THE ACUTE EFFECTS OF AMBIENT TEMPERATURE EXPOSURE ON MENTAL ILLNESS RELATED EMERGENCY ROOM VISITS IN THE CITY OF TORONTO.

by

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A thesis submitted to the Department of Community Health and Epidemiology.

In conformity with the requirements for

the degree of Masters of Science

Queen's University

Kingston, Ontario, Canada

(May 2013)

Abstract

Objectives: The purpose of this study was to assess the effects of extreme ambient temperature on hospital emergency room (ER) visits related to mental and behavior disorders in Toronto, Canada.

Methods: A time series study was conducted using health and climatic data from April 1st 2002 to March 31st 2010. Relative risks for increases in ER visits were estimated for specific mental and behavior disorders (MBD) after exposure to hot and cold temperatures while using 50th percentile of the mean temperature distribution as the reference. The non-linear nature of the exposure–outcome relationship was accounted for using a distributed lag non-linear model (DLNM). The effects of seasonality, humidity, day of the week and outdoor air pollutants (CO_2, O_3, $PM_{2.5}$, NO2, and SO_2) were also adjusted.

Results: We observed positive associations between elevated mean temperatures and hospital ER visits for MBD. For hot temperatures, significant increases in ER visits for MBD were observed after a mean temperature threshold of about 24°C. The association generally lasted about 3 to 4 lag days with the strongest effect occuring at lag 0 (RR = 1.06; 95% CI: 1.03 - 1.09). Similar trends and associations were observed for specific mental illnesses such as mood, neurotic, substance abuse, and schizophrenia related disorders. Cold temperature associations were only observed for schizophrenia.

Conclusions: Our findings suggest that extreme temperature poses a risk to the health and wellbeing for individuals with mental and behavior disorders. Patient management and education may need to be improved as extreme temperatures become more prevalent.

Co-Authorship

This research was conducted by Xiang Wang, under the supervision of Dr. Eric Lavigne and Dr. Hélène-Ouellette-Kuntz. The study protocol was developed by Xiang Wang with feedback from Dr. Lavigne and Dr. Ouellette-Kuntz. Data collection was developed and collected by Xiang Wang with the help of Dr. Lavigne. All data analyses were conducted by Xiang Wang with help from Dr. Lavigne. Dr. Bingchu Chen provided some proofreading assistance for the methods.

Acknowledgements

This work could not have been completed without the advice and support from: Eric Lavigne, Rose Dugandzic, Antonio Gasparrini, Hélène Ouellette-Kuntz, and Harriet Richardson. Also I would like to thank all my colleagues at the Public Health Agency of Canada/Environmental Issues Division and the Leslie Dan Faculty of Pharmacy University of Toronto for granting me a deferral to finish this work. I would also like to thank my two best friends Erin Liu and George Huang for their support and friendship. Finally, I would like to thank my parents for many years of nurture and love.

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Chapter 1

General Introduction

In this section, background information about the rates and burden of mental illness in Canada will be presented. A section will be devoted to describe the healthcare resource utilization of patients with mental illness and some barriers to access. Subsequently, the biological relationship between ambient temperature and health morbidities will be presented. Finally, the current research on the relationship between ambient temperature and mental illness will be summarized followed by a rationale for this study.

1.1 Epidemiology of Mental Illness in Canada

Mental illness is a health condition characterized by significant dysfunction in an individual's cognitions, emotions, or behaviors that reflects a disturbance in the psychological, biological, or developmental processes underlying mental functioning (Ang et al. 2004). Mental illnesses take on several forms such as mood disorders, schizophrenia, anxiety disorders, personality disorders, eating disorders, substance abuse, and gambling addictions. The burden of mental illness is significant. It affects individuals with various levels of education and income, from different cultures, with different occupations, of different ages, gender, and geographical locations.

According to the Report on Mental Illness in Canada (Health Canada, 2002), approximately one in five Canadian adults will have experienced a mental illness at some point during their lifetime and over 70% of all mental illness will occur during childhood or adolescence. The Human Face of Mental Health and Mental Illness in Canada (Public Health

Agency of Canada, 2006) reports that individuals 14 to 25 years of age are most likely to report a mental illness and Canadians with the lowest income will be three to four times more likely to experience a mental illness compared to individuals in the highest income group.

The most recent Canadian Mental Health and Wellbeing survey (CCHS1.2) (Public Health Agency of Canada, 2006) revealed that one out of every 10 Canadians aged 15 and over reports symptoms correlated with mood, anxiety, and substance dependence issues. Some of the most prevalent forms of mental illness among Canadians aged 15 and over are: mood disorders (~4.9%), anxiety disorders (~4.9%), schizophrenia (~1%), and substance abuse disorders (~3.6%). In addition, the Canadian Study of Health and Aging found that the rates of neuro-degenerative disease such as dementia among Canadian seniors aged 65 and over is ~ 8% and for individuals 85 and over, the rate is ~ 34.5%.

For the affected individual, mental illness can result in loss of productivity, limitation to career opportunities, loss of earning, and increased risk of suicide (Health Canada, 2002). In addition, recent research (Himelhoch et al. 2004, McIntyre et al. 2006) indicates that having a mental illness can increase the individual's risk of acquiring certain cardiovascular and respiratory conditions. For the affected family, the burden of mental illness can be significant as there are numerous difficulties they may face such as coping and making decisions regarding treatment, housing, and hospitalization (Pinquart and Sorensen 2007, Pinquart and Sorenson 2003). Primary and secondary caregivers, have an increased risk of psychological distress, loss of productivity, increased financial burden, impaired health habits, physical illness, mental illness such as depression, and in some extreme cases death (Vitaliano et al. 2003, Pinquart and Sorenson 2003, Schulz and Sherwood 2008).

1.2 Economic Burden of Mental Illness

In Canada, the economic burden of mental illness on society is considerable. Studies which consider only the direct medical cost of mental illness have reported estimates of ~ $5.7 billion annually on the health care system (Jacobs et al. 2008). Recent studies adopting a societal perspective (economic evaluations which considers both direct medical costs and loss of income to the individual) reported that the primary cost of mental illness stems from short term and long term loss of productivity in the workplace and losses in health related quality of life years (HRQOL) resulting in costs of $51 billion annually (Lim et al. 2008) to society.

1.3 Mental Health Service Utilization in Ontario

The Mental Health and Wellbeing survey (CCHS Cycle 1.2) reports that in Ontario, on average ~8.7% of the individuals (aged 15+) used a health care provider for reason of mental illness during a one year period. With respect to utilization by health care provider type, ~5.3% of individuals (aged 15+) visited general practitioners as their initial point of contact for reasons due to mental illness. 2.2% and 2.0% of individuals (aged 15+) with mental illness had a psychiatrist or a psychologist as their first point of contact. Finally, ~1.6% of the individuals (aged 15+) sought care from social workers as their initial point of contact for reasons related to mental illness. In addition, hospital emergency departments may represent the first point of contact for individuals with mental illness requiring immediate medical intervention. According to the report: *Exploring Hospital Mental Health Service Use in Ontario*, the rate of hospitalization related to mental illness in Ontario was 608 admissions per 100,000 (Canadian Institute of Health Information, 2008). Schizophrenia, mood disorders, anxiety disorders, and substance abuse issues accounted for over 85% of hospital admissions (Canadian Institute of Health Information, 2008).

1.4 Barriers to Mental Health Utilization in Ontario

Despite the broad spectrum of health care services offered to patients with mental illness, there are still significant barriers to mental health service utilization in Ontario. Currently, a number of attitudinal and structural barriers exist for access to mental health services. Sareen et al. (2007) conducted a survey among individuals with a diagnosed mental illness in Ontario to examine the perceived attitudinal and structural barriers for access to health care services. The study revealed that individuals with mental illness do not seek help from healthcare services due to: (1) a perception that the problem would resolve on its own (46%), (2) a desire to resolve the issue by themselves due to privacy concerns (15%), (3) a feeling that seeking help would not do any good (23%), (4) a fear of being hospitalized against their will (6%), (5) a concern for what others might think (15%), and (6) a lack of satisfaction with the available services (10%). In addition, Ontarians identified structural barriers to accessing mental health services, including the lack of insurance coverage for services not covered under OHIP (14%), the loss of productivity from too much time spent on treatment (19%), not being able to get an appointment (4%), and being unsure where to go to seek help (18%). Similar results have been reported by Mackenzie et al. (2006) who also conducted a survey among the general population regarding perceived barriers to care for patient with mental illness. There are also age and gender differences regarding mental health service utilization. Men are less likely compared to women to seek mental health services (Addis and Mahalik 2003) Also, some studies have indicated that older adults are more sensitive to the stigmatization associated with mental illness compared to the younger generation (Currin et al. 1998, Robb et al. 2003, Berger et al. 2008, Sirey et al. 2001).

1.5 Relationship between Ambient Temperature and Morbidity

The effect of ambient temperature on morbidity in recent years is arousing significant public health interest due to steady increases in global ambient temperature. Increases in daily ambient temperature are associated with increased daily morbidity based on hospital admission data (Ye et al. 2012, Schwartz et al. 2004, Michelozzi et al. 2009). Both extreme hot and cold temperatures can have adverse effects on human health. The effects of hot temperatures on morbidity are primarily found within a lag period of 0 to 5 days while the lag period for cold temperatures are generally longer, up to periods of two weeks (Gosling et al. 2008, Conti et al. 2005, Green et al. 2010). The increased risk of hospital admissions for cardiovascular, respiratory, and cerebrovascular outcomes with exposure to increased ambient temperature above a specific threshold has been demonstrated (Lin et al. 2009, Panagiotakos et al. 2004, Schwartz et al.2004, Michelozzi et al. 2009, Dawson et al. 2008, Wang et al. 2012). A recent systematic review and meta- analysis of 21 studies reported pooled effect estimates of 2.0% increase (95% confidence interval: 1.4% to 5.5%) in respiratory morbidity after 1 °C increase in temperature (Turner et al. 2012). Turner et al. (2012) also reported no effect of temperature on cardiovascular morbidities when all 21 studies were pooled.

1.6 Relationship between Ambient Temperature and Mental Illness: Biological Plausibility

Thermoregulation is the process where the body maintains its steady state temperature when a change in the external environment occurs. The main regulating center for human thermoregulation resides in the anterior hypothalamus and pre-optic region (Boulant 2000, Ishiwata et al. 2002, Hasegawa et al. 2005). The pathophysiologies of some mental illnesses (i.e., schizophrenia) have been shown to induce alterations in central dopamine neurotransmission which is associated with human thermoregulation through its interactions with the hypothalamic regions of the brain (Crandall et al. 2002, Kapur and Remington 1996, Shiloh et al. 2001, Lindvall et al. 1983). These alterations may lead to epigenetic changes such as imprinting, DNA methylation, and histone acetylation which are associated with thermo-regulatory dysfunction (Shiloh et al. 2001). These theories are supported by studies which report abnormal thermo-regulation (i.e., hyperthermia and hypothermia) in both drug free and medicated patients with mental illnesses (Chong and Castle 2004, Hermesh et al. 2000, Schwaninger et al. 1998). Although, some animal studies (Yuan et al. 2006, Wiste et al. 2008) have demonstrated the impaired dopaminergic transmission empirically, the plausible link between impaired dopaminergic transmission and impaired thermoregulation has not been conclusively proven. Also there is some literature suggesting possible exacerbation of the hazardous psychiatric effect by air pollution (Lundberg et al.1996); however, the link has only been theorized and not investigated empirically.

1.7 Purpose and Rationale

Given the public health importance of mental illness and climatic changes experienced around the globe, the thesis will seek to illustrate , at a population level, the relationship between ambient temperature and mental illness and how best to study this relationship. The thesis includes a systematic review of the literature linking ambient temperature to mental illness morbidity and mortality (Chapter 2 – Manuscript 1) and a study of the association between ambient temperature and daily mental illness related hospital emergency visits (Chapter 3 – Manuscript 2).

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Chapter 2

The Impact of Ambient Temperature on Mental Illness related Mortality and Morbidity: A Systematic Review.

2.1 Abstract

Objectives: The purpose of this study was to summarize the current literature between extreme ambient temperature exposure and mental illness morbidity and mortality.

Methods: A systematic review of the current literature was undertaken to identify relevant studies examining the effect of ambient temperature on mental illness or health related morbidity and mortality. Studies investigating the effects of ambient temperature on mental illness morbidity and mortality published up to August 12th 2012 were retrieved using the following electronic databases: PubMed MEDLINE, EMBASE, Web of Science, Scopus and PsycINFO.

Results: 15 studies examining the relationship between ambient temperature exposure and mental illness related morbidity and mortality were reviewed. All studies reported statisically significant increases in ER visits, hospital admissions, mortality, and ambulance call outs for individuals with mental illness during periods of elevated ambient temperature. Studies examining cold temperature associations were not found.

Conclusions: Our findings suggest that extreme temperature poses a risk to the health and wellbeing for individuals with mental and behaviour illnesses. Further research is needed which accounts for the lagged structure of these exposure–outcome relationships and adjustw for relevant confounders.

2.2 Introduction

The effect of ambient temperature on morbidity in recent years is arousing significant public health interest due to steady increases in global ambient temperature. Increases in daily ambient temperature have been shown to be associated with increased daily morbidity and mortality (Ye et al. 2011, Michelozzi et al. 2009). Both extreme hot and cold temperatures can have adverse effects on human health. The effects of hot temperatures on morbidity and mortality are primarily found within a lag period of 0 to 5 days while the lag period for cold temperatures are generally longer, up to periods of two weeks (Gosling et al. 2009, Conti et al. 2005). Current literature has demonstrated the increased risk of hospital admissions and mortality for cardiovascular, respiratory, and cerebrovascular outcomes with exposure to increased ambient temperature above a specific threshold (Lin et al. 2009, Schwartz 2004, Michelozzi et al. 2009, and Wang et al. 2012).

While the association between ambient temperature and cardiovascular and respiratory illnesses has been well investigated, there is limited evidence indicating that individuals with mental illness may be at significantly higher risk of hospital admission, emergency visits and mortality during periods of extreme high and low ambient temperature. In contrast with the general population, individuals with mental illness often experience poorer states of health (McMichael et al. 2006). It has also been well established that the use of psychotropic medication interferes with thermoregulation (Martin-Latry et al. 2007). Thus, individuals with mental illness are highly susceptible to the effects of extreme ambient temperature. Recently, there has been increasing interest in assessing the impact of ambient temperature on individuals with mental illness as significant fluctuations in ambient temperatures are becoming more prevalent.

However, to date, no review has specifically focused on the relationship between temperature and mental illness. Thus, we will try to fill this knowledge gap and illustrate the effects of ambient temperature on mental illness morbidity and mortality.

2.3 Methods

A systematic review of the current literature was undertaken to identify relevant studies examining the effect of ambient temperature on mental illness or health related morbidity and mortality. Studies investigating the effects of ambient temperature on mental illness morbidity and mortality published up to August 12th 2012 were retrieved using the following electronic databases: PubMed MEDLINE, EMBASE, Web of Science, Scopus and PsycINFO. Limitations were applied to include only peer-reviewed full English journal articles. The reference lists of identified papers were searched to make sure all relevant papers were captured.

Adults aged 18+ were the targeted population of this review. The primary search strategy used the following U.S. National Library of Medicine's Medical Subject Headings (MeSH Terms) and keywords: "Temperature", "Ambient Temperature", "Heat Waves", "Heat wave", "Mental Illness", "Mental Disorder", "Cold Weather", " Cold Temperature", "Cold Spells", "Psychiatric Illness", "Emergency Admissions", "Emergency Visits", "Hospital Admissions", "Hospitalization", "Mortality", and "Morbidity".

