The physical health and lifestyle of young people at ultra-high risk for psychosis

A thesis submitted to the University of Manchester for the degree of Doctor of Philosophy in the Faculty of Biology, Medicine and Health

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Appendix

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Abbreviations

APS: Attenuated Psychotic Symptoms

ARMS: At Risk Mental State

BCT: Behaviour Change Technique

BMI: Body Mass Index

CAARMS: Comprehensive Assessment for At-Risk Mental State

CBT: Cognitive Behavioural Therapy

CHR: Clinical High Risk

COM-B Model: Capability, Opportunity and Motivation Model

CUD: Cannabis Use Disorders

CVD: Cardiovascular Disease

DALY: Disability Adjusted Life Years

EDIT: Early Detection and Intervention Team

EI: Early Intervention

EPOS: European Prediction of Psychosis Study

FEP: First Episode Psychosis

iBeep: Investigating the Benefits of Exercise for Early Psychosis

MRC: Medical Research Council

NAPLS: North American Prodrome Longitudinal Study

NHS: National Health Service

NICE: National Institute for Health and Care Excellence

PPI: Patient and Public Involvement

PRIMROSE: Prediction and Management of Cardiovascular Risk in People with Severe Mental Illness

PUFA: Poly-Unsaturated Fatty Acids

RCP: Royal College of Physicians

SMI: Severe Mental Illness

SUD: Substance Use Disorder

UHR: Ultra-High Risk

WHO: World Health Organisation

YLD: Years with Lived Disability

Abstract

A PhD thesis (Medicine) submitted to the University of Manchester for the Faculty of Biology, Medicine and Health by Rebekah Carney, July 2017.

The findings of this PhD provide a significant contribution to early intervention research. The ability to detect those at ultra-high risk for psychosis (UHR) has been made possible in recent years. It is well known that people with serious mental illness have poor physical health, yet prior to this PhD little was known about the physical health of UHR individuals. This PhD explores the physical health and lifestyle of the UHR group, and makes recommendations for the development of a physical health intervention.

A range of methods have been used including quantitative and qualitative methods, systematic reviews and meta-analyses, and a clinical audit. Therefore, a multifaceted approach to investigate the physical health and lifestyle of UHR individuals has been taken. Papers 1-3 suggest UHR individuals are more likely to live an unhealthy lifestyle than their peers. This includes lower levels of physical activity, and higher levels of substance use (generally cannabis, tobacco and alcohol). Paper 4 contains a clinical audit showing physical health and lifestyle factors are not monitored routinely in early detection services, despite the UHR phase being an ideal opportunity to intervene.

Living an unhealthy lifestyle can have a detrimental effect on physical and mental health. Papers 1-4 emphasise the need to intervene to promote a healthy lifestyle for the UHR group. In line with the Medical Research Guidelines for the development of complex interventions, a theoretical model is applied in Paper 5. The final paper presents a qualitative study with UHR individuals, their parents and clinicians to explore barriers and facilitators to living a healthy lifestyle and inform the development of a physical health intervention. A final evidence synthesis includes recommendations for future work and the clinical implications of this thesis.

The findings of this PhD provide an important and timely contribution to early intervention research. Prior to this work, the physical health of UHR individuals had been largely under researched. For the first time, this PhD presents evidence to suggest individuals at ultra-high risk for psychosis experience cardiovascular risk, and there is an opportunity to intervene to promote physical health. Although not all UHR individuals will develop psychosis, many will continue to experience difficulties with their mental health. Given that this group are also more likely to live an unhealthy lifestyle, it is important to take a holistic approach to treating those at imminent risk for psychosis, considering both mental and physical health.

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This thesis is dedicated to my lovely Nan, Marie Dillon who taught me to read and ask questions, and who herself never got the chance to shine.

The Author

In 2014 I was granted a highly competitive award to complete my PhD from the Economic and Social Research Council, based in the Faculty of Biology, Medicine and Health (Health and Wellbeing Pathway). I have a MSc in Cognitive Brain Imaging (Distinction) from the University of Manchester, and a First Class (BSc Hons) Psychology degree from the University of Liverpool.

During my time at Manchester I have contributed to the teaching of undergraduates, postgraduates and tutored as part of the Manchester Access Programme. I have assisted with public engagement events, including a week-long festival 'Think Physical', to address poor physical health in mental illness. Prior to this I worked as a research assistant on trials of exercise for early psychosis. However I noticed there was a missed opportunity for physical health promotion. Preventing the onset of ill-health is something I feel passionate about and the reason why I pursued funding for this PhD. Although I had a relatively strong academic background, my research experience prior to this PhD was limited. I therefore took advantage of the opportunity for personal development and engaged in courses on qualitative and quantitative methods, intervention development, clinical skills and behaviour change.

I have co-authored over 20 papers since starting at Manchester on a range of topics which extend beyond the scope of this PhD including: exercise for psychosis, mHealth, and sleep research. In addition to my PhD studies, I have two commissioned book chapters in the textbook 'Health promotion and wellbeing in people with mental health problems' (Bradshaw & Mairs, 2017). I have also published two letters to disseminate my findings, which are included in the appendices:

> Carney, R., Bradshaw, T., Firth, J., Cotter, J., and Yung, A.R. (2017). Lifestyle factors may be linked to symptoms of metabolic syndrome in people at risk for psychosis. *Schizophrenia Research.* 183, 47-48.

> Carney, R., Bradshaw, T., and Yung, A.R. (2016). Physical health promotion in people with schizophrenia: why we should consider the ultra-high risk state. *Acta Psychiatrica Scandinavica.* 133 (2), 166-167.

I was awarded additional funds to visit mental health services in Australia including Orygen: The National Centre for Excellence in Youth Mental Health, and Keeping the Body in Mind Program: Sydney. This has resulted in ongoing international collaborations. I have presented my research at local and international conferences, including the Early Intervention in Mental Health Conference (IEPA Milan, 2016), and MQ Mental Health Scientific Meeting (London, 2017), and will present at the International Association for Youth Mental Health conference in Dublin later this year (2017). I was also invited to participate and present at two international Medical Research Council workshops (Doha, Qatar, 2015; Jakarta, Indonesia, 2016).

Introduction

'If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health' Hippocrates (460-377BC).

Background

Physical and mental health

Living a healthy lifestyle can have profound benefits to a person's overall health and wellbeing. The link between physical and mental health is becoming much more apparent in both clinical and research settings. Terms such as "healthy body, healthy mind" and "no health without mental health" illustrate the shift in attitudes towards a more integrated approach to health care (Millard & Wessley, 2014; Prince et al., 2007), rather than treating mental and physical health in isolation. The link between physical and mental health can be demonstrated in a number of ways. First, living a healthy lifestyle and engaging in positive health behaviours such as exercise and eating a balanced diet, is associated with positive mental health and wellbeing (Harvey et al., 2010; O'Neil et al., 2014). On the other hand, poor mental health is associated with high levels of co-morbidity, cardiometabolic risk and the development of non-communicable diseases, suggesting both should be considered for overall wellbeing (De Hert et al., 2011; Osborn et al., 2007; Shiers, Bradshaw & Campion, 2015).

The benefits of living a healthy lifestyle are well known. A number of reviews have shown that exercise has a positive effect on mental health (Harvey et al., 2010; Firth et al., 2015; Rosenbaum et al., 2014; Schuch et al., 2016). Engaging in physical activity for example, improves mood and reduces anxiety and stress. It has also been linked to increased levels of happiness and life satisfaction (Richards et al., 2015). In light of this, the National Institute for Health and Care Excellence (NICE) recommend exercise as a non-pharmacological treatment to help with depression (NICE, 2010), and there is a growing interest in using exercise interventions for a range of other mental health disorders.

One area of research where the link between physical and mental health is particularly pertinent is the health of people with severe mental illnesses (SMI) such as psychosis and schizophrenia.

Psychotic disorders

Psychotic disorders, such as schizophrenia, affect approximately 1% of the population and cost society an estimated £12 billion per year (The Schizophrenia Commission, 2012). The symptoms of psychosis include positive symptoms of delusions, hallucinations, disorganised thoughts, speech or behaviour, and negative symptoms such as lack of motivation and interest (American Psychiatric Association, 2013). Psychotic disorders are associated with high economic and societal impact. According to the Global Burden of Disease Study, schizophrenia accounts for 1.1% of the world's total disability-adjusted life years (DALYs) and 2.8% of overall years lived with disability (YLD), (Theodoridou & Rossler, 2010). Looking after the physical and mental health of people with SMI has therefore become a clinical priority.

The 'scandal' of premature mortality

People with psychotic disorders experience significant physical health problems at a young age (Mitchell et al., 2013; Osborn et al., 2007; Shiers, Bradshaw & Campion, 2015). Increased rates of comorbid conditions such as diabetes, obesity, cardiovascular disease (CVD) and cancer contribute to an overall reduction in life expectancy between 10 and 25 years (Laursen, Munk-Olsen & Vestergaard, 2012; McGrath et al., 2008). For example, people with schizophrenia are almost three times more likely to have type 2 diabetes than the general population (Papanastasiou, 2013) and are significantly more likely to die from CVD or stroke (Osborn et al., 2007). Recently, there has been a decline in the number of CVD related deaths in the general population; yet people with SMI continue to be at increased risk, thus widening the health inequality gap further (Nielsen et al., 2013). This has been labelled a national

'scandal' which Thornicroft (2011) argues represents a cynical disregard for the lost lives of people with mental health problems.

Multiple factors contribute to the development of poor physical health in this group, many of which are modifiable (De hert et al., 2011; Henderson et al., 2015; Osborn et al., 2007). First, antipsychotic medication, the primary treatment for psychosis, is associated with rapid weight gain and metabolic disturbances (Alvarez-Jiminez et al., 2008). Sudden and sustained weight gain significantly increases the risk of an individual developing 'metabolic syndrome'; which is a cluster of co-occurring risk factors for CVD such as obesity, hyperglycaemia, hypertension and increased waist circumference (Alberti, Zimmet & Shaw, 2008; De Hert et al., 2011).

Second, health inequalities are further widened by inadequate monitoring and treatment of physical health in mental health services (Shiers, Bradshaw & Campion, 2015). NICE recommend all patients with psychotic disorders receive regular physical health assessments, including Body Mass Index (BMI), blood pressure, substance use, and blood testing (NHS England, 2016). However, the National Audit of Schizophrenia found that assessment and treatment of physical health fell substantially below standard (Crawford et al., 2014). BMI was only recorded in 50% of over 5000 people with schizophrenia, and in just 33% of patients who had a diagnosis of comorbid CVD. Further, even when cardiovascular risk factors are recognised in people with schizophrenia, research has shown they often do not receive appropriate treatments or physical health interventions to reduce this risk (Crawford et al., 2014; Davies, 2014).

Finally, high-risk behaviours such as smoking, substance use and physical inactivity are responsible for a large proportion of the physical health burden experienced by this group. People with psychotic disorders are significantly more likely than the general population to engage in behaviours that are detrimental to their health, (Henderson et al., 2015). For example, they are three times more likely to smoke (Royal College of Physicians; RCP, 2013), less likely to be physically active (Stubbs et al., 2016), and more likely to consume a poor diet (McCreadie, 2003), and misuse substances (Addy et al.,

2012; Koskinen et al., 2010). Even when socio-economic factors such as social class and urbanicity are taken into account, the link between schizophrenia and increased rates of substance use remains (Henquet et al., 2005).

Smoking and physical inactivity are two of the largest behavioural risk factors for cardiovascular related mortality in the general population (World Health Organisation, 2009). In the general population, levels of CVD risk are commonly assessed by taking into account a range of factors such as age, gender, family history, and metabolic health. For example, Framingham Heart Study risk scores are used in primary care to calculate a person's risk of CVD (D'Agostino et al., 2008). However, traditional methods do not account for additional risk factors affecting people with SMI, such as antipsychotic medication and psychiatric diagnoses. An alternative risk profile which successfully predicts CVD risk in people with SMI is the Prediction and Management of Cardiovascular Risk in People with Severe Mental Illness (PRIMROSE; Osborn et al., 2015). The PRIMROSE risk profile includes indicators such as BMI, blood pressure, presence of diabetes, lipid profile, risk behaviours (smoking and alcohol abuse), demographic information (age, social status) and SMI-specific factors (diagnosis, antidepressant/antipsychotic medication).

Early intervention to prevent co-morbidity

Identifying when cardiometabolic risk first occurs is critical. Intervening at the earliest possible stage may prevent or delay the onset of poor physical health. Previous research has shown that cardiometabolic risk factors, and indicators of poor physical health are present at an early stage, during the first episode of psychosis (FEP), and increase considerably with duration of illness (Beary, Hodgson & Wildgust, 2016; Foley & Morley, 2011; Perry et al., 2016). High rates of obesity in people with FEP have resulted in what has been described as 'an epidemic within an epidemic' (Bailey et al., 2012).

People with FEP display signs of metabolic abnormalities within just weeks of commencing antipsychotic treatment (Foley & Morley, 2011; De Hert et al.,

2006; Perry et al., 2016). FEP patients are particularly susceptible to antipsychotic induced weight gain, and experience sudden increases in body weight up to 4 times higher than people who have used antipsychotics before (Alvarez-Jiminez et al., 2006; 2008). However, there is also evidence of poor metabolic functioning in antipsychotic naïve patients with FEP (Misiak et al., 2017; Zhai et al., 2017), and first-degree relatives of people with psychosis (Baptista et al., 2011; Spelman et al., 2007). People with FEP are also significantly more likely to engage in high-risk behaviours at an early stage, including smoking (Myles et al., 2012), physical inactivity (Stubbs et al., 2016), and poor diet (McCreadie et al., 2003; Wang et al., 2012), at a similar level to people with SMI. This suggests that even in the absence of long-term antipsychotic use, FEP patients exhibit a range of potentially modifiable CVD risk factors.

Over recent years an international consensus has been established known as 'Healthy Active Lives' or the HeAL declaration, (Shiers & Curtis, 2014). Endorsed by health providers, governing bodies, policy makers and charities worldwide, the HeAL declaration focuses on looking after the physical health of people experiencing FEP. Several resources are available for health care providers including the '*Positive Cardiometabolic Health Resource'* to improve the physical health of people with psychosis and schizophrenia, the '*Primary Care Guidance on Smoking and Mental Disorders'* and a specific resource for people with FEP, '*Early Intervention in Psychosis – Keeping the Body in Mind',* (Campion et al., 2014; Lester et al., 2012; Shiers, Jones & Field, 2009).

There has also been growing interest in developing lifestyle interventions to reduce some of the CVD risk associated with SMI, particularly to prevent long-term physical health problems. Typically behavioural interventions have aimed to address risk behaviours such as inactivity in order to reduce antipsychotic induced weight gain (Curtis et al., 2016; Lovell et al., 2014). Although lifestyle interventions can improve a person's physical health, they can also have wider benefits to mental health and symptoms, cognitive functioning, and general wellbeing (Firth et al., 2016a). For example, a previous review and meta-analysis found that just 90 minutes of moderate-to-vigorous exercise per week was sufficient to reduce psychiatric symptoms in people with schizophrenia

(Firth et al., 2015). Behavioural interventions therefore appear to be an appropriate way to promote positive outcomes for people in the early stage of illness.

The UHR criteria

Typically research has focused on intervening during the first-episode, when people start taking antipsychotic medication. Yet it is unclear when cardiometabolic risk factors first arise, and whether it is possible to intervene even earlier. One way to investigate this further is to look at people in the stages preceding FEP.

Prior to the onset of psychosis, individuals typically experience a decline in their mental health and functioning. In recent years the ability to detect prodromal symptoms and identify young people at high or 'ultra-high risk' of psychosis (UHR) has been made possible. The UHR criteria, otherwise known as clinical high risk (CHR), or at-risk mental state (ARMS) enables individuals in the putative prodrome for psychosis to be identified (Fusar-Poli et al., 2013; Yung et al., 2003; Yung et al., 1996). The idea to map the onset and trajectory of psychosis originated in Melbourne, Australia in the 1990s (Yung et al., 1996) and a tool to identify the UHR state was developed; the Comprehensive Assessment for At-Risk Mental States (CAARMS; Yung et al., 2005). In order to meet UHR status a person must present with one or a combination of the following criteria; attenuated or sub-threshold psychotic symptoms (APS), brief limited intermittent psychotic symptoms (BLIPS) which spontaneously resolve, or a genetic risk (first degree family member with a psychotic disorder) combined with a recent decline in functioning (Yung et al., 2004).

UHR individuals are significantly more likely to experience a FEP within the next 2 years compared with the general population. Approximately 22% of UHR individuals will develop a psychotic disorder within 12 months, rising to 36% after 3 years (Fusar-Poli et al., 2012). The largest proportion of individuals at UHR present with APS, and it is suggested those with BLIPS are at greatest risk of experiencing psychosis (Fusar-Poli et al., 2016; Nelson, Yuen & Yung,

2011). In addition to being at risk for psychotic disorders, the UHR group are at-risk for a range of other mental health problems, including non-psychotic disorders and chronic poor functioning (Cotter et al., 2014; Lin et al., 2015). A large proportion of UHR individuals also have pre-existing comorbid diagnoses, mainly depressive and anxiety disorders at the time of presentation for mental health care, (Addington et al., 2017). This suggests that this group has an inherent vulnerability to poor mental health.

High rates of social disability and functional impairments are observed throughout the UHR phase (Cotter et al., 2014; Yung et al., 2015), and have been identified up to 15 years prior to the onset of psychosis (Velthorst et al., 2016). Prodromal symptoms typically occur during late adolescence or early adulthood; an important stage in many young people's lives for education, employment and becoming independent. A recent study found that UHR individuals were significantly less likely to be in long-term employment, and unemployment risk was associated with duration of untreated illness (Cotter et al., 2016). Functional impairments persist even in the absence of psychological symptoms and many individuals continue to experience long-term difficulties with their mental health (Addington et al., 2017; Cotter et al., 2014; Michel et al., 2017; Rutligliano et al., 2016).

Early clinical findings were based on a selection of large UHR cohort studies. Primary research was taken from the Personal Assessment and Crisis Evaluation (PACE) Clinic in Melbourne, Australia (Yung et al., 2004). Other cohorts which formed important contributions to UHR research include the North American Prodrome Longitudinal Study (NAPLS; Addington et al., 2007; Addington et al., 2012), and the European Prediction of Psychosis Study (EPOS; Klosterkotter et al., 2005; Ruhrmann et al., 2010). Interest in the UHR state has grown exponentially over the past decade, with early detection and intervention becoming an area of clinical importance across the world. Research in this group has typically had 3 main aims; (1) identifying people in the putative prodrome for psychosis and examining risk factors within the UHR group for poor outcomes (Yung et al.,1996; 2003; 2004; Klosterkotter et al., 1997, 2001; Haroun et al., 2006; Olsen & Rosenbaum, 2006; Cannon et al., 2008; Ruhrmann et al., 2010), (2) using the UHR group to make inferences

about the aetiopathology of schizophrenia (Pantelis et al 2003; Wood et al., 2011; Mechelli et al., 2011, 2017; Koutsouleris et al., 2012; McGorry, 2013); and (3) early intervention to prevent the onset of psychosis (Olsen & Rosenbaum, 2006; Stafford et al., 2013; Van der Gaag et al., 2013; Ruhrmann et al., 2014).

Measures such as the CAARMS have been found to have high predictive validity and enable those at-risk to be identified (Yung et al., 2005; Daneault & Stip, 2013). In order to understand more about the development and onset of psychotic disorders, the UHR group have been monitored and assessed to identify specific risk factors for psychosis (Davies et al., 2016). A recent review by Fusar-Poli et al., (2017) published after this PhD work, summarised risk factors for transition across the lifespan, beginning with what has been defined as 'first-wave hits'. This includes prenatal and perinatal factors such as obstetric complications which have been linked with the development of psychotic experiences (Millan et al., 2016). 'Second-wave hits' then occur during the course of the lifespan and include risk factors such as trauma, childhood adversity (Yung et al., 2015), stress (Valmaggia et al., 2014, 2015), socio-economic status (Kirkbride et al., 2015), poor functioning (Kraan et al., 2015), and negative behaviours such as substance use (Kraan et al., 2016). Identifying risk factors for transition informs future research into the prevention of psychosis. However, there is a lack of information regarding the physical health and lifestyle behaviours of UHR individuals, and whether engaging in behaviours such as physical inactivity has an effect on the long-term outcome of this group.

Subsequent early intervention research has focused on establishing effective treatments and identifying risk factors for transition to psychosis. For example, previous research has shown it is possible to delay and prevent the onset of psychosis by intervening during the UHR phase, (Van der Gaag et al., 2013). The majority of trials have investigated the efficacy of psychosocial interventions on transition rates, such as cognitive behavioural therapy (CBT), (Morrison et al., 2004, 2012; Addington et al., 2011; Van der Gaag et al., 2012; McGorry, 2013; Ising et al., 2016), and general psychological interventions (Nordentoft et al., 2006; Bechdolf et al., 2012). A meta-analysis of 11 trials of

both psychosocial and pharmacological interventions, found early intervention can reduce the risk of developing psychosis by 54% within 12 months, (Van der Gaag et al., 2013). Psychological treatments are the preferred intervention for this group, based on positive findings from high quality trials, (Van der Gaag et al., 2013). Although there is evidence that pharmacological treatments also reduce the risk of FEP, serious metabolic side-effects confound their use as a primary treatment, (McGorry et al., 2002; McGlashan et al., 2006). For example, patients in one trial experienced significant weight gain of 8.8kg (McGlashan et al., 2006).

More recently polyunsaturated fatty acids (PUFA) have been trialled as a potential alternative to psychological therapies. When compared with a placebo, omega-3 PUFAs reduced the risk of transition to psychosis and showed prolonged symptomatic benefits over a median follow-up time of 6.7 years (Amminger et al., 2010; Amminger et al., 2015). Omega-3 PUFAs seemed to be a viable, safe and potentially low cost intervention for UHR individuals. However, since the start of this PhD, the recent NEURAPRO study has demonstrated that the intervention was no more efficacious than a placebo when combined with psychological therapies (McGorry et al., 2017). Therefore, in line with the National Service Framework for Access and Waiting Time Standards (NHS England, 2016), UHR individuals in the UK are currently offered psychological therapies, such as CBT, and mental health monitoring upon entry to specialised early detection and intervention services. However, more research is needed in this area to develop novel, non-invasive treatment options for this group.

In recent years there has been growing interest for the use of a clinical staging model of treatment (McGorry, 2010). The UHR cohort is a heterogeneous group, presenting with symptoms of varying intensity, duration and frequency. The trajectory of ongoing mental ill-health and diagnostic outcome also varies. Therefore, adopting a more general clinical staging model focusing on intervening to prevent distress and general psychopathology has been proposed to address broader mental health difficulties in this group (Fusar-Poli et al., 2013, 2014; McGorry, 2013; McGorry & Van Os, 2013). Behavioural interventions could be a useful, low-cost option for individuals who do not

require intensive support, yet this is an area which has not yet been explored in the UHR group. Continued advances in research with at-risk youth will help identify the most effective treatments to prevent long-term difficulties.

Gaps in research

The majority of research in the UHR group has focused on identifying risk factors for transition, and intervening early to improve mental health. Whilst this type of research is important, physical health has remained under-researched in this group. Little is known about the physical health and lifestyle of UHR individuals, and whether they are also experiencing heightened CVD risk. Prior to this PhD research there had been no attempt to investigate the lifestyles or health-behaviours of the UHR group. Yet, this group may be a valid target for healthy lifestyle interventions to improve mental health outcomes and reduce the risk for CVD, given the early onset of physical health problems in those with FEP and the serious health inequalities experienced later in illness. The UHR phase therefore represents a novel and unique opportunity to investigate this issue further, in people prior to the onset of psychosis.

Aim

The aim of this PhD was to assess the physical health and lifestyle of young people at ultra-high risk for psychosis in order to inform the development of a lifestyle intervention for this group.

Overview of thesis

This PhD thesis contains six separate but inter-related studies focusing on the physical health and lifestyle behaviours of the UHR group. This thesis will be presented in 'Alternate Format' style, to reflect the breadth of different studies conducted, all of which have been published in peer reviewed journals. Included research consists of two systematic reviews and meta-analyses, a clinical audit,

a cross-sectional quantitative analysis of existing cohort data, the application of a theoretical model and a qualitative study.

The Medical Research Council (MRC) framework for developing and evaluating complex interventions was used as a guide for this PhD research (Craig et al., 2008; Appendix C). Papers 1-4 focus on identifying an evidence base for a physical health intervention for the UHR group. Paper 5 builds on this evidence and describes a theory to underpin the development of an intervention. Paper 6 is a qualitative study which details a behavioural analysis of lifestyle factors in this group to further explore potential targets for an intervention for this group.

Papers and rationale

Physical health problems are present at an early stage, during FEP, however, it is unclear when these problems first arise, and if they are present prior to the onset of psychosis, during the UHR phase. Therefore, **Paper 1** describes a systematic review and meta-analysis of the existing literature in order to identify whether UHR individuals have higher rates of cardiometabolic risk factors than their peers. Both physiological measures of health and behavioural risk factors including smoking, diet, physical activity and alcohol use were explored. 47 eligible studies were included in the review, covering a range of risk factors. UHR individuals were 2.3 times more likely to smoke than controls and the rates of smoking were approximately 33%, (n=629, 17 studies). This is similar to the rates of smoking across all mental health conditions, (RCP, 2010). UHR individuals had low levels of physical activity, poor diet and high rates of alcohol abuse. Despite exhibiting a wide range of behavioural risk factors, UHR individuals were not more overweight than controls. This contrasts with FEP groups which have significantly higher rates of obesity than their peers (Foley & Morley, 2011). However, at the time of the review, studies assessing physical and metabolic health in this group were limited.

Substance use in this group was also relatively under-researched. The initial systematic review revealed (amongst other factors) tobacco and alcohol use were high in UHR cohorts, however, many studies did not have lifestyle

behaviours as a primary outcome, and some control groups were selected from healthy populations, which specifically excluded people with substance misuse. Therefore, in **Paper 2** pre-existing data from a large Australian cohort were analysed to examine the prevalence of substance use in a group at-risk for psychosis compared with help-seeking psychiatric controls. Here, substances such as cannabis, (which were not included in the initial physical health review) were also considered to establish whether this unhealthy profile extended to other behaviours.

Paper 2 showed UHR individuals have higher rates of substance use compared with an age-matched psychiatric control group. This relationship was not mediated by psychological distress, or other mental health symptoms such as depression or anxiety. Alcohol, tobacco and cannabis use often co-occurred in both groups suggesting this group are likely to engage in a cluster of behaviours which are detrimental to their overall wellbeing. Many existing studies examine the effect of cannabis use on the development of psychosis (Marconi et al. 2016). For example, previous reviews have shown cannabis use does not increase the risk of transition in the UHR group (Kraan et al., 2016); however, it was unclear whether UHR individuals were more likely to use cannabis than their peers. Previous reviews have shown individuals with FEP and schizophrenia are more likely to use cannabis or have cannabis use disorders (CUD) than controls (Koskinen et al., 2009; Myles et al., 2012). Given the findings from paper 2, a second review and meta-analysis was conducted focusing solely on cannabis use, to clarify whether cannabis use was also more common in the UHR group.

Paper 3 consists of a meta-analysis of 30 studies reporting cannabis use in the UHR group. The rates of cannabis use in this group were high and CUDs were significantly higher than controls. Further analyses were also conducted on the data to assess whether there were any clinically relevant differences in the UHR cannabis users compared with non-users. There was an association between cannabis use in the UHR phase and symptoms. UHR cannabis users had significantly higher rates of unusual thought content and suspiciousness than non-cannabis users. In the paper, possible reasons for this association are discussed and recommendations for early intervention are made.

From the initial three papers, there is evidence to suggest that not only are UHR individuals at increased risk for poor mental health; they are also at-risk for poor physical health, largely as a result of unhealthy lifestyle behaviours. High rates of cardiometabolic risk factors in this group are predominantly linked to living an unhealthy lifestyle. Given that people with schizophrenia experience significant physical health problems, the extent to which these factors were monitored and assessed in clinical services was considered. **Paper 4** contains a clinical audit of Early Detection and Intervention Services (EDIT) in Greater Manchester West. The case notes of a 12 month intake of UHR individuals were audited to identify whether physical health or lifestyle factors were monitored. Physical health and lifestyle factors were in fact poorly monitored in UHR services, and not assessed routinely. The implications for this are presented within Paper 4 along with recommendations for why physical health monitoring is important within this group.

The MRC framework recommends first identifying an evidence base for an intervention. From papers 1-4, there is evidence to suggest UHR individuals are engaging in a range of unhealthy lifestyle behaviours which can have an impact on both physical and mental health. As this group are often not on antipsychotic medication and it is usually the first time they have presented for mental health care, the UHR phase represents an important opportunity for early intervention. Behavioural interventions could help ameliorate potential risk for CVD in this group. Despite this, there have been no published interventions focusing on promoting physical health of UHR individuals.

The next stage of the MRC framework recommends identifying a theoretical basis to guide behaviour change. Existing behavioural theories were subsequently reviewed in an attempt to identify a framework to help inform intervention development. **Paper 5** contains a summary of the Capability, Opportunity and Motivation model of behaviour (COM-B Model; Michie, Van Stralen & West, 2011). The COM-B model states for behaviour to occur a person must have the capability, opportunity and motivation to do so. In Paper 5 this model is discussed in relation to the UHR cohort and need for a structured lifestyle intervention for UHR individuals is recommended.

Finally **Paper 6** contains a summary of the findings from a qualitative study conducted with twenty UHR individuals and a sample of their parents and clinicians. Using semi-structured interviews based around the COM-B model (Appendix D), the barriers and facilitators to living a healthy lifestyle were explored. A large scoping interview was conducted regarding all lifestyle factors including diet, exercise, and substance use to inform the development of a suitable intervention for this group. Participants reported a range of barriers to living a healthy lifestyle and a strong preference emerged for help with diet and exercise. Guided by the principles of the COM-B model, and the responses of all three groups, thematic analysis revealed the main barriers to living a healthy lifestyle were a lack of motivation and reduced opportunity as a result of emerging psychological difficulties and increased social withdrawal. The provision of social support and promoting autonomy were seen as important factors in facilitating the uptake of healthy behaviours.

In line with the MRC guidelines, an evidence synthesis is included prior to the discussion which makes recommendations for the development of future interventions for the UHR group. The final discussion chapter combines the findings of all six studies and raises the clinical importance of this work so far. Strengths and limitations of the work are discussed, along with how the findings from across these studies can be used to inform future work.

