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Mental illness and increased vulnerability to negative health effects from extreme heat events: a systematic review

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ABSTRACT

Rationale: Across countries, extreme heat events are projected to increase in frequency and intensity because of climate change. Exposure to extreme heat events can have a substantial negative impact on human health, and extant research suggests that individuals with mental illness are particularly vulnerable. To date, there has been no review of evidence regarding this vulnerability to inform response strategies and future research.
Objective: A systematic review was undertaken to investigate mental illness as an effect modifier of the relationship between heat exposure and morbidity or mortality.
Methods: Six databases (Medline, Embase, Global Health, PsychInfo, CINAHL and Scopus) were searched for studies published between the years 2000 to 2022. Twenty-two observational studies that met the inclusion criteria were investigated through narrative synthesis. The RoBANS tool, ROBIS and GRADE were used to assess the certainty of evidence including the risk of bias.
Results: Individuals with mental illness experience worse morbidity and mortality outcomes compared to their counterparts without mental illness in all studies investigating high temperature over a single day. This did not hold for studies examining heatwaves, which reported mixed findings.
Conclusions and implications: People with diagnosed mental illness should be targeted for policy and service attention during high temperature days. Further research should investigate specific mental illness and adjust for a wider range of confounding factors.

1. Introduction

Around 30 % of the world's population is exposed to harmful climatic conditions (mean surface temperature and relative humidity) for at least 20 days each year (Mora et al., 2017). Projections suggest that under 1.5 °C warming, severe heatwaves will impact 13.8 % of the world population at least once every five years (Dosio et al., 2018). It is anticipated that extreme heat events will intensify in the future and there is strong evidence that extreme heat events pose a serious threat to human health (Ebi et al., 2021; Kovats and Hajat, 2008). This can be from transient heat exposure over a single day, or cumulative heat exposure during a heatwave (Ebi et al., 2021; Kovats and Hajat, 2008). In both instances, this can result in a range of heat-related illnesses including heat exhaustion, heat cramps, heat syncope and heatstroke (Kovats and Hajat, 2008). Exposure to extreme heat events has also been found to exacerbate a range of chronic diseases leading to increases in morbidity and mortality (Liu et al., 2022).

Vulnerability to the negative health effects of extreme heat events is determined by exposure, sensitivity and adaptive capacity, meaning the impacts of heat exposure are not uniform across the population (Lõhmus, 2018; Pörtner et al., 2022). Systematic reviews support that people with chronic physical health conditions, including cardiovascular, respiratory, cerebrovascular and renal diseases, and diabetes mellitus, are particularly vulnerable to the impacts of extreme heat events (Bunker et al., 2016; Liu et al., 2022). The elderly, children, individuals of lower socioeconomic status, and individuals with existing chronic health conditions are also particularly at risk (Ellena et al., 2020; Liu et al., 2021; Pörtner et al., 2022; Son et al., 2019).

Pre-existing mental illnesses can cause adverse reactions to climate-related stressors, leading to increased sensitivity to heatwaves and impeded behavioural adaptation (Ellena et al., 2020; Li et al., 2023; Pörtner et al., 2022). Reduced thermoregulatory capacities, medication use, maladaptive behaviour and social isolation have been charted as some of the mechanisms for this (Lõhmus, 2018; Page et al., 2012).

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There is research evidence that people with mental illness may be less likely to be aware of the health risks posed by extreme heat and less likely to follow public health directives and to receive and comprehend warnings (Kaiser et al., 2001; Kovats and Hajat, 2008). They can be prone to a range of maladaptive behaviours such as wandering and psychomotor agitation which puts them at greater risk of heat exposure (Lõhmus, 2018; Page et al., 2012). This is compounded by the selection of people with mental illness into lower status occupations, poorer housing quality and homelessness (Kaiser et al., 2001). They are also more likely to be socially isolated and have chronic physical health conditions as comorbidities (Page et al., 2012).

In addition, psychotropic medications including anxiolytics/hypnotics, antidepressants and antipsychotics used to treat anxiety, sleep and mood disorders, and psychoses affect thermoregulation (Lõhmus, 2018; Page et al., 2012). Strong evidence suggests that people on these medications may be less able biologically to maintain their internal body temperature under extreme heat conditions (Lõhmus, 2018).

To better understand whether people with mental illness have worse health outcomes during extreme heat events, we undertook a systematic review of studies published between 2000 and 2022 that quantitatively test whether pre-existing mental illness alters the magnitude of the effect of high temperatures and heat on health (measured by hospitalisation and mortality). This review addresses the following research question:

Does having an underlying mental illness make people more vulnerable to morbidity and mortality from extreme heat or heatwaves?

Importantly, by investigating mental ill-health as an effect modifier in a systematic review that considers study quality, this paper contributes to the development of evidence-based policy responses to extreme heat events and provides guidance on how future studies should be conducted, thereby improving the overall quality of research (Gopalakrishnan and Ganeshkumar, 2013).

2. Methods

This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) guidelines to search for, screen, extract, analyse and evaluate all relevant research regarding mental illnesses as effect modifiers of the heat-health relationship (Page et al., 2021). The study protocol was registered on Prospero (CRD42022326993).

2.1. Search strategy

The research question was translated into key concepts to conduct a systematic search of databases and find an exhaustive list of all studies on the topic which met the inclusion criteria (Dana et al., 2014). Six databases were searched: Ovid MEDLINE, Ovid EMBASE, Ovid Global Health, Ovid PsycInfo, EBSCOhost CINAHL and Elsevier Scopus.

The search strategy (appendix 1) was formulated by identifying the exposure, comparator and outcomes of interest as key concepts (Dana et al., 2014; Harari et al., 2020). These were "heat-related morbidity and mortality", "mental illness" and "effect modification". Synonyms were generated for each concept. Truncation and wildcards were applied to ensure that all relevant synonyms were searched for efficiently and accounting for any variations in spelling (Dana et al., 2014). Synonyms comprised of multiple words were structured as phrase searches such as "mental health condition" (Dana et al., 2014). Specific mental illnesses were also included in the search terms.

Each database was searched to find relevant controlled vocabulary or Medical Subject Headings (Dana et al., 2014). Explosion was only used, if applicable, when all sub-terms were relevant to the research question (Dana et al., 2014). Free text search terms and controlled vocabulary were combined using proximity and Boolean operators (Dana et al., 2014). The search was restricted to only include results published in English between 2000 and 2022, to reflect the most up-to-date evidence and account for the most dramatic changes in climate. Climate change literature has consistently identified the 21st century as a period of significant increase in the frequency, duration and intensity of high temperatures and heatwaves (Klingelhöfer et al., 2023). The most intensive heatwave seasons have generally occurred post 2000 (Perkins-Kirkpatrick and Lewis, 2020). The final search strategy for each database (appendix 1), recorded using PRISMA-S guidelines was run on July 15, 2022 (Page et al., 2021; Rethlefsen et al., 2021).

2.2. Eligibility criteria

Eligible study designs were randomised controlled trials, cohort, case-control, case-crossover, cross-sectional and ecological study designs. Case reports, case series and grey literature were excluded because they provide lower quality evidence at a higher risk of bias (McDonagh and Peterson, 2014). The criterion for heat exposure was any high temperature or heatwave event as defined by each article. No strict definition of high temperature was used because heat is relative based on location and historical data and there is no one accepted method on how it should be defined in the literature. Outcomes investigated included mortality and morbidity measures such as hospitalisation and self-reported morbidity. Finally, the comparator included in this systematic review was mental illness. This included a diagnosis or history of mental illness and a range of specific mental illnesses including depression, anxiety, bipolar disorder, schizophrenia, psychoses, substance misuse and eating disorders. A broad definition of mental illness was used which included diagnoses from mental health practitioners and hospitalisation records as well as self-reported mental illness from participants or their family members. Studies which examined the effect of mental health medications on susceptibility to heat were also included in the review. This review focusses specifically on mental illness –which has been measured in wide range of ways in included studies. To reduce heterogeneity in our narrative synthesis, we have excluded studies that focus exclusively on neurological disorders (e.g., dementia) rather than mental illness. While there are overlapping issues faced by the population of people with these conditions, the underlying cause, progression of symptoms and treatments vary (Yudofsky and Hales, 2002).

