distress Trajectory Group Membership: multinominal analysis, NPHS, 1994-2011

	Low-Distress	Pr>t	Moderate-Distress	Pr>t	High-Distress	Pr>t	Type 3 Analysis Pr>F
	OR	.	OR	.	OR	.	
	(95%CI)		(95%CI)		(95%CI)		
Financial stress (High vs. Low*[1])	1.69 (1.301,2.194)	<.01	2.763 (2.035, 3.753)	<.0001	5.776 (3.473, 9.608)	<.0001	<.0001
Chronic condition (Dieseased v.s. D-free*[2])	1.541 (1.18, 2.011)	<.0001	2.041 (1.456, 2.861)	<.0001	2.608 (1.348, 5.045)	<.0001	<.0001
Overall health (Substandard vs. Good*[3])	2.103 (1.216, 3.637)	0.0079	4.505 (2.548, 7.967)	<.0001	10.529 (5.346, 20.738)	<.0001	<.0001
Income (Low vs. High*[4])	1.026 (0.806,1.305)	0.834	1.344 (1.001, 1.805)	0.0492	2.063 (1.235,3.445)	0.0057	0.0073
Marital status							<.0001
Married at early 20 group	REF	.	REF	.	REF	.	
Married at early 30 group	1.108 (0.843 ,1.457)	0.4609	1.271 (0.879, 1.839)	0.2023	1.589 (0.725,3.479)	0.247	
Divorced group	1.385 (0.974, 1.971)	0.0701	0.918 (0.56,1.504)	0.7339	1.774 (0.763, 4.125)	0.1832	
Not married group	1.709 (1.352,2.16)	<.0001	2.204 (1.624,2.991)	<.0001	3.97 (2.136, 7.381)	<.0001	
Smoking	.	.	.	.	.	.	<0.0005
Sex	.	.	.	.	.	.	<.0001
Smoking*Sex							0.0006
Female							
CS*[5] vs. Non-smoker*[6]	0.8959 (0.6177,1.2994)	0.5622	0.6311 (0.4007,0.9940)	0.047	0.4941 (0.2128,1.1471)	0.1008	0.0859
DP-smoker*[7] vs. Non-smoker	1.1651 (0.7229, 1.8779)	0.5302	1.6175 (0.9424, 2.7764)	0.081	2.5078 (1.1138,5.6467)	0.0264	0.0022
Male							
CS*[8] vs. Non-smoker*[9]	1.0365 (0.7346,1.4625)	0.8381	1.0205 (0.6162, 1.6900)	0.9372	1.3586 (0.4248, 4.3446)	0.6053	0.2524
DP-smoker*[10] vs. Non-smoker	1.2862 (0.8654, 1.9117)	0.213	1.4765 (0.8552,2.5492)	0.1618	1.8204 (0.5860, 5.6549)	0.3002	0.7075

*1 Low: We set people in the low financial stress trajectory group as the reference group

*2 D-free: Meaning diesease-free. We set peope in the disease-free trajectory group as the reference group.

*3 Good: We set people in the good overall health trajectory group as the reference group.

*4 High: We set people in the high income trajectory group as the reference group.

*5CS: Constant smoker in females.

*6 Female non-smoker: Among females, we set people in the non-smoker trajectory group as the refrence group.

*7 DP-Smoker: Dereased probability of being a smoker in females

*8 CS: Constant smoker in male

*9 Male non-smoker: Among males, we set people in the male non-smoker trajectory group as the reference group.

*10 DP-smoker: Decreased probability of being a smoker in males

2.4 Discussion

This study mainly revealed that the young Canadian adults' population is not homogeneous in distress trajectories, and there are 4 identified trajectory groups using the LCGM method, which are (1) Distress-Free group, (2) Low-Distress group, (3) Moderate-Distress risk group, (4) High- Distress group. We used the multinomial logistic regression to examine the association between multiple covariates (e.g., smoking, drinking, and income) and group membership. Our findings suggest that having a poor overall health condition, higher financial stress, lower-income, not married, as well as chronic conditions have impacts on people's distress trajectories. Most covariates are time-varying, which can better capture the developmental changes in the risk factors compared with the cross-sectional studies in the literature. This study may contribute to the growing body of research on mental health and its relationship to the potential risk factors.

Our study findings on the association between financial stress and psychological distress trajectories are consistent with prior studies. American researchers stated that people who are on student loans are more prone to high psychological distress [11]. A cross-sectional Australia study by Taylor et al. examined the prevalence of psychological distress among 439 parents aged between 18-45 years in Sydney [94]. Their study showed that compared with low distress people, the odds ratio for high psychological distress people to report having lower self-reported health is 4.48 (95% CI 1.88-10.64) and serious difficulty in mortgage or rent payments. Taylor et al. demonstrated that among all the examined stressors, including job loss, alcohol/drug use, and chronic condition, financial stress showed the strongest association with distress. Our study results demonstrated that people with financial stress had larger odds of falling into relatively high distress groups, which agreed with former studies.