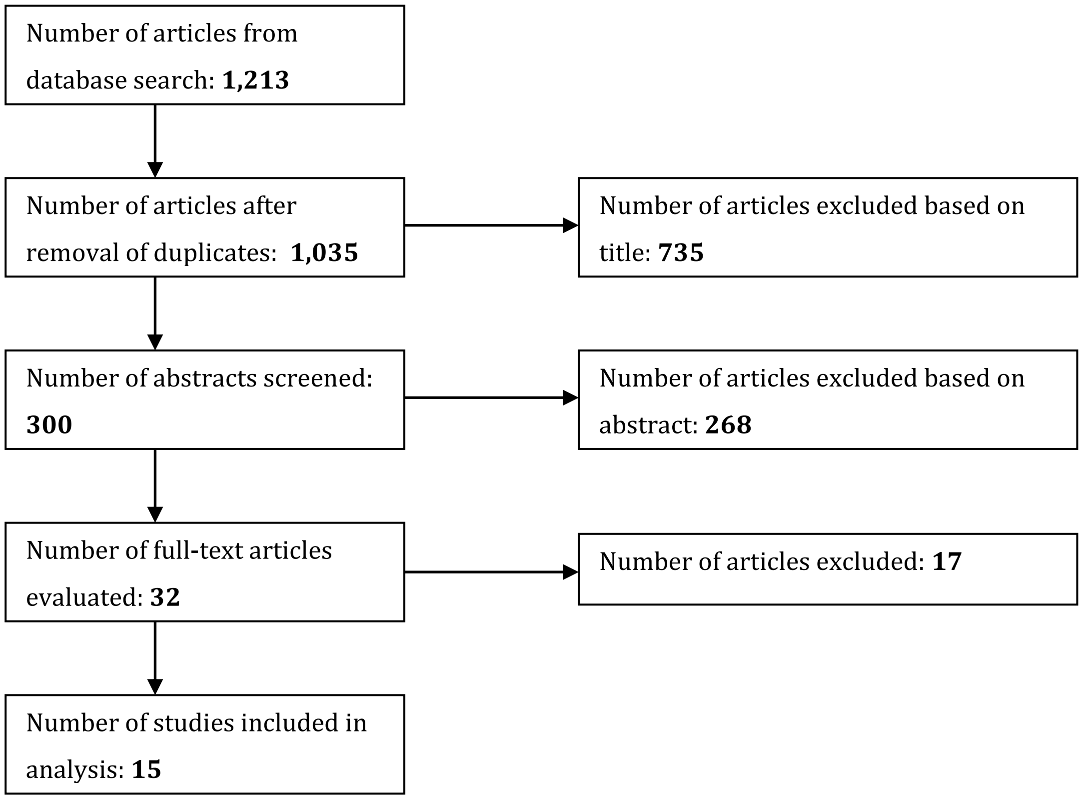
The title and abstract were initially used to exclude studies not related to the research question. The remaining results were merged into a refworks account and duplicates were removed. Full texts of the remaining studies were then reviewed against the inclusion criteria to determine eligibility.

Eligibility was determined based on the study design, the use of original data, the use of appropriate effect estimates, and the use of relevant exposure and outcomes. Study designs were required to be case control, time-series, or case crossover. Each study had to include the use and collection of original data and the presence of appropriate effect estimates (Odds Ratios, Relative Risk, Percent change in morbidity and mortality due to extreme temperature, and Incidence Rate Ratio). Furthermore, the main exposure of the study had to be an appropriate indicator /measure of ambient temperature. Finally, the outcome had to include measures of mental illness related morbidity (Hospital Admissions and/or Emergency Visits) and/or mortality.

2.4 Results

We identified 1324 papers in the literature search. Based on the inclusion criteria, 15 articles were included in the final review (Figure 2-1). All included studies examined elevated temperatures. Among the included studies, five examined the effects of temperature related mental illness mortality; five studies examined effects of temperature on mental illness related hospital admissions and emergency rooms visits, and five studies examined both temperature related mental illness mortality and morbidity.

Figure 2-1 Flowchart of Literature Search Results



2.4.1 Ambient Temperature and Mental Illness Related Morbidity

The studies examining ambient temperature and mental illness morbidity are listed in Tables 2-1 and 2-2. Nine studies examined the effects of ambient temperature on mental illness related morbidity. Morbidity was measure in terms of emergency department visits and/or hospital admissions.

Three studies used a case series study design and six used a time series design. Statistical analyses were conducted using GLM (General Linear Modeling), GEE (General Estimation Equations), or GAM (General Additive Models). In some studies, confounding variables were considered, such as various gaseous pollutants (NO_2, CO, O_3, and SO_2), particulate matter (PM_{10}, $PM_{2.5}$), humidity, and different seasons. However, adjustments for these variables were undertaken by a minority (2) of the studies.

The most commonly used metrics for ambient temperature were daily mean temperature and daily maximum temperature, although one study used apparent temperature. It is well known that the potential impacts of ambient temperature are often lagged over a period of several days for heat effects and up to periods of two weeks for cold effects (Ye et al. 2011). However, none of the studies considered the lagged effects of the ambient temperature.

Several methods were used to model the relationship between ambient temperature and mental illness/mental health-related morbidity. Nine studies examined heat effects using either a linear relationship or a linear relationship incorporating a particular threshold. For specific temperature thresholds, most studies used >35°C as extreme heat exposure. In the absence of specific thresholds for temperature, various percentiles were used to evaluate the effects of heat.

Generally, the studies found that exposure to extreme heat had significant effects on mental illness/mental health related morbidity in Australia, England, Taiwan, and the United States. All of the studies were conducted in high income countries.

In Chicago, Semenza et al. (1999) found that during periods of elevated temperatures, the number of hospital admissions for several neurological conditions such as Parkinson's disease and Alzheimer's disease significantly increased. In Adelaide, Australia, Nitschke et al. (2007) reported that during periods where the temperatures was > 35°C, mental illness related hospital admissions increasingly significantly by 7% across all ages. The greatest increase of 17% was seen in individuals 75+.

Khalaj et al. (2010) explored the effect of ambient temperature on emergency hospital admissions during periods of extreme heat in New South Wales, Australia, while adjusting for various air pollutants (NO_2, PM_{10}, and O_3). They reported that during periods of extreme temperature ($\geq 99^{th}$ percentile of max and min temp), emergency hospital admissions directly related to mental and behavior disorders (ICD 10 F00-F99) increased significantly by 4% at lag 0, and 7% using a three day average. In addition, they reported a 7 to 11% increase for emergency hospital admissions for heat related injuries among individuals with mental illness. This suggested that mental illness may act as a modifier of the association between extreme heat events and emergency hospital admissions. Similar results were reported by Williams et al. (2012a, 2012b).

In Adelaide, Australia, Hansen et al. (2008) explored the effects of heat waves on cause specific mental illness/disorders/health related hospital admissions during 1993-2006. They found that above thresholds of 26.7°C, a significant positive association existed between ambient temperature and hospital admissions for mental and behavior disorders (ICD10 F00-F99).

Specifically, hospital admissions significantly increased for organic and symptomatic mental disorders (F00-F09), dementia (F00-F03), mood (affective) disorders (F30-F39), neurotic stress related (F40-F48), somatoform (F60-F69), disorder of the psychological development (F80-F89); and senility (R54). There were no significant differences in hospital admission across strata by sex and by age.

Sung et al. (2011) evaluated the effects of ambient temperature on schizophrenia admissions and reported positive associations for temperatures in the 1st and 99th percentile. Nitschke et al. (2011) examined the pattern of several years of heat waves on ambulance call outs, hospital admissions and emergency room presentations. They found that in comparison with previous heat waves, the risk for ambulance call outs, hospital admissions, and emergency room admissions for individuals with mental illnesses/disorders have been consistently decreasing. Finally, Wang et al. (2012) found no significant association across all ages between ambient temperature and mental illness-related emergency room visits.

No studies investigating the effect of cold temperature on mental illness morbidity were identified in the review. Most studies evaluating the effects of ambient temperature on mental illness used a heat wave approach, only a few used daily temperatures as an exposure variable. Also the distributed lagged effects of ambient temperature on mental illness-related morbidity have not been investigated. In addition, none of the studies used a non-linear relationship to describe the potential association between ambient temperature and mental illness related morbidity. Finally, only 2 studies investigated the relationship between ambient temperature and specific mental and behavior disorders.

2.4.2 Ambient Temperature and Mental Illness Related Mortality

The studies examining ambient temperature and mental illness/disorder related mortality are listed in Tables 2-1 and 2-2. Associations between mental illness-related mortality and periods of elevated temperature were found in Chicago (US), New York (US), Cincinnati (US), Perth (AUS), Adelaide (AUS), New South Wales (AUS), Brisbane (AUS), and England.

Naughton et al. (2002) (OR 5.7 95%CI1.9-16.8) investigated the effect of heat waves on mental illness/disorder mortality in Chicago. They found that individuals with mental illness are significantly more likely to die from extreme heat exposure than individuals without. Similar results were reported for other US cities by Kaiser et al. (2001) and Semenza et al. (1999).

Nitschke et al. (2007), Hansen et al. (2008), Nitschke et al. (2011) and Wang et al. (2012) investigated the association between extreme temperature and mental illness mortality in Brisbane and Adelaide, Australia. Nitschke et al. (2007) reported no increased risk of mental illness-related mortality for all ages during periods where temperature exceeded 35°C for 3 or more consecutive days. Hansen et al. (2008) investigated the effects of heat wave on specific mental illness mortality above heat thresholds of 26.7°C. They reported significant increases in risk of mortality during heat waves for individuals with a diagnosis of mental illness (ICD 10 F00-F99) and ages 65-74 (IRR: 2.39 95%CI 1.16-4.92) . In addition, they found significant increases in risk of mortality for dementia (F00-F03), disorders due to psychoactive substance abuse (F10-F19), and schizophrenia, schizotypal, and delusional disorders (F20-F29). Wang et al. (2012) also reported an increased risk of mortality for individuals 75+ with mental health during period of heat waves. In addition, they explored the lagged effects of ambient temperature on mental illness mortality and reported that the greatest risk occurred with a lag of 1 and the risk decreased thereafter suggesting a possible harvesting effect. However, none of the findings were statistically significant.

Finally, Page et al. (2012) examined the effect of ambient on mortality among individuals with psychosis, dementia, and substance misuse. They reported that each 1°C increase above a heat threshold of 18°C is associated with significant increased risk of mortality for patients with psychosis, dementia, and substance abuse. In addition, risk did not increase with age; patients under the age of 65 had a greater risk than patients over 65.

No study has investigated the effect of cold temperature on mental illness related mortality and ambient temperature. Although mortality risk has been investigated in specific mental illnesses, the number of studies is relatively small and contains some of the methodological issues described above. Furthermore, only one study incorporated adjustments for potential air pollutant confounders or effect modifiers such as, CO_2, CO, $PM_{2.5}$, and NO_2.

Although one study incorporated a limited evaluation of the distributed lagged effect of ambient temperature on mental illness mortality, the lag period was extremely short (2 lags). It would be relevant to evaluate the effect for much wider range of lags. In addition, all of the studies assumed a linear relationship between ambient temperature metrics and mortality. Current studies have indicated the relationship between ambient temperature and adverse health outcomes to be S, J, or V shaped; thus, prompting the use of nonlinear methods such as spline functions to model this relationship (Ye et al. 2011). A methodology which allows for the adjustment of lagged and non-linear effects is the recently developed distributed non-linear modeling (DLNM) (Gasparrini et al. 2011).

2.5 Discussion

This review presents the main findings on the current relationship between temperature and mental illness related mortality and morbidity. The vulnerability of individuals with mental and behavior disorders to extreme temperature can be potentially explained by the following reasons:

(1) Psychiatric/Mental Illness: The pathophysiology of certain mental and behavior disorders can contribute to dysfunction of normal thermo-regulatory mechanism through interference of neurotransmitters involved in thermoregulatory pathways (i.e., schizophrenia spectrum disorder and delusional disorders)(Sung et al. 2011, Kapur et al. 1996, Hermesh et al. 2000). Also, certain pre-existing genetic factors for the development of specific mental and behavior disorders can induce thermoregulatory dysfunction resulting in hypothermia or hyperthermia after exposure to extreme temperature (Hasawaga et al. 2005). What occurs from here onwards is a bit unclear; there is literature to indicate that these changes can exacerbate the frequency and severity of the symptoms of the individuals while others indicate that these changes increase the individual's susceptibility to heat related illness such as a heat stroke. Thus, they may be admitted to the emergency room or hospital for treatment related to an exacerbation of their condition triggered by high temperature or heat related illnesses. In more severe cases, death may result.

(2) Medication/Substance Usage: The use of certain psychotropic medications (neuroleptics, anxiolytics, anti-depressants, and anti-cholinergic) are known to interfere with thermoregulation and increase susceptibility to temperature induced morbidity and mortality (Hansen et al. 2008, Martin-Latry et al. 2007, Hermesh et al. 2000). Also, the use of specific

psychoactive substances such as alcohol, hallucinogens (LSD), and stimulants (cocaine, methamphetamine) can induce hyperthermia increasing the risk of both temperature related morbidity and mortality (Marzuk et al. 1998, Romanovsky and Blatteis 1998, Crandall et al. 2002).

(3) Behavioral: In many cases, it is possible for individuals with mental and behavior disorders to be cognitively unaware of their condition and surroundings; thus, disregarding thirst sensations resulting in possible dehydration (Conti et al. 2007, Kaiser et al. 2001, Green et al. 2001). In some individuals with mental and behavior disorders, more than one of these factors may be responsible for the temperature-related morbidity and mortality.

To fully evaluate the studies linking temperature to mental and behavior disorders, several methodological issues should be considered: 1) exposure assessment, 2) outcome measures, and 3) use of statistical models.

2.5.1 Exposure Assessment

Ten studies used heat waves while others used a combination of mean, minimum, and maximum temperature for measurement of the exposure. Since heat waves are generally defined as greater than 35°C (Hansen et al. 2005), they are less informative measures of exposure as the effect of lower range temperatures and variations in temperature ranges are not well captured; this may introduce uncertainty in the results. The timing of the heat waves can also have an impact on effect estimates. For instance, the impact of heat waves on morbidity and mortality may be stronger earlier in the summer /spring season than heat waves later since the most vulnerable individuals will be affected by the first heat wave; thus, depleting the pool of susceptible individuals leaving a smaller pool of susceptible individuals (Basu and Samet 2002).

Also, individuals may have acclimatized to heat waves occurring late in summer due to behavior changes (staying indoors, use of air conditioning, drinking adequate fluids to stay hydrated, wearing appropriate clothing, etc.) (Goldberg et al. 2011). Thus, the timing of heat waves may explain some of the heterogeneity among results between heat wave studies.

For studies using temperature (Mean, Min, or Max) as their main exposure metric, several issues arise as well. For example, most of the studies used an ecological measure of temperature as a proxy for the entire geographical region of their study. This approach is made on the assumption that all individuals in the region will experience the same exposure. Thus, some degree of misclassification is inherent since temperature vulnerabilities do vary with geography and study temperature may not reflect the actual temperature experienced by the individual at that particular location (Goldberg et al. 2011). A disadvantage of this approach is that some regression dilution will likely occur resulting in an underestimation of the true exposure–outcome relationship (Gasparrini and Armstrong 2010). However, the magnitude of this underestimation will largely depend on the extent of correlation between the study temperature metric and the actual temperature experienced by the individual. Also, often one temperature indicator is used (Mean, or Max, or Min); however, the literature on which temperature metric is most suited for either morbidity and/or mortality investigations is limited. Thus, it may be more appropriate to include several temperature metrics and examine the robustness and sensitivity of each indicator to specific outcomes first before making a selection.

2.5.2 Outcome Measurements

Hospital admissions and emergency room (ER) visits are most often used as measures of morbidity. Some methodological issues to consider largely pertain to the capture of morbidity data. Usually, hospital admissions and ER visits for mental illness are included in the study. This approach may not be adequate in capturing individuals admitted for other illnesses triggered from both temperature and their mental illness. For example, an individual with dementia is exposed to extreme heat; however, due to the impaired cognitive awareness as a result of the dementia, he/she did not take the appropriate preventive measures (drinking water, removing excessive clothing, using air conditioning, staying indoors, etc.) to mitigate thermal stress, becomes dehydrated, and is admitted to the ER for treatment of dehydration. The ability of the currently used outcome measurements to capture these individual may not be ideal given that the clinical manifestations of temperature induced outcomes in patients with mental illness are difficult to predict and can often encompass a wide range of conditions. Thus, it may be helpful to include ER visits and hospital admissions where although the primary reason for the visit was not related to mental illness, the individual had an underlying mental illness condition. However, this method of outcome measurement for temperature induced morbidity may introduce additional difficulties in the study design and data collection process.

Some non-acute manifestations of temperature induced health issues experienced by individual with mental illness may not present to hospital or ER settings at all, but instead present at family physician offices or social services settings. Inherently, this will induce some level of underestimation and regression dilution. The exact impact of these issues on the effect estimate of the study will largely be disease specific. For the measurement of mortality, similar issues will arise as mental illnesses are not likely to be the immediate cause of death. For instance, an individual with mental illness susceptible to extreme temperature may die of a cardiovascular event, dehydration, or heat-stroke induced by exposure to temperature (Semenza et al. 1999).