2.3. Screening

Search results were imported into Covidence systematic review software where duplicate items were removed. Two reviewers (JM and MG) screened title and abstract and full text independently, to reduce reviewer bias (McDonagh and Peterson, 2014). In the case of a discrepancy between reviewers that could not be resolved through discussion, a third reviewer (AM) made the final inclusion/exclusion decision. Eligibility criteria were used to derive a title and abstract screening guide which was extended with further detail into a second full-text screening guide (appendices 2 and 3). These were developed by JM in collaboration with AM, RB and AL. After a list of studies for inclusion was identified, forward and backward searching of references was completed by JM to minimise the omission of relevant papers (Harari et al., 2020).

2.4. Data extraction

Key data was extracted by JM and checked by MG. This included PICO criteria (population, heat exposure, mental illness and morbidity/mortality outcomes), study design, setting, timing, aims and objectives, population characteristics, analysis methods and confounding factors adjusted for in the analysis.

2.5. Quality assessment

Risk of bias assessment for each individual study was conducted using the RoBANS tool which covers bias from selection, confounding, exposure, outcome assessment, loss to follow up and selective reporting (Kim et al., 2013). The assessment was completed independently by JM and MG. Any disagreements were resolved through discussion with the research team.

2.6. Data analysis and synthesis

Narrative synthesis was chosen because of the substantial clinical and methodological heterogeneity expected, making a meta-analysis inappropriate (Campbell et al., 2020). This was conducted by JM according to published guidance documents (Campbell et al., 2020; Popay et al., 2006). Risk of bias was assessed using the ROBIS tool which identifies concerns with the review process and provides an overall judgement of risk of bias, and GRADE, which assesses overall quality and certainty of evidence (Guyatt et al., 2008; Whiting et al., 2022). The ROBIS tool and GRADE assessment were conducted independently by JM and MG and discrepancies were resolved in collaboration with the research team.

3. Results

3.1. Eligible studies

The initial literature search yielded 767 results (MEDLINE = 70, EMBASE = 158, Global Health = 53, PsycInfo = 8, CINAHL = 50, Scopus = 418) (Fig. 1). Two hundred and twenty-eight duplicate articles were removed, and the remaining 539 papers were screened by title and abstract. One hundred and thirteen full-text studies were assessed for eligibility. Ninety-nine were excluded for not meeting eligibility criteria (appendix 4). Three papers which met eligibility criteria were conducted by the same authors using the same data, therefore only the first paper published was included (De'Donato et al., 2008; Stafoggia et al., 2008, 2006). This left 14 studies which met the eligibility criteria, and forwards and backwards searching identified a further eight studies. Therefore, a total of 22 studies were included in the review (Bélanger et al., 2014; Davido et al., 2006; Hall et al., 2021; Holstein et al., 2005; Kaiser et al., 2001; Kim et al., 2014; Larrieu et al., 2008; Layton et al., 2020; Mangoni et al., 2017; Martin-Latry et al., 2007; Naughton et al., 2002; Nitschke et al., 2013; Nordon et al., 2009; Oudin Åström et al., 2015; Pillai et al., 2014; Rocklöv et al., 2014; Schifano et al., 2009; Stafoggia et al., 2006; Stivanello et al., 2020; Vandentorren et al., 2006; Zhang et al., 2017, 2013). The characteristics and variables used in each study are outlined in Tables 1 and 2. The results of the studies in examining mental health effect modification are discussed below and grouped in terms of the type of heat exposure (high temperature or heatwave) and outcome (morbidity or mortality) used (Table 3).

All studies included in the review were observational. This included eight case-control (Hall et al., 2021; Kaiser et al., 2001; Kim et al., 2014; Martin-Latry et al., 2007; Naughton et al., 2002; Nordon et al., 2009; Vandentorren et al., 2006; Zhang et al., 2017), six cohort (Davido et al., 2006; Holstein et al., 2005; Mangoni et al., 2017; Oudin Åström et al., 2015; Pillai et al., 2014; Schifano et al., 2009), five case-crossover (Layton et al., 2020; Rocklöv et al., 2014; Stafoggia et al., 2006; Stivanello et al., 2020; Zhang et al., 2013), and three cross-sectional studies (Bélanger et al., 2014; Larrieu et al., 2008; Nitschke et al., 2013). All studies were conducted in high income countries. Namely, France (Davido et al., 2006; Holstein et al., 2005; Larrieu et al., 2008; Martin-Latry et al., 2007; Nordon et al., 2009; Vandentorren et al., 2006), United States (Hall et al., 2021; Kaiser et al., 2001; Layton et al., 2020; Naughton et al., 2002; Pillai et al., 2014), Australia (Mangoni et al., 2017; Nitschke et al., 2013; Zhang et al., 2017, 2013), Italy (Oudin Åström et al., 2015; Schifano et al., 2009; Stafoggia et al., 2006; Stivanello et al., 2020), Sweden (Oudin Åström et al., 2015; Rocklöv et al., 2014), Canada (Bélanger et al., 2014), and South Korea (Kim et al., 2014). Studies investigated populations at country (Kim et al., 2014; Layton et al., 2020; Nordon et al., 2009), state (Hall et al., 2021; Nitschke et al., 2013; Pillai et al., 2014), county (Kaiser et al., 2001; Martin-Latry et al., 2007; Naughton et al., 2002; Rocklöv et al., 2014), city (Bélanger et al., 2014; Larrieu et al., 2008; Oudin Åström et al., 2015; Schifano et al., 2009; Stafoggia et al., 2006; Stivanello et al., 2020; Vandentorren et al., 2006; Zhang et al., 2017, 2013), and hospital levels (Davido et al., 2006; Holstein et al., 2005; Mangoni et al., 2017). Nine studies focused on elderly populations defined using various age thresholds and settings such as nursing homes (Holstein et al., 2005; Larrieu et al., 2008; Layton et al., 2020; Mangoni et al., 2017; Nordon et al., 2009; Oudin Åström et al., 2015; Schifano et al., 2009; Vandentorren et al., 2006). The general population was often defined as individuals aged 18 years and over (Bélanger et al., 2014; Hall et al., 2021; Stivanello et al., 2020; Zhang et al., 2017). However, three studies placed no restrictions on age (Kim et al., 2014; Pillai et al., 2014; Rocklöv et al., 2014), and five studies did not specify any age restriction (Davido et al., 2006; Kaiser et al., 2001; Martin-Latry et al., 2007; Naughton et al., 2002; Zhang et al., 2017).

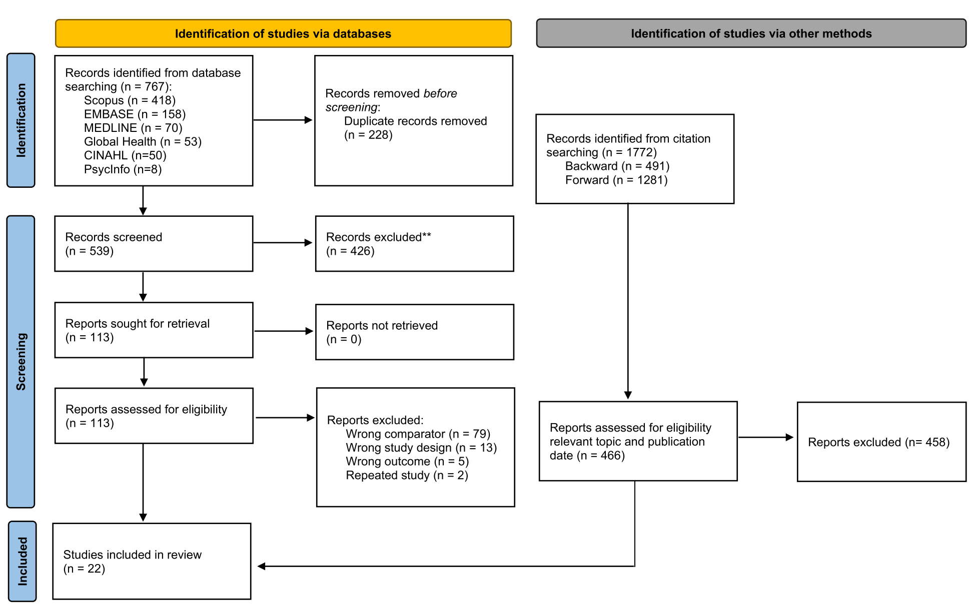

Fig. 1. PRISMA flow diagram.