Taylor et al. conducted a univariate analysis of the association between some stressors and psychological distress [94]. The univariate analysis in this showed that chronic disease/disability had a significant association with distress. However, in the multinomial analysis, this variable was dropped due to insignificance. One possible reason is that chronic condtions cover a large spectrum, after introducing other factors into the model, the importance of chornic condtion on distress was weakened. In both the univariate and multinomial models of our study, choric diseases both significantly associated with distress. This difference might be explained by the difference in the data type, where Taylor et al. 's study has a cross-sectional nature, and our study is longitudinal.

Bulloch et al. conducted a cross-sectional study using the combination of the National Population Health Survey of 1996 and the Canadian Community Health Surveys from 2000 to 2013 [96]. Bulloch et al. tested the association between marital status and depression among individuals aged above 18, and their study showed that people who are widowed, separated, divorced, and single had a larger risk of developing depression compared with people who are married [96]. The interaction between sex and marital status showed that, compared with men, women are less impacted by marital status. Women who are singled (OR=0.87 95% CI 0.78-0.96), widowed (OR=0.68 95% CI 0.55-0.84), and separated (OR=0.74 95% CI 0.63-0.87) have a lower odds ratio of developing depression compared with men who were in similar situations. Strine et al. conducted a study to investigate the sex-specific effect of psychological distress on the relationship between adverse childhood experiences and current smoking among adults on 7210 Kaiser-Permanente members in San Diego [95]; their study showed that after controlling for sociodemographic factors, the association between smoking status and psychological distress were statistically significant for both men and women. After adjusting for adverse childhood experiences, the association was only significant for women [95]. Our study showed that women who quit smoking as they age had a larger chance to fall

into the high psychological distress group, compared with female non-smoker; but the association is not significant for long-term female smokers. The difference may due to (1) we defined the levels of the smoking status into three, but Strine et al. defined the level of smoking into two levels, which are current smoker and non-smoker. (2) The average studied population of Strine et al. was over 55, but our studied population was young adults. Our results revealed that women who quit smoking might need more support to reduce possible psychological stress after quitting smoking. Similar results were obtained by Dahne et al., which examined the association between anxiety sensitivity and motivation to quit smoking among women and men [74]. Their studies showed that women with higher anxiety sensitivity had more motivation to quit smoking, but not for men. Women higher in anxiety sensitivity might be more likely to attempt cessation or engage in smoking cessation treatment [74]. Since psychological distress manifest as anxiety and depression, this study by Dahne implies that a subgroup of women who had higher anxiety level was more likely to quit smoking. A Japanese study by Fujiwara et al. investigated people whose psychological distress scale scored high than 13 (i.e., severe psychological distress) based on a national survey [34]. Their cross-sectional study stratified the sample by gender and age group. It was shown that severe psychological distress (SPD) is significantly related to smoking status in the 20-49 age group and >50 age group in women. SPD is significantly associated with smoking status among men aged over 50, which is different from our study result. This difference might come from the difference in definition and study design(i.e., cross-sectional vs. longitudinal. Fujiwara et al. 's study defined the smoking category as a current non-smoker and current smoker, but our study studied the long-term pattern of the smoking status and divided the smoking status into three categories, which are non-smoker, consistent smoker and DP-smoker (i.e., decreased the probability of being a smoker). Our study captured the long-term change of smoking status instead of using a single time-point data .

The first limitation to my study is that all the data are self-reported; the responses might not accurate. The second limitation is that smoking and drinking are defined based on the frequency of consumption instead of the amount of consumption. For example, among participants who are assigned into the constant drinking membership group, the amount of alcohol consumption may vary largely. We could not differentiate participants with alcohol abuse or participants' normal level of alcohol consumption.; thus, this may influence the significance of these risk factors.

In general, our study results regarding the effect of financial stress, income, overall health, physical activity, chronic disease, and marital status are in line with prior studies. The strength of our study is using the LCGM model to conduct trajectory analysis. Compared with prior cross-sectional studies of psychological distress, our study can better capture the change of developmental patterns of covariates and the dependent variable. In summary, our study filled the gap of the existing studies and contributed to a more comprehensive understanding of the psychological distress of the young adults' group.