2.5.3 Statistical Methods

Currently, only linear regression models are used to represent the relationship between ambient temperature and mental illness morbidity and mortality. Although such methods may be feasible, some limitations are inherent. The assumption of linearity usually requires the analysis to be partitioned into specific strata either based on month or season (Gasparrini et al. 2011). Thus, some flexibility to model heterogeneity of the exposure–outcome relationship across an entire timeframe of the study is lost. Hot and cold temperatures may need to be investigated by separate models in order to achieve reasonable model fit. Lastly, the ability to account for delayed/lagged effects of ambient temperature induced outcomes is important given the "harvesting "nature of these relationships.

2.6 Suggestions for Future Research

The relationship between ambient temperature and mental illness morbidity and mortality is an important public health issue. To date, numerous studies have demonstrated increases in both mental illness mortality and morbidity (hospital admissions and emergency room visits) during periods of elevated temperature. However, given the limited number of studies, knowledge gaps do exist.

First, no studies have investigated the effects of cold temperature on mental illness morbidity and mortality. Second, only a few studies have investigated the relationship between ambient temperature and specific mental diseases such as anxiety disorders, mood disorders, schizophrenia, and substance abuse related disorders. Third, previous studies have illustrated that the relationship between ambient temperature and health effects are best described by the J, V, or U shaped curve and that the impacts of ambient of temperature are often lagged over several days. No study has investigated the distributed lagged effects of temperature on mental illness related mortality and morbidity.

In addition, the effects of other covariates such as common air pollutants (CO_2, NO_2, O_3, CO, SO_2, $PM_{2.5}$, PM_{10}) on the relationship between ambient temperature and mental illness related mortality and morbidity are not well understood. Moreover, most of the studies have used heat waves as the temperature metric; thus, few studies have investigated these exposure-outcome relationships using a daily temperature measure (Mean, Min, or Max Temperature) as the exposure. Also, individual level information such as the use of air conditioning, the use of certain medications and substances which can increase vulnerability to temperature exposure, and other lifestyle factors are not accounted for; thus, the extent to which these influence the exposure-outcome relationship is not well known.

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2.8 Tables

Table 2-1 Descriptive Statistics of Included Studies

Author and Year of Publication	Location and Time Frame of Study	Study Objective of Interest	Study Design and Statistical Analysis	Study Population and Data Source	Exposure Variables	Outcomes Measurements	Variables Adjusted For	Lags(Days)
Semenza et al. 1996	Chicago, United States July 12-16, 1995	Determining risk factors for death due to heat	Case Control Matched Pair Analysis	Patients in all 47 non-VA (Veteran Administration) hospitals in Cook County Illinois during 1995 heat wave. Computerized Inpatient hospital discharge data for cook county obtained from Illinois Health Care Cost Containment Council (IHCCCC) Chicago weather data for O'Hare airport obtained from Midwestern Climate Center.	Heat Waves	Heat Related Mortality	Age, Race, Gender, Type of residence, Access to air condition Social Contacts, various comorbidities	None
Bark 1998	New York City United States 1950-1984	Examining mortality risk among psychiatric patients during periods of heat waves.	Time Series Relative Risk Calculation	Psychiatric Patients from ten state hospitals within 50 miles of New York City from 1950 to 1984.	Heat Wave Periods (>89 ° F) for a period of 3 days or more.	Mortality	Gender, Age	None

Semenza et al. 1999	Chicago, United States July 1995	Characterization of the population at risk for heat related morbidity.	Time Series	Eligible individuals were persons older than 24 who died from July 14 to 17 Data collected by Vital Statistics Division of Department of Public Health in Chicago.	Heat Waves	Hospital Admissions	Age, various comorbidities	None
Kaiser et al. 2001	Cincinnati, Ohio, United States July 21st to August 2nd 1999	Examining the heat related death of people with mental illness.	Case Control Study Matched Pair Analysis	All heat related death reported by Hamilton County Coroner Office in Cincinnati during heat emergency from July 21 to August 2	Heat index peaks (41.6°C & 46.1°C) Median Ambient Temperature	Mortality	Age, Sex, Race, Access to air conditioning, Outside Activity, Income, use of psychotropic medication, lived alone	None
Naughton et al. 2002	Chicago, United States July 29-August 1999	Determining risk factors for heat related death.	Case Control Study Matched Pair Analysis	Chicago residents who died in from July 26 to August 6, 1999 where heat was the primarily reason identified by Cook County Medical Examination's Office. Controls were matched to patients by neighbourhood and age (within 10 years)	Heat Wave Periods	Heat related death	Age, Gender, Race, Income, Living alone, access to air conditioning. Number of Social Contacts, Behaviour during heat wave (Extra bath/showers)	None

Nietschke et al. 2007	Adelaide, Australia. 1993-2006	To Investigate the association between morbidity, mortality and heat waves in Metropolitan Adelaide using ambulance, hospital admissions, and morality data.	Case Series Study Poisson Regression	Ambulance data from South Australian Ambulance Services from 1993 to 2006. Daily cases of hospital admission and mortality from 1993 to 2006 Daily Maximum temperatures were obtained from Bureau of Meteorology Kent Town Location.	Heave waves where maximum temperature was (>35 ° C) for 3 consecutive days.	Hospital Admissions (1993-2006) Mortality (1993-2004) Ambulance Transport (1993-2006) For Renal, Mental Illness, Cardiovascular Respiratory Conditions,	Age	None

Hansen et al. 2008	Adelaide, Australia 1993-2005	To identify mental, behavioral, and cognitive disorders that may be triggered or amplified during heat waves.	Time Series Poisson regression	Residents of Adelaide. Climatic data were obtained from Australian Bureau of Meteorology Kent Town Location. Morbidity data for Adelaide are were obtained from South Australian Department of Health. Principle hospital discharge using ISAAC (Integrated South Australian Activity Collection). Mortality data were obtained from July 1993 to December 2004 from the Australian Bureau of Statistics.	Daily Maximum Temperature	Hospital Admission and Mortalities for MBD ICD(F00F-99) Organic, including symptomatic, mental disorders(F00-F09) Dementia(F00-F09) Mental and Behavioural disorder due to psychoactive substance use (F10-F19),Schizophrenia (F20-F29),Mood(affective disorders) F30-F39,Disorders of Adult personality and behaviour(F60-F69) Mental retardation(F70-F79) Disorders of psychological development(F80-F89) (F90-F98) Behavioral and emotional disorders G30-G30.9 Alzheimer’s disease, G31.1 Senile degeneration of brain, R54 senility	Age and Gender	None

Khalaj et al. 2010	New South Wales, Australia 1998-2006	To determine and characterize health impacts or extreme heat events on population in five regions of New South Wales.	Case Only Design Logistic regression	Residents of New South West, Australia. Daily Hospital Admission data from 1998 to 2006 taken from New South West Health Climatic Data from New South West Bureau of Meteorology. Air Pollution data taken from NSW department of Environment, Climate Change and Water.	Heat defined by Distribution of Daily Minimum Temperature & Daily Maximum Temperature (Both >99th Percentile)	Hospital Admissions (1993-2006) Mortalities (1993-2004)	Adjustments of relevant air pollution variables (NO_2, PM_{10}, and O_3) Using daily mean levels.	Lag0 Lag1 3 day moving average
Nietschke et al. 2011	Adelaide, Australia. 1993-2007	Comparison of the health impacts of tow unprecedented heat waves and investigating the association between health impacts and during & intensity of Adelaide heat waves.	Case Series Poisson Regression	Ambulance call outs and Hospital Admission were taken from July 1993 to March 2009. Mortality data were available up until 2007.	Heave waves where maximum temperature was (>35 ° C) for 3 consecutive days Or more.	Emergency Hospital Admissions	Age Group	None

Sung et al. 2011	Taiwan, Republic of China 1996-2007	Investigating the risk of diurnal temperature range contributes to the risk of hospital admission in individual with schizophrenia.	Time Series GLM	Patient data were taken from Psychiatric Inpatient Medical Claim from the National Health Insurance Research Database from 1996 to 2007. Climatic data were taken from Central Weather Bureau of Taiwan.	Mean Diurnal Temperature	Hospital Admissions for Schizophrenia (ICD-9 295.0- 295.6 and 295.8-295.9) Schizoaffective (ICD-9 295.7)	Age Groups, Gender, Geographical Region	None

Williams et al. 2012 (a)	Perth, Australia 2003-2009	Examining the heat thresholds and temperature relationships for mortality and morbidity outcomes in Adelaide.	Time Series Generalised Estimating Equations (GEEs)	Residents of Adelaide. Daily Mortality, Hospital admissions, and emergency department visits from July 2003 to March 2009 were acquired from South Australian Department of Health. Ambulance call outs for the same period were obtained from South Australian Ambulance Service. Climate Data were taken from the Australian Bureau of Meteorology.	Heat threshold based on minimum and maximum temperature	Hospital Admission and Emergency Room Admissions for Renal, Mental, Cardiovascular, Ischaemic, respiratory, and directed heat related category comprising dehydration, heat and sunstroke and exposure to excessive heat.	Adjustments were made for $PM_{2.5}$, O_3, and NO_2.	None

Williams et al. 2012(b)	Adelaide South Australia 1983-2009	Examining the relationships between high temperatures and adverse health outcomes for the population of Perth and identify specific health outcomes that are sensitive to extreme heat.	Time Series Generalized Estimation Equations (GEEs)	Residents of Perth. Daily all-cause Mortality (January 1983 – November 2006), hospital admissions (January 1980 – July 2008), emergency presentation (January 2002 – April 2009). All data were obtained from Government of Western Australia. Daily Weather variables were taken by the Australian Bureau of Meteorology. Air Pollutant data were taken from Department of Environment and Conservation.	Maximum and Minimum Daily Temperature	Daily Mortality, Hospital Admission , and Emergency Room Admissions for Renal, Mental, Cardiovascular, Ischaemic, respiratory, and directed heat related category comprising dehydration, heat and sunstroke and exposure to excessive heat.	Age, PM_{10} and Ozone	None

Wang et al. 2012	Brisbane, Australia 1996-2005	Assessing the impact of heat waves on mortality and emergency hospital admission and from non-external causes.	Time Series Case Crossover	Residents of Brisbane. Data from 1996 to 2005. Daily Climate data were taken from five monitoring station in Brisbane from the Australian Bureau of Meteorology Air Pollution data was provided by the Queensland Department of Environment and Resource Management. Mortality data was provided by the Office of Economic and Statistical Research of the Queensland Treasury. Daily data on Emergency Hospital Admissions were provided by the Health Information Centre of Queensland Health.	Heat Waves defined as daily maximum temperature (≥37°C) for 2 consecutive days or more.	Mortality and Emergency Hospital Admissions for Renal, Mental, Respiratory, Ischaemic stroke, Diabetes, and Cardiovascular conditions.	Humidity, PM_{10}, NO_2, O_3, Age	Lag1 Lag2 Lag0-2

Page et al. 2012	UK 1998-2007	To determine the risk of mortality in individuals with psychosis, dementia, and substance misuse during periods of hot weather.	Time Series Poisson Regression	Individuals with primary diagnosis of psychosis, dementia, and alcohol misuse & and other substance abuse who had died between January 1998 and December 2007. Daily Temperature data for 1998-2007 were taken from the British Atmospheric Data Centre. Patient data were taken were taken using the UK General Practice Research Database (GPRD).	Daily Mean Temperature	Heat related mortality among individuals with psychosis, dementia, and substance misuse.	Geographical Region, age, use of antipsychotics, antidepressants, hypnotics, anxiolytics,	None

Table 2-2 Effect Estimates of Included Studies

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
Semenza et al. 1996	Heat Waves	3.5 (1.7-7.3)	Odds ratio during Heat waves for individuals with Mental Problem
Bark 1998	Heat Wave Periods (>89°F) for a period of 3 days or more.	1.36	Risk of Death for Psychiatric Patient during heat waves from 1950-1984
		1.36	Risk of Death for Psychiatric Patient during heat waves from 1950-1954
		1.29	Risk of Death for Psychiatric Patient during heat waves from 1955-1964
		1.52	Risk of Death for Psychiatric Patient during heat waves from 1965-1974
		1.74	Risk of Death for Psychiatric Patient during heat waves from 1975-1979
		1.19	Risk of Death for Psychiatric Patient during heat waves from 1980-1984
Semenza et al . 1999	Heat Waves	20% increase P value = 0.027	Percent Increase in hospital admission for individuals with Nervous system disorders
		50% increase P value = 0.001	Percent Increase in hospital admission for individuals with Degenerative Diseases
Kaiser et al. 2001	Heat index peaks(41.6°C & 46.1°C) Median Ambient Temperature	14.0 (1.8-633)	Odds ratio for risk of heat related death for individuals with mental illness
Naughton et al. 2002	Heat Wave Periods	5.7 (1.9-16.8)	Odds ratio for risk of death during heat waves for individuals with Psychiatric illness
		4.1 (1.3-12.5)	Odds ratio for risk of death during heat waves for individuals with Depressions
		11.7 (1.5-92.2)	Odds ratio for risk of death during heat waves for individuals with Other Mental Illness
Nietschke et al. 2007	Heave waves where maximum temperature was (>35 ° C) for 3 consecutive days.	1.07 (1.01-1.13)	Incidence Rate Ratio(IRR), Hospital Admission during Heat Waves, Mental Illness(ICD 10 F00-F99)
		1.52 (0.99-2.32)	IRR, hospital admissions during heat waves, all gender, age 0-4, Mental Illness(ICD 10 F00-F99)
		1.09 (0.85-1.39)	IRR, hospital admissions during heat waves, all gender, age 5-14, Mental Illness(ICD 10 F00-F99)
		1.05 (0.99-1.11)	IRR, hospital admissions during heat waves, all gender, age 15-64, Mental Illness(ICD 10 F00-F99)
		1.12 (1.00-1.26)	IRR, hospital admissions during heat waves, all gender, age 65-74, Mental Illness(ICD 10 F00-F99)
		1.17 (1.07-1.28)	IRR, hospital admissions during heat waves, all gender, age 75+, Mental Illness(ICD 10 F00-F99)
		1.01 (0.73-1.47)	IRR, mortality during heat waves, all gender, all ages, Mental Illness(ICD 10 F00-

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
			F99)
		1.24 (0.53-2.91)	IRR, mortality during heat waves, all gender, 15-64, Mental Illness(ICD 10 F00-F99)
		2.58 (0.96-6.93)	IRR, mortality during heat waves, all gender, 65-74, Mental Illness(ICD 10 F00-F99)
		0.87 (0.64-1.18)	IRR, mortality during heat waves, all gender, 75+, Mental Illness(ICD 10 F00-F99)
Hansen et al. 2008	Daily Maximum Temperature	1.073 (1.017–1.132)	IRR, hospital admission associated with heat waves, MBD(ICD F00-F99)
		1.213 (1.091–1.349)	IRR, hospital admission associated with heat waves, Organic, symptomatic, mental disorders(F00-F09)
		1.174 (1.017-1.355)	IRR, hospital admission associated with heat waves, Dementia (F00-F03)
		1.005 (0.913-1.105)	IRR, hospital admission associated with heat waves, MBD due to substance abuse (F10-F19)
		1.034 (0.969-1.102)	IRR, hospital admission associated with heat waves, Schizophrenia (F20-F29)
		1.091 (1.004-11.85)	IRR, hospital admission associated with heat waves, Mood Disorders (F30-F39)
		1.097 (1.018-1.181)	IRR, hospital admission associated with heat waves, Neurotic, stress, somatoform disorders (F40-F48)
		0.875 (0.678-1.130)	IRR, hospital admission associated with heat waves, Behaviour syndrome associated with physiological factors (F50-F59)
		1.049 (0.905-1.214	IRR, hospital admission associated with heat waves, Disorders of personality and behaviour (F60-F69)
		0.737 (0268-2.026)	IRR, hospital admission associated with heat waves, Mental Retardation (F70-F79)
		1.641 (1.086-2.480)	IRR, hospital admission associated with heat waves, Disorders of psychological development (F80-F89)
		0.578 (0.349-0.955)	IRR, hospital admission associated with heat waves, Childhood Emotional and Behaviour disorders (F90-F98)
		1.154 (0.894-1.489)	IRR, hospital admission associated with heat waves, Alzheimer’s disease(G30-G30.9)
		7.727 (0.701-85.217)	IRR, hospital admission associated with heat waves, Senile degeneration of the Brain (G31.1)
		2.366 (1.200-4.667)	IRR, hospital admission associated with heat waves, Senility (R54)
		2.395 (1.165-4.922)	IRR, mortality associated with heat waves, age 65-74 years, MBD(F00-F99)
		5.058 (1.205-21.232)	IRR, mortality associated with heat waves, age 15-64, Dementia (F00-F03)
		12.731 (2.064-78.516)	IRR, mortality associated with heat waves, males, 15-64 years, Dementia(F00-F03)
		3.098 (1.342-7.155)	IRR, mortality associated with heat waves, Females, all ages, Disorders due to substance abuse (F10-F19)
		3.211 (1.297-7.9848)	IRR, mortality associated with heat waves, Females, age 15-64 years, Disorders due