Table 1
Study characteristics.

Author, publication year	Country	Study design	Sample size	Population subgroup/age
Bélanger et al., 2014	Canada	Cross-sectional	3485	Residents of materially and socially disadvantaged census dissemination areas of nine cities in Quebec province aged 18 years and older, with the ability to converse in French or English.
Davido et al., 2006	France	Cohort	165	Patients attending the emergency department of an adult urban teaching emergency service in Paris with a heat related medical problem during the heatwave period. Heat-related medical problem was defined as “core temperature ≥38°C and/or clinical signs of dehydration” Excludes patient who departed from the emergency department prematurely before a sufficient medical evaluation could be done.
Hall, 2021	United States	Case-control	463	California residents aged 18 years and older who presented to a state-licenced emergency department between 1 January 2009 and 31 December 2013. Cases: individuals who presented to the emergency department and died from hyperthermia. Controls: individuals who presented to the emergency department within one day of the case's death matched on sex and age (±2 years).
Holstein et al., 2005	France	Cohort	4,403	Nursing home residents of the Assistance-Publique Hopitaux de Paris which is the largest French public hospital group with 41 hospitals and 22 nursing homes.
Kaiser et al., 2001	United States	Case-control	140	Hamilton County residents. Cases: individuals who died from heat-related illness during the heatwave. Controls: individuals age and neighbourhood matched (2 per case) from random neighbourhood recruitment method.
Kim et al., 2014	South Korea	Case-control	968	Patients diagnosed with heat illness by emergency physicians based on the patient's clinical presentation. Cases: patients diagnosed with heatstroke Controls: patients with mild heat-related illnesses such as heat exhaustion, heat edema, heat cramps, and heat syncope.
Larrieu et al., 2008	France	Cross-sectional	1416	Residents of Gironde, Dordogne, Bordeaux and Dijon who were aged 65 years and over and participants in the PAQUID or 3C cohort studies.
Layton et al., 2020	United States	Case-crossover	9,721	Medicare beneficiaries aged 65 years and older with chronic health conditions across the United States.
Mangoni et al., 2017	Australia	Cohort	1,721	Patients aged 65 years and older with at least one chronic illness admitted to the Flinders Medical Centre from the emergency department in Adelaide.
Martin-Latry et al., 2007	France	Case-control	1,176	Residents of the Aquitaine region. Cases: individuals admitted to the emergency department of the Saint Andre University Hospital in Bordeaux with a diagnosis of heat-related pathology over the study period Controls: individuals matched to cases on gender, age and residential area, not hospitalised over the heatwave period and with at least one prescription form submitted for refunding by the Social Security Insurance system during July 2003 randomly extracted from the SSI database of the Aquitaine region.
Naughton et al., 2002	United States	Case-control	51	Chicago residents. Cases: individuals who died from heat-

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Table 1 (*continued*)

Author, publication year	Country	Study design	Sample size	Population subgroup/age
				related illness during the heatwave. Controls: individuals age and neighbourhood matched from random neighbourhood recruitment method.
(Nitschke et al., 2013)	Australia	Cross-sectional	499	Residents aged 65 years and over living independently in South Australia with a landline telephone number.
Nordon et al., 2009	France	Case-control	23,248	French persons aged 70-100 years who use the SSI system. Cases: individuals who died in France during the heatwave. Controls: individuals who were still alive on 30 April 2004 matched to cases on age, gender and presence of chronic illness (yes/no).
Oudin Åström et al., 2015	Italy, Sweden	Cohort	1,106,511 (Rome) 512,964 (Stockholm)	Residents of Rome and Stockholm aged 50 years and older.
Pillai et al., 2014	United States	Cohort	13,562	Georgia residents with heat-related illness diagnosed from 2002 through 2008 in the emergency department (hospitalisation or discharge home).
Rocklöv et al., 2014	Sweden	Case-crossover	44,738	Stockholm residents who died between 1990 and 2002 excluding deaths from external causes.
Schifano et al., 2009	Italy	Cohort	624,561	Residents of Bologna, Milan, Rome and Turin aged 35 years and older who died from noninjury causes between 1997-2003.
Stafoggia et al., 2006	Italy	Case-crossover	205,019	Residents of Bologna, Milan, Rome and Turin aged 35 years and older who died from noninjury causes between 1997-2003.
Stivanello et al., 2020	Italy	Case-crossover	48,305	Bologna residents aged 18 years or older who died during the summer period of the years 2004-2017.
Vandentorren et al., 2006	France	Case-control	597	Community dwelling elderly aged 65 years and older who lived in Val de Marne in Paris, Tours and Orleans during the French heatwave between 8 August and 13 August 2003. Cases: randomly selected from death records. Controls: individuals matched to cases for age (±5 years), sex and residential area who were home between August 8 and August 13 were randomly selected from telephone records.
Zhang et al., 2013	Australia	Case-crossover	740	Metropolitan Adelaide residents admitted to a public hospital for heat-related illness over the study period. Excludes elective hospital admissions and individuals not living in Adelaide at the time of hospitalisation.
Zhang et al., 2017	Australia	Case-control	246	Adelaide residents aged 18 years and older who were in Adelaide at the time of the heatwave. Cases: individuals who died during the heatwave. Controls: individuals who lived in the same regions as controls during the heatwave.

3.2. Heatwaves and mortality

Eleven studies investigated how mental illness modifies the relationship between heatwaves and mortality (Davido et al., 2006; Holstein et al., 2005; Kaiser et al., 2001; Mangoni et al., 2017; Naughton et al., 2002; Nordon et al., 2009; Oudin Åström et al., 2015; Rocklöv et al., 2014; Schifano et al., 2009; Vandentorren et al., 2006; Zhang et al., 2017) (Table 2). Seven studies examined mental illness, two examined mental health medication, and two examined both mental illness and medication.

Eight studies conducted adjusted analyses to investigate this relationship (Holstein et al., 2005; Mangoni et al., 2017; Nordon et al., 2009; Oudin Åström et al., 2015; Rocklöv et al., 2014; Schifano et al., 2009; Vandentorren et al., 2006; Zhang et al., 2017) (Table 3). Of these, four studies found that individuals with mental illness were more likely to die following heat exposure compared to individuals without mental illness (Oudin Åström et al., 2015; Rocklöv et al., 2014; Vandentorren et al., 2006; Zhang et al., 2017). Two studies found that individuals with mental illness were less likely to die following heat exposure than individuals without mental illness (Mangoni et al., 2017; Schifano et al., 2009). The remaining two studies reported mixed results (Holstein et al., 2005; Nordon et al., 2009). Nordon et al (2009) found that individuals who took antidepressants and antipsychotics were at greater risk of dying during heat exposure than those not taking the medications whereas individuals taking anxiolytics were at reduced risk. Holstein et al (2005) examined three different exposure periods. Before and during heatwave exposure, individuals with psychotic states were at reduced risk of dying compared to individuals without psychotic states.

Table 2
Study variables.