Chapter 3

Alzheimer's Trajectories Analysis of the Older Population (aged 60-75 at baseline)

3.1 Introduction and Research Objective

Population aging is the trend in most developed and industrial countries due to the decline in birth rate and longer life expectancy. Although population aging has a similar pattern globally, the speed is different. The rate of the aging population in the older cohorts is fast [101]. The WHO reckons that Canada will be one of the 10 countries globally with the highest percentage of seniors by 2025. It is projected that the number of the senior Canadian population will reach 6.7 million by 2021 [103].

Although age is a determinant of people's health, the aging process varies significantly from person to person. Seniors are not a homogenous group, and the mental health condition of this group is also influenced by gender, family status, ethnicity, geographical locations and etc.[97]. Many underlying factors affecting senior mental health are closely associated with social inequities, which are disproportionally distributed in the senior population [97]. People with low economic status are more venerable to ill-health. All of these background factors and experiences shape the senior's belief and value, and we need to respect the uniqueness of each senior citizen and recognize the diversity of this group.

Health conditions can impact the life quality of the older population, and mental health is a crucial part of our overall wellbeing and is just as valuable as our physical health. Inadequate mental health service and emotional impact from social isolation stigma can

compound the wellbeing of seniors living with psychological issues [107]. Mental diseases, like Alzheimer's, are directly age-dependent. The Amerian Alzheimer's Association showed that the incidence of Alzheimer's disease among people aged 65 to 74 is 3 %, but it increases to 32% for people older than 85 [113]. The most common early symptom of Alzheimer's disease is having problems remembering newly learned information. As Alzheimer's disease progresses, it can cause more severe symptoms, including disorientation, mood, and behavior changes, deepen the confusion about the event, time, and place; baseless suspicion of family, friends, and professional nursing staff; this disease can also lead to difficulty in speaking, swallowing, and walking [113]. The Alzheimer's Society of Canada stated that over 500,000 Canadians are living with AD today, and 25,000 new cases of AD are diagnosed every year [114]. Alzheimer's disease can post a significant impact on people's quality of life, and the aging of the Canadian population makes the disease more prevalent over time. Although there is currently no cure for this disease, studies showed that early intervention could slow down the brain degeneration of this disease.

Alzheimer's disease trajectory analysis can better capture senior's mental health condition change over time and offer new insights on the developmental pattern of AD. However, there is limited knowledge on the AD trajectories of the older population. We only found two research investigated the heterogeneity of the trajectories of cognitive development. Wilkosz et al. investigated 201 Caucasian subjects with possible AD, and six trajectories with different paths and cognitive decline rates were identified using the LCGM model [39]. Another study by Small and Backman identified a 2-class model trajectory of cognitive development in preclinical Alzheimer's disease using the GMM model [15]. Neither of the two studies is Canadian-based; In addition, we found most studies investigating risk factors related to AD are cross-sectional rather than longitudinal.

There is currently a need for more longitudinal studies on the development of Alzheimer's trajectory and AD-related risk factors analyses. This chapter will investigate the heterogeneity of AD among the older population by using latent class growth modeling.

3.2 Method

We used the LCGM method to identify the potential subgroups of the Alzheimer's disease trajectory in the senior population. LCGM model is known as semi-parametric group-based trajectory modeling and this model is used for trajectory analysis. This model requires a major assumption that a whole population is composed of several sub-groups following similar patterns [55]. For the purpose of building a suitable model for the study population, we need to take 3 major criteria into account, which are Group Membership probability, Bayesian Information Criterion (BIC), and average posterior probability. The Bayesian Information Criterion (BIC) value is calculated for every model established and is a value designed for selecting the best model, which is used to compare two models with distinct numbers of trajectories or trajectories of different shapes (i.e., linear, quadratic, or cubic). Group membership probability shows the percentage of the population of each trajectory group (i.e., class). [81,90]. The Posterior Membership Probability (PMP) is used to the assigned individual to the trajectory group with the largest PMP. The average posterior probability (AvePP) is calculated by averaging the PMP, and the average posterior probability of each group should be higher than 70% to indicate that individuals with different developmental changes are appropriately classified into different groups, and people who are classified into the same group possess similar trajectory patterns. The estimation of the

parameters in LCGM and the assessment of the associated factors of trajectories were completed simultaneously in the same LCGM model.

The NPHS data set is a longitudinal dataset that consists of 17,276 people in the first cycle in 1994/1995, and the same individuals were interviewed every two years [23]. There were a total of nine cycles, and this survey ended in 2010/2011. We included 2036 participants who were aged between 60-75 at the baseline year (1994/1995), and they must have at least two cycles of records of Alzheimer's disease.