In the appendices some additional publications are included which are also relevant to this PhD work and have helped disseminate the findings further. The first includes a letter in response to a special edition of the journal *Acta Psychiatrica Scandinavica* which focused on improving the physical health of people with schizophrenia. The letter emphasises why physical health should also be promoted in the UHR group, citing relevant studies conducted for this PhD. A second letter is also presented which was published in response to a recent study published in *Schizophrenia Research* which found increased rates of metabolic syndrome in the UHR group (Cordes et al., 2016). The authors neglected to account for the potential role of lifestyle factors contributing to the development of poor metabolic health in this group, again highlighting the important findings from these PhD studies.

Paper 1

Cardiometabolic risk factors in young people at ultra-high risk for psychosis: A systematic review and meta-analysis

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Author Contributions:

Rebekah Carney conceived the original idea for the review, conducted the literature search, decided on eligibility criteria, screened the articles, conducted the data extraction and synthesis, conducted the meta-analyses and interpreted the findings. Rebekah created the first draft of the manuscript and completed all revisions following review by the co-authors.

Professor Alison Yung and Dr Tim Bradshaw also contributed to the design of the review, and provided methodological guidance and supervisory input. Jack Cotter and Joe Firth independently checked articles for eligibility. All authors critically reviewed and agreed on the submitted manuscript for publication.

Cardiometabolic risk factors in young people at ultra-high risk for psychosis: A systematic review and meta-analysis

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ABSTRACT

Background: The physical health of people with schizophrenia is poor, and associated with increased morbidity and mortality. Unhealthy lifestyles and side-effects of antipsychotic medication contribute to cardiometabolic dysfunction. Yet it is unclear when this unhealthy profile starts. We aimed to see if people at ultra-high risk for psychosis (UHR) have increased rates of cardiometabolic risk factors.
Method: An electronic search of MEDLINE, PsycINFO, Embase and the Cochrane Central Register of Controlled Trials was conducted on 1st May 2015 using terms associated with the ultra-high risk state and health. Eligible studies were peer-reviewed English language research articles with populations that met at-risk diagnostic criteria and reported cardiometabolic risk factors. A meta-analysis was conducted on smoking data, the cardiometabolic risk factor that yielded the most studies.
Results: Forty-seven eligible studies were identified. UHR samples had low levels of physical activity, and high rates of smoking and alcohol abuse compared with controls. No differences were found for body mass index. An overall pooled rate of smoking for UHR participants was 33% (95% CI = 0.24–0.42) and significantly more UHR individuals smoked compared with controls with a pooled odds ratio of 2.3 (P < 0.05; 95% CI = −1.48–3.48).
Conclusions: UHR samples display cardiometabolic risk factors which are largely modifiable. The UHR phase is an important opportunity for early intervention services to improve physical health.

1. Introduction

The physical health of people with schizophrenia is poor. They are at 2.5 times the risk of premature mortality and their life expectancy is 10 to 30 years lower than the general population (De Hert et al., 2011a; Saha et al., 2007; Wahlbeck et al., 2011). Despite advances in health care and pharmaceutical developments, the life expectancy gap continues to widen (Saha et al., 2007). A leading cause of premature mortality is cardiovascular disease, arising from increased rates of cardiometabolic risk factors such as obesity, hypertension, hyperglycaemia, and dyslipidaemia (Hennekens et al., 2005; Mitchell et al., 2013), as well as high rates of smoking (Control and Prevention, 2013; Krishnadas et al., 2012; McCreadie, 2003) and alcohol consumption (Addy et al., 2012; Drake and Mueser, 2002), poor diet (McCreadie, 2003) and low levels of physical activity (Daumit et al., 2005; Vancampfort et al., 2011).

The cause or causes of this poor cardiometabolic health is unclear. There is evidence of hyperglycaemia, dyslipidaemia and weight gain during the first episode of psychosis, within the first few weeks after initiating antipsychotic treatment (Correll et al., 2014; De Hert et al., 2006; Foley and Morley, 2011). Metabolic abnormalities increase considerably with illness duration (De Hert et al., 2006, 2011b). There is also evidence that antipsychotic-naïve individuals with non-affective psychosis have abnormal glucose tolerance (Fernandez-Egea et al., 2009), as do first-degree relatives of people with schizophrenia (Baptista et al., 2011; Spelman et al., 2007). This has led to the suggestion that cardiometabolic risk factors may be inherent to illness progression, and enhanced by antipsychotic medication (De Hert et al., 2006). Determining whether these factors are present before the onset of disorder and antipsychotic prescription could inform this debate.

One way this issue can be studied further is to consider the physical health of people prior to psychosis onset. The ultra-high risk (UHR) state (also known as the clinical high-risk (CHR) and at-risk mental state (ARMS) (Fusar-Poli et al., 2013)) allows the identification of people in the putative prodrome for psychosis (Miller et al., 2002; Yung et al., 1996). In order to meet UHR status an individual must exhibit one or a combination of the following characteristics: presence of attenuated psychotic symptoms, brief limited intermittent psychotic symptoms which spontaneously resolve or genetic-risk combined with recent decline in functioning (Yung et al., 2004). Approximately 30% of UHR individuals transition to full-threshold psychotic disorders within three years, and a large proportion of these individuals will develop

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schizophrenia (Nelson et al., 2013). These criteria have important implications for early intervention and allow us to examine the physical and psychological health of young people prior to onset of psychotic disorder.

We aimed to systematically review the literature to examine: (1) The prevalence of cardiometabolic risk factors in UHR populations; (2) Whether these cardiometabolic risk factors are related to psychological variables.

2. Method

This review was conducted according to PRISMA guidelines for reporting systematic reviews (Moher et al., 2009).

2.1. Eligibility criteria

Eligible studies were original research articles published in peer-reviewed journals, with populations meeting diagnostic criteria for 'at-risk', 'ultra-high risk' or 'clinical-high risk' (or similarly defined) of psychosis, based on a clinically validated instrument (Daneault and Stip, 2013). Studies reporting on either clinical or behavioural cardiometabolic risk factors within this population were included. Clinical assessments included body mass index (BMI), weight, blood pressure (BP), blood glucose and lipid levels. Behavioural cardiometabolic risk factors included tobacco and alcohol use, physical activity, fitness levels, and diet. Retrospective, cross-sectional and longitudinal studies were eligible. Intervention studies were included when relevant baseline measures were reported.

Studies including only subjects at genetic-risk, not meeting formal diagnostic criteria for being at-risk of psychosis were excluded, as were case studies, reviews and non-English language articles. When study samples overlapped across publications, the larger sample was included in the review. Studies reporting data solely relating to neuroimaging or neurotransmitters were excluded, as these are seen as a biomarker or psychosis endophenotype and not necessarily a marker of physical health.

2.2. Search strategy

An electronic database search was conducted on 1st May 2015 using Ovid MEDLINE, Embase, PsycINFO and the Cochrane Central Register of Controlled Trials (CENTRAL). The following keyword search terms were used: 'clinical high risk' or 'CHR' or 'ultra high risk' or 'UHR' or 'at risk mental state' or 'ARMS' or 'prodrom*' and 'psychos*' or 'psychot*' or 'schizo*' and 'health*'. The broad search term 'health*' was used to ensure that the maximum number of potential studies were retrieved, given the broad nature of the research topic. Reference lists of retrieved papers were hand searched, and experts in the field were contacted to identify additional relevant publications.

2.3. Study selection and data extraction

Three reviewers (R.C., J.C. and J.F.) independently screened articles for eligibility. Disagreements were resolved through discussion. A tool was developed to record: (1) study characteristics (author, year of publication, country of origin, study design); (2) sample demographics (sample size, gender, mean age); (3) instrument used to assess at-risk status; (4) cardiometabolic risk factors (measure, sample mean or prevalence reported); (5) psychological variables associated with cardiometabolic risk factors; and (6) summary of findings. Data extracted was grouped into specific risk factors, and narrative synthesis was conducted.

2.4. Meta-analysis

We also aimed to determine the prevalence of cardiometabolic risk factors in UHR samples, and compare this to healthy controls. Meta-analytic methods were applied to the most commonly reported risk factor, which was smoking. Individual study data for smoking prevalence among UHR individuals were pooled using proportional meta-analysis in StatsDirect 2.8 (StatsDirect, 2005). Additionally, an odds ratio meta-analysis was used to compare the rates of smoking in UHR with healthy controls. The amount of variance between studies was examined using Cochran's Q, and indexed using I^2 (which estimates the extent of variance caused by between-study heterogeneity rather than chance). A DerSimonian and Laird (1986) random-effects model was applied to all analyses to account for heterogeneity between studies (DerSimonian and Laird, 1986).

3. Results

3.1. Search results

The study selection and exclusion process is summarised in Fig. 1. Database searches retrieved 2281 unique citations after removal of duplicates, of which 1909 were excluded at the title-abstract stage and a further 327 after full-paper review. Full text articles were excluded if they did not examine cardiometabolic risk factors (n = 290), included an ineligible population (n = 7), were review papers or case studies (n = 23) or had an overlapping sample (n = 5). Two additional studies were also excluded due to insufficient detail being provided in the text or by the authors, following contact for further clarification. Two additional eligible papers were identified from reference lists and contact with researchers. Forty-seven unique citations were included (Table 1). Studies were conducted in Europe (n = 30; 63.8%), North America (n = 15; 31.9%), Australia (n = 1; 2.1%) and Asia (n = 1; 2.1%). Relevant data extracted from the studies can be found in Table 2.

3.2. Smoking

Seventeen studies reported smoking information (See Table 2). Proportionate meta-analysis revealed that 33% (95% CI = 0.24–0.42; I^2 = 82.4%; total pooled subjects n = 629) of UHR individuals were classed as smokers (Fig. 2). Furthermore, UHR individuals were more likely to be smokers compared with controls, with a pooled odds ratio of 2.3 (p < 0.05; 95% CI = 1.48–3.48; total pooled subjects n = 938), although substantial heterogeneity was observed between samples (I^2 = 78.8%) (Fig. 3). Most studies found UHR smokers consumed more cigarettes on average compared with controls (range 5–9 cigarettes per day; median 6). However, many of the studies excluded individuals with substance abuse (Amminger et al., 2010; Auther et al., 2012; Huber et al., 2014; Kristensen and Cadenhead, 2007; Smieskova et al., 2012), suggesting that the rate of smoking could have been even higher than that reported, given the co-occurrence between smoking and other substance use.

3.3. Alcohol use and abuse

Fourteen studies reported information about alcohol use (Table 2). The percentage of people who used alcohol was higher in control groups compared with UHR groups. Current alcohol use varied, ranging from 30% to 88%. Quantity of alcohol consumed per week did not differ between UHR and controls, varying from 1 unit to 8 units (median 6 units).

Ten studies reported alcohol abuse or alcohol use disorders. Comorbid alcohol use disorders were high, reaching up to 38% (Dragt et al., 2012) (Table 2). Self-reported rates of alcohol abuse ranged from 16% (Huber et al., 2014) to 40% (Hutton et al., 2011). However, the true prevalence may be higher, as many studies excluded subjects
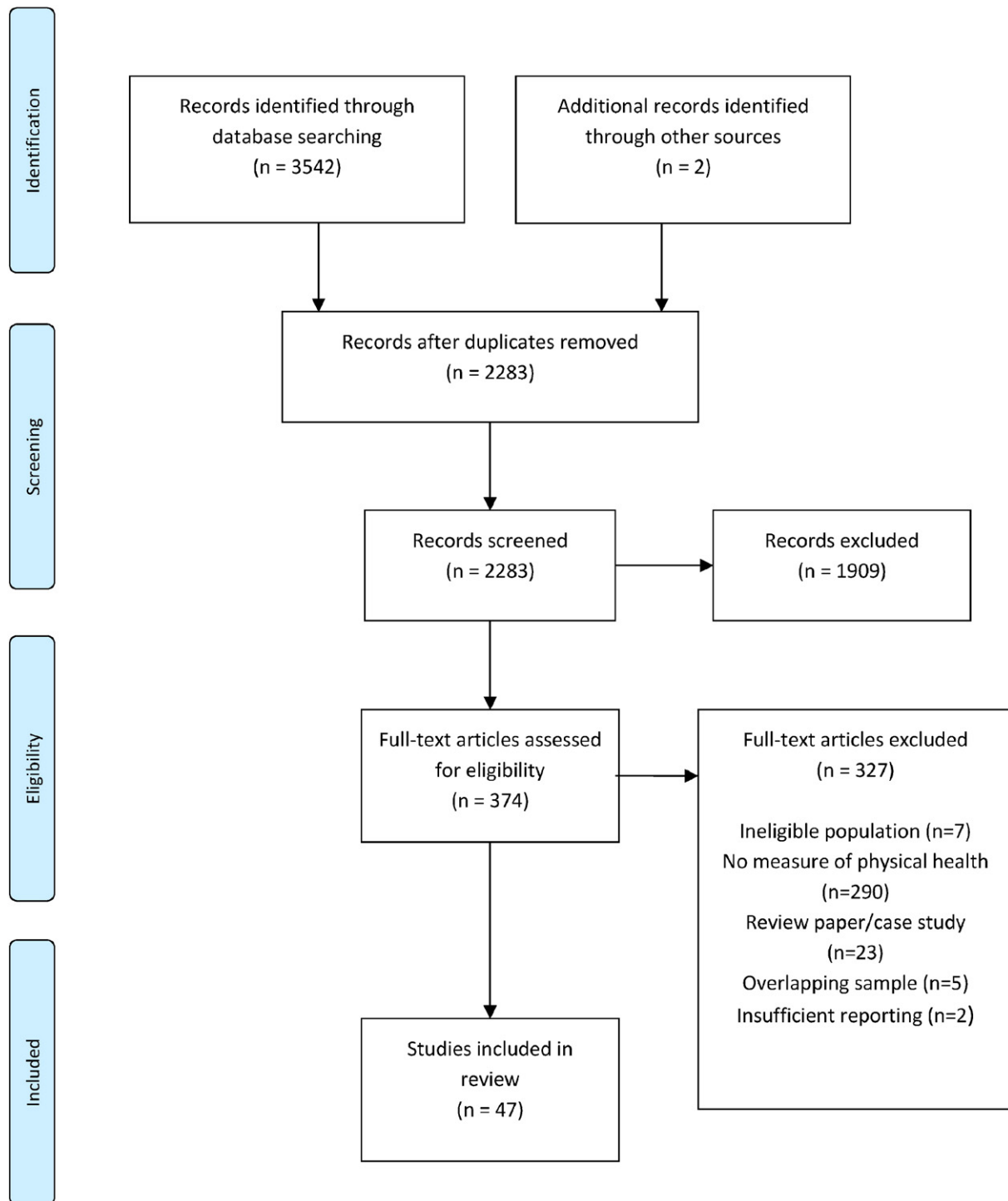
Fig. 1. PRISMA flow diagram.

who had current substance abuse or dependence (Amminger et al., 2010; Auther et al., 2012; Bernard et al., 2014; Huber et al., 2014; Kristensen and Cadenhead, 2007; Smieskova et al., 2012).

3.4. Physiological measures

Few studies reported physiological measurements. BMI values among the UHR group in five studies did not significantly differ from healthy controls, and fell within the normal weight range (range = 21–23; median 22); (Amminger et al., 2010; Bernard et al., 2014; Hayes et al., 2014; Labad et al., 2015; Stojanovic et al., 2014). In one study, systolic blood pressure was significantly lower in UHR subjects than controls, but diastolic blood pressure was no different (Pruessner et al., 2013). No studies documented blood glucose, cholesterol or lipid levels.

3.5. Physical activity levels

Four studies reported physical activity (Deighton and Addington, 2013; Hodgekins et al., 2015; Koivukangas et al., 2010; Mittal et al., 2013). UHR individuals had consistently lower levels of physical activity (Deighton and Addington, 2013; Hodgekins et al., 2015; Koivukangas

Table 1
Studies included in review.

Study reference and country	N (male/female)	At-risk screening instrument	Cardiometabolic risk factor	Study design
Addington et al. (2007) Canada	739 (432/307)	SIPS	Alcohol use	Longitudinal
Addington et al. (2012) Canada	468 (211/149)	SIPS	Alcohol use	Longitudinal
Amminger et al. (2010) Austria	81 (27/54)	PANSS	BMI, smoking, alcohol use	RCT
Andreou et al. (2014) Germany	58 (42/14)*	SIPS	Smoking	Cross-sectional
Auther et al. (2012) USA	160 (96/64)	SIPS	Smoking, alcohol use	Cross-sectional + longitudinal
Bernard et al. (2014) USA	58 (31/27)	SIPS	BMI, alcohol use	Cross-sectional
Brewer et al. (2003) Australia	112 (63/49)	SCID	Smoking	Cross-sectional + longitudinal
Brockhaus-Dumke et al. (2008) Germany	151 (106/45)	BSABS	Smoking	Cross-sectional + longitudinal
De Koning et al. (2014) Netherlands	28 (20/8)	CAARMS	Smoking	Cross-sectional
de la Fuente-Sandoval et al. (2011) Mexico	76 (52/24)	SIPS	Smoking	Cross-sectional
Dean et al. (2015) USA	87 (47/40)	SIPS	BMI	Cross-sectional + longitudinal
Deighton and Addington (2013) Canada	80 (39/41)	SIPS	Physical activity	Cross-sectional
DeVylder et al. (2013) USA	89 (74/25)	SIPS	Alcohol use	Cross-sectional + longitudinal
Dragt et al. (2012) Netherlands	245 (140/103)	SIPS/BSABS-P	Alcohol use	Cross-sectional + longitudinal
Egerton et al. (2013) UK	46 (25/21)	CAARMS	Smoking, alcohol use	Cross-sectional
Egerton et al. (2014) UK	131 (73/58)	CAARMS	Smoking, alcohol use	Cross-sectional + longitudinal
Fusar-Poli et al. (2011) UK	41 (24/17)	CAARMS	Alcohol use	Cross-sectional
Hayes et al. (2014) Germany	96 (65/31)	CAARMS	BMI, smoking	Cross-sectional
Hodgekins et al. (2015) UK	6840 (3218/3622)	CAARMS	Physical activity	Cross-sectional
Howes et al. (2011) UK	59 (37/22)	CAARMS	Smoking, alcohol use	Longitudinal
Hsieh et al. (2012) China	155 (73/82)	TP-DIS	Smoking	Cross-sectional + longitudinal
Huber et al. (2014) Switzerland	118 (81/37)	BSIP	Smoking, alcohol use	Longitudinal
Hutton et al. (2011) UK	34 (25/9)	CAARMS	Alcohol use	Cross-sectional
Koivukangas et al. (2010) Finland	6987 (3367/3620)	PROD screen	Physical activity	Cross-sectional + longitudinal
Korkeila et al. (2013) Finland	245 (137/108)	SIPS	Weight, smoking, alcohol use	Cross-sectional + longitudinal
Kristensen and Cadenhead (2007) USA	48 (26/22)	SIPS	Alcohol use, smoking	Longitudinal
Labad et al. (2015) Spain	83 (56/27)	CAARMS	BMI, smoking, alcohol, diet	Cross-sectional + longitudinal
Magaud et al. (2010) France	138 (92/46)	CAARMS	Alcohol use	Cross-sectional
Marshall et al. (2012) Canada	48 (33/15)	SIPS	Alcohol use	Longitudinal
Mittal et al. (2013) USA	56 (30/26)	SIPS	Physical activity	Cross-sectional
Mizrahi et al. (2012) Canada	34 (21/13)	SIPS	Smoking	Cross-sectional
Pruessner et al. (2013) Canada	42 (24/18)	CAARMS	Smoking, BP	Cross-sectional
Pruessner et al. (2011) Canada	92 (49/43)	CAARMS	Smoking	Cross-sectional
Quednow et al. (2008) Switzerland	113 (71/42)	ERIraos	Smoking	Cross-sectional
Rapp et al. (2013) Switzerland	60 (39/21)	BSIP	Alcohol	Cross-sectional
Russo et al. (2014) UK	120 (57/63)	CAARMS	Alcohol use	Cross-sectional + longitudinal
Schultze-Lutter et al. (2009) Germany	948 (590/358)	SIPS, BSABS, SPI-A	Alcohol use	Longitudinal
Smieskova et al. (2012) Switzerland	74 (50/24)	BSIP	Smoking, alcohol use	Cross-sectional
Stojanovic et al. (2014) Spain	119 (72/47)	CAARMS	BMI, smoking, alcohol use	Cross-sectional + longitudinal
Stone et al. (2012) UK	54 (27/27)	CAARMS	Smoking, alcohol use	Cross-sectional
UK	54 (27/27)	CAARMS	Smoking, alcohol use	Cross-sectional
Suridjan et al. (2013) Canada	37 (24/13)	SIPS	Smoking	Cross-sectional
Svirskis et al. (2005) Finland	157 (55/102)	SIPS	Alcohol use	Cross-sectional
van Tricht et al. (2013) Netherlands	98 (65/33)	SIPS	Smoking, alcohol use	Cross-sectional
Welsh and Tiffin (2014) UK	30 (14/16)	CAARMS	Alcohol use	Longitudinal
Wilquin and Delevoye-Turrell (2012) France	68 (29/39)	CAARMS	Alcohol use	Cross-sectional
Ziermans et al. (2011) Netherlands	74 (40/34)	SIPS	Smoking	Longitudinal
Zimbrón et al. (2013) UK	60 (36/24)	CAARMS	Alcohol use	Cross-sectional

*missing data for gender for 2 participants.
Abbreviations: BMI: Body Mass Index; BPRS: Brief Psychiatric Rating Scale; BSABS: Bonn Scale for the Assessment of Basic Symptoms; BSIP: Basel Screening Instrument for Psychosis: CAARMS: Comprehensive Assessment of At-Risk Mental States; ERIraos: Early Recognition Inventory; SCID: Structured Clinical Interview for DSM Disorders; SIPS: Structured Interview for Prodromal Symptoms; SPI-A: Schizophrenia Proneness Instrument; PANSS: Positive and Negative Syndrome Scale; RCT: Randomised Controlled Trial; TP-DIS: Thought/Perception Diagnostic Interview Schedule.

et al., 2010; Mittal et al., 2013), and exercised at a lower intensity than controls (Deighton and Addington, 2013; Mittal et al., 2013). Significantly more UHR individuals engaged in low intensity activity or sedentary behaviour compared with controls (Deighton and Addington, 2013). UHR males exercised more than females (Deighton and Addington, 2013; Mittal et al., 2013). A birth cohort study found those who later developed psychosis were more likely to be inactive during adolescence than those who did not (Koivukangas et al., 2010). UHR individuals reported more barriers to exercise than controls, such as anxiety when exercising ('I do not like how my body looks'), and fewer reasons to exercise than controls (Deighton and Addington, 2013).

3.6. Physical fitness

Cardiorespiratory fitness was assessed using a Vo2 sub-max cycle-ergometer test in 4803 adolescents (Koivukangas et al., 2010). There was no significant difference in cardiorespiratory fitness when individuals were grouped according to at-risk status and amount of prodromal symptoms in adolescence or whether they later developed psychosis (Koivukangas et al., 2010). However, a separate UHR group reported lower levels of perceived fitness than controls (Deighton and Addington, 2013).

3.7. Diet

One study reported dietary intake, and found UHR individuals consumed significantly more calories than controls (Labad et al., 2015).

3.8. Cardiometabolic risk factors and psychological variables

Low physical activity levels correlated with psychiatric symptoms (Koivukangas et al., 2010), poor occupational functioning (Mittal et al.,

Table 2
Data extracted from studies.

Cross-sectional Studies					
Study (Country)	Measure	UHR % (n)	Healthy control % (n)	Psychiatric control % (n)	Summary
Risk Factor—Tobacco Use					
Amminger et al. (2010)—Austria	% Smokers (current)	52% (42)	-	-	The majority of cross-sectional analyses found UHR individuals have higher rates of smoking compared with healthy controls. Most studies indicated that UHR smokers consumed on average more cigarettes per day than controls who smoked, but usually less than people with psychosis.
Andreou et al. (2014)—Germany	% Smokers (current)	50% (9)	32% (7)	61% SZ (11)	
Auther et al. (2012)—USA	% Smokers (current)	18% (19)	8% (4)	-	
	% Smokers (lifetime)	34% (31)	8% (4)	-	
Brewer et al. (2003)—Australia	% Smokers (current)	42% (34)	26% (8)	-	
Brockhaus-Dumke et al. (2008)—Germany	% Smokers (current)	31% (6)	4% (2)	39% FEP (18), 60% SZ (12)	
De Koning et al. (2014)—Netherlands	% Smokers (current)	50% (7)	29% (4)	-	
de la Fuente-Sandoval et al. (2011)—Mexico	% Smokers (lifetime)	6% (1)	23% (9)	33% FEP (6)	
Egerton et al. (2013)—UK	% Smokers (current)	39% (10)	25% (5)	-	
Egerton et al. (2014)—UK	% Smokers (current)	61% (46)	25% (14)	-	
Hayes et al. (2014)—Germany	% Smokers (current)	33% (5)	49% (17)	65% SZ (30)	
Hsieh et al. (2012)—China	% Smokers (current)	17% (5)	9% (5)	9% FEP (3)	
Kristensen and Cadenhead (2007)—USA	% Smokers (current)	17% (8)	-	-	
Mizrahi et al. (2012)—Canada	% Smokers (current)	8% (1)	8% (1)	40% SZ (4)	
Pruessner et al. (2011)—Canada	% Smokers (current)	13% (4)	17% (5)	31% FEP (10)	
Pruessner et al. (2013)—Canada	% Smokers (current)	14% (3)	14% (3)	-	
Stojanovic et al. (2014)—Spain	% Smokers (current)	41% (7)	24% (6)	69% PD (53)	
Stone et al. (2012)—UK	% Smokers (lifetime)	70% (19)	26% (7)	-	
Ziermans et al. (2011)—Netherlands	% Smokers (current)	21% (9)	0% (0)	-	
Auther et al. (2012)—USA	Daily smokers	50% (15)	50% (2)	-	
	Cigarettes per day	1–9 64% (11) 10–20 30% (5) 21–40 6%	1–9 50% (2) 10–20 50% (2) -	-	
Egerton et al. (2014)—UK	Cigarettes per day	6	2	-	
Howes et al. (2011)—UK	Cigarettes per day	5	3	4	
Huber et al. (2014)—Switzerland	Cigarettes per day	8	3	13 FEP	
Korkeila et al. (2013)—Finland	Cigarettes per day	8	-	-	
Stojanovic et al. (2014)—Spain	Cigarettes per day	5	1	10 PD	
Smieskova et al. (2012)—Switzerland	Cigarettes per day	9	3	13 FEP	
Stone et al. (2012)—UK	Cigarettes per day	5	2	-	
Kristensen and Cadenhead (2007)—USA	Packs of cigarettes per day	0.13–1.5	-	-	
Risk Factor—Alcohol Use					
Egerton et al. (2014)—UK	% Alcohol use	76% (57)	84% (47)	-	The percentage of people reporting alcohol use varied, but was usually higher in control groups compared with UHR groups. Average units consumed per week did not differ between UHR and controls, with the exception of one study.
Rapp et al. (2013)—Switzerland	% Alcohol use	49% (18)	-	48% FEP (11)	
Russo et al. (2014)—UK	% Alcohol use	30% (18)	57% (31)	-	
Smieskova et al. (2012)—Switzerland	% Alcohol use	88% (29)	95% (19)	81% FEP (17)	
Zimbrón et al. (2013)—UK	% Regular use	57% (17)	-	52% (15)	
Amminger et al. (2010)—Austria	% Daily use	17% (14)	-	-	
Stojanovic et al. (2014)—Spain	% Daily use	0% (0)	4% (1)	17% (13)	
Amminger et al. (2010)—Austria	% Weekly use	26% (21)	-	-	
Auther et al. (2012)—USA	% Weekly use	17% (7)	12% (3)	-	
Rapp et al. (2013)—Switzerland	% Weekly use	16% (6)	-	4% FEP (4)	
Auther et al. (2012)—USA	% Lifetime use	44% (43)	44% (26)	-	
Magaud et al. (2010)—France	% Occasional use	14% (11)	-	18% HSC (11)	
Smieskova et al. (2012)—Switzerland	% Moderate use	35% (6), 50% (8)*	75% (15)	50% FEP (10)	
	% Drunkenness	53% (9), 38% (6)*	20% (4)	33% FEP (7)	
DeVylder et al. (2013)—USA	Days per month	3	5	-	
Bernard et al. (2014)—USA	Frequency of alcohol use (1–5)	2	1	-	
Egerton et al. (2013)—UK	Units per week	1	6	-	
Egerton et al. (2014)—UK	Units per week	8	8	-	
Stone et al. (2012)—UK	Units per week	7	8		
Korkeila et al. (2013)—Finland	Drinks per day	1	-	-	
Risk Factor—Alcohol Abuse					
Hutton et al. (2011)—UK	% Alcohol abuse	38% (13)	-	-	Rates of self-reported alcohol abuse were high in UHR samples and ranged between 21%-38%. Co-morbid alcohol use disorders were also high reaching 38% in some UHR samples.
Svirskis et al. (2005)—Finland	% Alcohol abuse	21% (8)	-	-	
Wilquin and Delevoye-Turrell (2012)—France	% Alcohol abuse	27% (4)	-	24% FEP (4)	
Kristensen and Cadenhead (2007)—USA	% Lifetime alcohol abuse	33% (8)	-	-	
Huber et al. (2014)—Switzerland	% Uncontrolled alcohol use	16% (7)	8% (2)	15% FEP (7)	

Table 2 (continued)

Cross-sectional Studies

Study (Country)	Measure	UHR % (n)	Healthy control % (n)	Psychiatric control % (n)	Summary
Addington et al. (2012)—Canada	% SCID-IV Lifetime alcohol abuse	11% (40)	1% (1)		
Dragt et al. (2012)—Netherlands	% Alcohol use disorder	38% (76)	-	-	
Marshall et al. (2012)—Canada	% Alcohol use disorder	8% (4)	-	-	
Schultze-Lutter et al. (2009)—Germany	% Alcohol use disorder	4% (28)	-	-	
Welsh and Tiffin (2014)—UK	ICD-10 Alcohol dependence syndrome	3% (1)	-	-	
Risk Factor—Body Composition					
Amminger et al. (2010)—Austria	BMI	21	-	-	BMI values were all within the normal (healthy)
Bernard et al. (2014)—USA	BMI	22	24		weight range of 19–25 and were not significantly
Hayes et al. (2014)—Germany	BMI	23	23	23 SZ	different to healthy controls or people with
Stojanovic et al. (2014)—Spain	BMI	22	22	24 PD	psychosis/schizophrenia.
Korkeila et al. (2013)—Finland	Average weight	68 kg	-	-	
Risk Factor—Physical Activity					
Hodgekins et al. (2015)—UK	Hours of sport per week	1.7	2.0	3.2 FEP	The amount of physical activity was significantly
Mittal et al. (2013)—USA	Minutes of weekly activity	364	458	-	lower in the UHR group compared with healthy
Deighton and Addington (2013)—Canada	Duration (1–4)	2.5	2.9	-	controls. UHR individuals reported significantly
	Frequency (1–4)	2.4	2.8	-	more barriers and fewer reasons to exercise
	Intensity (1–4)	3.0	3.4	-	compared with controls.
	Amount of barriers to exercise	445	332	-	
	Amount of reasons to exercise	283	384	-	

Longitudinal studies

Study (country)	Measure	UHR-P	UHR-NP	HC	Time-point assessed	Summary
Risk Factor—Smoking						
Brewer et al. (2003)—Australia	% Smokers	41% (9)	42% (25)	26% (8)	Baseline	Most studies found UHR-P had lower rates of
Brockhaus-Dumke et al. (2008)—Germany	% Smokers	29% (6)	33% (6)	4% (2)	Baseline	smoking at baseline compared with UHR-NP.
Ziermans et al. (2011)—Netherlands	% Smokers	17% (1)	22% (8)	0% (0)	Baseline	However, those who did transition generally
		17% (1)	33% (12)	3% (1)	Follow-up (2 year)	smoked more per day or had higher lifetime
Howes et al. (2011)—UK	Cigarettes per day	5	5	3	Baseline	rates than controls, and non-transition subjects.
Labad et al. (2015)—Spain	Cigarettes per day	7	4	2	Baseline	
Brewer et al. (2003)—Australia	Lifetime quantity (cigarettes per day × years of use)	94	87	43	Baseline	
Risk Factor—Alcohol Use						
Howes et al. (2011)—UK	Units per week	7	5	10	Baseline	UHR-P consumed more units per week on
Labad et al. (2015)—Spain	Units per day	0	0	0	Baseline	average than UHR-NP.
Risk Factor—Body Composition						
Labad et al. (2015)—Spain	BMI	21	22	22	Baseline	BMI did not differ at baseline according to later transition.
Risk Factor—Physical Activity						
Koivukangas et al. (2010)—Finland	% Inactive	40% (13)	-	20% (1410)	Baseline	40% of a birth cohort who went on to experience psychosis were inactive at adolescence, compared with 20% who did not experience psychosis.
Risk Factor—Physical Fitness						
Koivukangas et al. (2010)—Finland	% Low physical fitness	46% (6)	-	33% (1569)	Baseline	46% of a birth cohort who went on to experience psychosis had low physical fitness at adolescence, compared with 33% who did not experience psychosis.
Risk Factor—Diet						
Labad et al. (2015)—Spain	Calories per day	2740 kcal	2368 kcal	1788 kcal	Baseline	UHR-P consumed more calories on average per day than controls and those who did not
	Protein intake per day	98 g	94 g	87 g	Baseline	transition. Both groups had significantly higher calorie intake than controls.