Author, publication year	Heat/heatwave measure	Mental health measure	Mortality measure Morbidity measure
Bélanger et al., 2014	Very hot and humid weather conditions	Self-reported mental disorder diagnosis via a questionnaire delivered face-to-face and computer-assisted methods. Questionnaire was based on a review of literature on health and climate change and various population survey questions and was tested twice prior to delivery for understanding, clarity and logic.	Self-reported adverse (not at all, slightly, moderately or greatly) physical and mental health impacts. Physical and mental health were assessed in separate questions and combined into an overall outcome score.
Davido et al., 2006	Hospital admissions between 8 August and 14 August 2003. "In Île-de-France, between 4 August and 12 August 2003, maximum temperatures were higher than 35 °C, and the minimum were never lower than 20 °C." Four experts decided blindly in pairs, whether a patient had presented with a heat-related problem.	"Any chronic pre-existing medical condition was assessed and recorded using the International Classification of Diseases, 10th edition. Following consensus between our staff, the diagnoses were grouped into 11 categories." The mental health condition is listed as depression. It is unclear how this was assessed and no corresponding ICD codes were provided. Use of psychotropic medications was also investigated but it was unclear how this was measured.	Short-term mortality defined as death in the emergency department or within the first month following the emergency department visit.
Hall, 2021	Heat is not strictly defined and is instead incorporated into the mortality outcome. However, 95 % of deaths did occur in the warmer months of May to September.	Prior emergency department visit for a mental health diagnosis. The mental health conditions examined are alcohol use disorders (ICD-9: 291, 303, 305.0, 357.5, 425.5, 535.3, 571.0, 571.1, 571.2, 571.3, 760.71, 790.3, V79.1, V11.3), drug use disorders (ICD-9: 292, 304, 305.2, 305.3, 305.4, 305.5, 305.7, 305.8, 305.9, 648.3, 655.5, 760.72, 760.73, 760.75, 779.5, 965, V65.42, 305.1) and psychiatric disorder (ICD-9: 293.81, 293.82, 295, 297, 298, 293.83, 296, 300.4, 311, 293.84, 300.00, 300.10, 300.2, 300.3, 300.5, 300.89, 300.9, 308, 309.81, 312, 313.81, 314, 312.30, 312.31, 312.32, 312.33, 312.34, 312.35, 312.39, 293.89, 293.9, 294.9, 294.8, 301, 307.1, 307.5, 307.2, 333.3, 307.3, 307.4, 307.80, 307.89, 307.9, 309, 309.21, 316, E950.0-E95.9, V62.84, E850-E858, E860-E869, E980, E981, E982, V11.0, V11.1, V11.2, V11.4, V11.8, V11.9, V70.1, V79.0, 648.4, V40.2).	Hyperthermia mortality (ICD-10: X30).
Holstein et al., 2005	3 periods were included. Before heatwave: 12 May to 31 July 2003 During heatwave: 1 August – 20 August 2003 After heatwave: 21 August to 30 November 2003	Annual survey of nursing home residents in May 2003 noted the absence or presence of severe or complex chronic diseases one of which was psychotic states with unstable behavioural disorders which was defined by geriatricians.	Mortality. A follow-up survey conducted in December 2003 asked each nursing home facility to report the status (died, returned home, transferred) of patients who participated in the May 2003 survey.
Kaiser et al., 2001	Cincinnati heat emergency period: 21 July to 2 August 1999	Cases: surrogate-reported in questionnaire to identify existing mental illness. Medical history from death investigation reports and toxicologic screening to determine psychotropic drug prescription and use. Three surrogates (next of kin, neighbours) per case.Controls: self-reported in questionnaire to identify existing mental illness and psychotropic drug prescription.	Heat related death determined by the Hamilton County Coroner according to the following criteria: 1. Body temperature of 40.6°C or higher at the time of death or immediately after death. 2. Substantial environmental or circumstantial evidence of heat as a contributor to death. 3. Absence of evidence of another cause of death if the decedent was found in a decomposed condition and was last seen alive during the heat wave.
Kim et al., 2014	Maximum ambient temperature	"Pre-existing neuropsychiatric condition was assessed through interviews with patients or the patient's family." "Patients were	Heatstroke (confirmed if a patient who had a body temperature greater than or equal to 38 1C with altered mental status).

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Table 2 (*continued*)

Author, publication year	Heat/heatwave measure	Mental health measure	Mortality measure Morbidity measure
		confirmed to have pre-existing medical conditions if they were diagnosed with the condition before developing heat illness or if they had taken medications for any of these conditions." Neuropsychiatric conditions include schizophrenia, Alzheimer's dementia, depression, Parkinson's disease, panic disorder, bipolar disorder, alcoholism, mental retardation, use of psychotropic drugs and unknown diagnosis of mental disorder.	
Larrieu et al., 2008	French heatwave: 1 August to 18 August 2003	Depressive symptomology assessed in both cohorts using the Centre for Epidemiology Studies Depression Scale (CES-D). In PAQUID it was referred to as "mood disorders" in 3C it was referred to as "depressive symptoms". PAQUID: psychologist administered the questionnaire in person with the participants at their home. Questionnaire included the CES-D. 3C: psychologist administered the questionnaire during a face-face interview. Questionnaire included the CES-D.	felt morbidity - "did you feel a deterioration of your health during the heatwave?" objective morbidity - occurrence of a morbid outcome during the heatwave declared by the subject or their close relative: dizzy spell, fall, loss of balance, hospitalisation or death. morbidity data was collected via phone interviewers and questionnaire completed between September to December 2003.
Layton et al., 2020	A heatwave was defined as two or more days above the 95th percentile of historical (1949-2010) zip code-specific maximum surface air temperatures (compared to normal summer temperatures). 14 days were added to the end of each heatwave period to capture lagged effects. If the grace period of one heatwave overlapped with the start of another heatwave event, they were considered one continuous event.	Heat-sensitising medication for mental health conditions: antipsychotics. Identified using Medicare pharmacy dispensing data from index hospitalisation discharge. Periods of heat-sensitising medication use vs non-use as the case and control periods. Use and non-use were defined based on individual patterns of medication initiation, refills and discontinuation.	heat-related hospitalisation (ICD-9) for heat-related illness in any diagnosis position in the hospital record. This includes explicit diagnoses of heatstroke and other closely-related conditions associated with excessive heat, including effect of heat and light, excessive heat, dehydration and exhaustion due to excessive exertion. Sensitivity analysis with a broader definition which included hyperosmolality and/or hypernatremia.
Mangoni et al., 2017	Heatwaves were defined as >=5 consecutive days of a maximum temperature of >=35C or >=3 consecutive days of a maximum temperature of >=40C. 5 heatwave periods occurred during the study period. There was a comparison of heatwave and non-heatwave periods.	Use of psychotropic medication was assessed by a trained pharmacist at the time of hospital presentation. Use of psychotropics, number of psychotropics used and specific categories of psychotropics were investigated. Categories of psychotropics: antidepressants, antipsychotics, drugs for bipolar disorder, drugs for anxiety and sleep disorders, drugs for ADHD, drugs for alcohol dependence, drugs for nicotine dependence and drugs for opioid dependence.	Morbidity: length of stay in hospital. Mortality: in-hospital mortality.
Martin-Latry et al., 2007	French heatwave: 1 August to 20 August 2003	Patients were considered as exposed if having taken at least one psychotropic drug. The name of the drug was recorded in clinical charts at admission. Subcategories of psychotropics: antidepressants, antiepileptics, anticholinergics, anxiolytics, hypnotics, antipsychotics and cholinesterase inhibitors.	Hospitalisation for heatstroke or hyperthermia. Heatstroke is defined as "body core temperature above 40.6°C with central nervous system symptoms". Hyperthermia is defined as "body core temperature above 38.3°C without identified aetiology (infection or other)".
Naughton et al., 2002	Chicago heatwave: 29 July to 6 August 1999	Standardised questionnaire administered to surrogates of the cases (telephone and in-person) and to controls in person. Questionnaires administered in person or by telephone by staff of the National Centre of for Environmental Health of the Centers for Disease Control and	Heat-related death determined by the Cook County Medical Examiner's Office according to the criteria published by the National Association of Medical Examiners, which includes: "an antemortem body temperature greater than or equal to 105°F, or if cooling has been attempted, a lower body temperature

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Table 2 (*continued*)