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
			to substance abuse (F10-F19)
		2.079 (1.045-4.138)	IRR, mortality associated with heat waves, All ages, Schizophrenia, Schizotypal, and delusional disorders (F20-F29)
		2.111 (1.018-4.380)	IRR, mortality associated with heat waves, 75+, Schizophrenia, Schizotypal, and delusional disorders (F20-F29)
		4.051 (1.386-11.840)	IRR, mortality associated with heat waves, male, all ages Schizophrenia, Schizotypal, and delusional disorders (F20-F29)
		5.255 (1.752-15.758)	IRR, mortality associated with heat waves, male, 75+, Schizophrenia, Schizotypal, and delusional disorders (F20-F29)
Khalaj et al. 2010	Heat defined by Distribution of Daily Minimum Temperature & Daily Maximum Temperature (Both >99th Percentile)	1.04 (0.99 -1.10)	Relative Odds, emergency hospital admission during heat waves vs. other condition, MBD(F00-F99), lag 0
		1.01 (0.96 -1.07)	Relative Odds, emergency hospital admission during heat waves vs. other condition, MBD(F00-F99), lag 1
		1.07 (1.00 -1.15)	Relative Odds, emergency hospital admission during heat waves vs. other condition, MBD(F00-F99), 3 day average
		1.07 (1.03-1.11)	Relative Odds, emergency hospital admission during heat waves vs. no condition , MBD(F00-F99), lag 0
		1.05 (1.01-1.09)	Relative Odds, emergency hospital admission during heat waves vs. no condition , MBD(F00-F99), lag 1
		1.11 (1.06-1.17)	Relative Odds, emergency hospital admission during heat waves vs. no condition , MBD(F00-F99), 3 day average
Nietschke et al. 2011	Heave waves where maximum temperature was (>35 ° C) for 3 consecutive days or more.	1.05 (1.00 -1.10)	IRR, daily hospital admission for Mental health during heat wave, All ages, Heat wave pre 2008
		1.48 (0.99 -2.21)	IRR, daily hospital admission for Mental health during heat wave, 0-4, Heat wave pre 2008
		1.03 (0.81- 1.32)	IRR, daily hospital admission for Mental health during heat wave, 5-14, Heat wave pre 2008
		1.04 (0.99 -1.09)	IRR, daily hospital admission for Mental health during heat wave, 15-64, Heat wave pre 2008
		1.12 (1.01-1.24)	IRR, daily hospital admission for Mental health during heat wave, 65-74, Heat wave pre 2008
		1.10 (1.01-1.19)	IRR, daily hospital admission for Mental health during heat wave, 75+, Heat wave pre 2008
		0.98 (0.84-1.14)	IRR, daily hospital admission for Mental health during heat wave, All ages, Heat wave 2008
		1.64 (0.70-3.87)	IRR, daily hospital admission for Mental health during heat wave, 5-14, Heat wave

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
			2008
		0.97 (0.83-1.12)	IRR, daily hospital admission for Mental health during heat wave, 15-64, Heat wave 2008
		0.87 (0.62-1.22)	IRR, daily hospital admission for Mental health during heat wave, 65-74, Heat wave 2008
		1.10 (0.85-1.41)	IRR, daily hospital admission for Mental health during heat wave, 75+, Heat wave 2008
		1.03 (0.88-1.20)	IRR, daily hospital admission for Mental health during heat wave, All ages, Heat wave 2009
		0.84 (0.34-2.09)	IRR, daily hospital admission for Mental health during heat wave, 5-14, Heat wave 2009
		1.03 (0.89-1.21)	IRR, daily hospital admission for Mental health during heat wave, 15-64, Heat wave 2009
		1.03 (0.74-1.42)	IRR, daily hospital admission for Mental health during heat wave, 65-74, Heat wave 2009
		1.05 (0.8-1.36))	IRR, daily hospital admission for Mental health during heat wave, 75+, Heat wave 2009
		1.11 (1.04-1.18)	IRR, daily emergency room admissions for Mental health during heat wave, All ages, Heat wave Pre 2008
		1.98 (0.78-4.99)	IRR, daily emergency room admissions for Mental health during heat wave, 0-4, Heat wave Pre 2008
		0.68 (0.41-1.14)	IRR, daily emergency room admissions for Mental health during heat wave, 5-14, Heat wave Pre 2008
		1.09 (1.02-1.17)	IRR, daily emergency room admissions for Mental health during heat wave, 15-64, Heat wave Pre 2008
		1.59 (1.22-2.08)	IRR, daily emergency room admissions for Mental health during heat wave, 65-74, Heat wave Pre 2008
		1.15 (0.93-1.43)	IRR, daily emergency room admissions for Mental health during heat wave, 75+, Heat wave Pre 2008
		1.05 (0.96-1.14)	IRR, daily emergency room admissions for Mental health during heat wave, All ages, Heat wave 2008
		0.56 (0.08-4.18)	IRR, daily emergency room admissions for Mental health during heat wave, 0-4, Heat wave 2008
		0.96 (0.53-1.73)	IRR, daily emergency room admissions for Mental health during heat wave, 5-14, Heat wave 2008
		1.04 (0.95-1.13)	IRR, daily emergency room admissions for Mental health during heat wave, 15-64,

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
			Heat wave 2008
		1.24 (0.85-1.82)	IRR, daily emergency room admissions for Mental health during heat wave, 65-74, Heat wave 2008
		1.15 (0.78 1.51)	IRR, daily emergency room admissions for Mental health during heat wave, 75, Heat wave 2008
		1.04 (0.95-1.13)	IRR, daily emergency room admissions for Mental health during heat wave, All ages, Heat wave 2009
		0.62 (0.83-4.60)	IRR, daily emergency room admissions for Mental health during heat wave, 0-4, Heat wave 2009
		0.96 (0.58-1.59)	IRR, daily emergency room admissions for Mental health during heat wave, 5-14, Heat wave 2009
		1.05 (0.96-1.10)	IRR, daily emergency room admissions for Mental health during heat wave, 15-64, Heat wave 2009
		0.66 (0.40-1.09)	IRR, daily emergency room admissions for Mental health during heat wave, 65-74, Heat wave 2009
		1.18 (0.85-1.64)	IRR, daily emergency room admissions for Mental health during heat wave, 75, Heat wave 2009
Sung et al. 2011	Mean Diurnal Temperature	1.22 (1.08-1.37)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 99th percentile of range
		1.16 (1.05-1.28)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 95-98th percentile of range
		1.17 (1.07-1.29)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 90-94th percentile of range
		1.13 (1.03-1.23)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 75-89th percentile of range
		1.13 (1.04-1.24)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 50-74th percentile of range
		1.15 (1.05-1.26)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 25-49th percentile of range
		1.10 (1.01-1.20)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 10-24th percentile of range
		1.02 (0.93-1.12)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 5-9th percentile of range
		1.01 (0.92-1.11)	Mean daily range of temperature and Relative risk of Schizophrenia Admissions, 1st percentile of range

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
Williams et al. 2012(a)	Heat threshold based on minimum and maximum temperature	1.027 (0.987-1.068)	IRR for daily Mental Health Emergency Room Visits per 10°C increase in Max Temp, Adjusted for O_3, NO_2, $PM_{2.5}$
		1.051 (1.027-1.074)	IRR for daily Mental Health Emergency Room Visits per 10°C increase in Min Temp, Adjusted for O_3, NO_2, $PM_{2.5}$
		1.030 (0.989-1.071)	IRR for daily Mental Health Emergency Room Visits during heat waves, Adjusted for O_3, NO_2, $PM_{2.5}$
Williams et al. 2012(b)	Maximum and Minimum Daily Temperature	1.154 (0.970-1.373)	IRR for daily Mental Health Emergency Room Visits per 10°C increase in Max Temp, Adjusted for O_3, PM_{10}, Age 65+
		1.079 (1.027-1.133)	IRR for daily Mental Health Emergency Room Visits per 10°C increase in Min Temp, Adjusted for O_3, PM_{10}, All ages
		1.143 (1.016-1.285)	IRR for daily Mental Health Emergency Room Visits per 10°C increase in Min Temp, Adjusted for O_3, PM_{10}, Age 65+
		1.001 (0.993-1.010)	IRR for daily Mental Health Emergency Room Visits per 1°C increase during elevated periods, Adjusted for O_3, PM_{10}, All ages
		1.006 (0.978-1.034)	IRR for daily Mental Health Emergency Room Visits per 1°C increase during extreme periods, Adjusted for O_3, PM_{10}, All ages
Wang et al. 2012	Heat Waves defined as daily maximum temperature (≥37°C) for 2 consecutive days or more.	0.88 (0.71-1.11)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 15-64, Adjusted for O_3
		0.88 (0.70-1.10)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 15-64, Adjusted for PM_{10}
		0.90 (0.72-1.12)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 15-64, Adjusted for NO_2
		0.88 (0.71-1.11)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 15-64, Adjusted for O_3, PM_{10}, NO_2
		1.50 (0.45-4.99)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 65-74, Adjusted for O_3
		1.53 (0.46-5.08)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 65-74, Adjusted for PM_{10}
		1.52 (0.46-5.05)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 65-74, Adjusted for NO_2
		1.49 (0.45-4.98)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 65-74, Adjusted for O_3, PM_{10}, NO_2
		0.60 (0.20-1.75)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 75+, Adjusted for O_3
		0.59 (0.20-1.74)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 75+, Adjusted for PM_{10}

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
		0.60 (0.20-1.75)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 75+, Adjusted for NO_2
		0.59 (0.20-1.73)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Aged 75+, Adjusted for O_3, PM_{10}, NO_2
		0.87 (0.70-1.08)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Total, Adjusted for O_3
		0.86 (0.70-1.07)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Total, Adjusted for PM_{10}
		0.88 (0.71-1.09)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Total, Adjusted for NO_2
		0.86 (0.70-1.07)	OR of Mental Health Emergency Hospital Admissions during Heat waves, Total, Adjusted for O_3, PM_{10}, NO_2
		1.05 (0.27-4.10)	OR of Mental Health Mortality during Heat waves, Age 75+, Adjusted for O_3
		1.33 (0.34-5.16)	OR of Mental Health Mortality during Heat waves, Age 75+, Adjusted for PM_{10}
		1.21 (0.31-4.72)	OR of Mental Health Mortality during Heat waves, Age 75+, Adjusted for NO_2
		1.08 (0.27-4.23)	OR of Mental Health Mortality during Heat waves, Age 75+, Adjusted for O_3, PM10, NO2
		0.80 (0.21-2.98)	OR of Mental Health Mortality during Heat waves, All ages Adjusted for O_3
		1.04 (0.28-3.86)	OR of Mental Health Mortality during Heat waves, All ages Adjusted for PM_{10}
		0.92 (0.25-3.42)	OR of Mental Health Mortality during Heat waves, All ages, Adjusted for NO_2
		0.82 (0.22-3.06)	OR of Mental Health Mortality during Heat waves, All ages Adjusted for O_3, PM_{10}, NO_2
		1.16 (0.30-4.40)	OR of Mental Health Mortality during Heat waves, Adjusted for O_2,PM_{10},NO_2, Lag 1
		1.13 (0.30-4.28)	OR of Mental Health Mortality during Heat waves, Adjusted for O_2,PM_{10},NO_2, Lag 2
		0.92 (0.24-3.42)	OR of Mental Health Mortality during Heat waves, Adjusted for O_2,PM_{10},NO_2, Lag 0-2
		0.85 (0.69-1.06)	OR of Mental Health Related Emergency Visits, Adjusted for O_2,PM_{10},NO_2, Lag 1
		0.86 (0.70-1.07)	OR of Mental Health Related Emergency Visits, Adjusted for O_2,PM_{10},NO_2, Lag 2
		0.87 (0.70-1.08)	OR of Mental Health Related Emergency Visits, Adjusted for O_2,PM_{10},NO_2, Lag 0-2

Authors and Year of Publication	Temperature Variable and Range	Effect Estimate	Outcome(Subgroups)
Page et al. 2012	Daily Mean Temperature	1.10 (1.05-1.16)	RR of Mortality and Temperature for Psychiatric Patients Per 1°C increase in Temp above 93rd Percentile , Age<65
		1.01 (1.01-1.07)	RR of Mortality and Temperature for Psychiatric Patients Per 1°C increase in Temp above 93rd Percentile , Age65+
		1.03 (1.00-1.07)	RR of Mortality and Temperature for Dementia Per 1°C increase in Temp above 93rd Percentile
		1.02 (0.95-1.09)	RR of Mortality and Temperature for Psychoses Per 1°C increase in Temp above 93rd Percentile
		1.08 (1.04-1.13)	RR of Mortality and Temperature for Alcohol Misuse Per 1°C increase in Temp above 93rd Percentile
		1.20 (1.08-1.35)	RR of Mortality and Temperature for Other substance abuse Per 1°C increase in Temp above 93rd Percentile
		1.04 (1.00-1.08)	RR of Mortality and Temperature for All Psychiatric Patients Per 1°C increase in Temp above 93rd Percentile
		1.07 (1.01-1.13)	RR of Mortality and Temperature for Antipsychotics Per 1°C increase in Temp above 93rd Percentile
		1.02 (0.96-1.09)	RR of Mortality and Temperature for Anti-depressants Per 1°C increase in Temp above 93rd Percentile
		1.08 (1.02-1.15)	RR of Mortality and Temperature for Hypnotics/Anxiolytics Per 1°C increase in Temp above 93rd Percentile
		1.11 (1.02-1.20)	RR of Mortality and Temperature for Hypnotics/Anxiolytics excluding alcohol or drug misuse Per 1°C increase in Temp above 93rd Percentile

Chapter 3

Acute Impacts of Extreme Temperature Exposure on Emergency Room Visits Related to Mental and Behavior Disorders in the City of Toronto, Canada.

3.1 Abstract

Objectives: The purpose of this study was to assess the effects of extreme ambient temperature on hospital emergency room (ER) visits related to mental and behavior disorders in Toronto, Canada.

Methods: A time series study was conducted using health and climatic data from April 1st 2002 to March 31st 2010. Relative risks for increases in ER visits were estimated for specific mental and behavior disorders (MBD) after exposure to hot and cold temperatures while using 50th percentile of the mean temperature distribution as the reference. The non-linear nature of the exposure–outcome relationship was accounted for using a distributed lag non-linear model (DLNM). The effects of seasonality, humidity, day of the week and outdoor air pollutants (CO_2, O_3, $PM_{2.5}$, NO2, and SO_2) were also adjusted.

Results: We observed positive associations between elevated mean temperatures and hospital ER visits for MBD. For hot temperatures, significant increases in ER visits for MBD were observed after a mean temperature threshold of about 24°C. The association generally lasted about 3 to 4 lag days with the strongest effect occuring at lag 0 (RR = 1.06; 95% CI: 1.03 - 1.09). Similar trends and associations were observed for specific mental illnesses such as mood, neurotic, substance abuse, and schizophrenia related disorders. Cold temperature associations were only observed for schizophrenia.

Conclusions: Our findings suggest that extreme temperature poses a risk to the health and wellbeing for individuals with mental and behavior disorders. Patient management and education may need to be improved as extreme temperatures become more prevalent.