Abbreviations: BMI: Body Mass Index; FEP: First-episode psychosis; HC: Healthy control; HSC: Help-seeking control; kcal: kilocalories; PD: Psychotic disorder; SZ: Schizophrenia; UHR: Ultra-high risk; UHR-P: Ultra-high risk who transitioned to psychosis; UHR-NP: Ultra-high risk who did not transition to psychosis.

2013) and later development of psychosis (Koivukangas et al., 2010). Individuals who transitioned to psychosis also smoked more cigarettes on average per day (Labad et al., 2015), had higher rates of overall cigarette use (Brewer et al., 2003), consumed more alcoholic units per week (Labad et al., 2015) and had a higher daily calorie intake (Labad et al., 2015) when assessed during the UHR phase. However, overall smoking status was not associated with transition (Brewer et al., 2003; Ziermans et al., 2011).
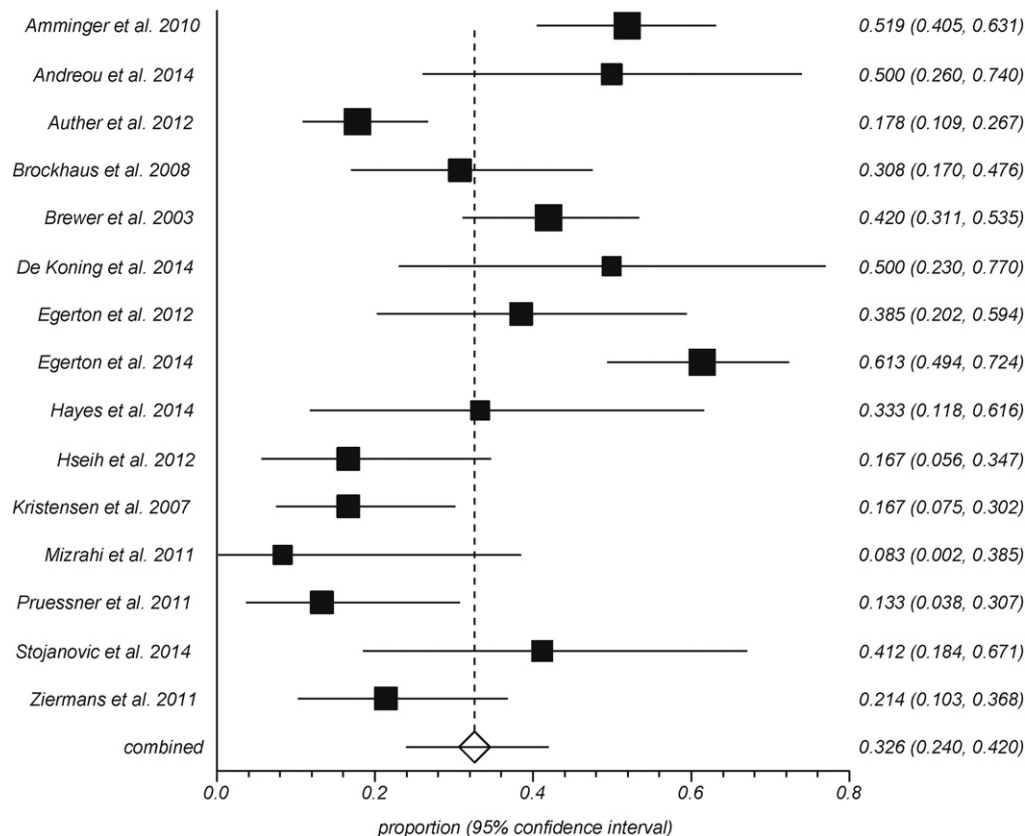
Proportion meta-analysis plot [random effects]

Amminger et al. 2010	0.519 (0.405, 0.631)
Andreou et al. 2014	0.500 (0.260, 0.740)
Auther et al. 2012	0.178 (0.109, 0.267)
Brockhaus et al. 2008	0.308 (0.170, 0.476)
Brewer et al. 2003	0.420 (0.311, 0.535)
De Koning et al. 2014	0.500 (0.230, 0.770)
Egerton et al. 2012	0.385 (0.202, 0.594)
Egerton et al. 2014	0.613 (0.494, 0.724)
Hayes et al. 2014	0.333 (0.118, 0.616)
Hseih et al. 2012	0.167 (0.056, 0.347)
Kristensen et al. 2007	0.167 (0.075, 0.302)
Mizrahi et al. 2011	0.083 (0.002, 0.385)
Pruessner et al. 2011	0.133 (0.038, 0.307)
Stojanovic et al. 2014	0.412 (0.184, 0.671)
Ziermans et al. 2011	0.214 (0.103, 0.368)
combined	0.326 (0.240, 0.420)

proportion (95% confidence interval)

Fig. 2. Summary of Smoking Rates of UHR samples.

4. Discussion

This is the first review assessing cardiometabolic risk factors and physical health in the at-risk population. UHR individuals have high rates of behavioural cardiometabolic risk factors with elevated rates of smoking, physical inactivity and alcohol abuse, but were not more overweight than controls. Longitudinal studies indicate that the increased unhealthy lifestyle factors may be associated with later transition to psychosis. These findings are consistent with a recent meta-analysis that found smoking may be a causative factor in the onset of psychosis (Gurillo et al., 2015).

4.1. Why do UHR individuals have unhealthy lifestyles?

4.1.1. Smoking

UHR individuals have high levels of depression, anxiety and negative symptoms (Fusar-Poli et al., 2014; Rietdijk et al., 2013; Yung et al., 2004). Smoking may reduce these symptoms through relaxation or alleviation of boredom (the self-medication hypothesis) (Kumari and Postma, 2005). Additionally, nicotine consumption may help to reduce deficits in information processing, by acting on nicotinic receptors in the temporal cortex (Bridgman et al., 2014; De Luca et al., 2004).

It could be that there is a shared proneness to developing schizophrenia (or sub-threshold psychotic symptoms) and smoking. There may be underlying neurobiological causes for this vulnerability (de Leon and Diaz, 2005), or it may occur through social mechanisms. For example, it is known that social deprivation increases psychosis risk through social defeat, poverty and increased likelihood of trauma (Allardyce et al., 2005; Cotter et al., 2015) and that socially deprived areas have high rates of unhealthy lifestyle factors including smoking,

substance abuse and physical inactivity (Barbeau et al., 2004; Hanson and Chen, 2007; Wardle and Steptoe, 2003).

Finally, it could be that smoking increases the risk of developing schizophrenia through inducing dopamine dysregulation in the brain (Gurillo et al., 2015), and the UHR group represents the first manifestation of the illness. However, further research is needed to explain the relationship between smoking and schizophrenia.

4.1.2. Physical inactivity

We can speculate that increased levels of depression, anxiety and negative symptoms in the UHR group contribute to decreased motivation to exercise and increased sedentary behaviour. UHR individuals often report reduced vitality levels, or motivation, energy and drive (Bechdolf et al., 2005; Grano et al., 2014; Hauser et al., 2009; Ruhrmann et al., 2008). Additionally, as noted above, factors such as social deprivation may present a shared risk for both physical inactivity and schizophrenia (Barbeau et al., 2004).

Exercise decreases inflammation and increases Brain Derived Neurotrophic Factor (BDNF) (Cotman and Berchtold, 2002; Mondelli et al., 2011; Singh and Chaudhuri, 2014). We could speculate that there is a link between physical inactivity, increased inflammation and decreased BDNF. However, it is unclear whether a reduction in physical activity has a causative role in increasing inflammation or whether it is a result of underlying neuro-inflammation occurring as the illness progresses.

4.1.3. Alcohol use and diet

Preliminary evidence indicates that UHR individuals may be more likely to abuse alcohol and consume more calories than generally healthy populations. The reported rates of alcohol abuse and misuse were higher than that of the general public. For example, it is estimated

Odds ratio meta-analysis plot [random effects]

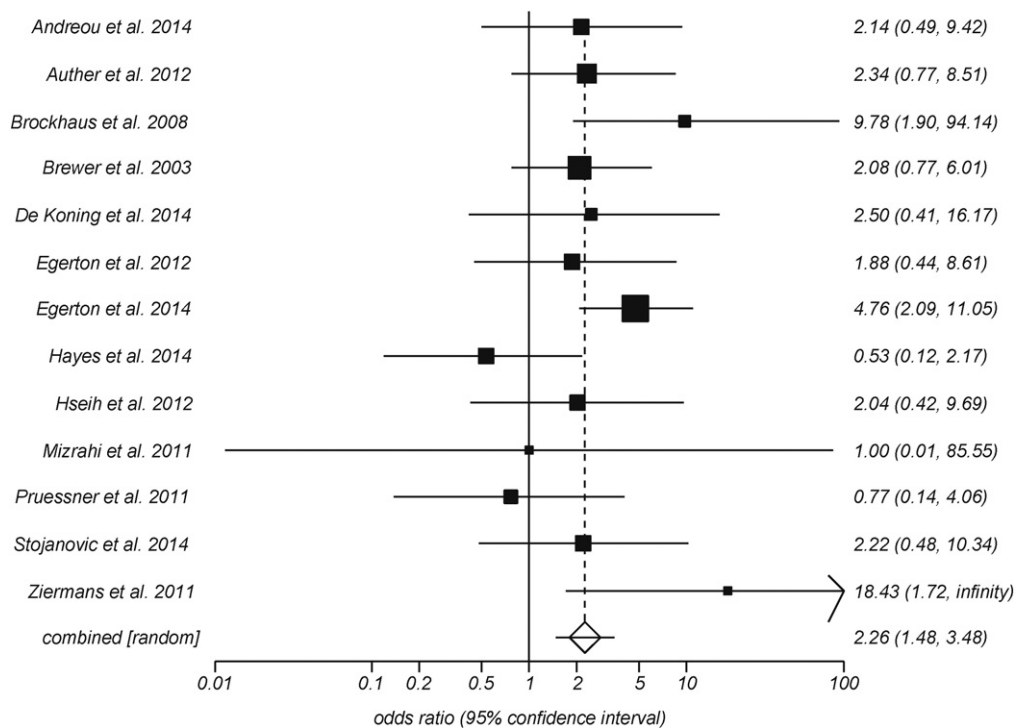| Andreou et al. 2014 | 2.14 (0.49, 9.42) |
Auther et al. 2012	2.34 (0.77, 8.51)
Brockhaus et al. 2008	9.78 (1.90, 94.14)
Brewer et al. 2003	2.08 (0.77, 6.01)
De Koning et al. 2014	2.50 (0.41, 16.17)
Egerton et al. 2012	1.88 (0.44, 8.61)
Egerton et al. 2014	4.76 (2.09, 11.05)
Hayes et al. 2014	0.53 (0.12, 2.17)
Hseih et al. 2012	2.04 (0.42, 9.69)
Mizrahi et al. 2011	1.00 (0.01, 85.55)
Pruessner et al. 2011	0.77 (0.14, 4.06)
Stojanovic et al. 2014	2.22 (0.48, 10.34)
Ziermans et al. 2011	18.43 (1.72, infinity)
combined [random]	2.26 (1.48, 3.48)

odds ratio (95% confidence interval)

Fig. 3. Odds ratio of smoking status in UHR individuals and control groups.

that in the UK 3.8% of individuals are alcohol dependent, and 6.8% of young people 16 to 24 years engage in hazardous drinking (McManus et al., 2009). Therefore, although many studies did not include a control group, the rates of alcohol abuse were often higher compared with the general population, reaching up to 38% for alcohol abuse (Hutton et al., 2011) and alcohol abuse disorders (Dragt et al., 2012). We can again speculate that this may be attributable to social and environmental factors, since low socioeconomic status is a common risk factor for psychosis and is also associated with substance misuse and poor diet (Darmon and Drewnowski, 2008; Galea et al., 2004; Marcenko et al., 2000). However, it could also be that eating a healthy diet has a neuroprotective effect, such as the consumption of omega-3 fatty acids and other vitamins, (McGrath et al., 2004; Peet, 2008). This arises from recent findings which suggest treatment with long-chain omega-3 fatty acids could lead to longitudinal symptomatic and functional improvements in UHR individuals (Amminger et al., 2010, 2015a, 2015b).

4.2. Limitations

The scope of the review was intentionally broad. Many studies of varied content and methodological design were included, making direct comparisons difficult. This is also reflected in the high levels of between study heterogeneity reported in the meta-analyses. This is likely to have been driven by both clinical and methodological differences across the studies with regards to UHR screening measures, study inclusion criteria (such as the rates of comorbid disorders and whether those with substance use disorders were included), recruitment settings and methods of data collection. Quality assessments were not conducted, as most information came from demographic assessments and not the studies' primary outcomes. Most studies were cross-sectional and sample size was often underpowered to find significant differences. Control groups varied, sometimes including help-seeking controls which made comparisons difficult.

4.3. Clinical implications

High rates of cardiometabolic risk factors observed in the UHR group are due to unhealthy lifestyle factors. These behaviours are potentially modifiable. Thus, the UHR phase is an important opportunity for early intervention to improve physical health, as UHR groups may be amenable to lifestyle interventions, including smoking cessation programmes, exercise promotion and healthy diet. Although a large proportion of UHR individuals will not develop a psychotic disorder, many go on to develop anxiety, mood and substance use disorders (Addington et al., 2011) and many will continue to function poorly, regardless of transition or symptomatic remission (Cotter et al., 2014). Therefore, even among so-called "false positives" (Yung et al., 1996), interventions to improve physical health are likely to be of benefit and may improve comorbid symptoms such as depression (Cooney et al., 2013), along with physical health.

4.4. Future research

A current gap in the literature is the prevalence and trajectory of plasma measurements of lipid and glucose, and insulin insensitivity in the UHR group. This is of particular interest as it would allow us to examine the possible effects of vulnerability to psychosis on these metabolic markers without confounding effects of antipsychotic medication. Further research is also required in the UHR group to assess cardiometabolic risk factors discussed in this review, such as physical activity and fitness, diet and physiological measurements. Examination of the association between these metabolic and other physical health variables with psychiatric symptoms and transition to psychotic disorder is also of interest and may highlight possible mechanisms underlying the link between unhealthy behaviours and psychosis onset.

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Paper 2

Substance use in youth at-risk for psychosis

Author Contributions:

Rebekah Carney conceived the original idea for the paper having received access to cohort data from Professor Alison Yung and Associate Professor Rosie Purcell. Rebekah decided on the research aims for the current study, statistical analysis, interpreted the findings, wrote the first draft of the manuscript and completed subsequent revisions following comments from co-authors.

Professor Alison Yung, Professor Paul Amminger, Professor Nick Glozier, Associate Professor Daniel Hermens, Professor Ian Hickie, Professor Eoin Killackey, Professor Pat McGorry, Professor Christos Pantelis, Professor Stephen Wood and Associate Professor Rosie Purcell designed and obtained funding for the original study and managed the data collection across sites in Australia. Professor Alison Yung and Dr Tim Bradshaw provided clinical guidance and Professor Alison Yung and Professor Nick Glozier provided statistical guidance. All authors critically reviewed and agreed on the submitted manuscript for publication.

Substance use in youth at risk for psychosis

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ABSTRACT

Background: People with schizophrenia have high rates of substance use which contributes to co-morbidity and premature mortality. Some evidence suggests people at-risk for psychosis have high rates of substance use. We aimed to assess substance use in a help-seeking cohort, comparing those at-risk and not at-risk for psychosis, and to establish any relationship with clinical symptoms.

Method: Participants were help-seeking youth presenting to mental health services in Sydney and Melbourne. 279 (34.8%) were at-risk for psychosis, and 452 (56.4%) did not meet criteria for a psychotic disorder or risk for psychosis. The excluded individuals were made up of 59 (7.4%) young people who met criteria for a psychotic disorder and 11 (1.4%) who were unable to be evaluated. We assessed the association of substance use involvement with risk status and clinical symptoms using multivariate regression.

Results: Individuals at-risk for psychosis had significantly higher tobacco, alcohol and cannabis use than those not at-risk. Multivariate analysis revealed at-risk status was significantly associated with higher alcohol involvement scores when adjusting for age and gender, but no association was found for cannabis or tobacco. At-risk status was no longer associated with alcohol involvement when cannabis or tobacco use was added into the analysis.

Conclusion: Tobacco smoking, alcohol consumption and cannabis use are common in help-seeking youth, particularly those at-risk for psychosis. It is important to consider co-occurring use of different substances in adolescents. Early substance misuse in this phase of illness could be targeted to improve physical and mental health in young people.

1. Introduction

People with schizophrenia have high rates of substance use including tobacco, alcohol and cannabis use (Addy et al., 2012; Davidson et al., 2001; McCreadie, 2003). This increases the risk of later cardiovascular disease. Together with the metabolic side effects of antipsychotics, these unhealthy lifestyle factors contribute to the increased morbidity and premature mortality of this population, (De Hert et al., 2011; Saha et al., 2007; Wahlbeck et al., 2011). High rates of substance use are observed early in the illness course, in individuals with first-episode psychosis (FEP) (Barnett et al., 2007; Wade et al., 2006).

The ultra-high risk state (UHR), also called the prodromal, clinical high-risk (CHR) or at-risk mental state (ARMS) (Fusar-Poli et al., 2013), identifies people at imminent high risk of developing a psychotic disorder, that is, they may be in in the prodromal phase for psychosis. In order to meet UHR status an individual must exhibit one or a combination of the following characteristics: presence of attenuated psychotic symptoms, brief intermittent psychotic symptoms, or a genetic-risk combined with a recent decline in functioning (Yung et al., 2004). These are assessed with established criteria (Miller et al., 2002; Yung et al., 2002; Yung and McGorry, 1996; Yung et al., 1998).

Two recent reviews suggest UHR individuals have high rates of poor physical health and unhealthy lifestyle behaviours such as smoking, cannabis and alcohol use (Addington et al., 2014; Carney et al., 2016). In at-risk samples, more severe symptoms are also associated with higher levels of substance use (Auther et al., 2012; Svirskis et al., 2005). Previous research has indicated that cannabis significantly

increases the risk for psychosis, with the greatest risk associated with early age of first use (Donoghue et al., 2014; Helle et al., 2016), use of high potency cannabis or 'skunk'(Di Forti et al., 2014; Marconi et al., 2016) and in those with an underlying genetic predisposition for psychosis (Henquet et al., 2008). Additionally, recent meta-analyses suggest there is a dose-response relationship between heavy cannabis use and transition to psychosis in UHR individuals (Kraan et al., 2015).

Despite these findings, there is little research into physical health and associated risk behaviours in UHR youth and these factors are poorly monitored in clinical services (Carney et al., 2015). Studies assessing lifestyle factors in UHR individuals rarely have substance use as a primary outcome. Those that do are often underpowered, with small samples (Allen et al., 2014; Rapp et al., 2013). Additionally, many fail to include an adequate control group (Dragt et al., 2012; Kristensen and Cadenhead, 2007; Phillips et al., 2002; Rapp et al., 2013) and often use unvalidated measurement tools (Stone et al., 2012; van Tricht et al., 2013). There is also a lack of evidence to link psychological and psychosocial factors to rates of substance use, as this has not yet been assessed in large cohorts.

To address this gap we aimed to;

(1) Assess rates of substance use, in help seeking individuals, to establish whether those with a specific risk for psychosis have higher rates of substance involvement than those without, using a World Health Organisation substance use assessment tool (ASSIST; (WHO, 2002)) This tool measures degree of substance involvement, taking into account current and lifetime use of substances, frequency of use, desire, problematic use, failure to meet expectations, concern expressed by others and failed attempts to quit.
(2) Identify any relationship between substance involvement, clinical symptoms and other psychosocial variables.

2. Method

2.1. Participants and setting

Data from the Transitions Study (Purcell et al., 2014) were used to conduct a cross-sectional analysis of a help-seeking cohort presenting at youth mental health services in Australia. The Transitions Study has been described in detail elsewhere (Purcell et al., 2015; Purcell et al., 2014). Participants were help-seeking individuals aged 12–25 years who had engaged with one of four 'headspace' clinics in Melbourne and Sydney, Australia, between January 2011 and August 2012 (Rickwood et al., 2014). 'headspace' was established by the Australian Government to provide mental health services for young people. Of 1615 individuals receiving help from these services, 801 young people consented to participate in the study, of whom 279 were at-risk for psychosis, 59 had established psychotic disorder and 452 met neither psychosis risk nor psychosis criteria (at-risk for psychosis status could not be evaluated in 11 participants) (Fig. 1), (Purcell et al., 2014). Those who could not be evaluated or who had a psychotic disorder were excluded, leaving 731 individuals.

2.2. Procedure

Baseline assessment measures were administered after participants gave informed consent Research assistants (RAs) with a minimum of 4-years graduate psychology degrees administered assessments. RAs had very good (kappa > 0.8) inter-rater reliability on interviewer-rated measures. Self-report measures were completed by participants on an iPad. A $20 gift voucher was provided to each participant. The Human Research Ethics Committees at the University of Melbourne and University of Sydney approved the study.
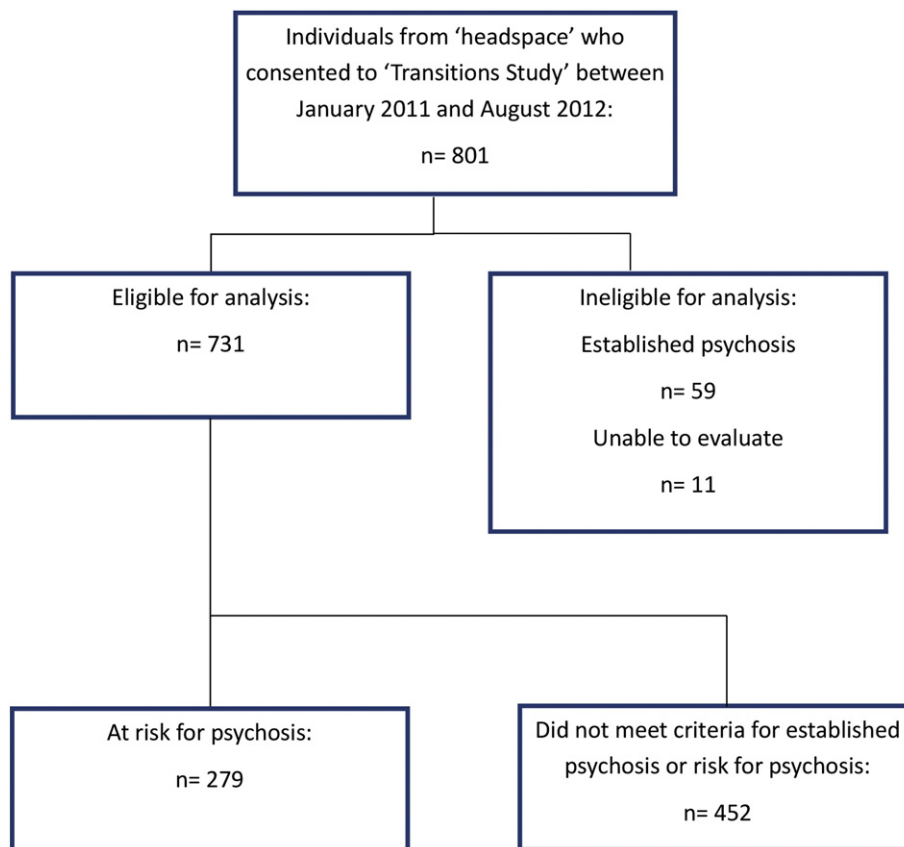

Fig. 1. Flow diagram of individuals included in the analysis.

2.3. Measures

The Positive Symptom Scale of the Comprehensive Assessment for At-Risk Mental State (CAARMS) (Yung et al., 2005) was used to determine whether an individual was at-risk for psychosis. This consists of four subscales: (i) unusual thought content; (ii) non-bizarre ideas; (iii) perceptual abnormalities; and (iv) disorganised speech. Scores for each of the subscales are rated according to intensity, frequency and duration of symptoms. An individual was considered at-risk of psychosis if they scored above a pre-set threshold on both intensity and frequency on any of these subscales, consistent with previous definitions (Yung et al., 2004).

Further clinician rated measures included; 16-item adolescent version of the Quick Inventory of Depressive Symptomatology (QIDS, (Rush et al., 2003)), Social and Occupational Functioning Assessment Scale (SOFAS, (Morosini et al., 2000)), and Young Mania Rating Scale (YMRS, (Young et al., 2000)). Self-report clinical measures included; Kessler 10 (K10, (Andrews and Slade, 2001)), Somatic and Psychological Health Report (SPHERE 12, (Berryman et al., 2012)), Generalised Anxiety Disorder scale (GAD-7, (Spitzer et al., 2006)), Overall Anxiety Severity and Impairment Scale (OASIS (Campbell-Sills et al., 2009)), WHO Disability Assessment Schedule (WHODAS-12, (Üstün, 2010)), a question on quality of life taken from the WHOQOL, (Group, T.W, 1998) and a 5-item eating disorder screening tool (SCOFF, (Morgan et al., 1999)). Substance use was assessed using the WHO Alcohol, Smoking and Substance Involvement Screening Test (WHO-ASSIST, (WHO, 2002)). Personality characteristics were assessed using the Behavioural Inhibition/Activation Scale, (BIS/BAS, (Carver and White, 1994)).

2.4. Statistical analysis

Categorical variables were analysed using a χ^2 test and continuous variables were compared using t-tests. When the assumptions for parametric statistics were violated, determined by distribution of data on histograms, non-parametric tests were employed (such as Mann Whitney U). Current use of substances was defined as use within the past three months (WHO, 2002). Use of substances other than tobacco, alcohol and cannabis was minimal; therefore, data was not included in further analysis. Substance involvement was calculated by taking into account current and lifetime use of substances, frequency of use, desire, problematic use and failure to meet expectations, concern expressed by others and failed attempts to quit.

Regression analyses were performed on the whole sample using each of the substance involvement scores (alcohol, tobacco and cannabis) as the dependent variables and risk-status, demographic information and clinical variables as independent variables (predictors). Where the outcome data was skewed, quantile median regression was used (alcohol and tobacco involvement). Predictors of cannabis involvement were modelled using mean regression, as median quantile regression models failed to converge. The clinical variables used in the multivariate analysis related to clinically significant outcomes such as depression, psychological distress, anxiety and functioning. Personality characteristics and symptoms of mania or eating disorders were therefore, excluded from the multivariate analysis, as they were deemed non-significant clinical variables. A significance level of 0.05 was used for all statistical tests, and two-tailed tests were applied. All data analysis was conducted using SPSS 22.0 (IBM, 2013).

3. Results

The sample consisted of young people presenting to youth mental health services in Australia. Individuals at-risk for psychosis and help-seeking controls did not differ according to age (psychosis risk 18.19; help-seeking control 18.33), or gender ratio (see Table 1). A higher proportion of females than males was found in both groups (psychosis risk 66.7% and help-seeking controls 65.7%), which is representative of the 'headspace' cohort (Rickwood et al., 2014).

3.1. Substance use in individuals at-risk for psychosis compared to help-seeking controls

3.1.1. Tobacco

Tobacco involvement scores were significantly higher in individuals at-risk for psychosis (7.90) than help-seeking controls (5.94; p = 0.01). Scores 0–3 indicate low risk, 4–26 moderate risk and 27 or higher suggests high risk. Compared to help-seeking controls, those at-risk for psychosis were more likely to have high risk tobacco use (5%, 1%; $X^2 = (1)12.79$, p = 0.001; OR 7.28, 95% CI 2.06, 25.79), daily, lifetime and current tobacco use. Problematic use (at least weekly use of tobacco) was not significantly different between the groups.