Author, publication year	Heat/heatwave measure	Mental health measure	Mortality measure Morbidity measure
		Prevention and the Chicago Department of Public Health. "History of condition below (and whether medication taken): Depression Other mental problems"	with known mental status changes or elevated liver enzymes."
Nitschke et al., 2013	Adelaide heatwave: 26 January to 7 February 2009	Self-reported use of medication for mental health. Questionnaire delivered using computer assisted telephone interviewing which was piloted twice before use in the study.	Self-reported heat-health outcomes including anxiety, loss of balance/ dizzy, a fall, headache, shortness of breath, heat stress, heart condition, something else or any of these symptoms in 2009.
Nordon et al., 2009	2 periods were compared Before heatwave: 1 August to 4 August 2003 During heatwave: 5 August to 13 August 2003	Use of psychotropic medication as indicated by drug dispensation in July 2003. Data was available at the therapeutic and pharmacological class as well. Therapeutic class: anxiolytics/ hypnotics, antidepressants, antipsychotics and mood stabilisers.	All-cause mortality.
Oudin Åström et al., 2015	A heatwave was defined as two consecutive days with temperatures exceeding the 95th percentile of the mean apparent temperature. The two days following a heatwave were also considered heatwave days to account for delayed effects. The percentile calculations were based on daily temperature observations for the summer months from 1995-2008 from airport weather stations in both cities.	Hospitalisation for a psychiatric condition extracted from the regional Hospital Information system in the Lazio region (Rome) and from the patient register at The National Board of Health and Welfare for the city of Stockholm (ICD9: 291–299, 300.4, 301.1, 309.0, 309.1, 311, ICD10: F20–F22, F31, F32, F34, F43)	All-cause mortality/daily death numbers.
Pillai et al., 2014	Extreme heat events: >=2 days above the 99th percentile for daily maximum temperature plus a 3-day buffer. Each hospitalisation was classified as to whether or not it occurred during an extreme heat event.	Non heat-related diagnostic codes: behavioural disorders (ICD-9: 290-319). It is unclear if these were identified as comorbidities on presentation to the emergency department or if they were extracted from existing diagnoses or previous hospitalisations.	Hospitalisation (vs discharge).
Rocklöv et al., 2014	Maximum ambient temperature: per 1C increase in temperature Heatwave duration: number of days in sequence above the 98th percentile of temperature (in summer June-August).	Mental disease: previous hospitalisation for mental disease more than 28 days before death (ICD-9: 290-319; ICD-10: F). Substance abuse: previous hospitalisation for substance abuse in a period 28 days to 2 years before death (ICD-9: 303-305; ICD-10: F10-19). Hospitalisation data was sourced from the National Hospital Discharge Register.	All mortality from non-external causes.
Schifano et al., 2009	The effect of apparent temperature at 30 °C versus 20 °C	Hospitalisation 2 years preceding death excluding the last 28 days before death based on primary cause of admission and secondary contributing diagnosis. Psychoses (ICD-9: 290-299) Depression (ICD-9: 300.4, 301.1, 309.0, 309.1, 311) Data extracted from the Regional Hospital Information System and the Municipality Population Registry.	Death due to noninjury causes in during the study period.
Stafoggia et al., 2006	The effect of apparent temperature at 30 °C versus 20 °C	Hospitalisation 2 years preceding death excluding the last 28 days before death based on primary cause of admission and secondary contributing diagnosis Psychoses (ICD-9: 290-299) Depression (ICD-9: 300.4, 301.1, 309.0, 309.1, 311) Data sourced from regional hospital discharge files.	Death due to noninjury causes in during the study period.
Stivanello et al., 2020	Mean apparent temperature from 18 monitoring stations of the Regional Agency for Prevention,	Mental Health Department (MHD) case registry covers ICD-9CM diagnoses. Psychiatric diagnoses of the	Primary outcome: death for all causes. Secondary outcomes: deaths due to natural, external causes and

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Table 2 (*continued*)

Author, publication year	Heat/heatwave measure	Mental health measure	Mortality measure Morbidity measure
	Environment and Energy of Emilia Romagna. Cut-off value of 24 °C (for every 1 °C above the cut-off value…)	MHD population include schizophrenia and other functional psychosis (ICD-9: 295, 297, 298 (excl. 298.0), 299 (excl. 299.0, 299.00, 299.01)), mania and bipolar affective disorders (ICD-9: 296.0, 296.1,296.4, 296.5, 296.6, 296.7, 296.8 (excl. 296.82)), depression (ICD-9: 296, 296.2, 296.3, 296.82, 296.9, 298.0, 300.4, 309.0, 309.1, 309.1, 311), neurotic disorders (ICD-9: 300 (excl. 300.4), 306, 307.4, 307.8, 307.9, 308, 309.2 (excl. 309.28), 309.8, 316), disorders of personality and behaviours (ICD-9: 301, 302, 312), alcoholism and substance abuse (ICD-9: 291, 292, 303, 304, 305), dementia and cognitive decline and other (ICD-9: 307 (excl. 307.4, 307.8, 307.9), 309, 309.3, 309.4, 309.5, 309.9, 313, 314, 315). Those who have accessed the MHD at least once compared to those who have never access the MHD.	causes categorised according to the ICD chapters.
Vandentorren et al., 2006	Thermal index: the mean surface temperature for a 200m radius around the subjects home measured from satellite pictures taken in the morning of 9 August 2003.	Family physicians of cases and controls were contacted to obtain information about pre-existing medical conditions. One of these conditions was mental disorders, however this was not clearly defined.	All cause deaths. Cardiovascular-related deaths. Heat-related deaths defined as those whose death certificates mentioned dehydration, hyperthermia or heat stroke as the primary cause of death.
Zhang et al., 2013	Heatwave defined as ≥35 °C for 3 or more days. Adelaide heatwave: 28 January to 1 February 2009 with the following maximum temperatures; 45.7 °C, 43.4 °C, 43.1 °C, 41.1 °C and 40.6 °C. Non-heatwave control periods: 16-25 January and 11-20 February each with an average maximum temperature of 30°C	Mental disorders as an existing co-morbidity collected from the medical records of patients admitted to the public hospitals in Adelaide.	Heat-related hospitalisation (ICD-10: X30, T67 and E86 as primary or additional diagnosis (maximum of 25 diagnosis codes for one patient).
Zhang et al., 2017	Heatwave period: 28 January to 1 February 2009. This was defined according to the methods of the Australian Bureau of Meteorology. The maximum temperatures on these days were 45.7, 43.4, 43.1, 41.1 and 40.6 °C.	Self-reported depression assessed using a questionnaire. "Did you have the following diseases in summer 2009? Depression: yes/no/ unsure." Questionnaire designed and developed based on literature review and was conducted face-to-face and over the phone by a trained interviewer.	All-cause mortality obtained from the South Australian Department of Health and Ageing or the South Australian Coroner's Office.

However, after the heatwave, individuals with psychotic states were at greater risk of dying. The three studies at the lowest risk of bias (appendix 5) were the two studies which found that individuals with mental illness were at a reduced risk of dying following heat exposure (Mangoni et al., 2017; Schifano et al., 2009), and the study which found that mortality risk was higher or lower depending on the type of mental health medication (Nordon et al., 2009). The remaining studies were at moderate risk of bias with a mixture of high, low and unclear risk of bias amongst RoBANS domains.

Three studies only included unadjusted analyses of mental illness (Davido et al., 2006; Kaiser et al., 2001; Naughton et al., 2002). All of these found that individuals with mental illness were more likely to die following heat exposure than individuals without the conditions.

3.3. Heatwaves and morbidity

Mental ill-health was investigated as an effect modifier of the relationship between heatwaves and morbidity in seven studies (Larrieu et al., 2008; Layton et al., 2020; Mangoni et al., 2017; Martin-Latry et al., 2007; Nitschke et al., 2013; Pillai et al., 2014; Zhang et al., 2013) (Table 2). Four studies investigated mental illness (Larrieu et al., 2008; Nitschke et al., 2013; Pillai et al., 2014; Zhang et al., 2013), and three examined mental health medication (Layton et al., 2020; Mangoni et al., 2017; Martin-Latry et al., 2007). Of six studies that adjusted for confounding, five found that individuals with mental illness were more likely to experience poor health/morbidity following heat exposure compared to individuals without mental illness (Larrieu et al., 2008; Layton et al., 2020; Martin-Latry et al., 2007; Nitschke et al., 2013; Pillai et al., 2014) (Table 3). In contrast, one study found that individuals taking psychotropic drugs were likely to spend less time in hospital following heat exposure than individuals not taking psychotropic drugs (Mangoni et al., 2017). This divergent study was at a lower risk of bias than the other adjusted analyses which were at moderate to high risk of bias across most RoBANS domains (appendix 5).