3.2 Introduction

Ambient temperature has long been suspected to play a role in the psychotic exacerbation of core symptoms for many specific mental and behavior disorders (McMichael et al. 2006). Individuals with mental illness are often susceptible to the effects of extreme temperature due the disruption of normal thermoregulation from psychotropic medication usage, psychiatric illness, and various behavior symptoms (Hansen et al. 2008; Shiloh et al. 2005). Several studies have demonstrated increases in hospital admissions and emergency rooms (ER) visits during periods of elevated temperature for individuals with mental illness in Australia (Nitschke et al. 2007, Nitschke et al. 2011, Williams et al. 2012(a), Williams et al. 2012(b), Wang et al. 2012, Khalaj et al. 2010), United States (Semenza et al. 1999, Semenza et al. 1996, Kaiser et al. 2001), Taiwan (Sung et al. 2011), England and Wales (Page et al. 2012). However, the distribution of these increases in morbidity with respect to specific mental illnesses (mood disorders, schizophrenia, substance abuse, etc.) is not well known. In addition, given that the effect of ambient temperature on human health is distributed over a period of several days to over one week (Ye et al. 2011), the lagged structure of the effects of ambient temperature on mental and behavior disorders remains unknown.

The aim of our study was to investigate the relationship between ambient temperature and mental illness related emergency room admissions in the City of Toronto. Toronto is located in the southern part of the province of Ontario; it is the largest city in Canada and the provincial capital of Ontario with approximately 2.7 million residents (Statistics Canada 2011). The city experiences a wide range of hot and cold temperatures throughout the year with daily mean temperatures ranging from -20.3 to 31.3°C (Environment Canada). How extreme temperature (Hot and Cold) can exacerbate specific mental illnesses in Toronto and the lagged effects of such associations are of interest.

3.3 Methods

3.3.1 Study Population and Morbidity Data

The study population included the residents of Toronto from April 1st 2002 to March 31st 2010. The study population was identified using relevant postal codes from a provincial computerized database for tracking emergency room admissions: the National Ambulatory Care Reporting System (NACRS). Access to the morbidity data was granted through data sharing agreement between the Canadian Institute of Health Information (CIHI) and the Public Health Agency of Canada (PHAC). The study protocol was reviewed and approved by the Queen's University Health Sciences & Affiliated Teaching Hospitals Research Ethics Board (see Appendix A).

Daily emergency room (ER) visits was selected as the outcome metric to represent the acute effect of ambient temperature on mental illness morbidity. This was done after reviewing the current literature between mental illness related morbidity and exposure to ambient temperature. Daily ER visits were obtained from NACRS for the city of Toronto from April 1st 2002 to March 31st 2010. ER records were retrieved if the primary reason of the visit was classified as related to mental and behavior disorders (F00-F99; under the International Classification of Diseases 10th Revision). We also investigated ambient temperature effects for specific diseases: Schizophrenia (F20-F29), Mood Disorders (F30-F39), Neurotic Disorders (F40-F48), and Mental and Behavior Disorders due to Psychoactive Substance (F10-F19).

3.3.2 Weather and Air Pollution Data

Hourly measurements of temperature and humidity for the city of Toronto from April 1st 2002 to March 31st 2010 were taken from Environment Canada using the monitoring station at

Toronto Pearson International Airport (latitude:43°40'36"N; longitude: 79°37'50"W) located approximately 26 km west of downtown Toronto. Daily mean, minimum and maximum temperatures and mean humidity were computed. Air pollution data were obtained from the National Air Pollution System (NAPS). It is comprised of hourly measurements of gaseous pollutants: sulfur dioxide (SO_2), nitrogen dioxide (NO_2), carbon monoxide (CO), and ozone (O_3). The air pollutants were measured using UV Fluorescence (SO_2) chemiluminescence (NO_2), infrared gas correlation (CO), and UV absorption (O_3) from multiple (Max8, Min4) fixed weather monitoring station within Toronto. Mean daily concentrations of each pollutant were computed by taking daily averages and then averaging across multiple stations for each day. The daily mean of particulate matter ($PM_{2.5}$) was computed using the same method and was measured using a combination of tapered element oscillating microbalances, gravimetric filters, virtual impactors, and beta radiation attenuation (Environment Canada).

3.3.3 Time Series Dataset

The time series dataset was based on the temporal structure of the data, where both the exposure (daily mean temperature), the outcome (daily counts of hospital emergency room visits for mental illnesses), and the confounders (daily concentration of pollutants and days of the week) were ordered within equally spaced time intervals of one day. A visual example of the dataset is provided in Appendix B along with two graphs to demonstrate the structure of the data.

3.3.4 Statistical Methods

Daily mean temperature was used as the exposure metric after model selection with several other indices of temperature and we assessed its association with emergency room visits related to mental and behavior disorders using a time series study design. Given that the relationship between adverse health outcomes and ambient temperature are lagged across specific timeframes and best described using a non-linear curve (J, S, or V) (Ye et al. 2011, Turner et al. 2012, Basu and Samet 2002), we employed the use of distributed lag non-linear models (DLNM). The DLNM is built on the foundation of combining two functions (temperature and lag) into a "cross-basis", a bi-dimensional matrix which allows the estimation of possible non-linear temperature and morbidity effects across specific lag periods (Gasparrini and Armstrong 2010; Gasparrini et al. 2011). In the context of our study, the DLNM was used to estimate the relative risk of increase ER visits from exposure to ambient temperature on mental and behavior disorders and specific diseases: schizophrenia, substance abuse related mental and behavior disorders, mood disorders, and neurotic disorders for both hot and cold temperatures.

For extreme hot temperatures, the 99^{th} percentile of the daily mean temperature was used as the exposure metric and the 1^{st} percentile of the daily mean temperature was used to represent exposure to extreme cold temperatures. We used the 50^{th} percentile of the temperature as a reference. A quasi Poisson regression was fitted using generalized linear modeling (GLM) to model the daily counts of emergency room visits based on the predictor variables: daily mean temperature and lag. The degrees of freedom for mean temperature and lag were set to 5. The lag period for the DLNM was set to 30 days. To account for the effects of season and sub-seasonal cycles, a categorical variable for day of the week was included. In addition, a smoothing function for time of 10 degrees of freedom per annum was included and we also investigated the sensitivity of the results by using varying degrees of freedom: 6, 7, and 8. An equation of the model is given in Appendix C. The quasi Akaike's information criterion (QAIC) was used to measure the relative goodness of fit for our statistical models. A lower QAIC value indicates an improvement in model fit.

3.3.5 Potential Confounders

We adjusted for the effects of air pollution by including mean daily concentration of NO_2, CO and O_3 as covariates in our analysis. Based on previous work, the effects of these pollutants were adjusted for lag periods of 0-2 days (Goldberg et al. 2011, Ye et al. 2011, Gosling et al. 2008). In addition, we accounted for humidity by using the daily mean concentration as a covariate. Finally, we adjusted for the effects of age by examining the association between ambient temperature and mental illness related ERV in specific age groups (0-14, 15-39, 40-59, 60+). Gender was adjusted using the same approach.

3.4 Results

3.4.1 Ambient Temperature and Environment Characteristics

Table 3-1 illustrates the descriptive statistics for weather and air pollution variables during the study period from April 1st 2002 to March 31st 2010. The average mean daily temperature was 8.7°C with range from -20.3°C to 31.5°C (Interquartile range 17.9°C). The mean relative humidity for the study period was 69.30% ranging from minus25.57 to 98.57%. Air pollution in the City of Toronto was low compared with other major Canadian cities. The average mean daily concentrations for collected air pollutants were: O_3 (22.05), CO (0.355Ug/m3), SO_2 (2.226Ug/m3), NO_2 (20.47Ug/m3, and $PM_{2.5}$ (8.39ppb). Table 3-2 indicates that temperature metrics (Mean, Min, and Max) were highly correlated with each other (Pearson Correlation Coefficients > 0.95), all negatively correlated with air pollutants NO_2, CO, and SO_2, and all positively correlated with O_3 and $PM_{2.5}$. Collinearity was not a concern since none of the air pollutants were significantly correlated with each other and with the temperature metrics.

Table 3-1Descriptive Statistics

	Units	Number of Days of Measurement	Mean	Standard Deviation	Maximum	Minimum	25^{th}	50^{th}	75^{th}	100th	Interquartile Range
Maximum Temperature	° C	2922	13.33	11.46	36.6	-17.4	3.7	13.7	23.4	36.6	19.7
Minimum Temperature	° C	2922	4.058	10.21	26.3	-24.7	-3.1	4.2	12.9	26.3	16
Mean Temperature	° C	2922	8.706	10.72	31.5	-20.3	0.3	9.0	18.2	31.5	17.9
Relative Humidity	%	2922	69.30	14.37	98.75	-25.57	61.87	70.54	78.32	98.75	16.45
$PM_{2.5}$	ppb	2922	8.39	6.85	49.2	0	3.833	6.33	10.5	49.2	6.66
NO_2	Ug/m3	2922	20.47	7.71	62.60	5	15.0	19.4	24.8	62.6	9.8
O_3	Ug/m3	2920	22.05	12.26	248.00	2.20	14.6	21	28	248.0	13.4
CO	Ug/m3	2915	0.355	0.210	1.8	0	0.2	0.3	0.45	1.8	0.25
SO_2	Ug/m3	2922	2.226	2.1158	17.33	0	1	1.5	3	17.33	2

Table 3-2 Correlation Coefficients

	MINT	MEANT	MAXT	$AVGSO_2$	$AVGPM_{2.5}$	$AVGSO_2$	$AVGNO_2$	$AVGO_3$	AVGCO
MINT	1	0.98626	0.95113	-0.11074	0.388	-0.11074	-0.24325	0.30521	-0.12671
MEANT	0.98626	1	0.98907	-0.07349	0.41595	-0.07349	-0.19674	0.33684	-0.11246
MAXT	0.95113	0.98907	1	-0.03843	0.43179	-0.03843	-0.15045	0.35778	-0.09724
$AVGSO_2$	-0.11074	-0.07349	-0.03843	1	0.41422	1	0.58108	-0.0779	0.55707
$AVGPM_{2.5}$	0.388	0.41595	0.43179	0.41422	1	0.41422	0.44632	0.25921	0.28585
$AVGSO_2$	-0.11074	-0.07349	-0.03843	1	0.41422	1	0.58108	-0.0779	0.55707
$AVGNO_2$	-0.24325	-0.19674	-0.15045	0.58108	0.44632	0.58108	1	-0.19843	0.54676
$AVGO_3$	0.30521	0.33684	0.35778	-0.0779	0.25921	-0.0779	-0.19843	1	-0.0945
AVGCO	-0.12671	-0.11246	-0.09724	0.55707	0.28585	0.55707	0.54676	-0.0945	1

MINT=Daily Minimum Temperature

MEANT= Mean Daily Temperature

MAXT= Daily Max Temperature

$AVGSO_2$= Daily Mean SO_2 Concentration

$AVGPM_{2.5}$= Daily Mean $PM_{2.5}$ Concentration
$AVGNO_2$ = Daily Mean NO_2 Concentration
$AVGO_3$ = Daily Mean Ozone Concentration
AVGCO = Daily Mean Carbon Monoxide Concentration

3.4.2 Distributed Effects of Ambient Temperature on Emergency Room Visits

Table 3-3 summaries the association between daily mean temperatures and mental and behavior disorders estimated through the use of DLNM. Results are shown for heat (99^{th} percentile of mean temperature) and cold (1^{st} percentile of mean temperature) effects. Adjustments were made for, humidity, NO_2, CO and $O_{3.}$ Cumulative effects were calculated by aggregating daily risks over a 7-day period. Sensitivity analyses were done with different lag periods to assess the robustness of the results. The regression results indicated that mental and behavior disorders (ICD-10 F00-F99), schizophrenia (F20-F29), mood disorders (F30-F39), neurotic disorders (F40-F48), and MBD due to substance abuse (F10-19) were all significantly associated with high temperature (99^{th} percentile) in the City of Toronto while schizophrenia (F20-F29) and neurotic (F40-F48) disorders related ER visits showed some associations with extreme cold temperature (1^{st} percentile). The specific associations are described in the subsequent sections.

Table 3-3 Distributed Lag Effects of Ambient Temperature on various Mental Illnesses

The Model was fitted using cubic b-spline using three equally space knots and 4 degree of freedom for mean temperature, a natural cubic spline with 5 df for the lag space, a natural cubic spline with 10 df per year was applied, adjustments were included for NO_2,CO,O_3, Days of the week, and Humidity.

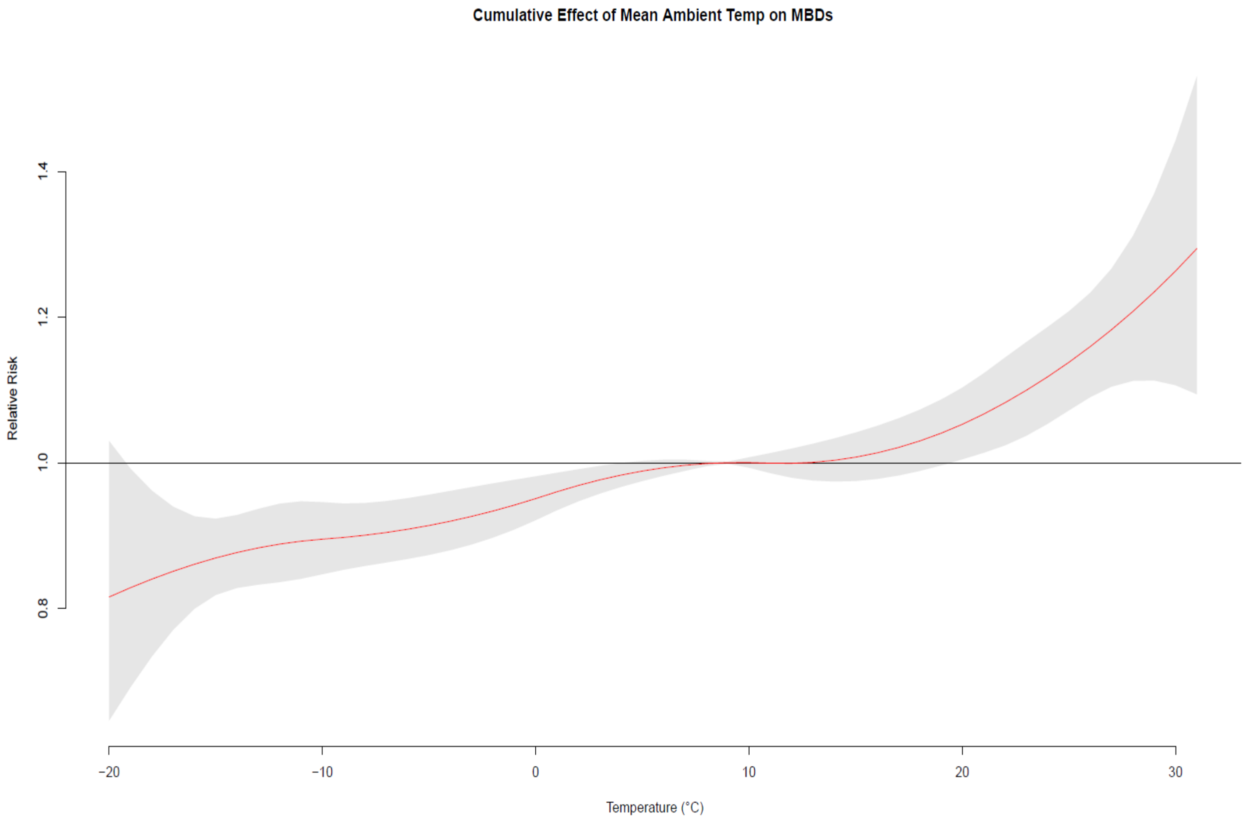
Effects of 99th percentile of Mean Ambient Temperature on Emergency Room Admissions (ERV) across all lags(0-30)					
	Mental Behavior Disorders (MBD) (F00-F99)	**MBD due to Psychoactive Substance (F10-F19)**	**Schizophrenia (F20-29)**	**Mood Disorders (F30-39)**	**Neurotic Disorders (F40-F48)**
Lag Days	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**
Lag0	1.056 (1.026 -1.087)	1.046 (0.986 - 1.110)	1.097 (1.026 - 1.172)	1.059 (0.996 - 1.126)	1.023 (0.943 - 1.108)
Lag1	1.040 (1.021-1.060)	1.028 (0.990 - 1.067)	1.078 (1.033 - 1.125)	1.050 (1.010 - 1.091)	1.031 (0.994 - 1.069)
Lag2	1.027 (1.014-1.400)	1.013 (0.978 - 1.040)	1.061 (1.030 - 1.094)	1.041 (1.013 - 1.071)	1.027 (0.987 - 1.068)
Lag3	1.017 (1.005-1.030)	1.003 (0.970 - 1.029)	1.047 (1.017 - 1.079)	1.034 (1.006 - 1.062)	1.014 (0.982 - 1.046)
Lag4	1.011 (0.998-1.024)	0.997 (0.970 - 1.235)	1.036 (1.005 - 1.068)	1.027 (0.998 - 1.056)	1.002 (0.977 - 1.028)
Lag5	1.006 (0.993-1.019)	0.993 (0.968 - 1.019)	1.026 (0.996 - 1.058)	1.021 (0.993 - 1.049)	0.994 (0.969 - 1.021)
Lag6	1.030 (0.991-1.015)	0.992 (0.968 - 1.017)	1.018 (0.990 - 1.048)	1.016 (0.989 - 1.042)	0.991 (0.964 - 1.019)
Lag7	1.001 (0.990-1.013)	0.991 (0.969 - 11.02)	1.011 (0.985 - 1.039)	1.011 (0.986 - 1.036)	0.989 (0.961 - 1.018)
Lag8	0.999 (0.989-1.010)	0.991 (0.969 - 1.014)	1.005 (0.980 - 1.032)	1.007 (0.983 - 1.030)	0.990 (0.965 - 1.017)
Lag9	0.998 (0.987-1.009)	0.991 (0.969 - 1.014)	1.000 (0.975 - 1.027)	1.003 (0.980 - 1.027)	0.992 (0.968 - 1.018)
Lag10	0.997 (0.986-1.008)	0.992 (0.969 - 1.014)	0.997 (0.971 - 1.023)	1.002 (0.977 - 1.024)	0.995 (0.972 - 1.018)
Lag11	0.997 (0.985-1.008)	0.992 (0.969 - 1.015)	0.993 (0.968 - 1.020)	0.998 (0.974 - 1.022)	0.998 (0.975 - 1.020)
Lag12	0.996 (0.984-1.007)	0.993 (0.970 - 1.016)	0.991 (0.964 - 1.018)	0.996 (0.972 - 1.207)	0.999 (0.977 - 1.023)
Lag13	0.996 (0.984-1.008)	0.993 (0.970 - 1.017)	0.989 (0.962 - 1.017)	0.994 (0.970 - 1.019)	1.001 (0.979 - 1.025)
Lag14	0.996 (0.984-1.008)	0.994 (0.971 - 1.018)	0.988 (0.962 - 1.016)	0.993 (0.968 - 1.019)	1.003 (0.980 - 1.027)
Lag15	0.996 (0.984-1.008)	0.995 (0.972 - 1.019)	0.988 (0.961 -1.016)	0.993 (0.968 - 1.018)	1.005 (0.982 - 1.029)
Lag16	0.997 (0.985-1.008)	0.997 (0.973 - 1.020)	0.988 (0.961 - 1.016)	0.992 (0.968 - 1.017)	1.006 (0.983 - 1.030)
Lag17	0.998 (0.986-1.009)	0.998 (0.974 - 1.020)	0.989 (0.962 - 1.016)	0.992 (0.968 - 1.017)	1.008 (0.985 - 1.031)
Lag18	0.999 (0.987-1.010)	0.999 (0.977 - 1.022)	0.989 (0.963 - 1.017)	0.993 (0.968 - 1.017)	1.009 (0.986 - 1.032)
Lag19	1.000 (0.988-1.010)	0.999 (0.977 - 1.023)	0.990 (0.966 - 1.018)	0.993 (0.970 - 1.017)	1.010 (0.988 - 1.032)
Lag20	1.000 (0.988-1.011)	1.000 (0.978 - 1.023)	0.994 (0.969 - 1.019)	0.994 (0.971 - 1.017)	1.010 (0.989 - 1.033)
Lag21	1.001 (0.989-1.012)	1.002 (0.983 - 1.024)	0.996 (0.971 - 1.021)	0.995 (0.973 - 1.018)	1.011 (0.990 - 1.033)
Lag22	1.000 (0.990-1.013)	1.004 (0.985 - 1.025)	0.999 (0.975 - 1.024)	0.997 (0.975 - 1.019)	1.012 (0.991 - 1.033)