3.1.2. Alcohol

Individuals at-risk for psychosis had significantly higher alcohol involvement (6.40) than help-seeking controls (5.16; p = 0.01). Scores 0–10 indicate low risk, 11–26 moderate risk and 27 or higher suggests high risk. High-risk alcohol use was no different between groups (2%). No differences were found between groups for current, daily, problematic, or lifetime use.

3.1.3. Cannabis

Those at-risk for psychosis had higher cannabis involvement scores (4.45) than help-seeking controls (3.20; p = 0.02). The criteria for low, moderate and high risk cannabis use were the same as tobacco use. Individuals at-risk for psychosis had higher rates of high risk cannabis use (psychosis risk 4.7%, help-seeking controls 1.6%) and moderate risk cannabis use (psychosis risk 25.4%, help-seeking controls 21.2%; $X^2 = (2)$ 8.67, p = 0.01). Significantly more participants at-risk for psychosis used cannabis in their lifetime, and currently used cannabis (33%), than help-seeking controls (26%). Problematic use was higher in those at-risk (16.1%) than help-seeking controls (14.4%) but the difference was not significant.

3.2. What predicts substance use in help-seeking youth?

Regression analyses controlling for at-risk status, age and gender can be found in Table 2. Independent of group (at risk or not at risk), substance involvement was associated with a range of clinical factors. For example, across the whole sample, a reduction in quality of life was associated with increased alcohol (b = −0.47, 95% CI −0.82, −0.12), tobacco (b = −1.24, 95% CI −2.34, −0.14) and cannabis involvement (b = −0.94, 95% CI −1.45, −0.44). An increase in depression was associated with increased substance involvement scores across the whole group; however, there was no association for anxiety (Table 2).

At-risk status was independently associated with a 0.90 increase in median alcohol involvement score after adjusting for age, gender and clinical variables (b = 0.90, 95% CI 0.11, 1.69). However, no significant association was found for tobacco use or cannabis involvement (Table 3).

Building on the initial analysis (Table 3), use of other substances was factored into the regression for alcohol involvement. Further multivariate analyses showed that at-risk status was no longer predictive of alcohol involvement scores when adjusted for tobacco (b = 0.51, 95% CI −0.34, 1.36), or cannabis use (b = 0.67, 95% CI −0.19, 1.52), as both scores significantly predicted alcohol use (Table 4). Additionally, no significant interactions were found between at-risk status and tobacco use, or at-risk status and cannabis use.

4. Discussion

In our large sample of help-seeking youth, those at-risk for psychosis had significantly higher tobacco, alcohol and cannabis use than help-

Table 1
ASSIST substance use analysis in help-seeking youth at risk and not at risk for psychosis.

	At risk for psychosis (n = 279)	Not at risk for psychosis (n = 450)	Statistic
Age: mean (S.D)	18.19 (3.16)	18.33 (3.32)	t (729) = 0.58, 95% CI (−0.35, 0.63)
Gender: (% female)	66.7% (186)	65.7% (297)	x^2 = 0.071, df 1, p = 0.79, OR 1.04, 95% CI (0.76, 1.43)
Tobacco			
ASSIST tobacco involvement: mean (S.D)	7.90 (9.38)	5.94 (7.88)	U = 56,450, p = 0.01
Lifetime use: yes (%)	196 (70.3%)	284 (62.8%)	x^2 = 4.21, df1, p = 0.04, OR 1.4, 95% CI (1.01, 1.92)
Current use: yes (%)	145 (52%)	205 (45.4%)	x^2 = 3.027, df1, p = 0.08, OR 1.3, 95% CI (0.97, 1.76)
Daily use: yes (%)	101 (36.2%)	127 (28.1%)	x^2 = 5.278, df1, p = 0.02, OR 1.5, 95% CI (1.06, 2.00)
Problematic use: yes (%)	113 (40.5%)	159 (58.5%)	x^2 = 2.094, df1, p = 0.15, OR 1.3, 95% CI (0.92, 1.71)
Alcohol			
ASSIST alcohol involvement: mean (S.D)	6.40 (6.84)	5.16 (6.25)	U = 55,644, p = 0.01
Lifetime use: yes (%)	244 (87.5%)	373 (82.5%)	x^2 = 3.189, df1, p = 0.07, OR 1.5, 95% CI (0.96, 2.27)
Current use: yes (%)	196 (70.3%)	300 (66.4%)	x^2 = 1.190, df1, p = 0.28, OR 1.2, 95% CI (0.87, 1.65)
Daily use: yes (%)	20 (7.2%)	22 (4.9%)	x^2 = 1.687, df1, p = 0.19, OR 1.5, 95% CI (0.81, 2.81)
Problematic use: yes (%)	97 (34.8%)	138 (30.5%)	x^2 = 1.419, df1, p = 0.23, OR 1.2, 95% CI (0.88, 1.67)
Cannabis			
ASSIST cannabis involvement: mean (S.D)	4.45 (7.99)	3.20 (6.55)	U = 57,468, p = 0.02
Lifetime use: yes (%)	157 (56.3%)	210 (46.5%)	x^2 = 6.644, df1, p = 0.01, OR 1.5, 95% CI (1.09, 2.00)
Current use: yes (%)	93 (33.3%)	119 (26.3%)	x^2 = 4.112, df1, p = 0.04, OR 1.4, 95% CI (1.01, 1.94)
Daily Use: yes (%)	25 (9.0%)	34 (7.5%)	x^2 = 0.481, df1, p = 0.49, OR 1.2, 95% CI (0.71, 2.08)
Problematic Use: yes (%)	45 (16.1%)	65 (14.4%)	x^2 = 0.413, df1, p = 0.52, OR 1.1, 95% CI (0.76, 1.73)
Cocaine			
ASSIST cocaine involvement: mean (S.D)	0.24 (1.72)	0.26 (1.42)	U = 62,664, p = 0.19
Lifetime use: yes (%)	40 (14.4%)	74 (16.4%)	x^2 = 0.514, df1, p = 0.47, OR 0.9, 95% CI (0.56, 1.30)
Amphetamines			
ASSIST amphetamine involvement: mean (S.D)	1.12 (3.74)	0.75 (3.02)	U = 59,974, p = 0.11
Lifetime use: yes (%)	80 (28.8%)	104 (23%)	x^2 = 3.038, df1, p = 0.08, OR 1.4, 95% CI (0.96, 1.91)
Sedatives			
ASSIST sedative involvement: mean (S.D)	0.09 (1.01)	0.12 (0.84)	U = 59,974, p = 0.11
Lifetime use: yes (%)	43 (15.5%)	57 (12.6%)	x^2 = 1.188, df1, p = 0.28, OR 1.3, 95% CI (0.83, 1.94)
Hallucinogens			
ASSIST hallucinogen involvement: mean (S.D)	0.45 (2.063)	0.31 (2.01)	U = 62,064, p = 0.28
Lifetime use: yes (%)	50 (18%)	75 (16.6%)	x^2 = 0.235, df1, p = 0.63, OR 1.1, 95% CI (0.74, 1.63)
Inhalants			
ASSIST inhalant involvement: mean (S.D)	0.51 (2.49)	0.33 (1.6)	U = 62,365, p = 0.93
Lifetime use: yes (%)	22 (7.9%)	36 (8%)	x^2 = 0.001, df1, p = 0.98, OR 1.0, 95% CI (0.57, 1.73)
Opioids			
ASSIST opioid involvement: mean (S.D)	0.27 (2.04)	0.27 (2.10)	U = 62,689, p = 0.65
Lifetime Use: yes (%)	15 (5.4%)	23 (5.1%)	x^2 = 0.029, df1, p = 0.87, OR 1.1, 95% CI (0.54, 2.07)
Other			
ASSIST other involvement: mean (S.D)	0.08 (0.54)	0.01 (0.14)	U = 62,700, p = 0.58
Lifetime use: yes (%)	15 (5.4%)	11 (2.4%)	x^2 = 4.355, df1, p = 0.04, OR 2.28, 95% CI (1.03, 5.03)

Abbreviations: S.D., standard deviation; ASSIST, Alcohol, Smoking and Substance Involvement Screening Test.

seeking controls. At-risk status predicted higher alcohol involvement, after adjusting for clinical and demographic variables, but did not predict cannabis or tobacco scores. Additionally, UHR status was no longer independently associated with alcohol involvement after controlling for tobacco and cannabis involvement scores, as these variables demonstrated much stronger associations with alcohol involvement.

Table 2
Regression analysis adjusting for UHR status, age and gender.

Clinical measure* all adjusted for at-risk group, age and gender	Alcohol involvement			Tobacco involvement			Cannabis involvement		
	Coefficient	p-Value	95% CI	Coefficient	p-value	95% CI	Coefficient	p-value	95% CI
K10	0.03	0.14	−0.01–0.08	0.1	0.12	−0.27–0.23	0.07	0.01	0.02–0.13
SPHERE Psych 6	0.02	0.69	−0.09–0.13	0.13	0.40	−0.18–0.44	0.22	0.01	−0.07–0.36
SPHERE Soma 6	0.13	0.02	0.02–0.23	0.17	0.32	−0.16–0.50	0.24	0.01	0.09–0.38
GAD7	0.14	0.69	−0.05–0.08	0.05	0.61	−0.15–0.25	0.08	0.08	−0.01–0.17
OASIS	−1.94	1.00	−0.08–0.08	−8.33	1.00	−0.24–0.24	0.08	0.14	−0.03–0.18
SCOFF	0.48	0.01	0.15–0.81	1.5	0.01	0.60–2.40	0.59	0.01	0.17–1.02
WHOQOL	−0.47	0.01	−0.82 to −0.12	−1.24	0.03	−2.34 to −0.14	−0.94	0.01	−1.45 to −0.44
WHODAS12	0.01	0.53	−0.03–0.06	0.14	0.03	0.02–0.26	0.09	0.01	0.03–0.15
QIDS	0.12	0.01	−0.04–0.20	0.24	0.03	0.02–0.46	0.22	0.01	0.12–0.33
SOFAS	0	1.00	−0.03–0.03	−0.07	0.14	−0.18–0.02	−0.11	0.01	−0.16–0.06
YMRS	0.11	0.03	−0.01–0.20	0.4	0.01	0.15–0.65	0.18	0.01	0.06–0.31
BAS drive	2.78	1.00	−0.15–0.15	−0.08	0.73	−0.51–0.36	−0.02	0.86	−0.21–0.17
BAS fun seeking	−0.21	0.01	−0.36–0.06	−0.40	0.05	−0.81–0.00	−0.28	0.01	−0.47–0.08
BAS reward	3.70	1.00	−0.14–0.14	0.07	0.76	−0.36–0.50	−0.01	0.98	−0.20–0.19
BIS	0	1.00	−0.11–0.11	0.18	0.27	−0.14–0.49	0.04	0.56	−0.10–0.18

Abbreviations: BAS, Behavioural Activation Scale; BIS, Behavioural Inhibition Scale; GAD, Generalised Anxiety Disorder Scale, K10, Kessler 10; OASIS, Overall Anxiety Severity and Impairment Scale; QIDS, Quick Inventory of Depressive Symptomatology; SCOFF, 5-item eating disorder scale; SOFAS, Social and Occupational Functioning Assessment Scale; SPHERE, Somatic and Psychological Health Report (P-Psychological, S-Somatic); WHODAS, World Health Organisation Disability Assessment Schedule; WHOQoL, World Health Organisation Quality of Life Scale; YMRS, Youth Mania Rating Scale.

Table 3
Regression analysis of UHR status and substance involvement scores, adjusting for age, gender and clinical variables.

	Variables		Coefficient	p-Value	95% CI
Alcohol involvement score	Model 1				
		At-risk status (UHR)	0.90	0.03	0.11–1.69
		Sex (female)	−0.08	0.84	−0.89–0.72
		Age	0.61	0.01	0.49–0.72
		K10	0.44	0.02	−0.28–0.12
		WHOQOL	−0.68	0.01	−1.15–0.21
		WHODAS	0.03	0.36	−0.03–0.09
		SOFAS	0.02	0.27	−0.02–0.06
		OASIS	−0.08	0.15	−0.19–0.03
		SPHERE psych 6	−0.19	0.04	−0.36–0.01
		SPHERE somatic 6	0.12	0.10	−0.02–0.26
		Constant	−7.51	0.01	−11.62–3.41
Tobacco involvement score	Model 1				
		At-risk status (UHR)	0.52	0.68	−1.94–2.97
		Sex (female)	−0.43	0.74	−2.93–2.07
		Age	0.51	0.01	0.15–0.87
		K10	0.18	0.12	−0.05–0.40
		WHOQOL	−1.26	0.10	−2.73–0.22
		WHODAS	0.08	0.40	−0.10–0.26
		SOFAS	−0.05	0.37	−0.16–0.06
		OASIS	−0.31	0.08	−0.66–0.04
		SPHERE psych 6	−0.27	0.33	−0.83–0.28
		SPHERE somatic 6	−0.04	0.85	−0.48–0.39
		Constant	−0.28	0.97	−13.06–12.50
Cannabis involvement score	Model 1				
		At-risk status (UHR)	0.61	0.25	−0.45 – 1.75
		Sex (female)	0.43	0.94	−1.08 – 1.16
		Age	0.40	0.01	0.24–0.56
		K10	−0.14	0.78	−0.11–0.86
		WHOQOL	−0.58	0.08	−1.25–0.08
		WHODAS	0.03	0.55	−0.57–0.11
		SOFAS	−0.08	0.01	−0.13–0.03
		OASIS	−0.12	0.13	−0.18–0.31
		SPHERE psych 6	0.07	0.59	−0.18–0.32
		SPHERE somatic 6	0.16	0.11	−0.04–0.35
		Constant	2.57	0.38	−3.17–8.32

Abbreviations: K10, Kessler 10; OASIS, Overall Anxiety Severity and Impairment Scale; SOFAS, Social and Occupational Functioning Assessment Scale; SPHERE, Somatic and Psychological Health Report (P-Psychological, S-Somatic); uhr, Ultra-high risk for psychosis; WHODAS, World Health Organisation Disability Assessment Schedule; WHOQoL, World Health Organisation Quality of Life Scale.

The strong association between substances indicates that polysubstance use is likely in both groups, and reflects observations from the general population in this age group (Redonnet et al., 2012), and the at-risk group (Auther et al., 2015). Both help-seeking groups had higher rates of smoking and substance use than the general Australian population (Scollo and Winstanley, 2008). For example, the National Drug Strategy Household Survey 2013 reported 18.6% of

Table 4
Alcohol involvement score adjusting for tobacco and cannabis involvement.

Alcohol involvement score				
Model	Variables	Co-efficient	p-Value	95% CI
Model 2	At-risk status (UHR)	0.51	0.24	−0.34–1.36
	Tobacco involvement	0.24	0.01	−0.20–2.93
	(+Model 1)	–	–	–
Model 3	At-risk status (UHR)	0.75	0.21	−0.43–1.93
	Tobacco involvement	0.25	0.01	0.18–0.32
Model 4	At-risk status (UHR)	0.33	0.66	−1.15–1.81
	Tobacco involvement	0.22	0.01	0.13–0.32
	Tobacco involvement × UHR	0.09	0.21	−0.05–0.22
Model 5	At-risk status (UHR)	0.67	0.13	−0.19–1.52
	Cannabis involvement	0.22	0.01	0.16–0.28
	(+Model 1)	–	–	–
Model 6	At-risk status (UHR)	0.6	0.18	−0.27–1.47
	Cannabis involvement	0.24	0.01	0.17–0.31
	Cannabis involvement × UHR	−0.04	0.47	−0.14–0.07
Model 7	At-risk status (UHR)	0.53	0.21	−0.31–1.38
	Tobacco involvement	0.21	0.01	0.16–0.27
	Cannabis involvement	0.08	0.01	0.02–0.15

young people (18–24) currently smoked tobacco (AIHW, 2014), compared with 52% of our at-risk sample and 45% help-seeking controls. Our findings therefore support previous research reporting elevated levels of substance use in help-seeking adolescents (Hermens et al., 2013).

People with schizophrenia have high rates of smoking (de Leon and Diaz, 2005), alcohol and cannabis use (Addy et al., 2012; Drake and Mueser, 2002). Our findings support recent research suggesting risk factors for poor health and long term outcome occur prior to the onset of psychosis (Addington et al., 2014; Carney et al., 2016). Substance use is linked to poor psychological outcome and high rates of relapse in patient groups (Hides et al., 2006; Lambert et al., 2005), particularly in individuals who continue to use substances after the onset of psychotic symptoms (Colizzi et al., 2015a). Therefore, in both help-seeking groups, high rates of substance use may have a detrimental effect on mental health.

Similar research has found help-seeking youth with mood disorders were significantly more likely to use substances such as cannabis and tobacco if they presented with a high degree of distress and functional disability (Scott et al., 2013; Scott et al., 2014). Additionally, previous research with the UHR group suggests enhancement in mood is the primary reason for using substances (Gill et al., 2015). Despite some significant results, the majority of associations between substance involvement and individual clinical variables were weak, and we did not clearly identify any significant clinical predictors of substance use. Therefore, despite these factors being higher in the at-risk group, our findings suggest there may be mediating variables not present in the analysis that explain the increased risk of substance use in the UHR group. We can speculate about several possibilities.

First, there may be a shared vulnerability to schizophrenia spectrum disorders and substance use disorders. Although early intervention may prevent the onset of full threshold psychotic symptoms, it may be that at-risk individuals are also at-risk for substance misuse. This possibility arises from the high degree of heritability and comorbidity of substance use disorders and schizophrenia (Chambers et al., 2001). An overlap in genes which are implicated in schizophrenia and substance abuse, such as those responsible for the modulation of dopamine systems could account for this (Volkow, 2009).

Similarly, shared psychosocial vulnerabilities such as social deprivation or childhood adversity have been found to increase the liability for both factors (Howes et al., 2004; Redonnet et al., 2012). At-risk status was not independently associated with cannabis use in our sample, despite rates being higher in this group. Therefore, some people may possess other underlying vulnerabilities to psychosis which may be moderated by the effects of substance use at an early age (Caspi et al., 2005; Colizzi et al., 2015b; Henquet et al., 2008). For example, cannabis use when combined with social adversity is believed to increase the risk for psychotic disorder beyond just the individual factors (Stilo et al., 2015).

Finally, substance use could increase vulnerability to schizophrenia, which may explain the higher rates of substance use in those at-risk for psychosis. Cannabis use, particularly at an early age, is associated with the onset of psychotic symptoms (Donoghue et al., 2014; Helle et al., 2016; Stefanis et al., 2013), and tobacco use may also contribute to the onset of psychotic symptoms (Gurillo et al., 2015). Recent research with the UHR group suggests that there is a dose-response relationship, where cannabis abuse or dependence increases the risk for transition, although this relationship is weakened when alcohol use is taken into account (Auther et al., 2015; Kraan et al., 2015).

4.1. Study limitations

Our cross-sectional study means we cannot determine causality. Longitudinal follow up will establish any variables which determine continued substance use, as well as highlighting any relationship with transition. Additionally, our sample may not represent the general UHR population. Although the CAARMS positive subscales were used to determine psychosis risk, additional criteria such as functioning and genetic risk, were not applied. However, we note that Cornblatt et al. used only the attenuated psychotic symptoms group in their recent study (Cornblatt et al., 2015). Another limitation is that individuals presented to youth mental health clinics and may differ from traditional help-seeking populations presenting to primary care. Finally, we did not control for multiple comparisons, which may have increased the risk of Type II error. As quantile median regression was not an acceptable approach to use for cannabis involvement scores (due to a failure of the models to converge), any conclusions derived about cannabis use should be made with caution.

4.2. Clinical implications

The increased substance use observed in at-risk youth has clinical implications. First, it places young people at increased risk of metabolic disturbances if they do transition to a first-episode of psychosis and receive anti-psychotic medication. Second, these behaviours are modifiable, and young people may wish to engage in lifestyle interventions such as smoking cessation programs. Regardless of whether an individual later experiences psychosis or not, the UHR phase represents an opportunity for early intervention to prevent or minimise future ill-health. Third, high rates of unhealthy lifestyle factors may increase the risk of psychosis (Di Forti et al., 2014; Gurillo et al., 2015). Co-morbid substance use disorders are common in people with schizophrenia (Volkow, 2009), depression (Boschloo et al., 2011), and anxiety (Conway et al., 2006). Therefore, promoting a healthier lifestyle and encouraging cessation of substances could improve outcome.

4.3. Conclusion

This current study adds to growing evidence suggesting increased rates of substance use are common in young people presenting with mental health difficulties, particularly those at-risk for psychosis. The negative consequences of continued substance use may be more pronounced in this group, who are already at risk for poor physical and mental health in the future. Therefore, this phase is an important stage to intervene with lifestyle interventions to promote healthy living, and has the potential to improve physical health, and benefit mental health and wellbeing.

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Paper 3

Cannabis use and symptom severity in individuals at ultra high risk for psychosis: a meta-analysis

Author Contributions:

Rebekah Carney conceived the original idea for the review, conducted the literature search, decided on eligibility criteria, screened the articles, conducted the data extraction and synthesis, conducted the meta-analyses and interpreted the findings. Rebekah created the first draft of the manuscript and completed all revisions following review by the co-authors.

Professor Alison Yung and Dr Tim Bradshaw also contributed to the design of the review, and provided methodological guidance and supervisory input. Jack Cotter and Joe Firth independently checked articles for eligibility. All authors critically reviewed and agreed on the submitted manuscript for publication.

Meta-analysis

Cannabis use and symptom severity in individuals at ultra high risk for psychosis: a meta-analysis

Carney R, Cotter J, Firth J, Bradshaw T, Yung AR. Cannabis use and symptom severity in individuals at ultra high risk for psychosis: a meta-analysis.

Objective: We aimed to assess whether individuals at ultra high risk (UHR) for psychosis have higher rates of cannabis use and cannabis use disorders (CUDs) than non-UHR individuals and determine whether UHR cannabis users have more severe psychotic experiences than non-users.
Method: We conducted a meta-analysis of studies reporting cannabis use in the UHR group and/or positive or negative symptoms among UHR cannabis users and non-users. Logit event rates were calculated for cannabis use, in addition to odds ratios to assess the difference between UHR and controls. Severity of clinical symptoms in UHR cannabis users and non-users was compared using Hedges' g.
Results: Thirty unique studies were included (UHR *n* = 4205, controls *n* = 667) containing data from cross-sectional and longitudinal studies, and randomised control trials. UHR individuals have high rates of current (26.7%) and lifetime (52.8%) cannabis use, and CUDs (12.8%). Lifetime use and CUDs were significantly higher than controls (lifetime OR: 2.09; CUD OR: 5.49). UHR cannabis users had higher rates of unusual thought content and suspiciousness than non-users.
Conclusion: Ultra high risk individuals have high rates of cannabis use and CUDs, and cannabis users had more severe positive symptoms. Targeting substance use during the UHR phase may have significant benefits to an individual's long-term outcome.

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Summations

- Ultra high risk (UHR) individuals are more likely to have used cannabis in their lifetime than controls.
- UHR individuals are more likely to have a comorbid cannabis abuse disorder than controls.
- UHR cannabis users had significantly higher levels of unusual thought content and suspiciousness compared with UHR non-cannabis users.

Considerations

- Included studies often had different methods of identifying cannabis users, and in some cases, use of cannabis was not a primary outcome but was reported as a mediating variable, or secondary area of interest.
- We were unable to account for the use of other substances in our meta-analysis which may have driven the relationship between cannabis use and increased severity of specific positive symptoms.
- Substantial heterogeneity was observed, which may have been the result of clinical and/or methodological differences across studies.

Introduction

Cannabis is one of the most frequently used illicit drugs worldwide (1). It significantly increases the risk of developing a psychotic disorder, particularly among those individuals who use it at an early age (2–4), who frequently use high-potency cannabis or 'skunk' (5, 6) and who have a genetic predisposition for psychosis (7).

People with schizophrenia are more likely to use cannabis and have comorbid substance use disorders than the general population (8). This increased comorbidity is associated with poor clinical outcomes: increased premature mortality, poor engagement with services and increased rates of hospitalisation (9, 10). Given the risks of continued substance use, it is important to identify when these problems first emerge. High rates of cannabis use are often observed at an early stage, in people with first-episode psychosis (FEP; (11)). Yet this unhealthy profile may even predate the onset of full psychotic symptoms, during the ultra high risk (UHR) phase.

Young people at UHR for psychosis (also referred to as 'clinical high risk (CHR)' or 'at-risk mental state') can be identified using operationalised criteria (12–14). An individual must fit one, or a combination of the following criteria: presence of attenuated psychotic symptoms, brief intermittent psychotic symptoms or a genetic-risk combined with a recent decline in functioning (15). Substance use research in the UHR group has mainly focussed on identifying whether cannabis use predicts transition to psychosis. A recent meta-analysis provides evidence for a dose–response relationship, where heavy cannabis use (including abuse or dependence) predicted increased likelihood of later transition to psychotic disorder (16).

Previous reviews have also explored the prevalence of substance use in the UHR group, (17, 18). However, the findings of these reviews were largely inconclusive, due to the lack of research available when the searches were conducted, and the main conclusions were that more prospective studies are required before any conclusions can be made regarding substance use in this group. To date, no meta-analyses have been conducted in this area to allow for more robust conclusions, and a meta-analysis comparing cannabis use in the UHR group to healthy controls (HCs) is lacking. Additionally, little is known about the relationship between cannabis use and attenuated positive and negative symptoms in the UHR group. This is despite many studies reporting a link between symptom severity and cannabis use in FEP and schizophrenia (19). For example, FEP individuals who used cannabis had more severe positive symptoms including hallucinations, suspiciousness and delusions, in addition to other clinical factors such as mania and poor general functioning than non-cannabis users (19).

Thus we aimed to provide robust, up-to-date statistical analyses of the literature examining cannabis use in the UHR group. Therefore, this review aimed to address the following questions:

i) Do UHR individuals have higher rates of current and lifetime cannabis use than HCs?
ii) Do UHR individuals have higher rates of cannabis use disorders (CUDs) than HCs ?
iii) Do UHR cannabis users have higher positive and negative symptoms than non-cannabis using UHR subjects?

Method

This review was conducted according to PRISMA guidelines for reporting systematic reviews (20).

Study inclusion

Eligible studies were original research articles published in peer-reviewed journals, with populations meeting criteria for being at 'UHR' or 'CHR' (or similarly defined) of psychosis, based on a clinically recognised instrument (21). Studies reporting the proportion of UHR individuals who claimed to currently use cannabis, or have done so in their lifetime, or having a current/lifetime CUD in accordance with DSM-IV/ICD criteria were included. Studies were also included if they reported positive or negative symptoms in both UHR cannabis users and non-users, as measured by a clinically validated tool. Eligible studies included cross-sectional and longitudinal analyses or intervention studies reporting baseline data on cannabis use in UHR individuals.

Studies including only subjects at genetic-risk, case studies, reviews and non-English language articles were excluded. Studies reporting general substance use and not cannabis use specifically were also excluded. Where participant samples overlapped, only the larger sample was included in the review. Where study samples overlapped but reported different outcomes, for example cannabis use and cannabis dependence, both were included in the respective meta-analyses. Authors were contacted if it was unclear whether samples overlapped. To avoid bias, studies using UHR individuals recruited solely from prisons, or young offender institutions were excluded (22) as substance use in these groups tends to be higher than in the general population (23).

On 8th December 2016, we conducted an electronic database search of Ovid MEDLINE, PsycINFO, EMBASE, AMED and the Cochrane Central Register of Controlled Trials (CENTRAL) using the following keyword search terms: ['clinical high risk' or 'CHR' or 'ultra high risk' or 'UHR' or 'at-risk mental state' or 'ARMS' or 'attenuated positive symptoms' or 'attenuated psychotic symptoms'] and ['psychosis' or 'psychotic' or 'schizophrenia'] and ['cannabis' or 'marijuana' or 'substance use' or 'substance abuse' or 'substance dependence' or 'substance misuse' or 'drug*' or 'recreational drug' or 'drug abuse' or 'hallucinogen']. In addition, a basic search of Google Scholar was conducted and the reference lists of retrieved papers were reviewed to identify any additional relevant publications.

Study selection and data extraction

Three authors (R.C, J.F & J.C) independently screened articles for eligibility. A tool was developed to extract the following data for eligible studies: (1) study characteristics (author, year of publication, country of origin, study design); (2) sample demographics (sample size, gender composition, mean age); (3) instrument used to assess at-risk status; (4) rate of cannabis use in UHR and control groups (measure, prevalence or sample mean); (5) ICD/DSM CUDs (measure, prevalence); (6) positive and negative symptoms for UHR cannabis users and non-cannabis users (sample size, measure, mean, standard deviation); (7) summary of findings. Studies that included a HC group were assessed for quality using the Newcastle–Ottawa Scale (24), a validated instrument for non-randomised trials and observational studies. The scale utilises a star system to assess selection of participants, comparability of groups and assessment of outcome or exposure of interest. Studies awarded 8–9 stars were classed as high quality, 4–7 medium quality and 0–3 low quality. Any disagreements were resolved through discussion.

Statistical analysis

All statistical analyses were performed using COMPREHENSIVE META-ANALYSIS Version 3.0 (25). Proportional meta-analyses using random-effects models were used to estimate logit event rates of current and lifetime cannabis use across the UHR samples. To assess the difference in cannabis use between UHR and HCs, odds ratios were used,

and 95% CI were calculated. Standardised mean differences (SMD) were calculated to assess differences in overall positive and negative symptom severity between UHR cannabis users and non-users using Hedges' g. SMDs were also conducted on individual positive symptoms if reported among three or more samples. Random-effects models were used throughout to account for heterogeneity between studies (26, 27). Heterogeneity across studies was quantified using the I^2 statistic (28).

Results

Study characteristics

The study selection process is summarised in Fig. 1. A total of 30 unique citations were included (UHR $n = 4205$; controls $n = 667$): 26 studies from the initial search and four additional studies from searching of reference lists (Table 1). Studies were conducted in 10 countries: Canada ($n = 6$), Netherlands ($n = 5$), USA ($n = 5$), Switzerland ($n = 3$), Austria ($n = 2$), Australia ($n = 4$), UK ($n = 2$), France ($n = 1$), Germany ($n = 1$) and Spain ($n = 1$). Study samples overlapped in three instances; however, different outcomes were included in separate meta-analyses (29–34). The majority of studies that included a control group were deemed medium quality, with only one study rated as high quality (35), (see Appendix S1 for individual scores).