3.4. Ambient temperature and mortality

Four studies examined the relationship between mental illness,

Table 3
Study results.

Author, publication year	Analysis	Confounding factors	Results
Bélanger et al., 2014	Chi square test. Univariate weighted logistic regression. Multivariate and weighted logistic regression using generalised estimating equations methods.	Sampling weights were used to compensate for possible over or underrepresentation of census dissemination areas and households given their total numbers can be different between cities Census deprivation areas were sampled in a such a way that the sampling and the population distributions of age and sex variables are as close as possible. Apart from the weighting between cities, no other variables were adjusted for in the bivariate analysis.	Prevalence of reported adverse health impacts during very hot and humid summer conditions. Individuals with mental disorders: 79.8 % (95 %CI 71.9-87.7) Individuals without mental disorders: 43.0 % (95 %CI 41.1-44.9) Crude odds ratio 5.3 (95 %CI 3.2-8.6)
Davido et al., 2006	Chi square test Fisher's exact test Significance level of $p < 0.05$	None	Prevalence Depression 9 % of survivors had depression compared to 6.5 % of non-survivors ($p \geq 0.05$). Psychotropic medications 46.1 % of survivors were on psychotropic medication compared to 68.2 % of non-survivors ($p < 0.05$).
Hall, 2021	Multivariate conditional logistic regression.	Matching on sex and age. Model 1: statistical adjustment for age. Model 2: statistical adjustment for age, patient race/ethnicity and insurance status. Model 3: statistical adjustment for all visitor history variables and sociodemographic factors visitor history variables: alcohol problems	Adjusted odds ratios Model 3 Alcohol use disorders: 11.15 (95 %CI 3.87-32.17) Drug use disorders: 0.45 (95 %CI 0.14-1.54) Psychiatric disorders: 1.35 (95 %CI 0.57-3.19)
Holstein et al., 2005	Poisson regression with 95 % Wald confidence intervals. Poisson model tested by Pearson's chi-square test.	Sex and age	Mortality rate ratios (individuals with psychotic states compared to individuals without psychotic states) for the 3 time periods. Before heatwave: 0.93 (95 %CI 0.64-1.33) During heatwave: 0.93 (95 %CI 0.65-1.34) After heatwave: 1.13 (95 %CI 0.83-1.54)
Kaiser et al., 2001	Univariate exact conditional logistic regression Age-stratified (<65 and ≥65) analysis was performed but results were not reported.	Matching on age and neighbourhood. No confounding factors adjusted for in analyses.	Crude odds ratios Mental illness: 14.0 (95 %CI 1.8-633) Psychotropic medication: 3.30 (95 %CI 0.5-38.1)
Kim et al., 2014	Chi square test. Fisher's exact test. *p*-value for significance<0.05 Multivariate logistic regression.	Age, sex, maximum ambient temperature, area of residence, relative wealth, place of occurrence, and all other diseases.	Adjusted odds ratio 7.69 (95 %CI 4.06-14.54)
Larrieu et al., 2008	Chi square test Multivariate logistic model built using stepwise forward regression to include variables associated with morbidity in the univariate analysis ($p < 0.25$)	PAQUID: living in a top floor apartment, presence of a bathroom, moment of time out, age, respiratory disease, neurological disease, diabetes, cardiovascular disease, possibility to ventilate the house and stopping usual activities 3C: living in a top floor apartment, possibility to ventilate the house, to dress lighter than usually, asthma, depression, age, primary educational level, living in a single room and stopping usual activities	Adjusted odds ratio (3C, felt morbidity outcome) 2.9 (95 %CI 1.4-5.8)
Layton et al., 2020	Conditional Poisson regression. Statistical interaction term between medication use and heatwave status.	Study design controls for time invariant confounding factors. Total follow-up time was a maximum of 3 months so it was anticipated that there would be little change in time-varying confounding factors.	Rate ratios Whole cohort Heatwave only: 1.26 (95 %CI 1.14) Drug only: 1.37 (95 %CI 1.14-1.66) Drug and heatwave: 1.51 (95 %CI 1.20-1.91) *p*-value for interaction term: 0.23
Mangoni et al., 2017	Chi square test. Univariate competing risks regression. Multivariate competing risks regression. Univariate logistic regression. Multivariate logistic regression.	Statistical adjustment for age, gender, ambulance arrival, metropolitan ambulance transport service priority code, weekend presentation, heatwave number, Charlson Comorbidity Index, arthritis,	Adjusted odds ratios Psychotropic use Heatwave: 0.35 (95 %CI 0.08-1.60, $p = 0.18$) Non-heatwave: 1.02 (95 %CI 0.55-1.89, $p = 0.94$) *Age-stratified*

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Table 3 (*continued*)

Author, publication year	Analysis	Confounding factors	Results
	Wald tests to assess differences in estimated effects for heatwave and non-heatwave periods. Type 1 error rate for all test of statistical significance was set at $p < 0.05$.	cancer, chronic kidney disease, osteoporosis, chronic obstructive lung disease, ischemic heart disease and stroke, and whether the patient was discharged home. Additional analysis which included age stratification (65-80 years vs 80+ years).	*results* Psychotropic use, 65-80 Non-heatwave: 0.38 (95 %CI 0.13-1.17, $p =$ 0.09) Psychotropic use, 80± Heatwave: 1.85 (95 %CI 0.30-9.46, $p = 0.51$) Non-heatwave: 1.79 (95 %CI 0.77-4.18, $p =$ 0.17) Sub-distribution hazard ratios Psychotropic use Heatwave: 0.89 (95 %CI 0.69-1.14, $p = 0.36$) Non-heatwave: 0.82 (95 %CI 0.72-0.94, $p =$ 0.003) *Age-stratified results* 65-80 Heatwave: 0.79 (95 %CI 0.57-1.09, $p = 0.15$) Non-heatwave: 0.88 (95 %CI 0.75-1.04, $p =$ 0.15) 80± Heatwave: 1.22 (95 %CI 0.78-1.91, $p = 0.37$) Non-heatwave: 0.73 (95 %CI 0.61-0.89, $p =$ 0.33)
Martin-Latry et al., 2007	Univariate conditional logistic regression. Multivariate conditional logistic regression model constructed by starting with all variables with a univariate analysis of p-value< 0.05 then using backward stepwise procedure so that all variables in the model have a p-value<0.05.	Matching on age, gender and residential area. Final multivariate model also included anticholinergic drugs anti- cholinesterase inhibitors (anti-Alzheimer drugs).	Adjusted odds ratios Anxiolytics: 2.4 (95 %CI1.3-4.4, $p < 0.05$) Antipsychotics: 4.6 (95 %CI 1.9-11.2, $p < 0.05$)
Naughton et al., 2002	Univariate conditional logistic regression. Multivariate conditional logistical regression model contained variables that remained significant $p < 0.05$ predictors of heat related death.	Matching on age and neighbourhood Multivariate model included: having a working air conditioner, living alone and not leaving the home daily.	Crude odds ratios Psychiatric illness (depression + other mental problem): 5.7 (95 %CI 1.9-16.8)
Nitschke et al., 2013	Chi square test Simple logistic regression Multiple logistic regression models developed by simultaneous insertion of plausible influential risk variables with $p <$ 0.2 at the univariate level	Inverse probability weighting for age, area and gender according to the Estimated Residential population of South Australia from the Australia Bureau of Statistics. The multivariate models for the anxiety, heat stress and any symptoms as outcomes also included use of mobility aid in the model. The multivariate model for the headache outcome also included reduced health status as a variable.	Adjusted odds ratios Anxiety outcome: 6.1 (95 %CI 2.5-15.1, $p < 0.001$) Headache outcome: 2.7 (95 %CI 1.2-6.0, $p < 0.05$) Heat stress outcome: 4.6 (95 %CI 2.2-9.4, $p < 0.001$ Any symptoms outcome: 2.9 (95 %CI 1.4-6.0, $p < 0.05$)
Nordon et al., 2009	Univariate conditional logistic regression. Bilateral Wald test to look at interaction between psychotropic drug use and heatwave period. Multivariate conditional logistic regression included all variables with a univariate analysis where $p < 0.1$	Matching on age, gender and presence of chronic illness. Statistical adjustment for cardiotropic anti-dementia and anti-parkinsonian drug use in sensitivity analysis.	Adjusted odds ratios Anxiolytics/ hypnotics Before heatwave: 0.81 (95 %CI 0.70-0.93) During heatwave: 0.85 (95 %CI 0.79-0.93) Antidepressants Before heatwave: 1.23 (95 %CI 1.02-1.49) During heatwave: 1.71 (95 %CI 1.57-1.86) Antipsychotics Before heatwave: 1.45 (95 %CI 1.14-1.85) During heatwave: 2.09 (95 %CI 1.89-2.35)
Oudin Åström et al., 2015	Poisson regression with 95 % Wald confidence intervals	Stratification by age (50-74 years and 75+ years) and gender. Statistical adjustment for time trends. Offset term for change in cohort size.	Rome Relative risks Total: 1.21 (95 % CI 1.06-1.38) Relative risk ratios Women vs men: 1.16 (95 %CI 0.89-1.52) 75+ vs 50-74: 1.05 (95 %CI 0.78-1.40) Stockholm Relative risks Total: 1.33 (95 % CI 1.10-1.61) Relative risk ratios Women vs men: 1.09 (95 %CI 0.74-1.61)