Trajectory Variable: Alzheimer's disease. Participants were asked, "Do you have Alzheimer's disease or any other dementia diagnosed by a health professional?" Participants responded "yes" or "no" to this survey question. In order to distinguish from a cross-sectional study, which only included a one-point measurement of the variable of interest, we included participants who have completed at least 2 cycles of the survey regarding the information on AD. Participants with only one Alzheimer's record were excluded.

Covariate (Risk Factors and Time-Varying Factors): The selection of covariates was based on previous literature reviews and the availability of the data in the NPHS survey. Many potential factors may have an impact on the development of Alzheimer's. sex (woman or man), smoking (daily smoker, occasional smoker, always an occasional smoker, former daily smoker, former occasional smoker, and never smoked), physical activity (active, moderate, and inactive), depression (Derived Depression Scale - Short Form 0-8), and social support (Derived social support –score rang from 0-4), marital status (married, living with a partner, single, separated, divorced, widowed). Covariates can be categorized as risk factors (time-invariant) and time-varying covariates.

Risk Factors (Time- Invariant): Sex (male/female) was included as a risk factor.

Time-Varying Covariates (TVCs): Time-varying covariates include depression, social support, marital status, smoking, and physical activity. NPHS used the short form depression scale as the measurement tool. The questions ask about "periods during which the respondent felt sad or depressed or lost interest in everyday things within the past 12 months." The score ranges from 0 to 8, and higher scores indicate higher depression levels.In the NPHS data, the derived variable of social support has a score range of 0 to 4, while high scores indicate more received social support. Social support is derived by NPHS based on multiple questions like "Do you have someone you can confide in or talk to about your private feelings or concerns?" "Do you have someone you can count on to help you out in a crisis?" "Do you have someone you can count on to give you advice when you are making important personal decisions?" For the marital status, In the NPHS survey, participants were asked "what is your current marital status?". There were 7 categories, which were married, common-law, had a partner, single, widowed, separated, and divorced.In the NPHS, the smoking status is based on participants' current smoking habits. The derived variable of smoking status consists of 6 categories in the NPHS dataset, which are daily smoker, occasional smoker, always an occasional smoker, former daily smoker, former occasional smoker, and never smoked. In the NPHS, physical Activity level was derived based on survey questions like "Have you done any of the following in the past 3 months? - Walking for exercise" "Have you done any of the following in the past 3 months? - Gardening or yard work" "Have you done any of the following in the past 3 months? - Exercise class or aerobics." NPHS defined the derived physical activity into three levels, which are active, moderate, and inactive.

In order to test the characteristics that each trajectory group holds, we extend the basic model presented in Chapter 2 by introducing the time-varying and time-invariant covariates in

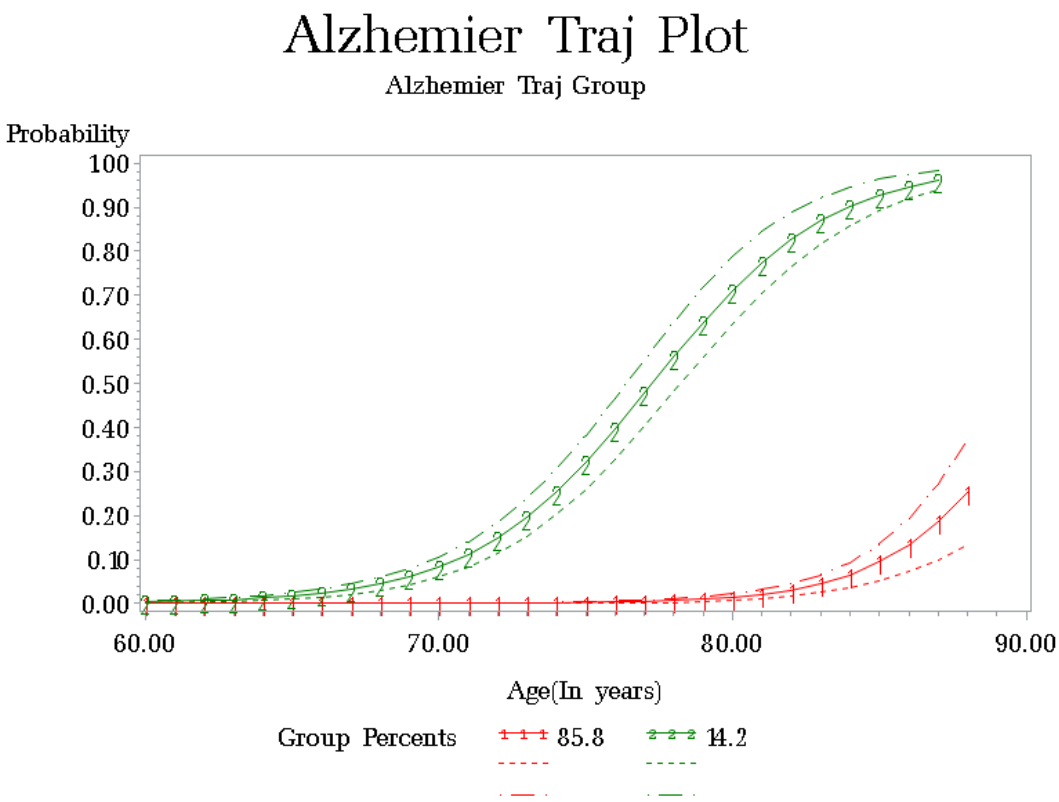
the LCGM trajectory model. In the LCGM analysis, sex was put in the fixed risk category; depression, smoking status, and social support, and physical activity were treated as a time-varying variable. In a model without covariates (i.e., time-invariant and time-varying factors), the trajectory does not condition on any event that might influence the development of trajectory [89]. Thus, the trajectory model with no covariates can be considered as measuring the "prototypical development path of trajectory group members", averaged over all the contingencies that might cause individual variation about this developmental course [89]. After introducing covariates in the LCGM model, the estimated parameters in age have a different interpretation. They specify the expected developmental course for the case where all of the covariates equal to zero [89]. Noted that the structure of the model allows for the possibility that the impact may vary by trajectory group [81]. In summary, the generalized LCGM was used to examine how the probability of trajectory group membership varies with risk factor (i.e., sex) and to examine whether TVCs affect trajectories within each group. The methods hold the assumption that TVCs do not directly affect the observed Alzheimer's developmental trajectories. Time-invariant covariates (risk factors) were incorporated into the model by assuming the risk factors are independent of the developmental trajectories, given group membership [81].