Current and lifetime cannabis use

Eighteen studies stated the proportion of UHR individuals who self-reported current cannabis use, defined as any use within the past month, with the exception of one study (39), which defined current use as any cannabis within the past 3 months. Proportionate meta-analysis revealed that 26.7% of UHR individuals currently used cannabis ($n = 3068$, 95% CI = 0.22–0.32; I^2: 85.70%; Fig. 2). A sensitivity analysis removing the study which defined current use as cannabis intake within the last 3 months (rather than last month) found that excluding this study had a negligible impact on the results. Comparisons of current cannabis use in UHR and non-UHR control groups indicated that UHR individuals were more likely to be current cannabis users than HCs, although the difference fell short of statistical significance (OR: 1.56; $P = 0.08$; 95% CI: 0.94–2.57; I^2: 59.52%; see Appendix S1).

Eleven studies reported lifetime cannabis use. Proportional meta-analyses found that 52.8% of UHR individuals had used cannabis at some point
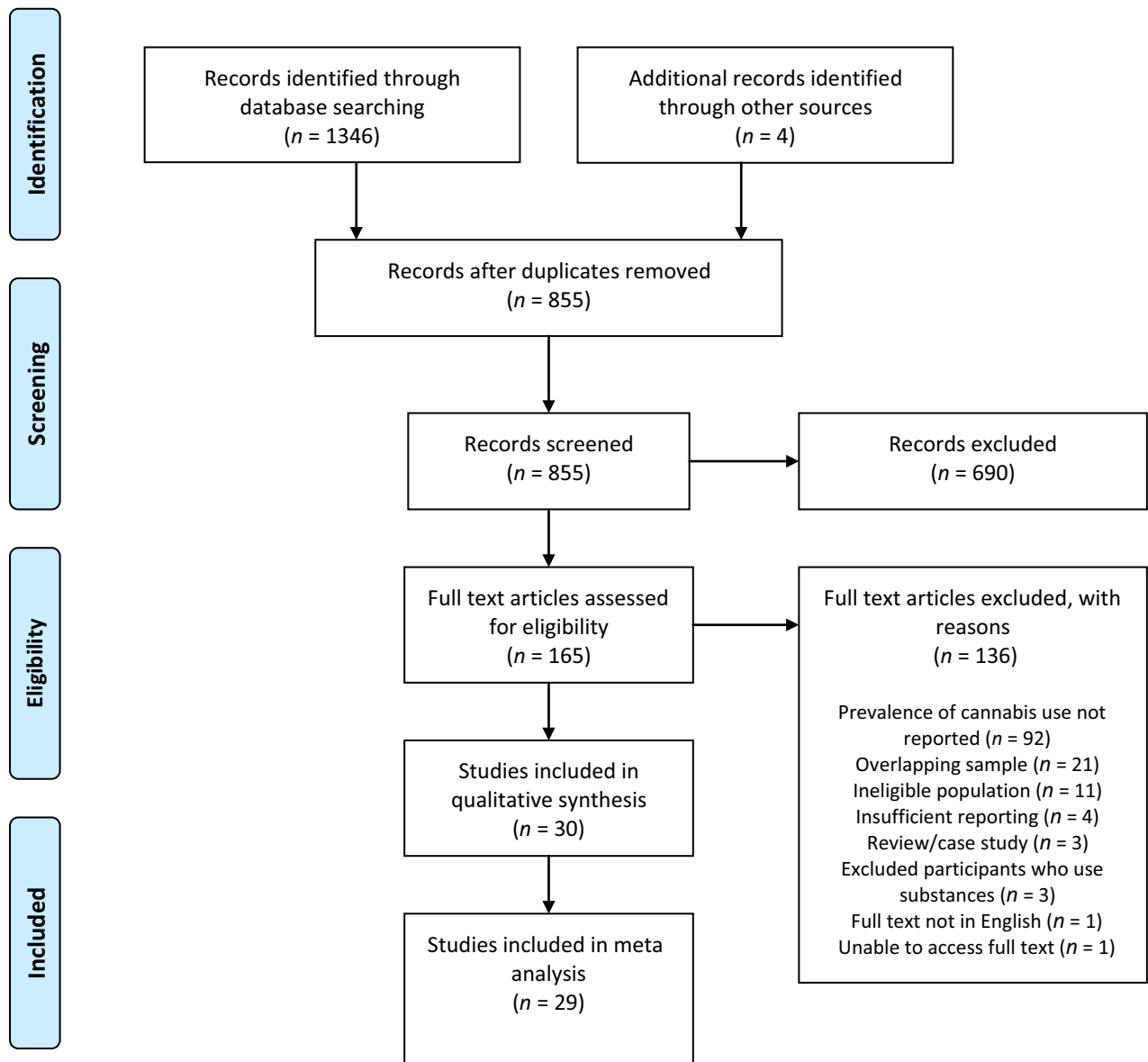
Fig. 1. PRISMA flow diagram. [Colour figure can be viewed at wileyonlinelibrary.com]

in their lifetime ($n = 2251$, 95% CI = 0.47–0.59; I^2: 84.02%). UHR individuals were also significantly more likely to have used cannabis in their lifetime compared with HCs (OR: 2.09; $P = 0.037$; 95% CI: 1.04–4.19; I^2: 67.63%; Fig. 3).

Cannabis use disorders (CUD)

Eleven studies reported comorbid cannabis abuse or dependence disorders (CUD) in UHR individuals, according to the DSM-IV criteria. Meta-analysis of prevalence rates indicated 12.8% of UHR individuals had a current comorbid CUD (95% CI = 0.09–0.19; I^2: 90.32%). UHR individuals were significantly more likely to have a CUD than controls (OR: 5.49, $P = 0.001$; 95% CI:

1.97–15.32; I^2: 0%). Lifetime CUDs were reported in only two studies and were not included in the meta-analysis (35, 41). The rates of lifetime CUDs were 12.8% ($n = 46$) and 26.7% ($n = 16$) respectively.

Positive and negative symptoms

Table 2 displays the effect and sample sizes, heterogeneity statistics and significance values of the relationships between cannabis use and symptoms in UHR individuals.

Scores for total positive symptoms were derived predominantly from overall scores on the positive items of the SIPS (42). Total positive symptoms did not significantly differ between UHR cannabis

Table 1. Studies included in review

Study reference and country	Group	N (male/female)	At-risk screening instrument	Outcome of interest	Study design
Addington et al. (35) — Canada	UHR	360 (211/149)	SIPS	Current cannabis use, DSM-IV current/lifetime cannabis abuse	Longitudinal
	HC	108 (87/21)			
Amminger et al. (29) — Austria	UHR	81 (27/54)	PANSS/GAF	Current cannabis use	RCT
Amminger et al. (30) — Austria	UHR	69* (27/54)	PANSS/GAF	DSM-IV cannabis abuse disorder	RCT
Auther et al. (32) — USA	UHR	101 (66/35)	SIPS	Current/lifetime cannabis use, DSM-IV cannabis abuse, SIPS-positive/negative symptoms in cannabis users	Longitudinal + cross-sectional
	HC	59 (30/29)			
Auther et al. (31) — USA	UHR	341 (210/131)	SIPS	Current cannabis use, DSM-IV cannabis abuse disorder, SIPS-positive/negative symptoms in cannabis users	Longitudinal + cross-sectional
Bechdolf et al. (57) — Germany	UHR	156 (106/50)	SIPS	DSM-IV cannabis abuse disorder	RCT
Bloemen et al. (58) - Netherlands	UHR	37 (26/11)	SIPS	Current/lifetime use of cannabis	Longitudinal
	HC	10 (8/2)			
Bousman et al. (33) — Australia	UHR	225 (93/132)	CAARMS	Lifetime cannabis use	Longitudinal
Buchy et al. (59) — Canada	UHR	735 (423/312)	SIPS	Current/lifetime cannabis use, DSM-IV cannabis abuse or dependence, SIPS-positive/negative symptoms in cannabis users	Longitudinal
	HC	278 (140/138)			
Buchy et al. (60) — Canada	UHR	170 (96/74)	SIPS	Current cannabis use, DSM-IV cannabis abuse or dependence	Longitudinal
Bugra et al. (61) — Switzerland	UHR	74 (47/27)	BSIP	Current/lifetime cannabis use, BPRS positive and SANS negative symptoms in cannabis users	Cross-sectional
Carney et al. (36) — Australia	UHR	279 (93/186)	CAARMS	Current/lifetime cannabis use	Cross-sectional
Corcoran et al. (62) — USA	UHR	32 (26/6)	SIPS	Lifetime cannabis use, DSM-IV cannabis abuse or dependence, SIPS-positive/negative symptoms in cannabis users	Longitudinal
Dragt et al. (63) — Netherlands	UHR	243 (140/103)	SIPS/BSABS-P	Lifetime cannabis use, DSM-IV cannabis use disorder, SIPS-positive/negative symptoms in cannabis users	Longitudinal
Gill et al. (37) — USA	UHR	102 (79/23)	SIPS	Current cannabis use, SIPS-positive symptoms in cannabis users	Cross-sectional
Hagenmuller et al. (64) — Switzerland	UHR	86 (53/33)	SIPS	Current cannabis use	Cross-sectional
	HC	47 (23/21)			
Machielson et al. (65) — Netherlands	UHR	59 (52/7)	SIPS	DSM-IV cannabis abuse or dependence, SIPS-positive/negative symptoms	Cross-sectional
Magaud et al. (66) — France	UHR	77 (92/46)	CAARMS	Current cannabis use	Cross-sectional
Marshall et al. (67) — Canada	UHR	48 (33/15)	SIPS	DSM-IV cannabis abuse disorder	Longitudinal + cross-sectional
McHugh et al. (38) — Australia	UHR	190 (76/114)	CAARMS	Lifetime cannabis use	RCT
Mizrahi et al. (68) — Canada	UHR	24 (13/11)	SIPS	SIPS-positive/negative symptoms in cannabis users	Cross-sectional
Nieman et al. (69) — Netherlands	UHR	147 (71/76)	CAARMS	Current cannabis use, CAARMS-positive/negative symptoms	Cross-sectional
Phillips et al. (34) — Australia	UHR	100 (49/51)	CAARMS	Lifetime cannabis use, DSM-IV cannabis dependence	Longitudinal
Pruessner et al. (39) — Canada	UHR	30 (16/14)	CAARMS	Current cannabis use	Cross-sectional
	HC	30 (15/15)			
Russo et al. (70) — UK	UHR	60 (31/29)	CAARMS	Current/lifetime cannabis use	Cross-sectional
	HC	60 (26/34)			
Simon & Umbricht (71) — Switzerland	UHR	72 (43/29)	SIPS	Current cannabis use	Longitudinal
Stojanovic et al. (72) — Spain	UHR	17 (12/5)	CAARMS	Current cannabis use	Cross-sectional
	HC	25 (12/13)			
Valmaggia et al. (40) — UK	UHR	182 (104/78)	CAARMS	Current/lifetime cannabis use	Longitudinal
Van Tricht et al. (73) — Netherlands	UHR	48 (32/36)	SIPS	SIPS-positive/negative symptoms in cannabis users	Cross-sectional
	HC	50 (33/17)			
Woods et al. (41) — USA	UHR	60 (39/21)	SIPS	Lifetime cannabis abuse or dependence	RCT

HC, healthy controls; BPRS, brief psychiatric rating scale; BSABS, bonn scale for the assessment of basic symptoms; BSIP, basel screening instrument for psychosis, CAARMS, comprehensive assessment of at-risk mental states; DSM-IV, Diagnostic and statistical manual of mental disorders IV; SIPS, structured interview for prodromal symptoms; UHR, ultra high risk; PANSS, positive and negative syndrome scale; RCT, randomised controlled trial.
*Long-term follow-up, missing data for 12 participants.

users and non-cannabis users. In two studies, UHR cannabis users also included those who had used in their lifetime and removal of these studies did not affect significance levels. When individual items of positive symptom scales were analysed, UHR cannabis users were found to have
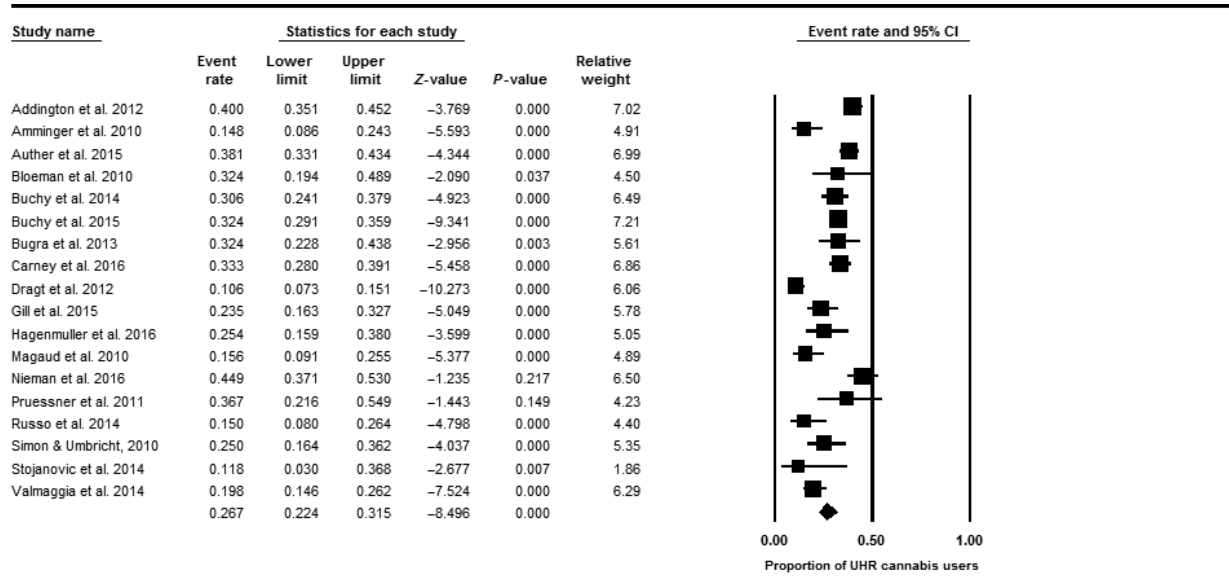
Fig. 2. Summary of rates of current cannabis use in ultra high risk individuals.
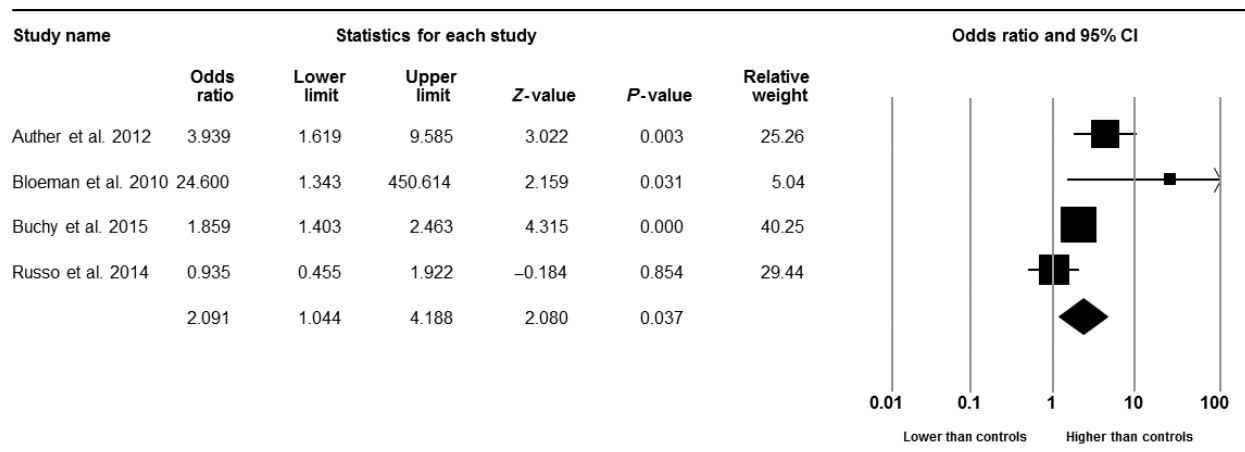
Meta−analysis

Fig. 3. Lifetime use of cannabis ultra high risk vs. healthy controls.

significantly higher levels of unusual thought content (UTC) and suspiciousness than non-cannabis users, but no differences were found for perceptual abnormalities, grandiosity or levels of disorganised speech (Table 2). Negative symptoms were reported less frequently, and no significant difference was found for overall scores between cannabis users and non-users.

Discussion

This meta-analysis indicates that UHR individuals have high rates of cannabis use. They are more than twice as likely to have used cannabis in their lifetime compared with HCs. UHR individuals were also more than five times as likely to have a

current cannabis abuse disorder compared to HCs. This is particularly problematic given the risks associated with continued cannabis use. Even prior to the onset of psychotic disorders, cannabis use is associated with increased severity of certain positive symptoms, as UHR cannabis users had significantly higher levels of unusual thought content and suspiciousness compared with non-users.

Cannabis use in UHR

We found that 52.8% of UHR individuals reported using cannabis in their lifetime, which is a similar proportion to FEP samples (11), and higher than that of healthy populations (43). Indeed, our analyses found significantly higher rates of lifetime

Table 2. Meta-analyses outputs

Cannabis use in UHR individuals	Studies Included (*k*)	N (UHR)	Event Rate	95% CI	I^2	-	-
Current cannabis use	18	3068	0.267	0.22–0.32	85.70		
Lifetime cannabis use	11	2251	0.528	0.47–0.59	84.02		
Current cannabis abuse disorder	11	2315	0.128	0.09–0.19	90.32		

UHR vs. HC	Studies Included (*k*)	*N* (UHR)	*N* (HC)	Odds Ratio	95% CI	I^2	Z	P-value
Current cannabis use	7	1289	622	1.56	0.94–2.57	59.52	1.73	0.08
Lifetime cannabis use	4	930	405	2.09	1.04–4.19	67.63	2.08	0.04
Current cannabis abuse disorder	2	1095	458	5.49	1.97–15.32	0	3.25	0.001

Symptoms in UHR-CU vs. UHR-NU	Studies Included (*k*)	*N* (UHR-C)	*N* (UHR-NC)	Hedges' g	95% CI	I^2	Z	P-value
Total Positive Symptoms	8	325	593	0.16	-0.05–0.37	45.70	1.52	0.13
Disorganised Speech	4	244	452	0.05	-0.27–0.38	71.05	0.31	0.75
Grandiosity	3	178	371	0.11	-0.11–0.32	19.96	0.96	0.34
Perceptual Abnormalities	4	244	452	0.05	-0.115–0.206	0.00	0.56	0.57
Suspiciousness	3	178	371	0.21	0.02–0.39	0.00	2.22	0.03
Unusual Thought Content	4	244	452	0.27	0.07–0.48	30.29	2.63	0.01
Total Negative Symptoms	7	301	515	-0.03	-0.29–0.23	59.77	-0.23	0.82

UHR, ultra high risk.

cannabis use in the UHR samples than in the HC groups. Meta-analyses also revealed approximately one in four UHR individuals currently used cannabis. We also found high rates of comorbid CUDs in UHR individuals (12.8%). This is slightly lower than that found in people with schizophrenia (16%) (8). However, it is important to consider that we focused on young people in the UHR phase; that is, those who are putatively prodromal and are not yet experiencing full psychotic symptoms. Therefore, even prior to the onset of psychosis, UHR individuals are likely to engage in risky cannabis use.

High rates of cannabis use in this group are perhaps unsurprising given that use of substances is common in young people who present for mental health care (44, 45) and people with early psychosis (11). As there is evidence to suggest frequent use of high-potency cannabis increases the risk for later transition (5, 6), it is important that early intervention services encourage substance use reduction upon first presentation. A previous review and meta-analysis found that UHR individuals are significantly more likely to smoke, abuse alcohol and have lower levels of physical activity than their peers (46). Here, we add to this evidence to suggest that this group is also more likely to have used cannabis or have a CUD, posing an additional risk factor to both physical and mental health.

Cannabis use and symptoms

Our meta-analysis is the first to find a statistically significant association between UHR cannabis use and more severe positive symptoms (unusual thought content and suspiciousness). This is in line with previous research in people with FEP. For example, the use of cannabis at the time of, and after FEP, is associated with increased positive symptoms and poorer psychosocial functioning and long-term outcome (10, 19). It also supports the findings of Valmaggia et al. (40) where UHR participants often reported that they stopped using cannabis due to exacerbation of positive symptoms. Similar to Seddon et al. (2016), we also found no association between cannabis use and negative symptoms. We were unable to analyse individual negative symptoms due to a lack of available data. As such, analysis of global symptom domains may have masked any differences in individual symptoms.

We can only speculate about the reasons for the association between cannabis and increased positive symptoms. Positive symptoms may occur as a direct result of substance use. Indeed, cannabis can induce symptoms of psychosis in healthy populations, and may therefore influence symptom severity in the UHR group (47). Alternatively, those with more pronounced positive symptoms may be more likely to self-medicate using substances such as cannabis (48). However, a study by Gill et al., (37) found that mood enhancement was the primary reason for cannabis use reported by UHR individuals. Therefore, it could be used as a way to alleviate other symptoms such as anxiety or low mood (45) that are frequently found in the UHR group (49, 50). Another possibility is that a separate factor is driving the increase in positive symptoms. Our meta-analysis does not take into account potential

confounders, such as alcohol or other substance use. Cannabis users are significantly more likely to engage in use of other substances, which may contribute to severity of positive symptoms (51). For example, a recent cohort study found alcohol confounds the relationship between cannabis use and transition to full-threshold psychotic disorders (31). We were also unable to account for the last time a person used cannabis across all studies. Therefore, increased positive symptoms could be due a result of the acute, intoxicating effects of cannabis.

From the studies included in our analysis, we were unable to account for the strength of cannabis young people were using. This may have been why we only found a significant difference for two of the positive symptoms. People with psychosis are more likely to use high-potency cannabis or 'skunk' (52). As high-potency cannabis has been shown to have the most harmful effects for both mental and physical health, it may be that those using the strongest forms of cannabis experience more severe symptoms. Similarly, the adverse health effects of synthetic cannabinoids such as 'spice' have been recognised, with the increased risk for psychotic-like experiences being a primary area of concern (53). As there has been a recent rise in the use of synthetic cannabinoids, more research is required to establish the effect these have on mental health as well as the patterns of use in people with emerging mental health difficulties.

Clinical implications

Irrespective of causation, high rates of cannabis use in the UHR group carries important clinical implications. Although many UHR individuals will not develop full-threshold psychosis, they may go on to have anxiety, mood or substance use disorders (50), and continue to function poorly regardless of transition or symptomatic remission (54, 55). Therefore, it is important to address any comorbid disorders at an early stage. Future research should assess the efficacy of interventions used to reduce cannabis use in UHR individuals upon first presentation to mental health services. For example, motivational interviewing and cognitive behaviour therapy have been found to be effective in reducing cannabis use among early psychosis groups (57), although a randomised control trial in the UHR group is yet to be conducted. Longitudinal studies are also required to highlight any relationship between continued cannabis use and factors such as long-term outcome, functioning and symptoms over time.

Limitations

High levels of heterogeneity were observed for all estimates which likely reflect clinical and methodological differences between studies. We performed sensitivity analyses in which we removed each study in turn and found that this had a negligible impact on the heterogeneity statistics, indicating that the I^2 values were not the product of the inclusion of a single study but instead reflected wider between-study differences. These may have been driven by different recruitment strategies, study locations, sample demographics and instruments that were used to define and report substance use. We included studies of varied content and design, which meant there were subtle differences in the definition of cannabis use between studies. The inconsistent nature by which cannabis use is classified is a key limitation of many of the studies and may have had an effect on our results. For example, some studies referred to lifetime use as any previous use; therefore, this may have included people with previous heavy cannabis use as well as people who have tried it just once.

The majority of studies were rated as medium quality, with only one high-quality study included in the analyses. The major source of bias related to exposure measurement as many studies did not use an objective method to classify cannabis use (such as blood/urine testing). Due to the classification of cannabis as an illicit substance in many countries, individuals may have been reluctant to admit use, leading to underreporting among both the UHR and control comparator groups. Another source of bias was that many studies also failed to control for confounding variables, such as age, gender, use of other substances and frequency of cannabis use. As mentioned previously, we were therefore, unable to control for other substances in our meta-analysis. Cannabis users are more likely to use other substances; therefore, comorbid substance use may have accounted for higher rates of UTC/suspiciousness. We also could not control for the strength or frequency of cannabis use, and the last time a person used cannabis.

Concluding remarks

Ultra high risk individuals have high rates of cannabis use and abuse which are significantly higher than HCs. Among UHR individuals, cannabis users have more severe unusual thought content and suspiciousness compared to non-cannabis users. The UHR phase represents an important opportunity to intervene, and targeting substance use at this stage may have significant benefits to an

individual's long-term outcome. Clinicians should be aware of comorbid substance use disorders in young people at UHR for psychosis, and reduction in substance use should be a priority in youth mental health services.

Acknowledgements

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. Quality assessment and meta-analyses outputs.

Paper 4

Monitoring of physical health in services for young people at ultra-high risk of psychosis

Author Contributions:

Rebekah Carney conceived the original idea for the paper, designed the audit form, extracted the data and interpreted the findings. Rebekah created the first draft of the manuscript and completed all revisions following review by the co-authors.

Professor Alison Yung provided access to the clinical files and supervised the data extraction process. Both Professor Alison Yung and Dr Tim Bradshaw provided clinical guidance, critically reviewed and approved the submitted manuscript for publication.

Original Article

Monitoring of physical health in services for young people at ultra-high risk of psychosis

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Abstract

Aim: People with schizophrenia have poor physical health and high rates of premature mortality. Risk factors for later cardiovascular disease are present from an early stage, and recording of these factors is recommended in first-episode services. However, it is unclear whether cardiometabolic risk factors are monitored prior to first-episode psychosis.

Methods: A retrospective analysis was conducted on case notes of individuals accepted into a specialized early detection service for young people at ultra-high risk for psychosis. Notes were assessed to determine whether the following physical health measures were recorded: height, weight, body mass index, blood pressure, blood glucose and lipids, physical activity levels, smoking status, substance use and alcohol intake.

Results: Forty individuals were deemed at ultra-high risk for psychosis and accepted into the service. The two measures reported most frequently were whether a person used substances (82.5%) or alcohol (72.5%), but more specific details were not commonly reported. A minority of case files contained information on height (2.5%), weight (7.5%), body mass index (5%), blood glucose (2.5%), smoking status (15%) and physical activity (7.5%). Six case files had no measure of physical health.

Conclusions: Physical health and unhealthy lifestyle factors were not assessed routinely in the specialized service. Clear monitoring guidelines should be developed to establish routine assessment of common metabolic risk factors present in this population.

Key words: clinical high risk, lifestyle, psychotic disorders, risk factors, schizophrenia.

INTRODUCTION

People with schizophrenia have high rates of physical ill health and premature mortality, with an average life expectancy of 13–30 years lower than the general population.[1–3] The leading cause of death is from chronic physical health conditions, such as cardiovascular disease and diabetes. People with schizophrenia have high rates of cardiometabolic risk factors such as central obesity, hypertension, hyperglycaemia and dyslipidaemia.[4,5] These cardiometabolic risk factors are associated with side effects of antipsychotic medication[6,7] and occur soon after starting treatment.[4,8,9] Additionally, poor cardiovascular health in people with schizophrenia is partly associated with unhealthy lifestyle factors. This includes high rates of alcohol, drug and tobacco use and poor levels of nutrition and low physical activity.[10–14] These unhealthy lifestyle factors may also be present prior to the initiation antipsychotic medication therapy.[15,16]

Despite available guidelines, rates of physical health screening and assessment in schizophrenia remain poor.[17] The National Audit of Schizophrenia[18] revealed only 50% of individuals with schizophrenia had their body mass index (BMI) recorded in secondary care services over 12 months.[19] As inadequate monitoring and health-care provision may contribute to poor long-term outcome, it is important that the disparities in physical health care are addressed.[2] First-episode services have developed guidelines emphasizing the importance

of capturing cardiometabolic data at regular intervals, starting before individuals begin antipsychotic treatment.[4] However, it is unclear whether it is necessary and possible to assess and monitor physical health in people before the onset of psychosis, that is, those meeting the ultra high-risk criteria.

The ultra high risk (UHR) state allows the identification of people in the putative prodrome for psychosis. Criteria have been developed to identify individuals vulnerable to developing a psychotic disorder.[20–22] These have been referred to as the prodromal, ultra-high risk (UHR), clinical high risk (CHR) and at-risk mental state (ARMS) criteria.[23] In order to meet UHR status, a patient must exhibit one or a combination of the following characteristics: presence of attenuated psychotic symptoms, brief limited intermittent psychotic symptoms that spontaneously resolve or a genetic risk combined with a significant recent decline in functioning.[24] Approximately one-third of UHR individuals transition to full-threshold psychotic disorders within 3 years.[25] These criteria have important implications for early intervention and allow us to examine both the physical and psychological health of young people prior to the development of a first psychotic episode.

Emerging evidence suggests that individuals at UHR for psychosis have high rates of unhealthy lifestyle factors, and poor physical health, prior to the onset of first-episode psychosis (FEP) (Carney et al.[26]). As the increased rate of cardiovascular disease may be partly due to modifiable risk factors, it seems appropriate to provide adequate monitoring and assessment at this early stage. However, it is unclear whether cardiometabolic risk factors are monitored effectively by UHR services. We therefore aimed to (i) review case notes of UHR individuals to see if cardiometabolic risk factors are recorded and (ii) assess the physical health of UHR individuals from the information available. Case notes were taken from a 12-month intake of referrals into a specialized UHR early detection service.

METHOD

A retrospective analysis was conducted on the case notes of clients accepted into a specialized early detection and intervention service based in Greater Manchester, UK.