Effects of 99th percentile of Mean Ambient Temperature on Emergency Room Admissions (ERV) across all lags(0-30)					
	Mental Behavior Disorders (MBD) (F00-F99)	**MBD due to Psychoactive Substance (F10-F19)**	**Schizophrenia (F20-29)**	**Mood Disorders (F30-39)**	**Neurotic Disorders (F40-F48)**
Lag Days	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**	**Relative Risk (95% CI)**
Lag23	1.000 (0.992-1.015)	1.006 (0.987 - 1.027)	1.000 (0.978 - 1.027)	0.998 (0.977 - 1.020)	1.012 (0.992 - 1.033)
Lag24	1.006 (0.994-1.016)	1.008 (0.989 - 1.029)	1.006 (0.982 - 1.030)	1.000 (0.978 - 1.022)	1.013 (0.993 - 1.033)
Lag25	1.008 (0.996-1.019)	1.011 (0.990 - 1.030)	1.009 (0.985 - 1.034)	1.002 (0.980 - 1.025)	1.013 (0.992 - 1.034)
Lag26	1.010 (0.997-1.020)	1.013 (0.992 - 1.033)	1.013 (0.988 - 1.040)	1.004 (0.981 - 1.028)	1.013 (0.992 - 1.035)
Lag27	1.010 (1.000-1.023)	1.015 (0.993 - 1.039)	1.017 (0.990 - 1.045)	1.060 (0.982 - 1.031)	1.014 (0.991 - 1.037)
Lag28	1.013 (1.001-1.026)	1.017 (0.993 - 1.043)	1.021 (0.993 - 1.051)	1.009 (0.982 - 1.035)	1.014 (0.991 - 1.039)
Lag29	1.016 (1.001-1.029)	1.020 (0.994 - 1.047)	1.026 (0.995 - 1.058)	1.019 (0.983 - 1.039)	1.014 (0.989 - 1.041)
Lag30	1.017 (1.002-1.032)	1.020 (0.994 - 1.051)	1.030 (0.997 - 1.065)	1.013 (0.983 - 1.044)	1.014 (0.987 - 1.044)

3.4.3 Mental and Behavior Disorders (MBDs) (ICD-10 F00-F99)

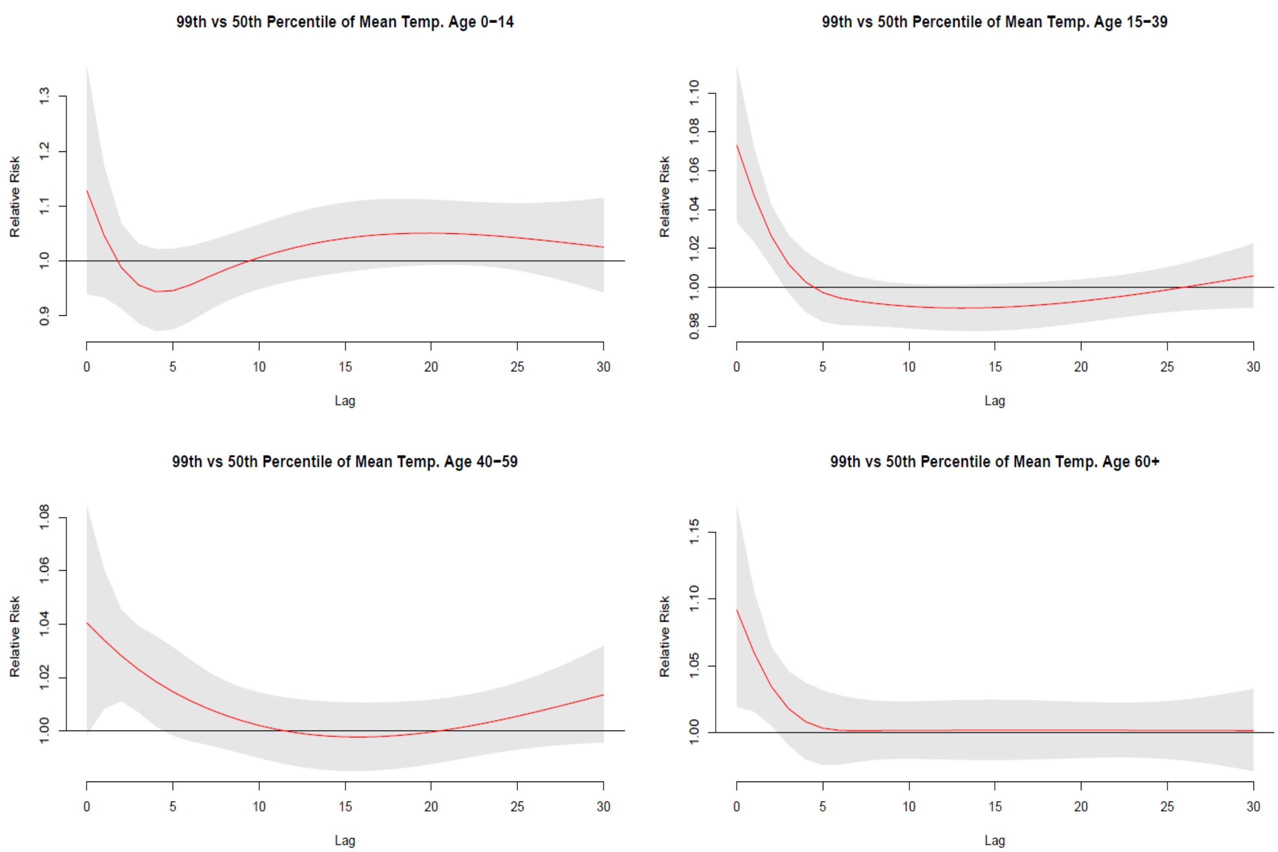
A total of 271,746 emergency room visits were related to mental and behavior disorders in Toronto during the study time frame. We observed a significant increase (RR1.06 95%CI 1.03-1.09) in ER visits at the 99th percentile of the mean temperature at lag 0. The significant increase in ER visits lasted for 3 days (RR1.04 95%CI 1.02-1.06 lag 1, RR1.03 95%CI 1.01-1.04 lag 2, RR1.02 95%CI 1.01-1.03 at lag 3) gradually decreasing and eventually falling back around RR of 1.00 (Table 3-3). Although, there was an increase in risk at lag 28-30 for high temperatures (Table 3-3), this should be interpreted with caution as the stability of estimates generated by DLNM at extremely long lags are more prone to variability. Cumulatively, a 29% increase (RR1.29 95%CI 1.09-1.53) in daily ER visits was observed over one week after the initial high temperature day (Figure 3-1).

Figure 3-1 Cumulative Effect of Ambient Temperature on Mental and Behavior Illnesses-Related ER Visits (The grey portion of the figures indicates confidence intervals and the red line represents the relative risk estimates. The figure was produced from model using 4 degrees of freedom for lag and 5 degrees of freedom for temperature. Adjustments were made for NO_2, CO, O_3, day of the week and daily humidity levels. Seasonality smoothing was set to 10 per annum.)



No increase risk in admissions was observed for cold temperatures. Age and gender effects were also examined. The effect of high temperature on MBDs related ER visits was greatest among individuals aged 60+ (Figure 3-2). There were no gender effects.

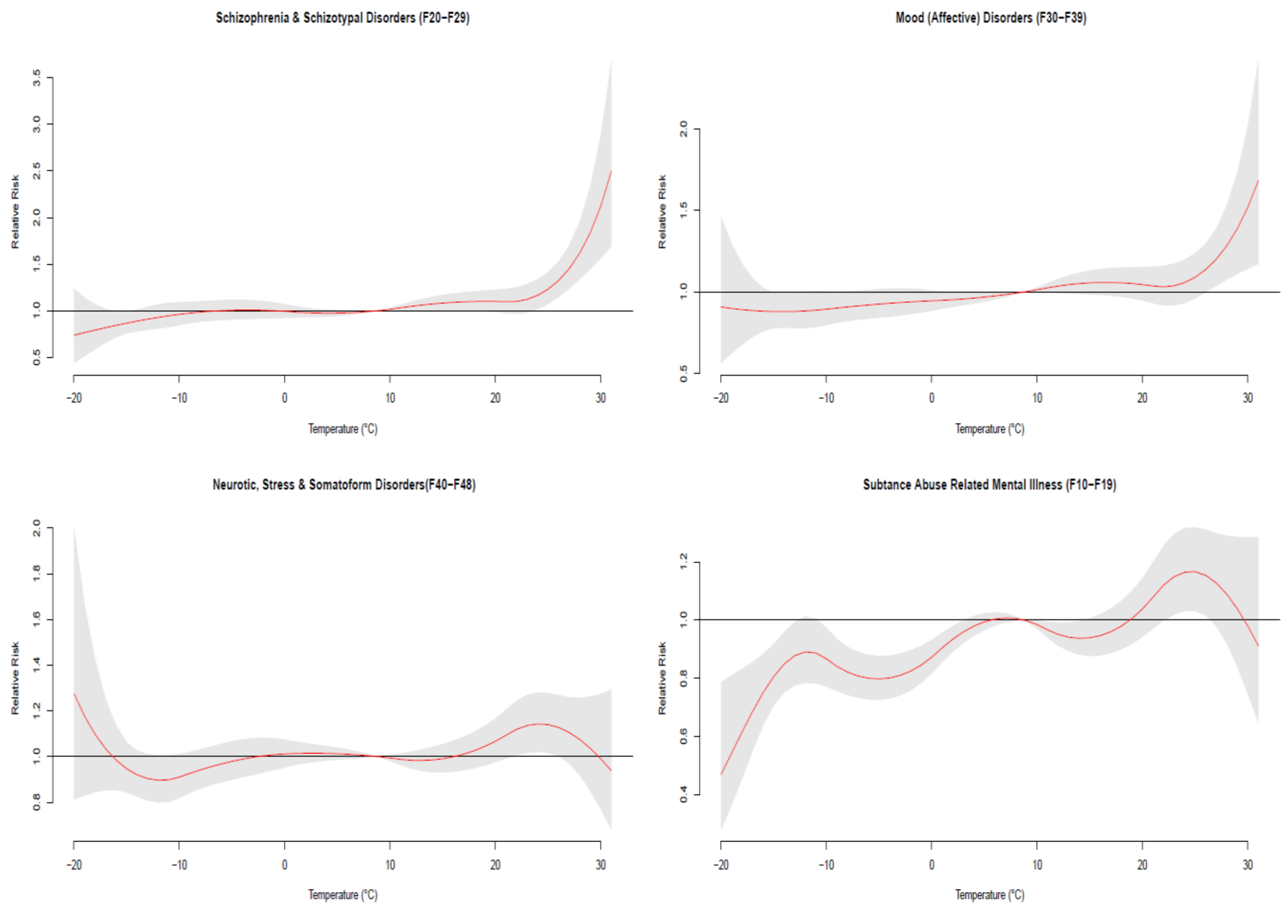
Figure 3-2 Lagged Effects of Mean Ambient Temp on MBD based on age (The grey portion of the figures indicates confidence intervals and the red line represents the relative risk estimates. The figure was produced from model using 4 degrees of freedom for lag and 5 degrees of freedom for temperature. Adjustments were made for NO_2, CO, O_3, day of the week and daily humidity levels. Seasonality smoothing was set to 10 per annum.)



3.4.4 MBDs due to psychoactive substance abuse (ICD-10 F10-F19)

In this category, we observed 73,050 emergency room visits related to MBDs due to psychoactive substance abuse over the study timeframe in Toronto. Increased ER visits at high (99^{th} percentile) mean temperatures were observed from 0 to 3 lag days (Table 3-3). The highest increase in ER visits was observed at lag 0 (RR 1.05 95%CI 0.99-1.11). After a period of 3 days the effect of ambient temperature on substance abuse ER visits fell to null levels. Finally, a 14% increase (7 day cumulative) (RR 1.14 95%CI 1.03-1.32) in daily emergency room visits was observed after a high temperature day (Figure 3-3). No increases in ER visits for cold temperatures were observed.

Figure 3-3 Cumulative Effects of Mean Temp on Various Mental and Behavior Disorders (The grey portion of the figures indicates confidence intervals and the red line represents the relative risk estimates. The figure was produced from model using 4 degrees of freedom for lag and 5 degrees of freedom for temperature. Adjustments were made for NO_2, CO, O_3, day of the week and daily humidity levels. Seasonality smoothing was set to 10 per annum.)