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Table 3 (*continued*)

Author, publication year	Analysis	Confounding factors	Results
			75+ vs 50-74 years: 1.21 (95 % CI 0.79-1.85)
Pillai et al., 2014	Univariate logistic regression. Multivariate logistic regression.	Demographic variables, comorbidities, SES, geographic and temperature variables	Adjusted odds ratios 3.68 (95 %CI 3.08-4.40, $p <$ 0.0001)
Rocklöv et al., 2014	Multivariate logistic regression.	Stratification by age (<65 years and ≥65 years). Adjusted for time trends, weekday patterns and national holidays. Adjusted for air pollution (daily mean levels of nitrogen oxides and ozone).	Adjusted odds ratio associated with heat wave duration Mental disease, <65: 1.054 (95 %CI 0.9032-1.230) Mental disease, ≥65: 1.099 (95 %CI 1.027-1.175) Adjusted odds ratio associated with a one unit increase of maximum temperature lag 0-1 Mental disease, <65: 1.004 (95 %CI 0.990-1.017) Mental disease, ≥65: 1.011 (95 %CI 1.002-1.019)
Schifano et al., 2009	Multivariate Poisson regression model developed using manual backward stepwise procedure. Relative effect modification index	Stratification by age (65-74 and 75+ years) Statistical adjustment for age, gender and presence/absence of heatwave. Multivariate model also included: socio-economic status, civil status, presence or absence of each of the selected groups of diagnosis and the number of hospitalizations for conditions not associated with an increased mortality risk from high temperatures.	Adjusted mortality relative risk 65-74 years Psychiatric disorders: 1.08 (95 %CI 1.01-1.15) No psychiatric disorders: 1.27 (95 %CI 0.91-1.77) 75± years Psychiatric disorders: 1.14 (95 %CI 1.10-1.18) No psychiatric disorders: 1.16 (95 %CI 0.99-1.35) REM index (*p*-value) 65-74 years: 1.18 (0.350) 75± years: 1.02 (0.894)
Stafoggia et al., 2008	Concentration response curve to determine relationship between apparent temperature and noninjury mortality. Conditional logistic regression with the exposure variable modelled as a cubic penalised spline. Relative effect modification index (REM).	Case-crossover study design controls for time-invariant confounding factors. Selection of exposure and non-exposure periods were on the same day of the week in the same month. Statistical adjustment for temporary population decrease in the summer period, holidays, coarse particulate matter and barometric pressure. Sensitivity analyses using different temperatures as comparisons for heat and non-heat exposure, ozone and age restriction.	*Combined cities results* Adjusted odds ratios Psychoses: 1.70 (95 %CI 1.39-2.09) Depression: 1.71 (95 %CI 1.23-2.38) REM index (*p*-value) Psychoses: 1.28 (0.024) Depression: 1.28 (0.149)
Stivanello et al., 2020	Conditional logistic regression z-test to study effect modification	Study design controls for time invariant confounding factors. Statistical adjustment for ozone levels and population decrease over holidays.	Adjusted odds ratios All cause of death Non-MHD population: 1.019 (95 %CI 1.012-1.026, $p <$ 0.001) MHD population: 1.055 (95 %CI 1.024-1.086, $p <$ 0.001) Z test *p*-value All cause of death: 0.0255
Vandentorren et al., 2006	Univariate conditional logistic regression. Multivariate conditional logistic regression model included variables which had $p < 0.20$ in the univariate analysis and had $p < 0.10$ in the multivariate model. 3 separate analyses for each cause of death: all cause, cardiovascular-related, heat-related	Matching on age, sex and residential area. Additional statistical adjustment for age in multivariate model using a linear term. Other variables in all-cause model: occupation, living conditions, going out, dressing, mobility and history of disease (cardiovascular disease, high blood pressure and neurological disease) Other variables in cardiovascular-related deaths model: occupation, living conditions, going out, dressing, mobility and history of cardiovascular disease	Adjusted odds ratios All-cause death: 5.02 (95 %CI 1.44-17.50, $p <$ 0.10) Cardiovascular-related death: 5.35 (95 %CI 1.36-21.01, $p <$ 0.10)
Zhang et al., 2013	Chi square test Multivariate conditional logistic regression which included variables with a $p < 0.1$ in the univariate analysis.	Humidity and ozone levels as well as patterns of the days of the week were investigated but found to not be sufficiently different to include in the analysis	Prevalence of mental disorders Individuals hospitalised during the heatwave: 20 % Individuals hospitalised during the non-heatwave: 19 % $p = 0.792$
Zhang et al., 2017	Chi square test. Simple conditional logistic regression Multivariate conditional logistic regression. Multivariate model was developed by including all	Matching on age and gender. Multivariate analysis adjusted for: non-European ethnic, married/de facto, north facing building, living alone, having pets, air conditioning	Adjusted odds ratio (standard error, *p*-value) 5.36 (5.16, 0.081)

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Table 3 (*continued*)

Author, publication year	Analysis	Confounding factors	Results
	variables that were significantly ($p < 0.2$) associated with the outcomes in the univariate analysis.	in house, air conditioning in bedroom, easy ventilation, having private health insurance, having emergency button, having a social activity more than once a week, heart disease, asthma, respiratory disease, kidney disease, diabetes, dementia, depression, confined to bed, need of assistance for daily activities, use of air conditioning and use of refreshment.	

ambient temperature and mortality (Hall et al., 2021; Rocklöv et al., 2014; Stafoggia et al., 2006; Stivanello et al., 2020) (Table 2). All four studies found that individuals with mental illness exposed to high ambient temperatures were more likely to die than individuals without mental illness (Table 3). These studies tended to be at a low to moderate risk of bias across RoBANS domains (appendix 5).

3.5. Ambient temperature and morbidity

Only two studies investigated mental illness in the context of ambient temperature and morbidity (Bélanger et al., 2014; Kim et al., 2014) (Table 2). Both studies found individuals with a mental illness were more likely to experience morbidity outcomes following high temperature exposure than individuals without a mental illness (Table 3). However, one study only conducted unadjusted analysis with mental ill-health and was at a high risk of bias across most RoBANS domains (Bélanger et al., 2014) (appendix 5).

3.6. Bias assessments

The RoBANS results demonstrated variability in study quality (appendix 5). The ROBIS assessment found that overall, this systematic review was at a low risk of bias (appendix 6). However, in keeping with this review being largely based on observational studies, GRADE assessment suggests findings may change on publication of future studies that provide further evidence on effect modification of health effects of heat exposure by mental health status.