Sample

The study population consisted of a 12-month intake into the Early Detection and Intervention Team (EDIT) between October 2013 and October 2014. EDIT is based in a UK National Health Service primary care setting in Salford and Wigan and accepts referrals of people aged between 14 and 35 who are at UHR for developing psychosis, defined according to the Comprehensive Assessment of At-Risk Mental States.[27]

Outcome measures

A structured audit tool was used to assess whether the following physical health measures were recorded: height, weight, body mass index (BMI), blood pressure, blood glucose, blood lipids, physical activity levels, smoking status and substance use and alcohol intake. To maintain patient confidentiality, no personal identifiable information was extracted. Demographic information consisted of age at time of acceptance, location of service and whether an individual transitioned to psychosis. For each individual measure, we noted (i) whether the variable had been assessed and (ii), if so, relevant information was recorded. If no reference to the variable was made, it was assumed that it had not been assessed. For example, if tobacco or alcohol use was measured, the frequency and quantity of use was recorded. For substance use, the name of substance was also recorded, in addition to any previous drug use. If information on physical activity were available, the type of exercise and total time spent per week was extracted.

Statistical analysis

Data analysis was conducted in SPSS version 22.0 (IBM Corp., Armonk, NY, USA).[28]

RESULTS

A total of 131 referrals were accepted for assessment by EDIT (Fig. 1). Of these 131, 40 individuals met the UHR criteria and were accepted into the clinical service. Case notes of these individuals were reviewed using a structured audit tool created by the researchers. Ninety-one referrals were not accepted as they were under-threshold ($n = 35$), met criteria for first-episode psychosis ($n = 12$), met criteria for bipolar or bipolar at risk ($n = 9$) or moved out of the area ($n = 3$). A further 32 were not assessed due to failure to attend appointments ($n = 24$), or failure to provide consent ($n = 8$).

Demographic data

The mean age at time of acceptance to EDIT was 21.4 (standard deviation (SD) = 5.5, range 14–35).

FIGURE 1. Flow chart of referrals.
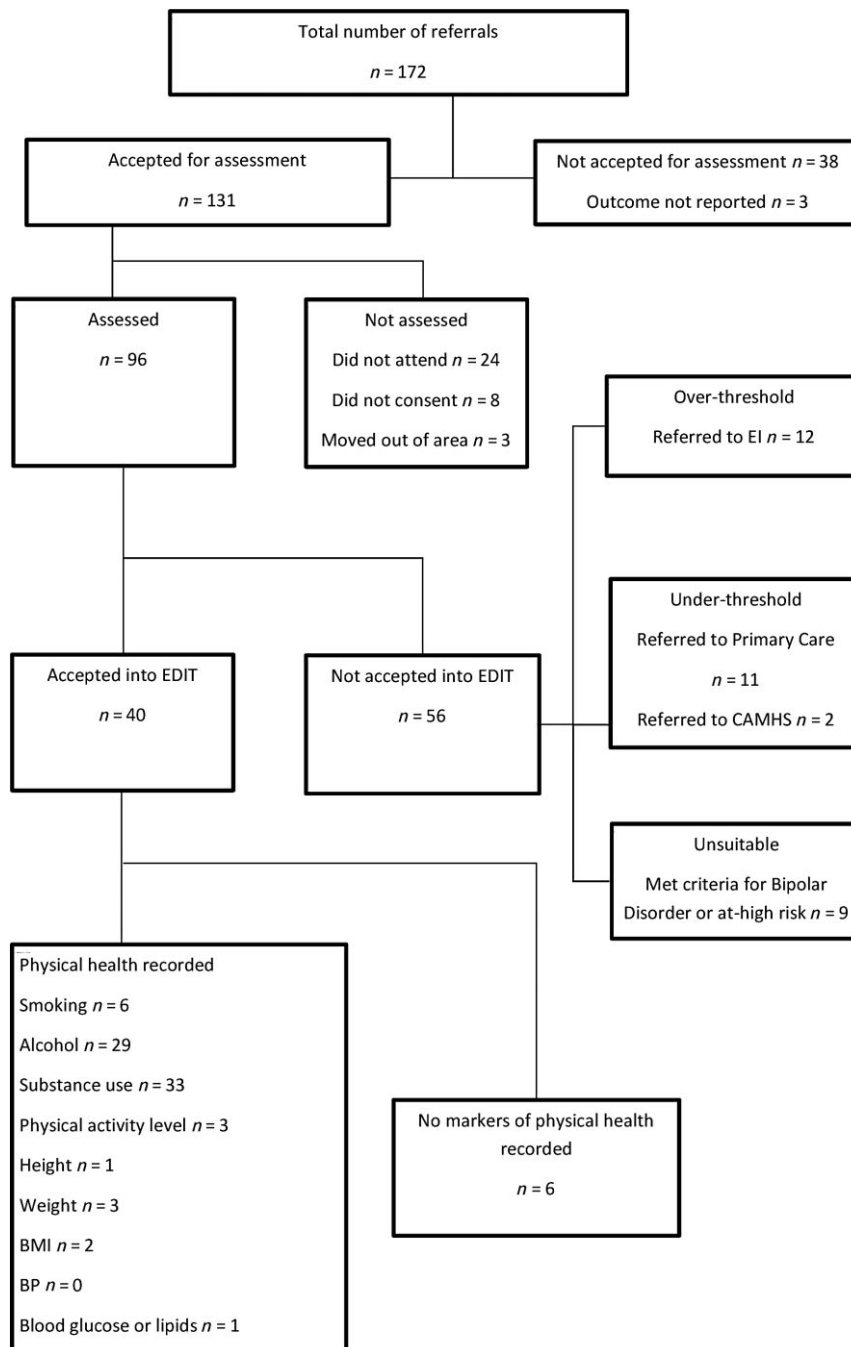
Slightly more service users came from the Wigan site ($n = 23$, 57.5%) than Salford ($n = 17$, 42.5%). A small percentage of case files contained information on transition to psychosis after being referred to EDIT ($n = 3$, 7.5%).

Information recorded

The physical health of UHR individuals was not assessed routinely (see Table 1). None of the files recorded physical health data for all factors. In total, six (15%) of the individuals accepted into the EDIT service over the previous 12 months did not have any documentation of physical health measures or information on unhealthy lifestyle factors. Anthropometric variables were reported in a minority of case files: height ($n = 1$, 2.5%), weight ($n = 3$, 7.5%), BMI ($n = 2$, 5%). Blood pressure was not documented for any referral accepted into EDIT, and blood glucose and lipid testing was provided for

TABLE 1. The proportion of case notes containing physical health information

Factor	Physical health measures noted, n (%), (n = 40)
Height	1 (2.5%)
Weight	3 (7.5%)
Body mass index	2 (5%)
Blood pressure	0 (0%)
Blood glucose/lipids	1 (2.5%)
Smoking status	6 (15%)
Alcohol use	29 (72.5%)
Substance use	33 (82.5%)
Physical activity	3 (7.5%)

TABLE 2. Proportion of people reporting tobacco, alcohol or substance use

Factor	Additional measures recorded n (%)
Smoking recorded (n = 6)	
Smoking frequency	5 (83.3%)
Smoking quantity	5 (83.3%)
Alcohol use recorded (n = 29)	
Alcohol frequency	15 (51.7%)
Alcohol quantity	12 (41.2%)
Substance use recorded (n = 32)	
Substance frequency	28 (87.5%)
Substance quantity	25 (78.1%)

only one individual. Physical activity levels were not routinely assessed, as reference to physical activity was only made in three cases (7.5%).

Current alcohol use was measured in 29 cases (72.5%). Approximately half of these cases also recorded alcohol frequency (n = 15, 51.7%) (Table 2). Quantity of alcohol consumed was also recorded in 12 cases (41.2%). The majority of case files contained a reference to substance use (n = 32, 82.5%). In these cases, the frequency of substance use was reported more often than the quantity (n = 28, 87.5%; n = 25, 78.1%). Smoking status was only available in a minority of cases (n = 6, 15%). From the six case files that reported smoking status, five contained information on frequency and quantity of tobacco use (n = 5, 83.3%).

Physical health data

Anthropometric measurements

Height was reported for one individual (180 cm), and weight was recorded in three cases (mean = 52.38 kg, SD 16.26, range 34.92–67.10 kg). BMI

values were available in two instances (m = 18.75, SD 2.62, range 16.9–20.6).

Alcohol use

From the information available, the majority of people used alcohol (n = 24, 82.8%). Alcohol abuse or misuse was documented for a high percentage of alcohol users (n = 9, 37.5%). For people who reported alcohol use, some case notes contained information about the specific drinks consumed, for example, one bottle of wine per week. This was then converted using the NHS unit calculator to provide the best estimate of alcoholic units per week. The average weekly intake of alcoholic units was 96.03 (SD 60.64, range 8–186). Nine referrals disclosed how frequently they consumed alcohol. The highest proportion of people used alcohol daily (n = 4), followed by 1–2 days per month (n = 2), 3–5 days (n = 1), 6–9 days (n = 1) and 10–19 days per month (n = 1).

Substance use

A high percentage of individuals reported no current drug use (n = 21, 65.6%). The remaining data reported drug use (n = 8, 25%), abuse (n = 2, 6.3%) or dependence (n = 1, 3.1%). Where applicable the substance name was reported in all but one case (n = 10, 90.9%). Almost all substance users used cannabis (n = 8, 72.7%); other substances included cocaine, heroin, ketamine and legal highs. Lifetime or previous substance use was reported in eight cases. The frequency and quantity of substance use was difficult to quantify, as it was often reported in terms of how much a person spent on the substance per week, for example, £100 per week. However, from the limited information available, it appears that most people who used substances did so on a daily basis (n = 5).

Smoking

From the limited information available, 50% (n = 3) of service users smoked. UHR smokers smoked daily (n = 2) and the amount ranged from two to five cigarettes per day (n = 1) to 6 to 10 per day (n = 1).

Physical activity

When physical activity was reported, all three stated the type of activity: daily jogging (n = 1), pole fitness (n = 1) and yoga (n = 1). One case stated classes were attended twice per week averaging 120 min of exercise.

DISCUSSION

Physical health monitoring and assessment in this specialized UHR service is low. None of the referrals had a complete documented assessment of physical health upon intake to the service, and six case files contained no measure of physical health. Anthropometric assessments were substantially lacking within case notes, and blood glucose assessments were found for only one individual. Although it was often reported whether a person used alcohol, substances or tobacco, more specific details relating to the extent of use were not recorded.

Because of the limited data available from the case notes, we are unable to assess the physical health and proportion of lifestyle risk factors with any certainty. However, in a large proportion of cases specific details on alcohol and substance use were only documented when it was of concern to the clinician or client. This is reflected in the large amount of average units per week provided for alcohol use. The most commonly reported drug used was cannabis. This is consistent with the findings of a previous review that also found the most commonly reported drug in UHR individuals was cannabis, and the rates of cannabis use were much higher than found in the general population (Carney et al.[26]).

The findings from this service evaluation are similar to the national audit conducted by Crawford et al.,[19] which found that assessment and treatment of physical health complaints in severe mental illness are below recommended standards. This is an important failure of care considering that a large proportion of premature mortality and morbidity seen in these patients may be preventable.[29,30] Early monitoring of physical health is possible through UHR services; however, at least in this service in Greater Manchester it does not occur.

Barriers to providing effective management and assessment of physical illness in mental health services have previously been discussed.[2,31] A key issue is a lack of clarity and consensus regarding with whom the responsibility lies.[2,31–33] Additionally, the lack of integration between mental and physical health services contributes to suboptimal health care. In many cases, people with schizophrenia only access health care via mental health services, suggesting a more holistic approach to service provision is required. Other factors reported by mental health outreach clinicians include uncertainty over what should be monitored and when, lack of confidence interpreting abnormal results and limited access to equipment.[31,34] A large proportion of mental health professionals fail to discuss meta-bolic side effects of medication due to issues around non-adherence.[34] Although this does not usually apply to the UHR group, it is an important reflection of how motivations of the clinician may affect screening in mental health care.

Clinical implications and recommendations

This audit provides evidence that improvements are needed for physical health-care provision in UHR. NICE guidelines currently recommend routine monitoring of weight, cardiovascular and metabolic parameters for people with psychosis and schizophrenia.[35] The implementation of these recommendations in early intervention services is a national priority. A leading C-QUIN target for 2014/2015 focuses on improving physical health care for people with psychosis to reduce premature mortality. Local trusts are paid for routine monitoring and assessment of cardiometabolic parameters, including lifestyle information, BMI, blood pressure, glucose regulation and blood lipids.[36]

Despite substantial national targets for psychosis, the same recommendations are not given for at-risk populations. This is concerning, as UHR individuals display a wide range of risk factors for future ill health, which are largely preventable. Therefore, clear monitoring guidelines are required within early detection services to encourage screening of early risk factors. One way this could be implemented is to use a concise physical health assessment tool, administered at, or soon after intake to the early detection service. The Health Improvement Profile was a tool designed to aid mental health nurses with physical assessments in people with severe mental illness.[37,38] A similar approach could be used in the UHR group.

It is important to gather metabolic information during the UHR phase, as individuals are usually antipsychotic naïve, thus allowing baseline cardiometabolic risk to be assessed. Therefore, if later transition to psychosis occurs, metabolic indices can be compared to see whether any abnormalities that may be present are an inherent part of the illness progression or a result of later antipsychotic medication.

Strengths and limitations

This service review is the first to be conducted within a specialized early detection and intervention setting. The findings carry important implications for future service development and provide a baseline to improve upon. However, the small sample size and cross-sectional design are

limitations. As this assessment was restricted to one UK service in Greater Manchester, the findings may not be representative of other early detection services. However, a lack of existing literature on the topic indicates that physical health may not have been assessed routinely across the majority of UHR services. The large proportion of missing information meant no statistical analysis could be conducted on the sample to assess markers of physical health.

CONCLUSIONS

Physical health was not assessed routinely in the EDIT service. Clear monitoring guidelines should be developed to establish routine assessment of common metabolic risk factors present in this population. Appropriate interventions can then be targeted to prevent future ill health.

ACKNOWLEDGEMENTS

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Paper 5

Physical health promotion for young people at ultra-high risk for psychosis: An application of the COM-B model and behaviour-change wheel.

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Rebekah Carney conceived the original idea for the paper, reviewed existing theories, applied the theoretical model and created the first draft of the manuscript.

Professor Alison Yung and Dr Tim Bradshaw provided clinical input and all critically reviewed and agreed on the submitted manuscript for publication.

ORIGINAL ARTICLE

Physical health promotion for young people at ultra-high risk for psychosis: An application of the COM-B model and behaviour-change wheel

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ABSTRACT: *People with psychotic illnesses, such as schizophrenia, have high rates of unhealthy lifestyle factors, such as smoking and physical inactivity. Young people who seek help for mental health care, particularly those at high risk for psychosis, often also display high rates of these unhealthy behaviours. Although healthy living interventions have been applied to people with established psychosis, no attempt has been made to offer them to young people at risk for developing psychosis, despite potential benefits to mental and physical health. We propose that the COM-B model (consisting of capability, opportunity and motivation) and behaviour-change wheel might be an appropriate framework that mental health nurses and other health professionals could apply. Using a systematic and theoretically-based approach to intervention development could result in effective methods of health promotion in this group. Further training and development for mental health nurses could encourage a greater integration of mental and physical health care.*

KEY WORDS: *lifestyle, mental health nursing, physical health, ultra-high risk.*

INTRODUCTION

The physical health disparities of people with schizophrenia and severe mental illness are an area of increasing concern (Shiers *et al.* 2015). Together with the unwanted side-effects of antipsychotic medication, this increased morbidity is partly due to adverse lifestyle factors, including tobacco use, poor diet, and physical inactivity (Addy *et al.* 2012; Hennekens *et al.* 2005; Vancampfort *et al.* 2013). However, these lifestyle factors are also present from an early stage (first-episode of psychosis (FEP)), and might even occur prior to the onset of psychosis, in those who are at ultra-high risk (UHR) for psychosis or putatively 'prodromal' (Addington *et al.* 2015; Carney *et al.* 2016).

UHR individuals (otherwise referred to as the 'at-risk mental state' (ARMS) group are characterized by the presence of attenuated psychotic symptoms, brief limited intermittent psychotic symptoms that spontaneously resolve, or genetic-risk combined with recent decline in functioning (Yung *et al.* 2004). Within 3 years, we can expect approximately one-third of UHR individuals to progress to a full-threshold psychotic illness, with a large proportion developing schizophrenia (Nelson *et al.* 2013). Other psychological illnesses are also prevalent in this group, such as anxiety, mood, or substance use disorders (Addington *et al.* 2011; Lin *et al.* 2015), and many continue to function poorly, regardless of symptomatic remission (Cotter *et al.* 2014).

Existing interventions for UHR cohorts focus primarily on addressing poor mental health and providing supportive psychological therapies to prevent the onset of psychotic illnesses (van der Gaag *et al.* 2013; Yung *et al.* 2011). Physical health and lifestyle behaviours are generally not addressed or monitored routinely in services (Carney *et al.* 2015), and to date, healthy lifestyle interventions have not been applied to this group. This is despite potential benefits to

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future physical and mental health. First, if a UHR individual develops a FEP, he or she will almost certainly receive antipsychotic medication. The side-effects of antipsychotics might then further exacerbate already compromised physical health due to the unhealthy lifestyle factors noted earlier (De Hert *et al.* 2006). Second, even if a psychotic illness does not develop, encouraging a healthy lifestyle might protect against future ill health and health implications arising from these unhealthy behaviours, such as continued tobacco use. Finally, there is evidence to suggest that high rates of unhealthy lifestyle factors could contribute to the onset of psychosis. This includes the use of high-potency cannabis (Di Forti *et al.* 2014), tobacco (Gurillo *et al.* 2015), and physical inactivity (Koivukangas *et al.* 2010). Therefore, the UHR group represents an important target for health professionals when applying healthy lifestyle interventions. Mental health nurses might be an appropriate target to deliver such interventions, as they are frequently in contact with service users and are seen as having a holistic role in managing mental and physical health (Bradshaw and Pedley, 2012).

Unique Characteristics of the UHR Group

In addition to subthreshold psychotic symptoms, UHR individuals frequently report depression and anxiety (Fusar-Poli *et al.* 2013; Yung *et al.* 2004). Although they are usually no different to their peers with regards to weight and body composition, they do have high levels of unhealthy lifestyle behaviours (Addington *et al.* 2015; Carney *et al.* 2016). Designing an intervention must take these characteristics into account. However, issues which usually have to be considered when developing lifestyle interventions for people with schizophrenia might not be relevant, such as long-standing illness, high levels of negative symptoms, cognitive impairment, and antipsychotic side-effects, such as weight gain and metabolic disturbance. We aimed to assess which behaviour-change theories and techniques might be useful to underpin a healthy living intervention for the UHR group, given their unique characteristics. We also aimed to discuss how this can be related to clinical practice, and how mental health nurses might have an important role in promoting physical health.

Existing Interventions

Happell *et al.* (2012) discuss how physical health interventions are required to promote the well-being of people with mental health difficulties. A focus on developing health-behaviour interventions within the nursing and wider health-care professions might encourage significant benefits in the general health of young people who use mental health services. One

approach recommended by the Medical Research Council (Craig *et al.* 2008) is to use a theoretical background to develop methods of health promotion. A sound theoretical framework will assist the delivery of an intervention through the application of a well-developed structure, based on the best available evidence (Hillsdon *et al.* 2004). The alternative is to simply apply interventions in the hope that they might work. However, behaviour change is a complex area, with many overlapping concepts and theories. The most common social cognition models applied to behaviour-change research are social learning theory (Bandura, 1986), the Health Belief Model (Rosenstock, 1974), theory of planned behaviour (Ajzen, 1991), and the Transtheoretical Model (Prochaska and Velicer, 1997).

These models are useful to predict and explain human behaviour; however, their application to behaviour-change interventions is less clear. National Institute for Health and Care Excellence (NICE) guidelines (2007) state that evidence supporting any specific psychological model to inform behaviour change is limited (Abraham *et al.* 2009). A recent meta-analysis concluded that the relationship between the use of theory and effectiveness of an intervention is weak (Prestwich *et al.* 2014). Additionally, despite MRC (Craig *et al.* 2008) recommendations, many health-behaviour interventions lack a clear and specific theoretical foundation (Davies *et al.* 2010; Hardeman *et al.* 2002; Prestwich *et al.* 2014). Even those that include a theoretical model often fail to link the mechanisms of change back to theoretical constructs (Michie and Prestwich, 2010; Prestwich *et al.* 2014). This could be due to the inconsistency in existing frameworks when describing how to apply theory to an intervention.

Promoting Behaviour Change

Creating an intervention involves the initial difficulty of identifying which behaviour should be targeted to achieve a desired health outcome. For example, in a healthy living intervention for young people, the aim might be to promote weight loss, for which many types of behaviours could be targeted, including dietary intake, physical activity, and sedentary behaviour. Once a behaviour is identified, techniques to promote this change can be applied.

Behaviour-change techniques (BCT) are the active components which make up an intervention, and are observable and replicable (Michie and Johnston, 2012). The behaviour-change technique taxonomy consists of 93 'active ingredients' that can be used to facilitate behaviour change (Abraham and Michie, 2008; Michie and Johnston, 2012); for example, the use of goal setting and the provision of instructions in a physical activity

intervention. Individual taxonomies have also been refined containing a smaller set of techniques, which could be most effective for smoking cessation (Michie *et al.* 2011b), or interventions for physical activity and diet (Michie *et al.* 2011a), and alcohol consumption (Michie *et al.* 2012).

NICE suggests a number of BCT that might be effective for driving behaviour change, including self-monitoring techniques (NICE, 2007; NICE, 2014). Self-monitoring involves recording behaviours (i.e. keeping a food diary), setting goals, and obtaining feedback (Abraham and Michie, 2008). NICE (2014) also suggest applying these techniques using remote methods via text messaging or mobile apps (NICE, 2014). Self-monitoring techniques are recommended for the general population (Michie *et al.* 2009), obese adults and those with obesity related comorbidities (Dombrowski *et al.* 2012), and people with recently-diagnosed diabetes (Hankonen *et al.* 2014).

Interventions For Clinical Populations

NICE guidelines (2014) emphasize that techniques used in lifestyle interventions should match service users' needs. Therefore, the characteristics of the UHR cohort need to be considered to ensure any new lifestyle interventions are appropriate. As noted earlier, health promotion for UHR individuals is currently limited. While interventions designed for the general population might not be appropriate, neither might those developed for people with schizophrenia. Given that UHR individuals frequently experience high levels of depression (Fusar-Poli *et al.* 2014; Yung *et al.* 2004), we examined the techniques commonly used in populations with clinical depression to promote physical activity.

A recent Cochrane review examined the effectiveness of exercise interventions for depression (Cooney *et al.* 2014). Individuals with clinical depression from inpatient or community outpatient settings usually receive supervised, guided exercise sessions conducted by a professionally-qualified physical activity trainer (Carta *et al.* 2008; Knubben *et al.* 2007; Martinsen *et al.* 1985; Mota-Pereira *et al.* 2011; Pilu *et al.* 2007; Schuch *et al.* 2011). Individuals are also given information about correct exercise technique (Knubben *et al.* 2007), and receive positive feedback from trainers throughout sessions (Carta *et al.* 2008; Pilu *et al.* 2007). However, it is unclear whether other BCT are employed, as many studies lack sufficient detail for further analysis.

As UHR individuals present with subthreshold, emerging psychotic symptoms, we also considered physical activity interventions for people with early psychosis. Although there are many such interventions for people with schizophrenia (Firth *et al.* 2015), to date, only one review has assessed the active components of physical activity interventions for first-episode samples (Rosenbaum *et al.* 2014). Similar to interventions for people with depression, the most common techniques employed are the provision of information and guidance about exercise (Alvarez-Jimenez *et al.* 2006; Abdel-Baki *et al.* 2013; Curtis *et al.* 2015a; Fredrikson *et al.* 2014; Killackey *et al.* 2011; Lin *et al.* 2011; Lovell *et al.* 2014; Smith *et al.* 2014), supervised sessions (Curtis *et al.* 2015a; Lin *et al.* 2011; Smith *et al.* 2014), and the use of goal setting (Fredrikson *et al.* 2014; Killackey *et al.* 2011). A further qualitative study found FEP individuals value the peer support of a training partner and an individualized approach to designing an exercise intervention (Firth *et al.* 2016).

Common techniques used for FEP populations and individuals with depression are the provision of a professionally-qualified trainer who is available to supervise, demonstrate, and give instructions during exercise sessions. Therefore, increasing the opportunity to exercise by providing facilities, or allocating time for physical activity and enhancing a person's knowledge so they feel capable to exercise, might be particularly useful. Nonetheless, we should look further than the methods used for these patient groups, as they might not be the only effective techniques to employ for UHR individuals. Additionally, many existing interventions are vague and do not provide sufficient detail for replication.

COM-B Model of Behaviour and Behaviour-Change Wheel

Despite MRC (Craig *et al.* 2008) recommendations of using theory to guide intervention development, little advice is given on how mental health nurses and allied health professionals can apply theory to behaviour-change interventions in practice, and how health professionals can select the most appropriate techniques to use. The behaviour-change wheel is a new framework that aims to promote a systematic method of intervention development, (Michie *et al.* 2011c; Michie *et al.* 2015).

The behaviour-change wheel has been described elsewhere (Michie *et al.* 2011c; Michie *et al.* 2015). To summarize, the behaviour-change wheel is made up of three layers (Fig. 1). At the centre of the framework sits a theoretical model that proposes three ways in which a behaviour occurs: capability, opportunity, and motivation (the COM-B model; Michie *et al.* 2011c; Michie *et al.* 2015). This helps identify which source of behaviour should be targeted. Surrounding the COM-B model are intervention categories that provide methods to promote behaviour change and
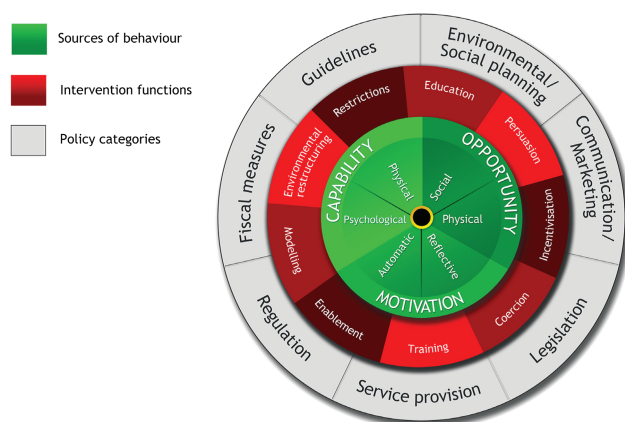
FIG. 1: *Behaviour change wheel Michie et al. (2011c).   [Colour figure can be viewed at wileyonlinelibrary.com]*

include education, persuasion, incentivization, coercion, training, restriction, environmental restructuring, modelling, and enablement (see Table 1 for examples and definitions from Michie *et al.* (2011c)). The final layer of the behaviour-change wheel contains policy categories showing how intervention functions cab be applied on a wider scale (Michie *et al.* 2015).

Although a relatively new model, the COM-B model has been successfully applied as a framework to the English Department of Health 2010 tobacco control strategy (Health, 2010), the NICE guidance on reducing obesity (NICE, 2006), medication adherence and management (Jackson *et al.* 2014; Sinnott *et al.* 2015), management of spinal cord injury (Bérubé *et al.* 2015), childhood obesity (Curtis *et al.* 2015b; Robinson *et al.* 2013), and promotion of safe-sex practices (Newby *et al.* 2013). It has also recently been adopted by Improving Access to Psychological Therapy teams to guide the application of low-intensity lifestyle interventions for psychological well-being practitioners and other health professionals.

Application of the COM-B model to a UHR cohort

We propose that the COM-B model could be useful to develop a lifestyle intervention to promote the physical health of the UHR group. It provides a systematic and standardized approach to developing an intervention, and allows theoretically-based BCT to be applied to guide behaviour change. Using clearly-defined techniques proposed by the COM-B model and behaviour-change wheel taxonomy will ensure transparency and enable replication of an intervention (Abraham and Michie, 2008; Michie *et al.* 2011c). To date, there have been no published or recorded physical health interventions for the UHR group. We suggest that using a theoretically-based framework to develop an intervention will provide a good baseline to conduct further

research and develop health-service provision for this population. In the present study, we outline how each of the three components of the behaviour-change wheel could be addressed for the UHR cohort (Fig. 2).

Motivation

Amotivation or avolition is observed in some young UHR individuals, and can impact on a person's daily functioning (Piskulic *et al.* 2012). Targeting motivation according to the COM-B model could involve increasing knowledge about exercise and diet, and discussing the benefits of living a healthy lifestyle. Goal setting and self-monitoring, such as aiming for two gym sessions per week or eating five servings of fruit and vegetables daily, recorded in a diary might increase reflective motivation.

The concept of self-efficacy has an important influence on motivation (Bandura, 1977; Schunk, 1995; Zimmerman *et al.* 1992). Self-efficacy refers to an individual's belief in their own capacity to engage in a given behaviour (Bandura, 1977; Bandura, 1982). Motivation is enhanced when people have a greater sense of competency and self-belief that they can complete a task (Schunk, 1995; Zimmerman *et al.* 1992). Empirical evidence suggests self-efficacy has an important role in determining whether an individual engages in a given health behaviour and their motivation to change that behaviour (Holloway and Watson, 2002; Thirlaway and Upton, 2009). Programmes targeting self-efficacy to increase healthy eating in adolescents are effective in improving dietary choices and increasing physical activity in adults (Fitzgerald *et al.* 2013; Lee *et al.* 2008; Olander *et al.* 2013). Despite this, self-efficacy has not been explored in UHR individuals. However, in people with schizophrenia, a lack of self-belief and low physical competence (i.e. low self-efficacy) is related to physical inactivity (Vancampfort *et al.* 2011). Therefore, self-efficacy could be an appropriate target for the UHR group.