3.3 Results of Alzheimer's Disease Trajectory

Table 3.1 Characteristics of Subjects Aged 60-75 at Baseline Cycle(1994/1995)

Characteristics	Numbers
Sex	
Males	845 (41.5%)
Females	1191(58.5%)
Race	
White	1930 (94.8%)
Non-white	106 (5.2%)
Education	
Less than secondary	944 (46.37%)
secondary	267 (13.13%)
some post-secondary	373 (18.35%)
Post-secondary	451 (22.15%)
Financial Stress	
High	423 (20.8%)
Low	1613 (79.2%)
income	
High	1161(57%)
Low	875(43%)

Table 3.1 stated the descriptive statistics of the characteristics of the studied population at the baseline survey cycle (1994/1995). The studied population of older adults consists of 2036 subjects. Males consist of 41.5% of the studied population, while females comprised 58.5% of this elderly population. White people are the majority of the population (94.8%), and most people's education level was less than secondary (46.37%) at the baseline year 1994.



*Trajectory 1: Stable-Low
*Trajectory 2: Low-Increase

Figure 3.1 The trajectories of the probability of having Alzheimer's for older adults (60-91 years), with 95% confidence intervals (two-group model, no covariates included, NPHS, 1994-2011.)

Table 3.2 Parameters of Alzheimer's Trajectories (60-91), with 95% confidence intervals(two-group model, no covariates included), NPHS (1994-2011)

Trajectory Groups of Alzheimer's	Intercept (s.e.)	Linear Coefficients(s.e)	GMP	AvePP
Stable-Low	-35.64 (4.12)	0.39 (0.049)	85.80%	0.931
Low-Increase	-25.34 (0.33)	0.0045(0.0015)	14.20%	0.917

Figure 3.3 shows the resulting trajectories from ages 60 to 91 for a 2-group model with no covariates other than age in the specification of the trajectories.

Two Alzheimer's disease groups, a Stable-Low trajectory and the Low-Increase trajectory, were identified. The initial probability of developing Alzheimer's Disease of the two groups at age 60 was the same. The development of the two trajectories differed with the increase of age. The average posterior probability of each trajectory group exceeded 0.9.

The probability of developing Alzheimer's of the Stable-Low group started at nearly 0. It maintained stablility until the age of 80. Since age 80, the probability slightly rose with age, and the probability approached 0.3 at age 91.