3.4.5 Schizophrenia, Schizotypal and Delusional Disorders (ICD-10 F20-29)

In this group, we observed 46,765 emergency room visits in the city of Toronto during the study timeframe. At high (99th percentile) mean temperatures, increases in ER visits were observed from lags 0 to 7 (Table 3-3). The strongest significant increase in risk occurred at lag 0

(RR1.10 95%CI 1.03-1.17). From lag period 1 to 4, the effect was significant (Table 3-3). Cumulatively, a 249% increase (RR 2.49 95%CI 1.69-3.69) in daily ER visits was observed over a period of 7 days after initial exposure to high temperatures (Figure 3-3). A clear dose response relationship was observed with higher ERV increases occurring at higher temperatures (99th percentile). Interestingly, sensitivity analyses revealed increases in ER visits at cold temperatures (1st percentile range) when the lag period was altered to 30 days.

3.4.6 Mood Disorders (ICD 10 F30-F39)

Depression, mania, dysthymia, and bipolar disorders are included in this group. We observed a total of 64,284 emergency room visits in the City of Toronto during the study timeframe. During high temperatures, increases in ERV were seen from lag 0 to lag 5 (Table 3-3).The increase is highest at lag 0 and is significant for lags 1 to 3. Overall, a cumulative (7 day) 68 %(RR 1.68 95%CI 1.17-2.40) increase in ER visits was observed after an initial high temperature day (99th percentile) (Figure 3-3). No significant associations were observed for cold temperatures.

3.4.7 Neurotic Disorders (ICD 10 F40-F49)

This category includes various phobia disorders (Agora, Social), anxiety disorders, panic disorders, stress related disorders, and Obsessive Compulsive disorders. Increases in ER visits were observed for high temperatures from lag 0 to lag3 (Table 3-3). The strongest effect of high temperature occurred at lag 1(Table 4). Overall, a 12% (RR 1.12 95%CI 1.00-1.27) increase in ER visits was seen over a 7-day period after a high ambient temperature day. Also, a 9% (RR 1.09 95%CI 0.84-1.42) increase in ER visits was observed over a week after a cold ambient temperature day (1st percentile).

3.5 Discussion

This is the first ever study to investigate the lagged effects of ambient temperature on MBDs and specific mental illness ERV. For the population of Toronto, Canada, we found that exposure to high ambient (99^{th} percentile) mean temperature is significantly associated with increases in hospital emergency room visits for individuals with mental and behavior disorders. We illustrated the lagged structure of these relationships and found that the greatest effect/risk of emergency room admissions is limited between 0 to 4 lag days for hot temperatures. Age group stratified analyses revealed that the effect of high temperature on MBDs related ER visits was greatest among individuals aged 60 and over followed by individuals ages 0-14, 15-39, and 40-59. No significant differences were seen between genders and no significant cold associations were observed for overall MBDs.

With respect to specific mental illnesses, significant increases in hospital emergency room admission during high temperatures were shown for: Schizophrenia and Schizotypal disorders, Mood disorders, substance abuse related mental and behavior disorders, and Neurotic Disorders. These effects were restricted to a period of 0 to 7 lag days with peak admissions usually occurring at lag 0 or lag 1. Individuals with Schizophrenia and Schizotypal disorders and Mood disorders were affected by high temperatures more than other disease groups. Cold temperature increases in ER visits were observed for Neurotic and Schizophrenia and Schizotypal disorders. This was reported after sensitivity analyses with increased lag period indicating the effect of cold temperature is delayed to a greater extent than high temperatures; however, cold temperature associations were non-significant.

Although limited direct comparison to previous work can be made since the lag structure of mental and behavior disorders were not previously investigated, our results are comparable to some previous work of similar nature indicating that high temperature is significantly associated with increases in emergency room visits for MBDs. In Australia, Khalaj et al. (2010), using a logistic regression model, have reported increases (7-11%) in emergency hospital admissions during periods of heat waves for individuals with mental and behavior disorders compared against individuals without. Other studies, such as Nitschke et al. 2011, Wang et al. 2011, Nitschke et al. 2007, and Williams et al. 2012, have all reported similar findings between heat waves and MBDs emergency room visits. Similarly, studies have reported greater risk of hospital admission with increasing age (Hansen et al. 2008, Nitschke et al. 2011; Wang et al. 2012). For specific mental and behavior disorders, Hansen et al. 2008 reported significant increases in the risk of hospital admission after a threshold of 26.7°C for organic (~7.3%), dementia(~17.4%), psychoactive substance use (~0.5%), schizophrenia (~3.4%), mood disorders (~9.1%), and neurotic disorders (~9.7%). Although some of these findings were numerically similar to ours, potential confounders such as various air pollutants (NO_2, CO, O_3), humidity, and day of the week were not adjusted for; thus, the extent to which these confounders affect the associations are unknown and not directly comparable with our results.

Our results for schizophrenia and schizotypal disorders are also similar to studies in other regions. In Taiwan, Sung et al. 2011 have demonstrated increases in schizophrenia hospital admissions during periods of change in ambient temperature range. However, no associations were reported for cold temperatures and no associations were reported for schizoaffective disorders. In Israel, Shiloh et al. (2000, 2005) reported that mean daily temperature was significantly correlated with the severity of symptoms and hospital admissions among patients with schizophrenia. Thus, indicating that temperature may be a risk factor for psychotic exacerbation in patients with schizophrenia.

For Mood disorders, although our illustration of the lag structure of associations between increased emergency visits and ambient temperature is novel, previous findings have reported similar correlations. In Egypt, Amr and Volpe (2012) reported data that demonstrated a correlation between ambient temperature and hospital admissions for affective disorders. In Brazil, Volpe et al. (2008) and Volpe and Porto (2006) have reported a correlation between increasing temperature and specific clinical dimensions of mania and hospitalizations for mania. In Israel, Shiloh et al. (2005) reported a correlation between maximal temperature and admission rates for bipolar depressed patients. However, no effect estimates were reported; thus, the results are not directly comparable. Although increases in temperature related mortality have been reported in individuals with substance abused relate mental illness (Page et al. 2012), increases in morbidities due to temperature for individuals with this condition has been limited.

Extreme temperatures can exacerbate Mental and Behavior illnesses for various physiological and behavioral reasons. First, the nature of the psychiatric disorder/illness can increase an individual's physiological vulnerability to extreme temperature if specific neurotransmitters involved in thermoregulation are also involved in the disease process itself such as in schizophrenia, where impaired dopaminergic transmission have been demonstrated in animal models (Bark 1998, Sung et al. 2011, Hasegawa et al. 2005). Climatic variables such as temperature have been previously demonstrated to modulate relevant biological chemicals and its bioavailability such as plasma tryptophan, serotonin production, brain serotonin turnover, and platelet serotonin availability, which are potentially related to the psychophysiology of many affective disorders (Ljubici et al. 2007, Lambert et al. 2002, Maes et al. 1995, Sarrias et al. 1989).

Second, the individual's illness decreases the ability to remain cognitively aware of the surrounding environment; thus, neglecting appropriate prevention measures such as drinking extra fluids, taking off clothing when required, and avoiding going outside (Martin-Latry et al. 2007, Bark 1998, Hansen et al. 2008) all of which increase one’ s vulnerability to temperature modulated psychotic exacerbations. Although the presence of air conditioning is protective against temperature-related exacerbation of health conditions, individuals with mental and behavior disorders often tend to have lower socioeconomic status compared with the general population which could affect their ability to live in an air conditioned home (Semenza 1999). Finally, individuals with mental illness have higher risks of social isolation and acquiring chronic cardiovascular and respiratory co-morbidities, all of which are risk factors for increased vulnerability to the hazardous effects of extreme temperature (McIntyre et al. 2006).

Third, many psychotropic medications have been shown to cause disruption to normal thermoregulatory mechanisms due their pharmacological properties (Conti et al.2003, Shiloh et al. 2001, Schwaniger et al. 1998, Yuan et al. 2006). Medications such as anti-cholinergics, anti-depressants (serotoninergic), anti-histamines (H3), mood stabilizers, anti-psychotics, sedatives, and anti-epileptics have been associated with abnormal thermoregulation. Anti-cholinergics, anti-histamines, anti-depressants, and anti-psychotics can lower the elimination of high temperature through parasympathetic pathways and impairing sweat production. Antipsychotics and antidepressants may induce elevated body temperatures leading to hyperthermia. Many of these medications are used in the treatment of mood, stress, anxiety, psychosis, and personality disorders and when coupled with the nature of their psychiatric illness, behavior symptoms, and socioeconomic factors can further increase the susceptibility of these individuals to extreme ambient temperatures.

Dehydration can alter the pharmacokinetics of some of these medications and the side effects of many psychotropic medications may further add to an individual’s vulnerability to extreme temperature. For individuals with psychoactive substance abuse, numerous substances may impair physiological responses to extreme temperature. For example, opiates can interfere with skin vascularization and alter physiological heat responses (Page et al. 2012). Hypnotics (Alcohol) can cause depression of the central nervous system; thus, inducing dehydration and haemoconcentration which increases an individual’s vulnerability to heat (Marzuk et al.1998, Romanovsky and Blatteis 1998).

This study builds on previous literature which identified individuals with psychiatric illness as a susceptible population to the effects of extreme temperature (hot and cold). However, our study builds on previous work by investigating these effects with consideration for the lagged and non-linear nature of these exposure-outcome relationships. To our knowledge this is the first study in the literature undertaking this endeavor.

Our findings of specific temperature-morbidity relationships are not confounded by various air pollutants and humidity since adjustments were included for such factors. Additionally, the results were produced from the models with the best fit after multiple sensitivity analyses varying the degrees of freedom for the predictor, lag and different time smoothing functions.

There are some limitations that need to be considered when interpreting the results of our study. First, the small sample size in a few disease specific categories limited the statistical power of some disease specific temperature associations and restricted our ability to conduct in-depth analyses of age and gender per disease subgroup. Second, changes in the diagnostic criteria from ICD-9 to ICD-10 may have introduced some misclassification among certain diseases. As well, it is possible that some level of misdiagnosis in the ICD coding could have occurred since many psychiatric illnesses exhibit similar clinical presentations and psychopathology which can be difficult to distinguish. For example, individuals with bipolar disorder can sometimes be diagnosed as having schizophrenia since positive symptoms of schizophrenia can resemble manic episodes while negative symptoms of schizophrenia show resemblance to depressive episodes (Shiloh et al. 2001).

Moreover, given the wide range of clinical manifestations of psychotic exacerbation, it is possible some diagnoses were not included in our study due to non-mental health specific ICD coding. For instance, individuals with mania often exhibit certain dimensions of violence, aggression, and suicidality; thus, if temperature induced psychotic exacerbation prompted a manic individual to visit the ER due to physical injuries sustained from acts of violence and aggression, is possible that the ICD code assigned to the visit would be related to injury rather than for mania. Also, since mortality data such as suicides were not included in our study, we were only able to investigate effects on morbidity; thereby, leading to possible underestimation of the true effects of temperature on mental illness.

Given the lack of individual level data on drug usage/individual medication compliance and the ecological nature of the study, it was not possible to distinguish between susceptibility brought on by psychotropic medication usage and/or the presence of a psychiatric illness. Similarly, the presence of comorbidities and social factors such as financial status, the use of air conditioning, and whether the individual lived alone were not able to be accounted for in the study.

Spatial variations, especially in urban settings, are more likely to produce heterogeneous vulnerabilities to extreme temperature; thus, the usage of aggregated daily average of temperatures from a network of monitoring stations for a city is likely to result in some "regression dilution" resulting in a potential underestimation of the true effect (Goldberg et al. 2011).

Although we have demonstrated some significant associations between extreme temperature and mental and behavior disorders, we are unable to pinpoint the exact cause for them. Future research can build on these limitations by incorporating the usage of medication history, collection of information on comorbidities and various social indicators (income, air conditioning, etc.) in order to provide a more thorough understanding of the observed associations.

3.6 Conclusions

Individuals with mental illness are vulnerable to the effect of extreme temperatures and preventive measures/adaptation strategies should be developed to minimize the risk of hospitalization and more serious illnesses. Given that ambient temperature is predicted to rise in the future, our findings highlight the need for further research to understand the reported relationships between extreme ambient temperature and mental illnesses in order to mitigate the risk and reduce the burden of illness on the affected population.

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Chapter 4

General Discussion and Conclusions

4.1 Summary of Findings

A literature review identified limitations in the way the effects of extreme ambient temperatures on individuals with mental and behavior disorders have been studied:

-there has been little investigation on the effects of exposure to extreme cold temperatures,

-the lagged and non-linear nature of these exposure-outcome relationships has not been incorporated into the statistical analysis, and

-few studies have adjusted for many relevant potential confounders: humidity, various air pollutants, and day of the week.

A time series study concluded that exposure to heat (99^{th} percentile of the daily mean ambient temperature) was associated with a significant increase in ER visits related to mental and behavior disorders. Similar associations were observed for specific disorders such as schizophrenia, mood disorders, neurotic disorders, and substance abuse related mental illnesses. Although there is some indication that exposure to extreme cold temperatures (1st percentile of the daily mean ambient temperature) may increase ER visits for individuals with schizophrenia and neurotic disorders, the results are not statistically significant.

4.1 Limitations

Although our time series study was novel in its statistical methodology, limitations related to exposure and outcome measurements are acknowledged. The methodological issues regarding exposure measurement largely pertain to the potential underestimation of the actual temperature experienced by the individual. This occurs through a combination of the urban heat island effect, the location of temperature measurements, and the use of aggregate temperature metrics. These will be discussed further in depth regarding their specific impacts on the results reported.

4.1.1 Exposure misclassification

Our study used an ecological measure of temperature (daily mean temperature) as the proxy for the entire geographical region of the study. This approach assumes that all individuals in the study region will roughly experience the same exposure. However, geographical differences with respect to temperature vulnerabilities can exist in urban settings (Goldberg et al. 2011). The urban heat island effect is a phenomenon where the positioning of numerous large urban structures in close proximity can magnify the high temperatures felt by the individual (Basu and Samet 2002). Numerous factors such as building filtration and air conditioning can also affect the actual temperature experienced by the individual (Basu and Samet 2002).

The temperature monitoring station used in this study (Toronto Pearson International Airport) is approximately 28 kilometers from downtown Toronto. This may not represent the actual temperature conditions experienced in the metropolitan area of Toronto since the concentration of urban structures is sparser near the airport than in the downtown area; thus, lowering the urban island effect.

Consequently, some degree of misclassification is inherent. For high temperatures, this would lead to an underestimation of the actual temperature felt. For cold temperatures, it may be lead to overestimation of the temperature (colder at the airport than downtown due to fewer buildings to provide cover for wind-chill effects); however, this is not certain and there is limited literature to support this speculation. For high temperatures, this underestimation would result in some regression dilution and would lower the magnitude of the reported associations (Gasparrini and Armstrong 2010). The exact magnitude of this underestimation will largely depend on the extent of correlation between the study temperature metric and the actual temperature experienced by the individual. A recently published paper (Goldberg et al. 2011) reported that the exact magnitude of the underestimation was not significant with respect to the overall risk estimate for the study. The impact of this exposure measurement error on the association between cold temperatures and ER visits is unclear since there is very limited literature on the matter.

While daily mean temperature was the best overall temperature metric to use in our model as it produced the lowest QAIC value for model fit; the extreme ranges of the daily mean temperature are lower than the actual minimum and maximum temperature of the day. Although this difference between the actual temperature extremes and the daily mean temperature extremes is not significant, this may produce additional misclassification of the exposure and possibly lowering the associations reported.

Finally, a fixed temperature value may not be suited to represent the exposure since temperatures often fluctuate throughout the day (Sung et al. 2011). Thus, the daily temperature range may be the best metric to represent the exposure. Given the limitations of the distributed non-linear lag modeling in computing estimates based on a range of temperature values, we were not able to investigate the suitability of using temperature range as the exposure metric.

4.1.2 Outcome misclassification

The methodological issues surrounding outcome measurements are related to the gathering of morbidity data through NACRS and the use of relevant ICD codes. Hospital ER visits are currently the standard outcome metric used in measuring morbidity effects in time series study of temperature. ER visits related to mental and behavior disorders based on ICD-10 coding were included in the study. This approach may not be adequate in capturing individuals with mental illness admitted to the ER due to extreme temperature exposure but coded as seen for reasons other than mental illness.