Opportunity

Considering environmental factors and social opportunities could prove useful when developing interventions for the UHR group, as poor social environment, deprivation, and other socioeconomic factors are risk factors for psychosis, and UHR individuals tend to live in socially-deprived areas (Allardyce *et al.* 2005; Cotter *et al.* 2015; O'Donoghue *et al.* 2015). Working with young people to change the context in which a behaviour usually does (or does not) occur might be helpful to promote a healthy lifestyle. For instance, if a person lives in a deprived area, rather than encouraging them to exercise outdoors, sessions could be conducted in local gyms in a safe environment. Thus, the environmental setting can be developed to be as conducive to an individual

TABLE 1: *Possible intervention functions to encourage a healthy lifestyle in UHR cohorts*

Intervention class	Definition (from Michie *et al.* 2011, p7)	Example applied to a healthy living intervention for the UHR cohort
Education	Increasing knowledge or understanding	Provide instruction about exercise, increase understanding of why it is important for physical health.
Persuasion	Using communication to induce positive or negative feelings or simulate action	Discussing the benefits of a healthy lifestyle, such as improved mood, more energy; and provide general encouragement when behaviour is carried out.
Incentivization	Creating expectation of reward	Encourage goal setting, such as 2 hours per week exercise and allocating rewards when goals are met.
Coercion	Creating expectation of punishment or cost	Provide information about consequences of unhealthy habits; for example, smoking increases cancer risk.
Training	Imparting skills	Encourage the relevant skills to be developed that enable a person to be able to exercise, such as gym training.
Restriction	Using rules to reduce the opportunity to engage in the target behaviour (or to increase the target behaviour by reducing the opportunity to engage in competing behaviours)	Increase the minimum price of alcohol frequently used to target younger populations, such as alcopops.
Environmental restructuring	Changing the physical or social context	Private gym, diet, or behavioural support classes for young people who are taking part in the intervention with a trainer who has awareness of mental health.
Modelling	Providing an example for people to aspire to or imitate	Using a gym buddy system where UHR individuals are accompanied to exercise sessions by a peer or staff member.
Enablement	Increasing means/reducing barriers to increase capability or opportunity	Prompt practice of exercise sessions or cooking sessions, accompany an individual to gym until they feel confident to go alone.
Policy communication/ marketing	Using print/electronic/telephonic or broadcast media	Develop leaflets and materials to be used in the UHR service, which educate people about living a healthy lifestyle or provide warnings to stop smoking.
Guidelines	Creating documents that recommend or mandate practice, including changes to service provision	Ensure young people who access UHR services have a physical health assessment and are given information about their health.
Fiscal	Using the tax system to reduce or increase the financial cost	Increase taxation on tobacco and high-sugar products.
Regulation	Establish rules or principles of behaviour or practice	Reduce adverts for fast food in areas populated by young people such as around colleges and replace with healthy food or gyms.
Legislation	Making or changing laws	Enforce limits on the amount of alcohol one person can buy if under the age of 21 years.
Environmental/ social planning	Designing and/or controlling the physical or social environment	Encourage local areas to have accessible facilities, such as gyms and green spaces.
Service provision	Delivering a service	Encourage parity of esteem in mental health services.

UHR, ultra-high risk for psychosis.

as possible. A supportive social environment could be created by conducting small group sessions with other participants who are also motivated to improve their physical health.

Capability

Enhancing psychological capability might focus on breaking down some of the psychological barriers young people experience. This could include providing behavioural support for low mood and high levels of anxiety experienced by UHR individuals. Physical capability could also be targeted using education and training intervention functions to demonstrate correct exercise techniques, such as following a gym workout with a trainer.

Relevance for Clinical Practice

It is not only the behaviours of UHR individuals that should be targeted to promote a healthier lifestyle. Clinical services also need to be aware that monitoring physical health is important, and interventions to improve physical health in the UHR cohort are required. This arises from recent findings, which suggest physical health and associated health behaviours are not monitored on a routine basis by UHR services (Carney *et al.* 2015). Happell *et al.* (2012) also argue that despite being a rising topic, more research is required in
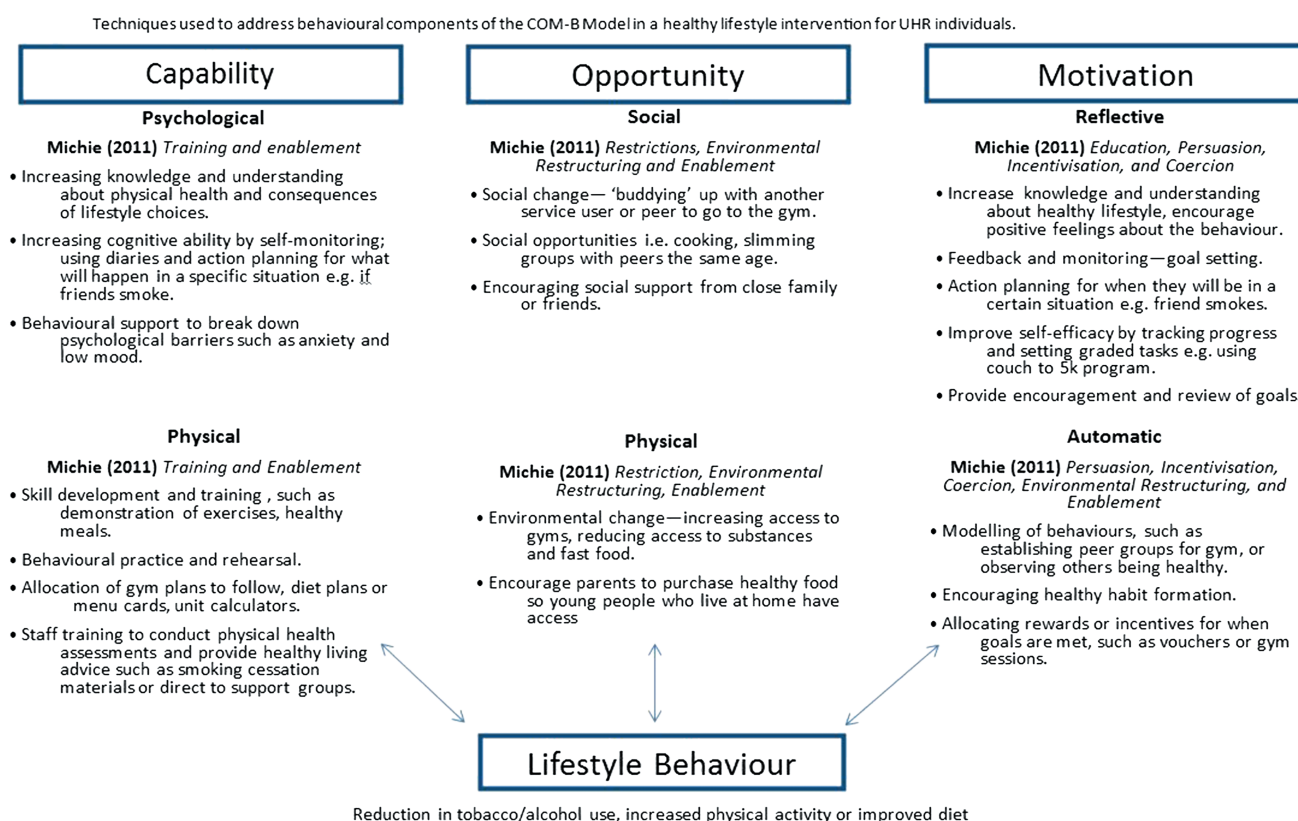
Techniques used to address behavioural components of the COM-B Model in a healthy lifestyle intervention for UHR individuals.

Capability

Psychological

Michie (2011) *Training and enablement*

- Increasing knowledge and understanding about physical health and consequences of lifestyle choices.
- Increasing cognitive ability by self-monitoring; using diaries and action planning for what will happen in a specific situation e.g. if friends smoke.
- Behavioural support to break down psychological barriers such as anxiety and low mood.

Physical

Michie (2011) *Training and Enablement*

- Skill development and training , such as demonstration of exercises, healthy meals.
- Behavioural practice and rehearsal.
- Allocation of gym plans to follow, diet plans or menu cards, unit calculators.
- Staff training to conduct physical health assessments and provide healthy living advice such as smoking cessation materials or direct to support groups.

Opportunity

Social

Michie (2011) *Restrictions, Environmental Restructuring and Enablement*

- Social change— 'buddying' up with another service user or peer to go to the gym.
- Social opportunities i.e. cooking, slimming groups with peers the same age.
- Encouraging social support from close family or friends.

Physical

Michie (2011) *Restriction, Environmental Restructuring, Enablement*

- Environmental change—increasing access to gyms, reducing access to substances and fast food.
- Encourage parents to purchase healthy food so young people who live at home have access

Motivation

Reflective

Michie (2011) *Education, Persuasion, Incentivisation, and Coercion*

- Increase knowledge and understanding about healthy lifestyle, encourage positive feelings about the behaviour.
- Feedback and monitoring—goal setting.
- Action planning for when they will be in a certain situation e.g. friend smokes.
- Improve self-efficacy by tracking progress and setting graded tasks e.g. using couch to 5k program.
- Provide encouragement and review of goals.

Automatic

Michie (2011) *Persuasion, Incentivisation, Coercion, Environmental Restructuring, and Enablement*

- Modelling of behaviours, such as establishing peer groups for gym, or observing others being healthy.
- Encouraging healthy habit formation.
- Allocating rewards or incentives for when goals are met, such as vouchers or gym sessions.

Lifestyle Behaviour

Reduction in tobacco/alcohol use, increased physical activity or improved diet

FIG. 2: *Techniques used to address capability, opportunity and motivation from the COM-B model. [Colour figure can be viewed at wileyonlinelibrary.com]*

order to facilitate integrated care for physical and mental health needs. One way to address this is to equip mental health nurses with the ability to promote physical health in this group.

The important role mental health nurses can have to improve the general health of people with mental health difficulties has previously been recognized (Bradshaw and Pedley, 2012; Happell *et al.* 2011; Robson and Gray, 2007) First, as many have daily contact with service users, this time could be used to work together to address unhealthy lifestyle factors (Bradshaw and Pedley, 2012; Stanton *et al.* 2015). Schemes, such as 'Making every contact count', might be effective, where health professionals are trained to facilitate behaviour change at every contact with a client (Lawrence *et al.* 2016). Second, nurses make up the largest component of the health-care workforce, which results in an increased chance of implementation if interventions are rolled out on a larger scale. Third, encouraging mental health nurses to focus on both the physical and mental health of an individual promotes a more holistic approach to health care; one that is required to address physical health disparities (De Hert *et al.* 2011).

The outer circle of the behaviour-change wheel focuses on changes to policy to encourage wider-scale behaviour change, such as service provision, or policy guidelines (Table 1). Mandatory training in physical health promotion for all health professionals could allow it to be incorporated into general nursing practice. This could include training for mental health nurses to conduct physical health assessments and provide advice about diet, or integrating a physical health specialist into mental health services (Happell *et al.* 2016). Changes to policy guidelines might also be an effective way to promote physical health, such as including reminders to conduct physical health checks on the files of service users.

Future Recommendations

Interventions to promote physical health are required for UHR individuals due to high rates of unhealthy lifestyle factors such as physical inactivity and substance use. We recommend mental health nurses and wider health professionals use the principles of the COM-B model and behaviour-change wheel to develop a new healthy lifestyle intervention for the UHR group. Developing an intervention using this systematic method may have advantages over traditional approaches used to promote healthy living in mental healthcare settings, which are often not linked to any underlying theoretical

framework, or developed structure and are applied on an ad-hoc basis. Due to limited existing research, further qualitative research should be conducted with this population and the clinical staff prior to developing any intervention to identify what behaviour would be the most appropriate target. Determining the barriers to and facilitators of healthy lifestyle in the group, and establishing which behaviours they wish to change (e.g. smoking, diet, and physical activity) will be useful. The perspective of mental health professionals should also be considered to determine which interventions they believe are feasible and acceptable approaches to use.

CONCLUSION

Training mental health nurses and other health professionals to use the COM-B model and behaviour change wheel could promote physical health for young people at risk for psychosis. Using a systematic and theoretically-based approach to intervention development could result in effective methods of health promotion in this group. Given the lack of physical health research with the UHR group, we suggest that using a theoretically-based framework to develop an intervention will provide a good baseline to conduct further research and develop health service provision for this population. The COM-B model could be an appropriate framework to use, given the flexibility of the approach and ability to account for a wide range of behaviours. Additional training and development for mental health nurses could encourage a greater integration of mental and physical health care for young people in clinical services.

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Paper 6

Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: a qualitative study involving service users, parents and clinicians

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Rebekah Carney conceived the original idea for the paper, created the study documents, obtained ethical approval, recruited study participants, designed the topic guides, conducted and transcribed qualitative interviews, conducted the qualitative analysis on the data and interpreted the data. Rebekah created the first draft of the manuscript and completed all revisions following review by the co-authors.

Professor Alison Yung and Dr Tim Bradshaw assisted with the design of the study, provided clinical input and contributed to the development of the topic guide. All authors reviewed the codes and themes to ensure interpretive rigour. Dr Tim Bradshaw provided methodological guidance on qualitative interviewing. Jack Cotter assisted with participant recruitment. All authors critically reviewed and agreed on the submitted manuscript for publication.

ELSEVIER

Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: A qualitative study involving service users, parents and clinicians

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A B S T R A C T

Emerging evidence suggests young people at ultra-high risk for psychosis (UHR) are also at-risk for poor physical health, and display high rates of modifiable cardiometabolic risk factors. However, before we can develop effective interventions there is a need to understand factors affecting lifestyle choices in the UHR group. We conducted semi-structured qualitative interviews with 20 UHR individuals (50% male; mean age 21.7), 5 parents (4 mothers, 1 father), and 6 clinicians from early intervention services in the Northwest of England to identify barriers and facilitators to living a healthy lifestyle, including achieving regular exercise, eating well and refraining from excessive substance use. Thematic analysis revealed the main barriers to living a healthy lifestyle related to psychiatric symptoms, beliefs about self, social withdrawal and practical considerations such as accessibility and cost. Provision of social support and promoting autonomy emerged as the two main themes which would facilitate a healthy lifestyle. Promoting physical health in people with emerging symptoms of psychosis is an important, yet neglected area of mental health practice and warrants further investigation. UHR individuals experience numerous barriers to living a healthy lifestyle, and interventions should focus primarily on targeting autonomous motivation and providing social support to facilitate this change.

1. Introduction

People with psychosis are more likely to live unhealthy lifestyles and experience poor physical health at a young age compared with the general population (Mitchell et al., 2013; Shiers et al., 2015). This results in a 10–25 year reduction in life expectancy, mostly due to cardiovascular disease, (Laursen et al., 2012). Physical inactivity, diets low in nutritional value or high in convenience food, smoking and excessive alcohol or substance use are all examples of unhealthy lifestyle behaviours common in people with psychosis. Emerging evidence suggests this unhealthy profile may begin even prior to the onset of full psychotic symptoms; that is in those at ultra-high risk (UHR) for psychosis (Carney et al., 2016, 2017).

The UHR criteria, also known as prodromal, clinical high risk (CHR), or at-risk mental state (ARMS criteria), enable the identification of individuals at high risk for psychosis (Yung et al., 2003; Yung et al., 1996; Fusar-Poli et al., 2013). In order to meet UHR status, an individual must fulfil one or a combination of the following criteria; attenuated psychotic symptoms, brief limited intermittent psychotic

symptoms (BLIPS), or a genetic risk combined with a recent decline in functioning (Yung et al., 2004). An individual meeting the UHR criteria is at greatly increased risk of developing a first episode of psychosis within 1–2 years compared to individuals in the general population (Fusar-Poli et al., 2012).

In a recent study, unmedicated UHR individuals displayed a higher prevalence of cardiometabolic risk factors compared with age matched controls, including higher blood pressure, increased waist circumference and increased fasting blood glucose (Cordes et al., 2017). A recent cross-sectional analysis of cardiometabolic risk factors in the UHR group also found evidence for low levels of physical activity and poor quality sleep (Lederman et al., under review). High rates of cardiometabolic risk factors can largely be attributed to lifestyle factors observed in this group, such as reduced physical activity, and increased rates of smoking and alcohol abuse (Carney et al., 2016). These behaviours are potentially modifiable. Therefore, the UHR phase represents an important opportunity for early intervention, to prevent future ill-health.

Despite the need for physical health interventions in this group, there remains a paucity of research examining physical health promo-

tion for young people in the UHR phase. Physical health measures are not routinely monitored in early detection settings (Carney et al., 2015) and there have been no documented physical health interventions for this group. However, before we can develop a feasible, acceptable and potentially efficacious intervention there is a need to understand more clearly why the UHR group have poorer lifestyle profiles compared to individuals who are not UHR (Carney et al., 2016; Carney et al., 2017; Lederman et al., under review). Qualitative research enables us to gain insight into a person's subjective experience of physical health and lifestyle. The limited amount of qualitative studies in this group have focused on functional impairment and experience of symptoms (Byrne and Morrison, 2010; Ben-David et al., 2014) however, this approach has not yet been used to explore the physical health of this group. Therefore, we conducted a qualitative study in order to assess the perceptions of UHR individuals, their families and the professionals who worked with them, regarding factors that prevent or promote them living more healthy lifestyles and how they could be supported to improve their physical health.

1.1. Aims

Using qualitative interviews, we aimed to identify:

- Barriers that UHR individuals face to living a healthy lifestyle.
- Facilitators to living a healthy lifestyle for UHR individuals.
- Support that would be useful to help this group improve their physical health.

2. Methods

2.1. Sample

Sampling was purposive. Eligible participants were aged 16 years or over, were English speakers, and fulfilled at-risk mental state criteria according to the Comprehensive Assessment for At-Risk Mental States (CAARMS; Yung et al., 2005). In line with the National Service Framework for Access and Waiting Time Standards (NHS England, 2016), all individuals were offered cognitive behaviour therapy and mental health monitoring in a specialised early intervention or early detection service in the Northwest of England. Twenty UHR individuals were recruited. Five of their parents, and 6 clinicians from the services also agreed to be interviewed, leaving a total sample size of 31.

2.2. Procedure

East Midlands Derby Research Ethics Committee approved the study (ref:15/EM/0559) which took place between January - December 2016. Clinicians were given study information to pass on to their clients and consent to contact was obtained. UHR individuals were contacted by the lead author (RC) and provided with further information before arranging to meet. Written informed consent was sought from all participants prior to all interviews taking place. After taking part, UHR individuals were asked for their consent to contact a parent to complete a similar interview about their physical health. Clinicians were also contacted again and invited to take part. Participants were reimbursed for their time. Data collection was finalised once data saturation had been reached in the UHR sample and no further parents or clinicians were willing or available to be interviewed.

2.3. Demographic information

Age, gender, ethnicity, marital, vocational and living status and highest educational qualification were recorded for UHR individuals (Table 1).

Table 1
UHR demographics.

Demographic variable		UHR (n = 20), n (%)
Age, mean (sd)		21.7 (5.59)
Gender	Male	10 (50%)
Ethnicity	White British	20 (100%)
Marital status	Single	11 (55%)
	In a relationship (not married)	9 (45%)
Employment status	Full-time employment	2 (10%)
	Part-time employment	2 (10%)
	Student	10 (50%)
	Unemployed	6 (30%)
Highest qualification	Undergraduate degree	3 (15%)
	A-level	6 (30%)
	GCSE	4 (20%)
	BTEC	5 (25%)
	NVQ Level 2	1 (5%)
	No qualifications	1 (5%)
Living status	Lives on own	3 (15%)
	Lives with family	9 (45%)
	Lives with partner	3 (15%)
	Lives with friends	5 (25%)

2.4. Qualitative interviews

A qualitative design was employed using semi-structured interviews. Topic guides were developed by the study team based on previous research (Carney et al., 2016; Bradshaw et al., 2012) (available on request). Semi-structured interviews were conducted by the lead author and covered a range of pre-specified topics regarding participant's lifestyles. Interviews consisted of questions about diet, exercise, alcohol and tobacco use as well as questions about barriers and facilitators to living a healthy lifestyle. Interview schedules were adapted to be appropriate for the three groups of participants, and lasted up to 1 h. Interview guides were flexible using prompts and open questions to encourage participants to talk in depth about their perceptions and experiences. All interviews were digitally recorded and transcribed verbatim for analysis. Participants were assigned pseudonyms to maintain anonymity.

2.5. Qualitative analysis

The current study had several pre-specified areas of interest relating to identifying barriers and facilitators to living a healthy lifestyle. A thematic approach was taken to analyse the data in order to identify key themes for each topic. Thematic analysis is a systematic approach whereby patterns and common themes are identified to describe a data set and understand a given phenomenon (Braun and Clarke, 2006). Despite having pre-specified areas of interest, we adopted a bottom up approach to identifying recurring themes in the data. This was conducted according to the method specified by Braun and Clarke (2006):

1. Transcripts were read and re-read to familiarise the researchers with the data
2. Systematic line by line coding to identify common features in the data
3. Codes were reviewed to determine potential themes
4. Themes were reviewed for internal homogeneity and external heterogeneity and ensure they were coherent and distinctive
5. Themes were defined and names generated for each

To reduce the risk of bias, all researchers were involved in the analytic process and codes and themes were discussed throughout. Quotes presented within the results section are used to illuminate the findings and add context to each theme. The perceptions of all three groups were synthesised to identify overarching themes and factors

Table 2
Barriers and facilitators to living a healthy lifestyle.

Barriers to living a healthy lifestyle	
Psychiatric Symptoms	Kate: it was easier to sit in my room and eat a load of crème eggs than to go outside for a walk and stuff. Even though the walk would have helped me more than a box of crème eggs.
	Parent: as he walks in a room he thinks every single person has eyes on him and they are judging him straight away. They are thinking look at him, look at the way he's looking, look at his hair, look at his glasses, look at his shoes, look at his….. So to him everybody's judging him, everybody's laughing at him.
	Clinician: when people are depressed, they don't have that motivation to look after themselves properly.
Beliefs about self	Anthony: the way they feel about themselves, if they're feeling tender and see themselves as not really having that high self-esteem that might be a barrier.
	Beth: it is always like portrayed as like happy people, like people being all like positive and like when you are in like a bad state of mind that is not me, that is not something I can do.
	Parent: They will gain self-confidence not just because they are more active, and that makes things more easier to achieve because you are fit, but because they are doing something for themselves and they are healthy and I think it all feeds into the mood.
	Clinician: a lot of the people I see, they are overweight, they've got poor self-image, they don't do any physical exercise
Social withdrawal	Alison: when you are having like quite a low day and you are feeling quite down or you are feeling like really agitated or really anxious and stuff you just, you don't want to go anywhere, you don't want to do anything, you don't want to see people, and don't want to be around anyone. So it puts you off doing that, especially with eating because you think I just don't wanna eat.
	Parent: They need to do like more exercise and not eat like loads of junk and keep going out. They don't go out and mix with people, like she doesn't go out and mix with anybody. She's just in her bedroom. She won't even come downstairs she just stays in her bedroom.
	Clinician: sat in their bedroom, not interacting with people, on the computer. You know and often I think how that can impact on them, you know it's bound to impact on not only their mood, but their social skills as well. And physical health in terms of they're not physically active.
Practical	Harriet: my diet has gone really bad recently because I've started college and I just haven't got the time to start making anything proper so I've just gone McDonald's or summat or buy like a pasty.
	Parent: there's not enough locally for him to do. There's no park facilities or anything like that. Erm, I would say that there really isn't anything for people his age. It would revolve around school or college and then home life. Because really where we live there's no, there's nothing.
	Clinician: Not having money…how can you afford a gym membership if you've not got any money? And if you have got money you wanna spend it on fags
Facilitators to living a healthy lifestyle	
Social Support	Tom: Arrange activities with someone who is in a similar situation to you, because you relate to people who are going through what you are going through? Because then you boost each other, because you are all there getting help anyway because you wouldn't be with the service. So if you have that then you know you could push each other.
	Andy: I love working in a team, I'd rather work in a team than on my own… it'll open up a lot of opportunities like teams, 'cause mates can be made, and it can, it can just help a lot, … just broaden your views and everything like that. 'Cause you're gonna see loads of different people from all different walks of life all going to do the same thing, no one's any different, you're there for the same reason aren't you
	Clinician: what we find with our clients, particularly with the ones who are more anxious or suspicious is that they will probably need a little bit of help or adaptation to access services
Promoting autonomy	Erin: That's the main thing that puts me off doing exercise when someone says have you done this, you should be doing this. And like that instantly makes me not want to do it.
	Parent: being told things all the time you tend to switch off whereas when you experience something it sticks with you.
	Clinician: It's got to mean something to that person, it's got to be important to them, they've gotta want to change. If you try and force it on them it's not gonna work….. Not only you encouraging them to be more active but for them to want to be more active.

affecting lifestyle. All data analysis was conducted using nVivo (Version 11) (NVivo Qualitative Data Analysis Software, 2015).

3. Results

UHR demographics can be found in Table 1. Four mothers and one father took part in an interview about their son/daughter. Clinicians had a range of healthcare backgrounds, (Clinical psychologist $n=3$, Mental Health Nurse $n=1$, Occupational Therapist $n=1$, Social Worker $n=1$).

3.1. Barriers to living a healthy lifestyle

UHR individuals experience numerous and frequent barriers to living a healthy lifestyle which result in low levels of physical activity, poor diet, and excessive substance use. The main barriers related to psychiatric symptoms, beliefs about self and social withdrawal (Table 2).

3.1.1. Psychiatric symptoms

A wide range of psychiatric symptoms impacted on the ability of UHR individuals to live a healthy lifestyle. These symptoms included suspiciousness, paranoid thinking, perceptual abnormalities, and affective symptoms such as depression and anxiety.

"Clinician: they don't do any physical exercise, and mainly it's because of the suspiciousness and the paranoia, linked with social anxiety and depression that they don't get out of the house."

Lack of motivation was a major barrier. This was linked to symptoms of depression, loss of interest in activities, and low energy. Relying on quick fixes was common, such as convenience food and highly caffeinated drinks to boost mood and energy.

"UHR: But on the days where you eat rubbish, partly it's because you are feeling rubbish that day anyway so I eat like the wrong stuff and then, that doesn't really make anything better… it's generally on a day when I'm feeling down and like lack motivation and I'm not up for anything so sometimes you go for like fizzy drinks."

Despite being aware of the benefits of a healthy lifestyle, UHR individuals were often unable to overcome barriers associated with positive symptoms and anxiety. Increased paranoia and suspiciousness prevented many from attending places such as gyms, through fear of being judged by other people. Additionally, diet was often poor and related to symptoms. For example, comfort eating when depressed, or under-eating when anxious.

"UHR: I normally snack, like with chocolate, crisps.. which I know I shouldn't do. I get that, but it's comfort eating. I still comfort eat. Like cause of the voices, like my voices I start like bottling inside it."

Substance use was also linked, with some people claiming they smoke more or use alcohol when they feel depressed or anxious as a way of calming themselves down.

"UHR: So half of the time everyone else is also drinking, but some of the time I'll be with everyone else and I'll be the only one drinking… possibly, but it's just to take the edge off the anxiety and stuff, so it just makes it

easier to interact with people."

3.1.2. Beliefs about self

UHR individuals often held a negative view about themselves, with many having low self-esteem, poor confidence and a lack of belief in their own ability.

> *"UHR: The biggest barrier I think a young person can ever have themselves is the opinion they have of themselves; which can act as maybe a positive thing or an actual barrier to self-improvement"*

This had a profound impact on their lifestyle for example, feeling self-conscious in public places, fearing judgement from others and comparing themselves to other people. Internalised self-stigma was also common. Many individuals reported feeling different to other people as a result of their mental health difficulties and poor self-image, which presented a further barrier to engaging in social opportunities.

> *"Parent: self-image, I think any of the young 'uns with mental health issues are very conscious of it and they think everyone else can see 'em. Because I know Joe has said that"*

3.1.3. Social withdrawal

Social withdrawal as a result of poor mental health and low self-esteem was also a barrier. Factors included fear of others, failure and ridicule, and finding unfamiliar situations or group tasks intimidating.

> *"UHR: I think the idea of group activities can be a bit intimidating and just…. I think sometimes it's hard to like tell yourself, that you like you need to do more exercise, or like you need to eat better"*

Increased isolation and avoidance of others often resulted in young people having fewer opportunities to engage in healthy behaviours such as walking, and playing sports. Although a proportion of individuals were in college or employment, many spent a lot of their time participating in unstructured activities, and isolating themselves from others.

> *"Parent: They need to do like more exercise and not eat like loads of junk and keep going out. They don't go out and mix with people, like she doesn't go out and mix with anybody. She's just in her bedroom. She won't even come downstairs she just stays in her bedroom."*

Social factors also impacted on whether a young person engaged in unhealthy behaviours. For example, many used alcohol and other substances as a way of improving social confidence and making them feel more relaxed around other people.

3.1.4. Practical issues

Finally, numerous practical barriers were presented, which generally related to accessibility and the surrounding environment. This included cost, time, and having the skills and knowledge to live a healthy lifestyle, for example not knowing how to prepare a healthy meal.

> *"Clinician: that would be around access really, so cost, availability, ease of access and then erm… for many people I think Salford wise it is you know, not only the cost of the exercise itself but the cost of transport."*

> *"UHR: it makes me feel down because like, I want to eat like, I want to eat healthier, but obviously I can't cook myself. Like I can't use a cooker, I can only just manage like the stove part of a cooker, I can only just manage to do that now, and I'm 17. That's embarrassing for a 17 year old not to cook, and because my mum would never let me touch anything."*

The physical and social environment affected the lifestyle choices people made, such as the behaviours of other people in the household, past experiences, availability of food, and opportunities available in the local area.

3.2. Facilitators to living a healthy lifestyle

The main facilitators to living a healthy lifestyle were linked to social support and promoting autonomy, (Table 2).

3.2.1. Social support

A range of social factors were acknowledged as useful facilitators to living a healthy lifestyle. A prevalent theme throughout was having someone to support this change in behaviour, such as having someone to exercise with or attend groups with. Parents and clinicians also discussed the value of having support from young people who may have had similar experiences with mental health issues, and who may represent useful role models. Social support may encourage UHR individuals to make positive changes to their physical health and may reduce self-stigma and low confidence in this group.

> *"UHR: If someone would come with me that I know… because I'd have someone there that would be able to say, they are not talking about you and just reassure me."*

Reassurance from people who they trust was also a facilitator in helping UHR individuals overcome some of the barriers they face associated with symptoms, such as distracting people in public places if they are thinking people are looking at them, or are feeling paranoid.

3.2.2. Making the choice for themselves

A strong theme which emerged across the data was that UHR individuals do not find it useful if they are told by a clinician or parent what to do.

> *"UHR: if you tell someone to do something, they're not gonna want to do it but if you got that option there to do it, it's gonna make people give it a go"*

Alternatively, when young people are empowered to make decisions themselves regarding their physical health they feel much more in control and motivated to do so. Providing individuals with the knowledge to enable them to make an informed choice was seen as useful throughout the interviews. Promoting self-efficacy and autonomy are therefore, facilitators in helping young people be more healthy and active and help address motivational difficulties.