For the Low-Increase group, the probability of developing Alzheimer's Disease started from 0 at age 60, and slowly increased to 0.1 at age 70. Since age 70, the probability increased quickly over the next ten years and reached 0.7 at age 80. Since age 80, the probability of developing depression kept increasing and hit nearly one at age 91

Table 3.3 Time-Varying Risk Factor Parameter Estimates, Errors, Tests, and P Values

Group	Time-Varying Parameter	Estimate	Error	Test	p Values
1	Intercept	-14.225	4.27	-3.328	0.0009
	Linear	0.176	0.059	2.991	0.0028
	Depression Score	0.38	0.16	2.374	0.0176
	Social Support	0.573	0.569	1.007	0.3139
	Marital Status	-1.214	0.607	-2.00	0.0455
	Smoking	-0.269	0.158	-1.705	0.0882
	Physical Activity	0.108	0.319	0.339	0.7343
2	Intercept	-3.027	1.52E+08	0	1
	Linear	-0.521	1.42E+06	0	1
	Depression	-0.0002	9.42E+06	0	1
	Social Support	-0.00076	5.77E+07	0	1
	Marital Status	-0.00265	4.50E+07	0	1
	Smoking	-0.03189	4.78E+06	0	1
	Physical Activity	-0.01705	3.22E+07	0	1

Table 3.4 Time-Invariant Risk Factor Parameter Estimates, Errors, Tests, and P Values

Trajectory Group	Time-Invariant Parameter	Estimate	Error	Test	p Values
Group 1	Reference	.	.	.	.
Group 2	Constant	2.945	0.685	4.298	0
	Sex	0.1514	0.39	0.388	0.6981

The impact of the time-invariant risk factors and TVCs on the Alzheimer's trajectory was examined based on the generalized model, which included all covariates. The model's parameter estimates measured the change in the response variable associated with changes in the explanatory variable. In Table 3.3, we presented the time-varying risk factor parameter estimates, standard errors, tests for the hypothesis that the parameters equal zero, and p values for the test. It is shown that in group 1, the stable-low group, depression score and marital status can significantly affect the observed Alzheimer's trajectory, while social support, smoking and physical activity did not pose a significant impact on the Stable-Low group (i.e., trajectory group 1). Due to the sparse data in NPHS, we cannot find meaningful results regarding the characteristic of the Low-Increase (i.e., trajectory group 2). Further research is needed to look up into the Low-Increase group.

Table 3.4 showed the parameter estimates of risk factor sex, which indicates the change of the relative odds of following the Low- Increase trajectory group as opposed to the reference group (i.e., group 1) with one unit increase in sex (from male to female). The p-value is larger than 0.05, which indicated sex is independent of the developmental trajectories, given group membership.

LCGM identified two Alzheimer's disease trajectory groups. Besides introducing the time-varying covariates: depression score, social support, marital status, smoking habit, and physical activity, we also added fixed covariates: sex, into the model. In summary, Table 3.3

shows that depression score and marital status posed a significant impact on the Stable-Low group, after controlling for social support, smoking habit, and levels of physical activity. Due to the sparse data in Low-Increase group membership, we cannot find the meaningful result to analyze the characteristics associated with trajectory 2. The older participants were included in our study if they have completed the 2 cycles of the survey (i.e, at least two records of Alzheimer's diseases). But information of the included participants regarding the measurements of depression, social support, marital status, smoking status, and physical activity might be absent. Since the participants in the Low-Increase group had a higher risk of developing AD, the information about above-mentioned factors are highly likely to absent in the survey after their cognitive decline. We do not have enough data about their self-reported information of potential risk factors in the NPHS, so we are not able to find meaningful results regarding the potential risk factors for the second group. Further research is needed to look into this trajectory group.

3.4 Discussion

In this chapter, we investigated the Alzheimer's trajectories of the elderly Canadian population using the latent class growth modeling.

The results indicate that a 2-class trajectory model is the best statistical fit for our AD data. Our results are consistent with a study conducted by Small and Backman, which examined the longitudinal trajectory of cognitive change using the growth mixture modeling [15]. Their study identified two cognitive trajectory groups; in their study, group 2 showed a relatively little decline over the follow-up period, and group 2 showed an accelerated rate of cognition decline after the third year of the follow-up period [15]. This study also indicated the heterogeneity nature in the deterioration of cognitive performance.

Our results showed that Stable-Low trajectory exhibits a slow increase in the probability of developing AD over time, and Low-Increase trajectory exhibits an accelerated

increase in the probability of developing AD after 70 years old. Even though AD is a common mental disease among the senior population, there is a lack of research regards the developmental trajectory of Alzheimer's disease in the Canadian population. Our study can provide us a better understanding of the growth pattern of AD.

Based on the data from NPHS, our epidemiological study also showed that depression was significant associated with the developmental trajectory of AD, which is in line with many studies [32, 92, 98,106]. Studies suggest that there is a strong relationship between depression and Alzheimer's disease. Modergo and Ferrandez investigated the association between depression and risks of developing Alzheimer's disease [32]. The study found that depressed patients are more than twice as likely to develop Alzheimer's disease compared with nondepressed patients. Another case-control study by Kokmen et al. showed that episodic depression and personality disorder are significantly associated with Alzheimer's disease [92].