4. Discussion

Studies investigating transient heat exposure found that individuals with mental illnesses were more likely to die or experience worse morbidity than individuals without mental illnesses (Bélanger et al., 2014; Hall et al., 2021; Kim et al., 2014; Rocklöv et al., 2014; Stafoggia et al., 2006; Stivanello et al., 2020). However, studies investigating heatwaves displayed greater variability in their findings. One possible explanation is that there was much greater variability in how cumulative heatwave exposures were defined, potentially leading to differences in the effect modification of mental illness observed across studies. Previous systematic reviews have also found that differences in heatwave definitions can alter the magnitude of effects (Liu et al., 2022). It may also be that heatwave periods compared to a single day of high temperature are easier to predict and prepare for. This applies for both individuals and for service providers (Kotharkar and Ghosh, 2022). In addition, we note that studies investigating mortality outcomes tended to be at a lower risk of bias than those investigating morbidity outcomes. This is because lack of blinding is unlikely to bias outcome assessment and studies are at a reduced risk of selective outcome reporting.

Regardless of whether mental illness modifies the effects of heat on health, individuals with mental illness tend to be more vulnerable to poor health outcomes (Lõhmus, 2018). Further, people who experience low income, unemployment, social exclusion and/or housing insecurity are more likely to have mental illness (Shim et al., 2014). Therefore, all public health interventions and strategies, including those for extreme heat events, should contain specific measures to target individuals with mental illness (Kotharkar and Ghosh, 2022; World Health Organization, 2008). This will help to improve conditions for individuals with mental illness which is an important part of working towards health equity and improving population health (Sampson et al., 2013; Shim et al., 2014; World Health Organization, 2008).

Strategies to target individuals with mental illness during extreme heat events could include monitoring use of psychotropic medication and targeted public health messaging to encourage adaptive behaviours in individuals with mental illness (Lõhmus, 2018; Sampson et al., 2013). Such strategies are likely to be a cost-effective public health measures that reduce the burden on hospitals and other healthcare facilities during heat events by reducing severe heat-related illnesses (World Health Organization, 2008). Likewise, improving mental health services overall is also likely to reduce the vulnerability of people with mental illness during extreme heat events.

This review has many strengths. Well-defined and reproducible methods, adherence with PRISMA guidelines for the reporting of the protocol, search strategy and the systematic review process, independent assessment by two reviewers in most stages of the process, and forward and backward searching all reduce bias and increase the sensitivity of the search process (Harari et al., 2020; Page et al., 2021; Rethlefsen et al., 2021).

However, this study is not withstanding limitations. For pragmatic reasons, studies were restricted to those published in the English language. The search strategy was restricted to the years 2000 to 2022, however one heatwave in 1999 was included. Despite the presence of heatwaves outside the 21st century, the 22-year period was sufficient to gather relevant and useful information to understand the recent relationship between heat, mental health and overall health outcomes.

Further, despite excluding neurological disorders in screening criteria, many studies screened used a broader definition of mental illness which encompassed neurological conditions such as dementia (Hall et al., 2021; Kim et al., 2014; Pillai et al., 2014; Stivanello et al., 2020). The decision was made to exclude studies which exclusively focused on neurological conditions and include those examining mental illness and neurological conditions. This has likely introduced further heterogeneity into the results however, it has likely had a minimal impact on the overall interpretations and findings of this review.

In addition, included studies used a wide variety of methods to investigate effect modification which is likely to be of vary quality and individually introduce different forms of bias. All included studies were observational which produce a lower quality of evidence than randomised controlled trials. However, randomised controlled trials are not appropriate for studies investigating heat exposure and existing mental illnesses as effect modifiers.

Another point of difference was how variables were measured with some relying on official registries and others using self-reported surveys. Further variability between studies occurred due to the different analytical methods and confounders used to investigate the effect modification. These differences are almost impossible to avoid in a systematic review of observational studies but are still likely to impact on the quality and consistency of results.

The impact of extreme heat also varies geographically (Ebi et al., 2021). The specific climate and environment of a region or country influences the apparent temperatures experienced by the population (Ebi et al., 2021). Moreover, the existing infrastructure available to care for vulnerable people and the capacity of healthcare systems to cope with the impact of climate on patient numbers also alters the health outcomes from extreme heat events (Pörtner et al., 2022). This requires further study to guide contextually appropriate implementation of recommendations based on research.

Finally, all studies included in this review were conducted in OECD countries which are likely to have better infrastructure and healthcare. Therefore, the results may not be generalisable to non-OECD countries. This lack of research on low- and middle-income countries may be due to the different ways in which mental illness is diagnosed and treated as well as the social determinants of health, mental health stigma and the amount and quality of data collected on mental illness (many studies relied on linking multiple high-quality datasets) (Rathod et al., 2017). Commonly these issues are known as the treatment gap and the 10/90 gap (Mascayano et al., 2015; Maselko, 2017). The treatment gap describes the reality that most individuals in low- and middle-income countries do not receive treatment for their mental illness. The 10/90 gap describes the phenomenon that only 10 % of health research investigates 90 % of the global population meaning that the amount of research in high income countries is disproportionate to the size of the population (Maselko, 2017). This is even more concerning due to the greater number of individuals with mental illness residing in low- and middle-income countries. Over 80 % of individuals with a mental illness live in low- and middle-income countries (Rathod et al., 2017). As low- and middle-income countries host most of the human population and are in areas which are likely to experience the worst heat impacts of climate change, these areas need to be a priority for future research on the impacts of climate change on human health (Klingelhöfer et al., 2023).

Some clear objectives for future research have arisen in this review. Specific mental illnesses and medications need to be investigated as effect modifiers of the relationship between extreme heat and poor health outcomes. For example, a specific examination of the impacts of heat on individuals with schizophrenia or individuals taking antidepressants. This would allow for a better understanding of the potential mechanisms (reduced thermoregulation, maladaptive behaviour or social isolation) underlying the effect modification. Moreover, it would ensure that future reviews do not need to compare studies which have different, inconsistent and broader definitions of mental health conditions with one another.

Any future reviews which continue to broadly investigate effect modification from mental illness should include neurological conditions within that definition. This is because of the overlap in the symptoms and treatment of mental illnesses and neurological disorders and their inclusion together in primary research. Consistency in the definition of mental illness would thus improve the overall quality and certainty of evidence.

Future studies should also investigate effect modification in a greater number of cities and regions, including non-OECD countries. This is important to understand how differing climates, environments, health care systems and infrastructure (among other factors) may alter the role of mental illness as an effect modifier. Moreover, greater consistency in the use of relative measures to examine extreme heat events would allow for clearer comparisons across geographic areas. Use of relative temperature measures can account for the impacts of local temperature ranges, acclimatisation and urban heat island.

Finally, future studies need to measure and adjust for a wider range of variables. Many of the included studies only adjusted for age and sex while some included other proxy measures for socioeconomic status and other variables. This does not account for a range of other social and environmental factors which are likely to confound the investigation of mental illness as an effect modifier. Potential confounders include comorbidities, race and ethnicity, the built environment and humidity. The more data that is collected and accounted for, the more accurate and useful the research generated is likely to be.

Individuals with mental illness represent a vulnerable population prone to poor physical and mental health outcomes (Shim et al., 2014). Understanding this vulnerability, in the context of extreme heat events, is essential to developing evidence-based interventions to protect those with and without mental illness from the growing public health threat of climate change. There are a range of targeted and general strategies available, however there is still a great need for more research to further investigate this vulnerability and to improve existing and develop new public health interventions.

CRediT authorship contribution statement

Julia Meadows: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Adelle Mansour:** Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis. **Maria Rosa Gatto:** Writing – review & editing, Formal analysis. **Ang Li:** Writing – review & editing, Supervision, Investigation. **Amber Howard:** Writing – review & editing. **Rebecca Bentley:** Writing – review & editing, Supervision, Investigation, Funding acquisition, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Rebecca Bentley reports a relationship with The University of Melbourne that includes: funding grants. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2023.115678.

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