For example, when persons with dementia are exposed to extreme heat; however, due to their impaired cognitive awareness of the surroundings as a result of dementia, they did not take the appropriate preventive measures (drinking water, remove excessive clothing, use air conditioning, stay indoors, and etc.). Consequently, they become dehydrated and are admitted to the ER for treatment of dehydration. These individuals would not be captured under the currently used method since they were treated for dehydration and not mental illness. This would result in an underestimation of the morbidity effects as these individuals were not included in the study. Thus, the ability of the currently used outcome measurements to capture these individual may not be ideal given that the clinical manifestations of temperature induced outcomes in patients with mental illness are difficult to predict and can often encompass a wide range of conditions.

For high temperatures, we hypothesize that this limitation in ER visit coding will result in an underestimation of the actual number of ER visit related to mental and behavior disorders and lower the magnitude of the relative risk. For cold temperatures, the impact of this limitation is unclear since the cold temperature associations reported earlier are not statistically significant.

Another issue arises concerning mental and behavior disorders which have similar clinical presentations that are difficult to distinguish. It is possible that some inherent level of misdiagnosis between extremely similar conditions will occur. An example using mania and schizophrenia was given earlier in the previous chapter.

It may be helpful to include ER visits where, although the primary reason for the visit was not related to mental illness, the individual had an underlying mental illness condition. However, since secondary diagnoses were not mandatory reporting fields under NACRS (CIHI, 2012), the completeness of this data is questionable. As such, their use would introduce additional uncertainty and potential for misclassification.

In addition, some non-acute manifestations of temperature-induced health issues experienced by individuals with mental illness may not be presented in hospital or ER settings. Instead, they are presented at family physicians and other social workers. Since we did not have access to this information, the overall morbidity impact of extremes in temperature on individuals with mental and behavior disorders are underestimated.

4.1.3 Statistical Challenges

Although the use of DLNM in our study was novel since it was able to simultaneously account for the lagged and non-linear nature of the exposure-outcome relationship, several limitations exist. First, the great degree of customization regarding model variable selection such as degrees of freedom, lag, and covariates can lead to unnecessarily complex models which are time consuming to construct and give marginally little accuracy over simpler models. Second, although the DLNM is able to adjust for various potential confounders such as air pollutants and humidity, we are unable to pinpoint exactly how these covariates influence the magnitude of the relative risk. Also, the use of lag periods for covariates without caution may decrease the reliability of the results since the model does not account for the interaction of these time dependent exposure-outcome relationships. Third, given that the casual pathway for temperature-exacerbated health outcomes are often complex and may involve many synergic pathways with air pollutants and humidity, the ability to investigate interactive effects between temperature, air pollutants, humidity, and the outcome variable is crucial. However, the ability of the DLNM to investigate interactive effects is limited given the rigid programing barriers in this regard.

4.2 Public Health Implications

Individuals with mental illness are vulnerable to the effect of extreme temperatures. The vulnerabilities differ with respect to age group and specific mental and behavior disorders. From a public health perspective, meaningful interventions, preventive measures, and adaptation strategies should be employed to minimize the risk of hospitalization and more serious illnesses where opportunity arises.

Given some individuals with mental and behavior disorders will be unaware of the risks from extreme temperature exposure, adequate patient counseling and education regarding information on exposure reduction and preventive measures such as intake of sufficient fluids, wearing appropriate clothing, taking showers, avoiding going out during periods of extreme heat or cold, use of air conditioning, and the use of heat shelters should be incorporated into outpatient care programs.

Issuing heat/cold alerts to the public and relevant health authorities, and the formulation of heat-wave/cold-spell response plans are needed. The establishment of early heat warning systems is also important since they often have lead times of 12 to 48 hours which offer valuable time for preparation to decision makers and public health practitioners (Basu and Samet 2002). In Europe after the heat waves in 2003, many early heat warning systems were implemented in 16 European countries to provide relevant officials time to prepare before heat waves (Basu and Samet 2002). However, no conclusion can be drawn regarding their effectiveness since they have not been evaluated.

Although not directly examined in our study, but given the relevant biological link, health care practitioners working with individuals with mental and behavior disorders should be trained to evaluate risk and apply interventions such as monitoring of indoor temperature during relevant months, conducting face to face interviews during periods of elevated temperature to check for symptoms of dehydration and other temperature-induced illnesses, and, when possible, switching medications that affect thermoregulation for alternative formulations that do not.

The public health measures listed above should be studied to demonstrate how they can contribute to improvements in the management and care of the individuals with mental and behavior disorders. Their ability to reduce the economic and social costs of extreme temperature events must also be demonstrated.

4.3 References

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4.4 Appendices

4.4.1 Appendix A: Ethics Certificate

QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW

April 17, 2013

Mr. Wang Xiang
Department of Community Health and Epidemiology
Queen's University

Dear Mr. Xiang
Study Title: EPID-423-13 Acute effects of ambient temperature exposure on mental illness related emergency room visits in the city of Toronto
File # 6008079
Co-Investigators: Mrs. H. Ouellette-Kuntz, Dr. C. Bingshu, Dr. E. Lavigne

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair's signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # **6008079** in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file **6008079** in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair's signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Albert F. Clark

Chair, Research Ethics Board
April 17, 2013

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete

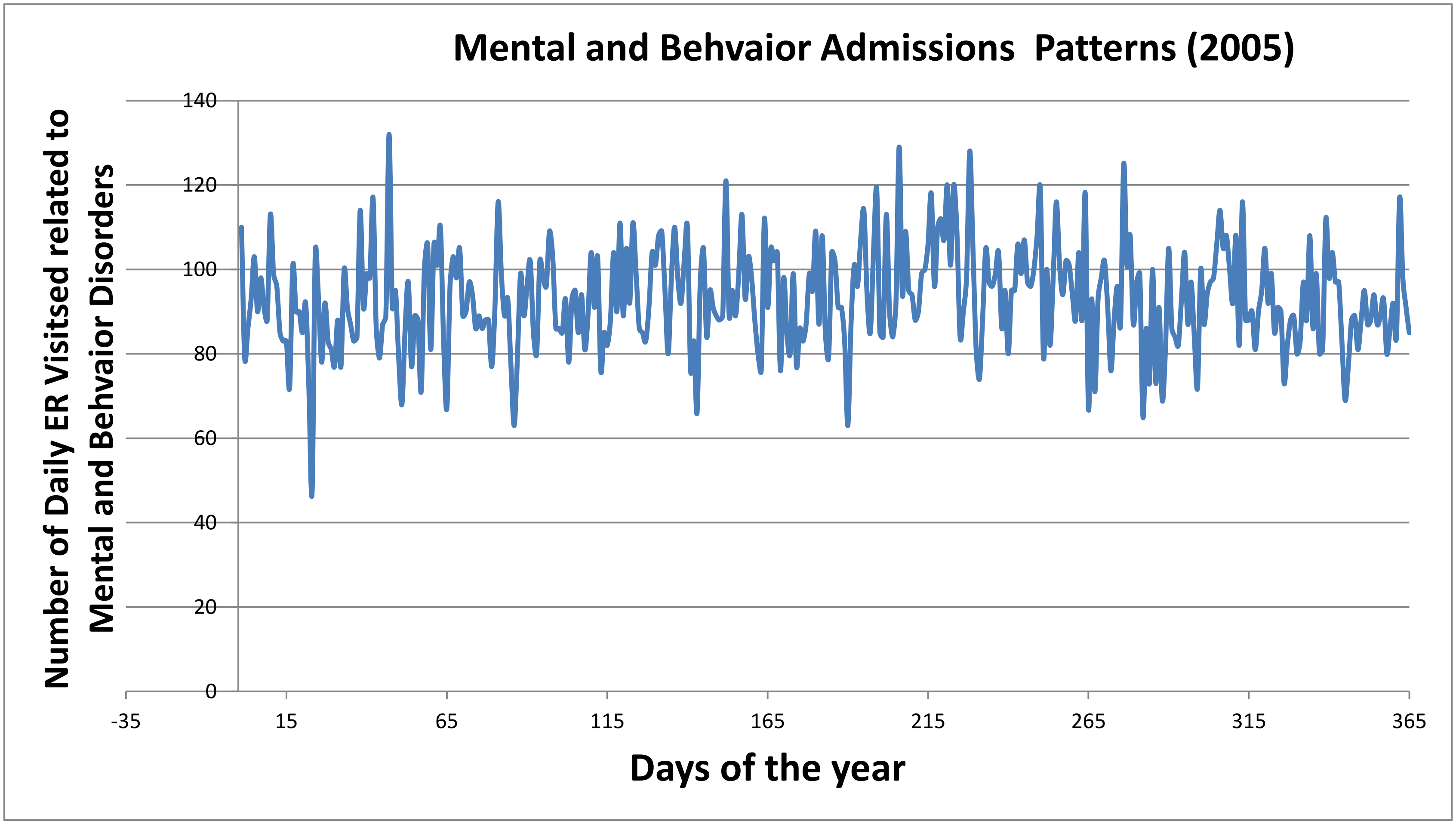
4.4.2 Appendix B: Example of Time Series Dataset, ER Visit Distribution over a year, and Temperature Distribution over a year

Example of Time series Dataset

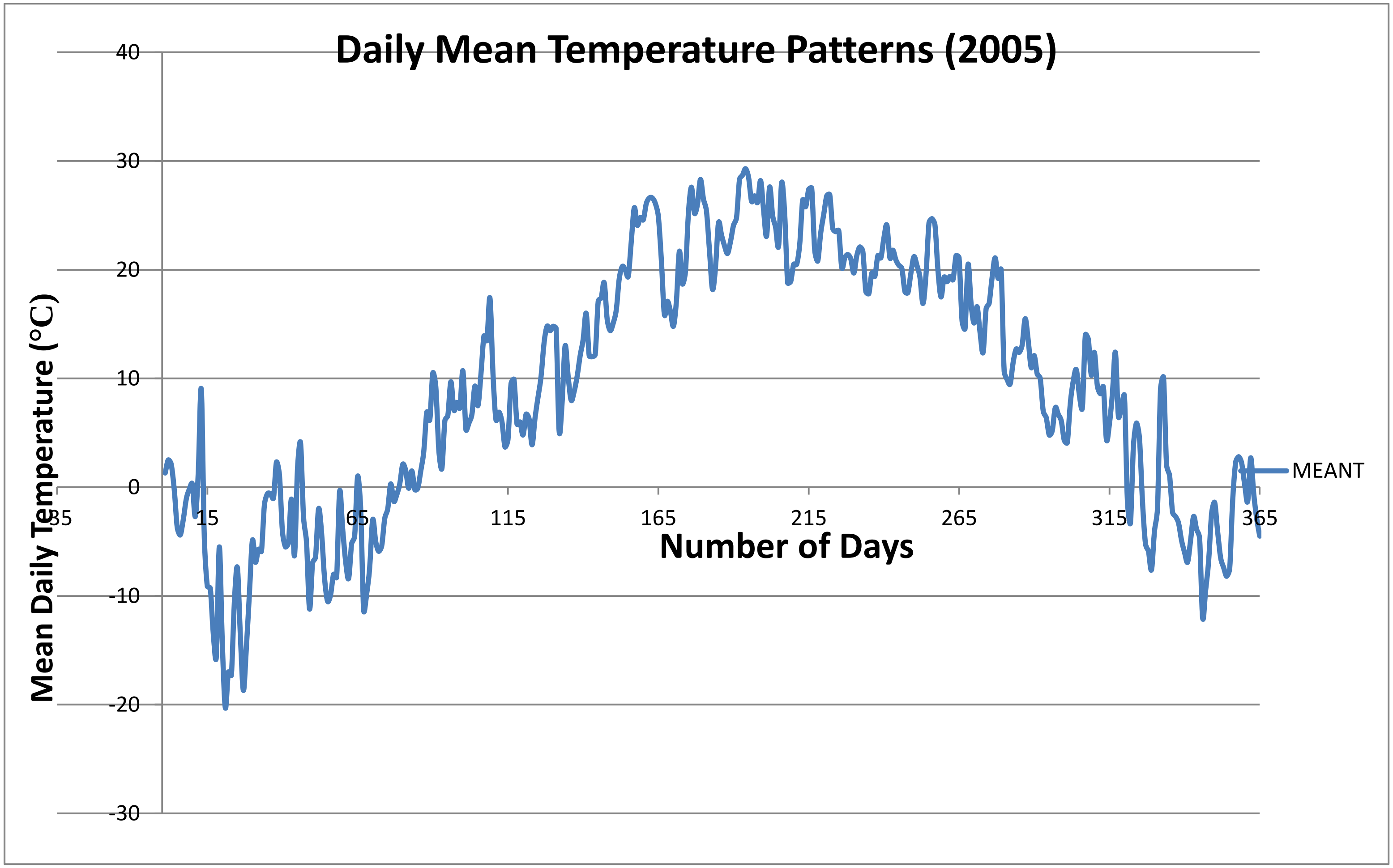
date	MBD	Year	Month	TIME	Day	MEANT	RELHUM	DOW	AVGNO$_2$	AVGCO	AVGO$_3$	AVGSO$_2$	AVGPM$_{25}$
1/1/2005	110	2005	1	1007	1	1.3	67.5	Saturday	11.2	0.4	14.8	0	2.4
1/2/2005	79	2005	1	1008	2	2.5	90.29	Sunday	15.2	0.6	13.6	1	4.2
1/3/2005	86	2005	1	1009	3	2.1	88.67	Monday	25.8	0.65	4.2	1	4.2
1/4/2005	93	2005	1	1010	4	-0.2	79.83	Tuesday	22.6	0.55	12.4	0.5	3.7
1/5/2005	103	2005	1	1011	5	-3.7	69.46	Wednesday	19.6	0.45	16.2	0.5	1.5
1/6/2005	90	2005	1	1012	6	-4.4	78.21	Thursday	20	0.5	16	1	3
1/7/2005	98	2005	1	1013	7	-3	72.96	Friday	26.2	0.45	17.4	2.5	5.2
1/8/2005	91	2005	1	1014	8	-1.1	80.5	Saturday	29.2	0.65	9.2	3.5	10.2
1/9/2005	88	2005	1	1015	9	-0.2	84.167	Sunday	25.2	0.6	8.6	5.5	12.8
1/10/2005	113	2005	1	1016	10	0.3	73.46	Monday	20.2	0.55	12.8	3	7
1/11/2005	99	2005	1	1017	11	-2.7	72.54	Tuesday	21.4	0.55	17	1	3.2
1/12/2005	96	2005	1	1018	12	1.4	91.58	Wednesday	23	0.55	8.6	1	5.2
1/13/2005	85	2005	1	1019	13	9	87.08	Thursday	25.4	0.3	10.8	4	7.5
1/14/2005	83	2005	1	1020	14	-4.6	71.92	Friday	16.4	0.2	25.4	0	3.7
1/15/2005	83	2005	1	1021	15	-9.1	67.25	Saturday	15.2	0.25	25.2	1.5	4
1/16/2005	72	2005	1	1022	16	-9.3	75.21	Sunday	24.2	0.4	15.6	1	4.2
1/17/2005	101	2005	1	1023	17	-13.5	75.08	Monday	25	0.35	16.4	1.5	3.8
1/18/2005	90	2005	1	1024	18	-15.6	60.54	Tuesday	20.6	0.3	20.2	3.5	5.5
1/19/2005	90	2005	1	1025	19	-5.5	78.96	Wednesday	26	0.3	13	10.5	6.8
1/20/2005	85	2005	1	1026	20	-14.4	71.08	Thursday	19.2	0.3	22.2	0	2.3

MDB =daily counts of ER visits related to mental and behavior disorders, MEANT= Daily mean temperature, RELHUM= Daily Humidity concentration, AVGNO$_2$= Daily NO_2 concentration levels, AVGCO= daily CO concentration, AVGO$_3$= daily ozone concentration, AVGSO$_2$= daily SO_2 concentration, AVGPM$_{2.5}$ = daily particular matter concentration, and DOW = day of the week, TIME= Number of days of Study.

ER visits pattern for 2005



Daily Mean Temperature Patterns for 2005



4.4.3 Appendix C: Statistical Model Equation

The equation for the quasi-Poisson regression will be:

Log [ut] = α +β BS [Tt, lag30], + [NO_2, lag2], + [CO, lag1] + [O_3, lag2] + nDOW + kHumidity,

Where α is the equation intercept, β is the vector of the coefficients for the Tt, and lag corresponds to the lag period in which the effect is investigated over. Furthermore, adjustments based day of the week (DOW) and humidity will be done.