In our study, gender was not a significant factor in terms of deflecting the growth of trajectories. This result is in line with a study from America, which investigated the risk of developing Alzheimer's disease between different gender. After following people aged over 65 years in Boston for up to 11 years, the study showed that the incidence of AD does not significantly associate with sex, after controlling for age [115]. A Canadian study showed similar results, where they examined the risk factors of Alzheimer's disease, and they found that sex was not significantly associated with the development of Alzheimer's disease after controlling a series of chronic diseases, lifestyle, age, and education [116].

Our research analysis demonstrated that social support did not pose a significant impact on Alzheimer's growth curve, which partially contradicts a Japanese study [62]. The Japanese study followed 14,088 older people from 2003 to 2013 [62]. After adjusting for age, health status, health behaviors, depression, cognitive complaints, and other socioeconomic

factors, the impact of support differs by gender. The Japanese showed that higher emotional support would contribute to better cognition ability among females. The study showed that males could benefit from receiving emotional support from co-residing family members, but this association was not observed among women. This difference might be explained by the difference in cultural background. Asian culture This difference might be explained by differences in cultural backgrounds. Asian culture emphasizes family unity and support, and emotional support from family members may be an important measurement for the quality of life.

Our results indicated that smoking was not a significant risk factor for developing Alzheimer's, and an American study by Norton et al. showed similar results[56]. Norton et al. examined the association between six lifestyle behaviors and dementia risk among 2,491 participants with an average 6-year follow-up. Their results showed that after adjusting for social activity, alcohol, church attendance, diet, as well as physical exercise, smoking abstention was not a significant factor in developing dementia.

In the results, we found that the marital status is related to the growth pattern of the AD trajectory group. The association between marital status and AD agreed with a cross-sectional study conducted in Taiwan [66]. It was shown that people in widowhood status had an elevated probability of developing dementia compared with another marital status.
The studies about Alzheimer's trajectories are currently under-explored. The LCGM method allows us to examine the developmental pattern of AD over time. Our research can fill in the gap and provide a more comprehensive understanding of Alzheimer's developmental trajectories of the senior Canadian population. Through the Alzheimer's trajectory curve, we can see the peak onset age of Alzheimer's disease. Early identification of Alzheimer's disease can ensure timely intervention and treatment planning. Although the result of the thesis is informative, this thesis has several limitations. When exploring the potential risk factors for

Alzheimer's disease, we only included social support, marital status, smoking, physical exercise, depression, and gender. Alzheimer's pathogenesis is not known yet, and it is a disease related to various potential risk factors; Second, the data regarding the subjects on trajectory 2 is sparse, which does not allow us to explore the characteristics of the subjects on trajectory 2; thus, further study and more abundant data are needed in this field.

Chapter 4 Summary

Our research demonstrated that mental health conditions are heterogeneous in young adults and the elderly population. We identified 4 psychological distress trajectory patterns in the young adults' age group (18-29 at baseline), and 2 Alzheimer's disease trajectories in the elderly population (60-75 at baseline).

For the young adult group, the 4 psychological distress trajectory patterns are the distress-free trajectory (26.2%), low-distress trajectory (48.3%), moderate-distress group (21.02%), and high-distress (4.47%) group. Our findings suggested that having a poor overall health condition, higher financial stress, lower-income, not married, as well as chronic conditions have an impact on people's psychological distress.

In the young adult group, compared with people without financial stress, people with financial stress had higher odds of being in the low -distress group, moderate-distress group, and high-distress group, relative to distress-free, with simultaneous adjustment for all other variables. The results also showed people with lower income had higher odds of experiencing psychological distress compared with people with higher income. In terms of the physical health aspect, having the chronic disease are associated with higher odds of being in the low-distress, moderate-distress, and high-distress, relative to distress-free after controlling for other variables. The overall health variables showed that the odds of having Low-Distress was higher for people who had decreasing overall wellbeing over time compared with stable high-quality overall wellbeing.

There are some differences regarding the impact of marital status on different trajectory groups. It is shown that for people who were never married relative to people who were married in the early 20s, the odds ratio for having high distress over distress-free is 3.97 (95%CI 2.136, 7.381), given all other predictors in the model are held constant. In other

words, people who were never married are more likely to have high distress. The interaction between smoking status and sex was statistically significant among the females who had a decreasing probability of being a smoker in the high-distress group.

For the elderly group, we identified two Alzheimer's disease trajectories, which are the Stable-Low group and the Low-Increase group. Our study showed that there are time-varying and time-invariant covariates affecting the observed Alzheimer's disease trajectory. Depression score and marital status posed a significant impact on Stable-Low Alzheimer's disease trajectory group, after controlling for social support, smoking habit, and levels of physical activity. In our study, gender, social support, smoking status, and physical activity were not significant factors in terms of deflecting the growth of trajectories in the Stable-Low group.

By adopting the LCGM method, we identified the heterogeneity in the psychological distress and Alzheimer's disease developmental trajectories. Moreover, the dataset we used is longitudinal data. Most covariates are time-varying, which can better capture the developmental changes in the risk factors compared with previous research. NPHS selected the representative population, which allows the results to be generalizable to young adults and the elderly population in Canada. The limitation of our study is that the questions in the NPHS survey were mainly self-reported; thus, the answer might be exaggerated or underestimated, and the participant's feelings influence the self-report response of the study at the time they filled out the survey questions. When analyzing the risk factors deflecting the Alzheimer's trajectory curves, we might ignore some other possible confounders, since Alzheimer's pathogenesis is not known yet, and it is a disease related to various potential risk factors; the sparse of data in Low-Increase AD group does not allow us to further explore the covariates associated with Low-Increase AD group. Further investigation and more rich data are needed to achieve this goal.

In summary, the main purpose of this study was to determine the different subgroups of individuals who followed similar mental health conditions during the 16-year follow-up and the characteristics of each trajectory group. Mental health trajectory analysis can show long-term age-related developmental changes in young people (baseline 18-29) and older population (baseline 60-75).

The results showed that the mental health status of the Canadian population is not homogeneous, and there exist different subgroups. Mental health trajectory group members are related to many variables, including gender, socioeconomic status, lifestyle, and physical condition. By analyzing the attributes of trajectories and development of trajectories, this research may help understand the psychological status of the Canadian population. Public health policymakers and mental health workers might gain inspiration from our study, and early intervention might be adopted to improve patients' health conditions.

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Appendix

Definition of the logistic function

Logistic regression is used to model data and to explain the association between one dependent binary variable , such as win/loss , and independent variables.

Logit (p)= log ($\frac{p(y=1)}{1-p(y=1)}$) = b_0+ b_1x_1+ b_2x_2

Where:
p(y=1) : probability of success

b_0 : y-intercept

b_1x_1: regression coefficient multiplied by some value of the predictor x_1.
b_2x_2: regression coefficient multiplied by some value of the predictor x_2

Definiton of the multinominal logistic regression

Multinomial logistic regression is a method that generalizes logistic regression to multiclass problems, which allows the dependent variable have more than two possible discrete outcomes. f(k ,i) predict the probability that observation *i* has outcome *k*.

$$f(k,i) = b_{0,k} + b_{1,k}x_{2,i} + \ldots\ldots + b_{m,k}x_{m,i}$$

where
$b_{m,k:}$ regression coefficient associated with the *m*th explanatory variable and the *k*th outcome.

for *K* possible outcomes, running *K*-1 independent binary logistic regression models, in which one outcome is chosen as a reference and then the other *K*-1 outcomes are separately regressed against the reference outcome.

$$\text{In}\ \frac{p(Yi=1)}{p(Yi=k)} = b_1 * x_i$$

$$\text{In}\ \frac{p(Yi=2)}{p(Yi=k)} = b_2 * x_i$$

.....

$$\text{In}\ \frac{p(Yi=k-1)}{p(Yi=k)} = b_{k-1} * x_i$$

After we exponentiate both sides, we get

$P(Y_i=1)= P(Y_i=k)\, e^{b_1 * x_i}$
$P(Y_i=2)= P(Y_i=k)\, e^{b_2 * x_i}$
……
$P(Y_i=k-1)= P(Y_i=k)\, e^{b_{k-1} * x_i}$

The summation of K possibilityies must equal to 1, we find

$P(Yi=k)=1-\sum_{k=1}^{k-1} p(Yi=k)$

$=1-\sum_{k=1}^{k-1} p(Yi=k) e^{b_k * x_i}$

Definition of Latent class growth model (LCGM)

LCGM is a semi-parametric statistical technique used to analyze the growth trajectory of variable of interest. It can identify the potential subgroups following similar trajectories within the large population.

$$f(y)=\sum_{k=1}^{k} p(c=k)p(Y=y|C=k)=\sum_{k=1}^{k} p_k f(y,\lambda_k)$$

where

$y= (y_1, y_2, y_3 \ldots y_t)$: longitudinal sequence of an individual's behavioral measurements over the T periods of measurement.

p_k : pk is the probability of belonging to class k with corresponding parameter(s) λ_k