4. Discussion

4.1. Summary of findings

Qualitative interviews were conducted to investigate physical health and lifestyle in an UHR cohort. Multiple barriers to living a healthy lifestyle were experienced resulting in high rates of cardiometabolic risk factors in this group. The main difficulties were linked to low motivation and psychiatric symptoms, including symptoms such as suspiciousness, anxiety and depression. These experiences increase the likelihood of becoming isolated and socially withdrawn, and reduce the opportunity to lead a healthy lifestyle. Despite this, many are keen to improve their physical health if activities were available and if they had appropriate support from others to help overcome their difficulties. These findings highlight the growing need to develop healthy lifestyle interventions for people at high risk of psychosis.

Our findings can be interpreted in the context of the COM-B model which states a person must have the *Capability, Opportunity* and *Motivation* to engage in behaviours (Michie et al., 2011; See Fig. 1). Firstly, UHR individuals displayed substantial deficits in motivation. Research in FEP groups has also found that motivation, particularly autonomous motivation, is one of the primary barriers to living a healthy lifestyle (Firth et al., 2016a, 2016b, 2016d). Autonomous motivation refers to a person valuing the importance of behaviour, taking control and making the decision to engage in behaviour by aligning it with their personal views (Deci and Ryan, 2010). Intrinsic
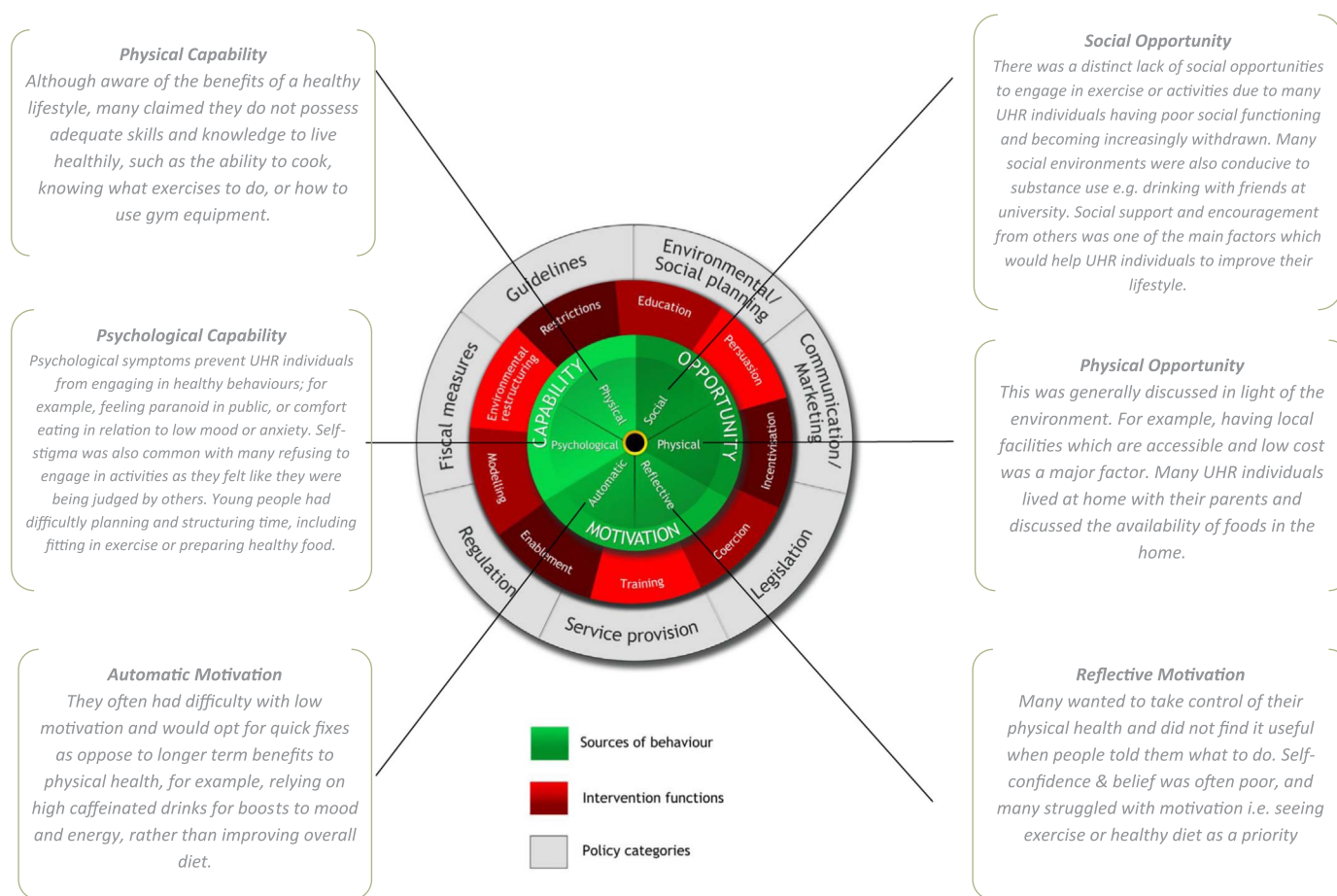
Physical Capability
Although aware of the benefits of a healthy lifestyle, many claimed they do not possess adequate skills and knowledge to live healthily, such as the ability to cook, knowing what exercises to do, or how to use gym equipment.

Psychological Capability
Psychological symptoms prevent UHR individuals from engaging in healthy behaviours; for example, feeling paranoid in public, or comfort eating in relation to low mood or anxiety. Self-stigma was also common with many refusing to engage in activities as they felt like they were being judged by others. Young people had difficultly planning and structuring time, including fitting in exercise or preparing healthy food.

Automatic Motivation
They often had difficulty with low motivation and would opt for quick fixes as oppose to longer term benefits to physical health, for example, relying on high caffeinated drinks for boosts to mood and energy, rather than improving overall diet.

Social Opportunity
There was a distinct lack of social opportunities to engage in exercise or activities due to many UHR individuals having poor social functioning and becoming increasingly withdrawn. Many social environments were also conducive to substance use e.g. drinking with friends at university. Social support and encouragement from others was one of the main factors which would help UHR individuals to improve their lifestyle.

Physical Opportunity
This was generally discussed in light of the environment. For example, having local facilities which are accessible and low cost was a major factor. Many UHR individuals lived at home with their parents and discussed the availability of foods in the home.

Reflective Motivation
Many wanted to take control of their physical health and did not find it useful when people told them what to do. Self-confidence & belief was often poor, and many struggled with motivation i.e. seeing exercise or healthy diet as a priority

Sources of behaviour
Intervention functions
Policy categories

Fig. 1. Barriers and facilitators to living a healthy lifestyle according to the COM-B model of behaviour (Michie et al., 2011).

motivation, one aspect of autonomy, plays an important role in facilitating initial uptake and long-term maintenance of exercise in people with FEP (Firth et al., 2016c; Vancampfort et al., 2016), however, promoting autonomy is often overlooked in youth mental health services, (Plaistow et al., 2014).

We found that costs and accessibility of attending a gym were barriers affecting opportunity to engage in healthy behaviours. Assisting with these issues could include the provision of low cost gym memberships, assistance with transport, or making people aware of local facilities they are able to access. This could then encourage long-term behaviour change, as young people may continue to access local facilities in the absence of support and guidance from mental health services.

Lack of knowledge about how to live a healthy lifestyle was also evident in some of our participants. Some participants reported that they were unsure how to prepare a healthy meal, and had relatively few cooking skills. Increasing this knowledge would increase their capability. For example, showing young people how to cook healthy food on a budget may be useful, in order to reduce the amount of convenience foods consumed, and over-reliance on caffeinated drinks as a source of energy.

However, providing advice and access to gym facilities is insufficient to encourage people with serious mental illness to increase their physical activity (Archie et al., 2003). Our findings support previous work that showed the importance of social support in overcoming psychological barriers to exercise (Firth et al., 2016c, 2016d). Providing social support increases people's capability to engage in healthy behaviours. Exercise and lifestyle interventions which draw on social support are feasible and useful for people with FEP (Firth et al., 2015; Bradshaw et al., 2012). Support to exercise could be facilitated by

employing physical health therapists and peer mentors within services. This holistic lifestyle approach has been trialled in Early Intervention for Psychosis services in Australia with demonstrable benefits to both physical and mental health (Curtis et al., 2016).

Providing social support can also help address factors associated with poor social functioning in this group. A culmination of factors including psychiatric symptoms, poor self-esteem and low motivation often result in UHR individuals becoming increasingly withdrawn and isolated from others (Cotter et al., 2014; Meyer et al., 2014; Glenthøj et al., 2017). For example, we found that emerging positive symptoms such as suspiciousness, paranoia and perceptual abnormalities reduce a person's psychological capability to engage in meaningful activities for physical health, and increase the likelihood of them becoming more withdrawn. This in turn reduces the amount of opportunities young people have to engage in health behaviours, such as attending sports groups, or going to the gym. Therefore, living a healthy lifestyle is difficult for this group, particularly for those with marked impairment in social functioning who spend a lot of time home alone, participating in unstructured activities.

UHR individuals are at an important stage in their life in terms of occupational functioning, and long-term employment outcomes are often poor in this cohort (Cotter et al., 2014, 2016). Therefore, it is important to adopt a multifaceted approach to health care provision for this group. An early qualitative study interviewed parents about the time leading up to a first-episode of psychosis, and identified similar themes to our study (Cocoran et al., 2003). For example, prior to FEP individuals experienced a decline in functioning, particularly social functioning which could have impacted on their ability to engage in exercise. Support to overcome psychosocial barriers may help increase people's capability to engage in physical activities to improve physical

health, and also open up further opportunities as a result of increased confidence and self-esteem. Support for this comes from a recent exercise intervention in a FEP group where participants reported the benefits of engaging in exercise extended to other aspects of their life such as improving social confidence and self-esteem (Firth et al., 2016c). Therefore, there may be a virtuous cycle whereby improving physical health can result in greater self-esteem and confidence, which in turn improves motivation and capability to engage in both healthy lifestyle activities and overall social functioning.

4.2. Clinical implications

Addressing the physical health of people with emerging psychological difficulties is an important, yet neglected area of mental health and warrants further investigation (Carney et al., 2015). Encouraging this group to live a healthy lifestyle is important for several reasons. First, it protects against future metabolic ill-health commonly associated with disease progression. Second, it may reduce the risk of developing psychosis, as a recent cohort study found low levels of physical activity during childhood and adolescence was an independent predictor of psychosis in adulthood (Sormunen et al., 2017). Third, although the majority of this cohort will not develop psychosis, a large proportion will develop mood, anxiety and substance use disorders, (Lin et al., 2015) and continue to function poorly even in the absence of symptoms, (Cotter et al., 2014; Yung et al., 2015). Therefore, even in those who do not develop psychosis, promoting physical health may be beneficial. Finally, intervening at the earliest stage and adopting a preventative approach is more cost-effective and associated with better long-term outcome (Tsiachristas et al., 2016).

4.3. Strengths and limitations

This is the first qualitative exploration of physical health in the UHR cohort. Interviewing parents and clinicians and integrating this data with opinions of the UHR individuals enabled us to gain a more holistic view of the factors affecting physical health in this group. Some of the barriers to living a healthy lifestyle may not be unique to the UHR cohort, and may be experienced by other young people, for example, cost, knowledge and accessibility. However, some of the key themes can be linked to symptoms and psychopathology of this group. Our findings suggest this cohort experience difficulties with motivation, social anxiety and symptomatic barriers which have an effect on their lifestyle and health behaviours. Given the importance of identifying appropriate methods of physical health promotion for this group, to ameliorate cardiometabolic risk, our findings provide an important contribution to the wider literature.

Our sample had an equal number of males and females, all of whom were white British. Although this is representative of the service, our findings may not be culturally representative of the whole UHR cohort. All patients met at-risk criteria on the CAARMS (Yung et al., 2005); however, due to the qualitative nature of the study individuals with more severe symptoms may not have volunteered.

4.4. Conclusion

UHR individuals experience numerous barriers to living a healthy lifestyle. We recommend the development of a structured lifestyle intervention to support UHR individuals to engage in healthy behaviours. Interventions should focus primarily on targeting autonomous motivation and providing social support to facilitate this change. Preventing physical ill-health and promoting wellbeing in this vulnerable group should be a priority for future development.

Conflict of interest

None.

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Intervention Development

There is a need to further develop and evaluate physical health interventions in the UHR group. Informed by the findings of this PhD, the following chapter discusses recommendations for a potential intervention to help promote physical health in people at UHR for psychosis.

Why an intervention is needed

Interventions to promote a healthy lifestyle are important for UHR individuals for several reasons. First, the findings of this PhD show that many UHR individuals lead an unhealthy lifestyle. This is mainly due to high rates of physical inactivity, smoking, substance use and poor diet (Carney et al., 2016b; 2017b-c). This group also experience numerous barriers to living a healthy lifestyle, such as emerging symptoms of psychosis, reduced social opportunities and low motivation (Carney et al., 2017a). Second, living an unhealthy lifestyle during adolescence predisposes individuals to unhealthy living in adulthood (Gordon-Larsen, Nelson & Popkin, 2004; Zhang et al., 2017). This increases the likelihood of long-term physical and mental ill-health (Ferriera et al., 2005; Suetani et al., 2017). For example, if during adolescence an individual engages in unhealthy behaviours such as eating irregular meals, consuming higher quantities of alcohol and sugary snacks, and being physically inactive, these behaviours are more likely to be continued into adulthood. This has long-term consequences on physical health and has been linked to the development of metabolic syndrome up to 27 years later (Wennberg et al., 2016).

Third, although promoting healthy living is important for all young people, it is even more important for UHR individuals as they are at-risk for a range of serious mental illnesses (Yung et al., 2003; Fusar-Poli et al., 2012; Rutligliano et al., 2016; Lin et al., 2015). This includes schizophrenia, bipolar disorder and major depression; conditions which are all associated with poor physical health. Therefore, encouraging healthy behaviours may provide some protection against the co-morbid conditions and poor physical health generally observed alongside these illnesses. Finally, exercise may lower the risk of UHR

individuals developing SMI. Recent cohort studies have shown that frequent exercise during adolescence is linked to lower levels of psychosis in adulthood, (Sormunen et al., 2017), and can have a protective effect on general mental health in later life (Suetani et al., 2017).

Previous interventions

To date there have been no published studies of physical health interventions for the UHR group. However, integrating mental and physical health services to provide a more holistic approach to healthcare is an area which is gathering momentum. In recent years a strong evidence base has been established which demonstrates the efficacy of structured exercise programmes to improve mental health in individuals with a range of psychiatric illnesses, from depression to psychotic disorders (Richardson et al., 2005; Rosenbaum et al., 2014; Schuch et al., 2016). Existing trials have largely focused on the use of formal exercise programmes, encouraging people to undertake an agreed amount of moderate-to-vigorous exercise per week (Firth et al., 2015; Gorczynski & Faulkner, 2010; Rosenbaum et al., 2014). Yet there is also evidence to suggest lower intensity activities such as yoga, tai chi, and walking interventions can have demonstrable benefits to a person's mental health (Cramer et al., 2013; Robertson et al., 2012; Vancampfort et al., 2012; Vollestad et al., 2012).

Given the health inequalities experienced by people with SMI, such as metabolic side effects of antipsychotic medication, increased comorbidity and premature mortality and poor monitoring of physical health in services, the inclusion of physical activity within mental health services has received considerable attention (Bailey et al., 2012; Richardson et al., 2005; Rethorst & Ttivedi, 2013; Shiers, Bradshaw & Campion, 2015). Exploring the utility of exercise and lifestyle interventions within early intervention services is a particular area of interest. The physical health benefits of exercise for FEP are highlighted in a recent pilot trial which found high intensity aerobic exercise reduces cardiometabolic risk in FEP by reducing waist circumference and resting heart rate and improves overall physical fitness (Abdel-Baki et al., 2013). A recent feasibility study also demonstrated benefits to both physical and

mental health in this group. A 10-week individualised exercise programme, 'investigating the benefits of exercise in early psychosis' (iBeep) showed significant improvements in psychiatric symptoms, physical fitness, cognitive functioning and psychosocial outcomes (Firth et al., 2016a). Active components of this intervention included individualised goal setting, personalised gym plans, intensive social support in the form of a gym buddy to attend gym sessions with, and access to local leisure facilities. The intervention had high levels of adherence, and the average amount of exercise achieved per week exceeded initial targets. Following the intervention, 55% of people continued to exercise, and showed sustained benefits to their mental health over 6 months (Firth et al., 2016b).

The growing evidence base supporting exercise for mental health has resulted in a shift from assessing whether physical activity interventions are useful, to identifying appropriate ways to implement them within services. The use of physical health practitioners or nurse specialists to deliver structured lifestyle interventions within mental health services is becoming increasingly popular (Happell et al., 2016; Richardson et al., 2005; Teasdale et al., 2017; Yung, 2016). This has also enabled the efficacy of nutritional interventions to be assessed, and provides evidence for the inclusion of both exercise and dietary components in early intervention (Teasdale et al., 2017; Teasdale et al., 2014).

The Bondi 'Keeping the Body in Mind' programme examined the use of a 12-week structured lifestyle and life skills program to reduce weight gain associated with antipsychotic medication in FEP (Curtis et al., 2015). The intervention was delivered by a team of specialists including a nurse, dietitian, exercise physiologist and peer wellness coach. Participants received individual consultations and group sessions to equip them with the skills and knowledge to cook healthy meals. Exercise sessions were conducted in an on-site gym, and individualised programmes were developed with participants in line with their personal goals and physical ability. Participants received motivational guidance throughout the programme, as well as being introduced to peer coaches who had lived experience of psychosis to accompany them to gym sessions and cooking classes, (Curtis et al., 2015). The intervention was successful and attenuated weight gain in people with FEP over a period of 12 weeks.

A similar approach has also been trialled in youth mental health services in Melbourne, Australia (Woodhead et al., 2017). Student exercise physiologists (supervised by accredited exercise physiologists) delivered a program within a youth mental health service to promote physical activity. 'Bod Squad' was offered to all young people attending the service with a range of psychiatric diagnoses, including FEP, bipolar disorder and depression. The intervention ran for 6 months and incorporated both one-on-one and group sessions which people could attend on a voluntary basis. Sessions were conducted in gyms on inpatient wards and in a specialist gym set up in a community centre for outpatients. Attendees were also given advice on how they could exercise at home. Over 6 months young people only attended 3 sessions on average. Despite low attendance rates, modest changes to physical health were observed. Additionally, the qualitative feedback from participants is useful for future intervention development. Participants valued the social aspect of attending groups, the individualised approach and the skills they had learned to incorporate physical activity into their daily life, (Woodhead et al., 2017). Similar findings were reported from the iBeep study, as participants enjoyed the social engagement of attending the gym with someone or being part of a wider community of 'gym goers' (Firth et al., 2016c).

Development of an intervention for the UHR group

The research in this PhD has helped inform the development of an intervention for the UHR group. Papers 1-3 combine systematic reviews, meta-analyses and cross-sectional comparisons to show that UHR individuals are more likely to live an unhealthy lifestyle than their peers and psychiatric controls. These papers also highlight the link between physical and mental health. The clinical audit showed that physical health and lifestyle behaviours have been neglected in early detection services. Given these findings, Paper 5 explains how a theoretical model, the COM-B model of behaviour (Michie et al., 2011), can be applied to inform an intervention for this group. According to the MRC Framework for complex intervention development, upon identifying the need for an intervention it should then be refined in a series of studies with the target

population. Therefore, in Paper 6, potential targets for a physical health intervention were selected by assessing the barriers and facilitators to living a healthy lifestyle (Carney et al., 2017a). As part of the qualitative study, 20 UHR individuals, 5 parents and 6 clinicians were asked about their views of a physical health intervention for use within early detection services. The findings from all 6 studies have led to a series of recommendations for future intervention development.

Overall physical health care

In the qualitative study, UHR individuals, their parents, carers, and clinicians believed having physical health care integrated within mental health services was important. Many participants reported that there was a lack of support available to help young people to live a healthy lifestyle. Many UHR individuals claimed that they wanted help to improve their physical health and become more active but did not know how to access this support. Therefore, even those who had the motivation to change their behaviour still felt like they could not as they did not have the opportunity to do so. This was also reflected in the audit (Paper 4, Carney et al., 2015) which found that physical health was not monitored, assessed or included as a part of routine health care in early detection services. Some examples of participant responses from study 6 are included below:

Service User: "I said to the doctor that I need to put on weight I need some dietician and I was waiting for months and nobody ever got in touch so they don't even help you. There's nothing. Not unless you are in the gym or you are paying for it you don't get no help."

Service User: "…I suppose it's not something that like people could be doing. I think it's that they don't have the ability to do it. It's not necessarily something that somebody could just step up and change and be like I'm gonna start doing this now, because they just can't access it."

Clinician: "…it's interesting that a lot of people who come into mental health services don't get asked those questions… it kind of is an issue but I think a lot of the time in services like EDIT the questions aren't necessarily asked."

Participants in this study also often referred to physical and mental health being linked and how both should be considered for overall wellbeing.

Parent: "If your lifestyle is healthier that potentially is gonna help with your mood. Mood and lifestyle, mood and physical health, are inextricably linked"

Recommendation 1

To develop a structured lifestyle intervention within EDIT services. This would enable UHR individuals to live a healthier lifestyle and improve their physical health.

Behavioural target and intervention content

A strong preference was expressed for an intervention focused on increasing physical activity and improving diet. Many young people reported enjoying some form of physical activity but did not feel confident enough to partake in these activities on their own. They also frequently reported feeling good about themselves when they have eaten a healthy diet, but would often consume convenience food such as junk food, crisps or chocolate, ready meals and fast food, as it was easier. This related to a lack of skill and motivation to look after their physical health.

Service User: "I think like cooking classes would probably be helpful, because trying to cook healthy food from scratch is hard. Like you don't know what you are doing."

Service User: "…Makes me feel down because like, I want to eat like, I want to eat healthier, but obviously I can't cook myself. Like I can't use a cooker, I can only just manage like the stove part of a cooker, I can only just manage to do that now, and I'm 17. That's embarrassing for a 17 year old not to cook, and because my mum would never let me touch anything."

Clinician: "I think recognising that a person's got to be motivated to address their physical health. And if they're really depressed they're not gonna be motivated. So it's how you enable someone to feel motivated to address the physical health."

Therefore an intervention which targets these barriers to exercise and healthy eating would be useful for this group. For example, showing young people how to quickly cook healthy foods, informing them of smart food swaps and healthy snack options.

Young people claimed having a focus on weight would be an unhealthy target for an intervention and would add to the growing pressures around body image during adolescence. As reported in Paper 6, the way young people felt about themselves was a barrier to exercise and healthy diet, for example having low confidence and feeling self-conscious (Carney et al., 2017a). A recent paper also highlights this issue and suggests moving beyond the paradigm of weight loss for physical health interventions (Firth et al., 2016e). Focusing on weight may also discourage some young people who feel like they have previously tried to lose weight and not succeeded. Furthermore, this group is actually likely to be a similar weight to their peers, in comparison with FEP individuals for example (Carney et al., 2015; Foley & Morley, 2011). More appropriate outcomes could include quality of life, fitness, or energy. Self-efficacy is an additional factor which could be considered, given that higher self-efficacy is associated with sustained changes to behaviour (Vancampfort et al., 2016).

Service User: "like eating healthy like you know this is what your body needs to function and be healthy, not just this is what you need to eat to be skinny because skinny is not necessarily healthy. But that's what young kids are seeing in the media."

Ensuring an intervention was low cost, accessible in terms of location and transport, and orientated to young people was seen as an important factor. This is in line with previous research (Bradshaw et al., 2012). Clinicians raised concerns that it is difficult ensuring activities are youth appropriate, as sometimes it can come across as patronising or 'trying too hard'. One of the key facilitators for young people changing their behaviour was promoting autonomy, rather than simply being told what to do (Carney et al., 2017a). A strong preference was expressed for a motivational intervention which empowers UHR individuals to take control of their own behaviour. Working with young people to change their behaviour in a way that is acceptable and meets their goals could avoid this conflict.

Options to engage in community activities could be discussed during goal setting meetings with the person delivering the intervention. Many UHR individuals wanted to learn how to incorporate physical activity and healthy eating into their daily routine. One of the main issues for young people was that they felt incapable of planning their time, often engaging in unstructured

activities. Helping UHR individuals to plan weekly activities and meals may help facilitate long-term change. The 'Bod Squad' study also found that participants with a range of mental health diagnoses valued the chance to learn how to incorporate exercise into their daily life and found it a useful component of the intervention (Woodhead et al., 2017). Preparing healthy meals and developing the skills and knowledge to be able to cook healthy meals from scratch were also examples of some of the content UHR individuals would like to see in an intervention.

Service User: "I think you should get help, sort of like with a timetable, like planning it out sort of like balancing it out with college and stuff, and then your gym and stuff like your revision and stuff like… I know it sounds simple but I struggle with stuff like that like balancing everything out and that."

For substance use, clinicians generally referred on to additional drug and alcohol services if it was raised as an issue during therapy. However, from the audit (Carney et al., 2015) although young people were assessed for comorbid substance use disorders at intake, they were not asked about general substance use and it was only known to clinicians if it was a goal they wanted to work on within their therapy sessions. Although not all UHR individuals smoke and use cannabis, and not all UHR individuals need help to exercise, we know that this group are significantly more likely to do so than their peers which can have a detrimental effect on their mental and physical health (Carney et al., 2016b; Carney et al., 2017a-c). As there are alternative services available for drug and alcohol use, it may be more appropriate to provide brief advice sessions as part of a wider intervention; sign posting young people to other services and places they can get advice. This could include smoking cessation which includes very brief advice as part of an intervention (Coleman, 2004).

Recommendation 2

A structured lifestyle intervention should include:

- psychoeducational components
- motivational counselling including goal setting

- social support

- guided skills based sessions (cooking demonstrations, warm-up workouts)

- very brief advice and signposting to drug and alcohol services

Recommendation 3

Behavioural targets should include both physical activity and diet. Potential targets could be:

- physical activity (90 minutes moderate to vigorous exercise per week)

- reducing sedentary behaviour (10,000 step goal per day)

- fruit and vegetable intake (5-7 servings of fruit-veg per week)

- overall diet (calorie controlled diet)

Overcoming potential barriers to engagement in the intervention

Conducting a physical health intervention for this group is challenging; Table 1 contains a summary of some challenges which may be experienced when developing an intervention and potential strategies to address these.

Table 1: Barriers to a physical health intervention for the UHR group and strategies

Barriers to physical health intervention	Quote from service users in Paper 6 (Carney et al., 2017a)	Strategies
Social anxiety	*"I know I've got to try but I would never want to go to the gym on my own unless a friend was coming with me."* *"Like fields, or swimming, or a gym… anywhere like that but where it's not too busy. So like certain times when they know it's not gonna be that busy so we can cope with it, people like me can cope with it."*	• Bring a friend or family member along • Taster sessions to observe • Offer 1:1 sessions as well as group • Have peer mentors involved in facilitating group sessions and to accompany people to the gym • Attending or visiting the gym at non-peak times so that it is not busy
Transport and accessibility	*"making sure it is not too far away and making sure it is easy to get to and so they know where it is"*	• Ensure sessions conducted in a central place with good access to public transport and local area • Use local gyms as oppose to running exercise sessions in areas which are difficult to get to • Discuss local supermarkets/food outlets that participants can use
Stigma	*"You are pointing out like, oh I'm going to slimming world tonight – why because you are fat? You're pointing out why you are doing it. Whereas if you called it a nicer name… more people would come to it."*	• Sessions to take place in a non-stigmatising venue e.g. community centre, local college, gym • Study materials to have service user input regarding the language used • Focus to not be on health and wellbeing not weight • Give information on how improving fitness is more important than losing weight • Visiting the gym at non-peak times to avoid comparing themselves to stereotypical gym goers
Delivery of intervention not appropriate for the UHR group	*"Yeah probably like a, erm somebody who has, yeah I guess who has that nutritional knowledge but who knows the effect like… like someone who specialises in diabetes, but someone who specialises in mental health."*	• Ensure the trainer has some experience of the psychopathology of the UHR group • User-led input to enable the intervention is appropriate for the age group (approximately 16-25) and not pitched too young
Low motivation	*"Maybe just like diet plans and exercise routines, stuff like that, depending on what you want to achieve, like if you want to build muscle, or cardio or whatever."*	• Not to be too prescriptive and work on empowering the individual to take control of their physical health, rather than simply telling them what to do • Trainer to work with the individual on personal goals

	"Maybe present them with a chart that they can use to see if you have done any exercise over the week, you can see if they have seen any improvements. And sort of record it on a chart and see if at the end of therapy if you've actually improved your physical appearance as well as your psyche"	and what they want to achieve, giving different exercise options to do to achieve a collective goal of 90 minutes moderate-to-vigorous exercise per week • Work with individuals to set small achievable goals which are updated throughout the program to keep motivated and celebrate small achievements
Time	*"I used to have like a 7 minute work out on my phone and then you just put it on in the morning for 7 minutes and that was it. So it is good in that sense, because you can just, it is there… you don't have to, you know it takes away one of the obstacles."*	• Trainers to show quick and effective exercise methods, how activity can be incorporated into active travel, short sessions in the gym • Key component of an intervention should be showing quick healthy recipes, meal planning and meal preparation to avoid young people consuming convenience foods
Financial costs	*"…having activities that are free or just like £1 or 2 an hour instead of like 5 or 6 pound, would be better because they will be obviously cheaper and because it is like cheaper for us it will be… bit more motivated because it won't costs us a fortune"* *"I suppose if like people could like show you how to eat well on a budget that would be helpful"*	• Keep costs incurred to the participants to a minimum, low cost or free exercise sessions offered by linking in with community activities • Recommend low cost options for foods and how to cook on a budget rather than showing expensive food recipes • Provide with information about low cost food options in a booklet form or via an app so that participants can take away and show to parents
Sustaining a healthy lifestyle	*"..they could take away different ideas on how to make their lives healthier. You could offer like leaflets and stuff to find for different activities, so like different clubs around areas that they may not have known about because there are a lot of hidden ones, you just don't know of them"*	• Focus of the intervention is to equip participants with the skills and knowledge to be able to include physical activity and a healthy diet in their daily routine • Education materials to be given throughout which participants can look back on e.g. recipe books, work out plans, planning lists • Focus on promoting autonomy and motivation to continue long-term changes • Link in with local community facilities throughout, but particularly towards the end of the intervention and ensure participants know where they can go to access further support for their physical health

Intervention delivery

Acceptable methods to facilitate support were discussed and could be grouped under two main categories:

1. The staff members who would deliver an intervention
2. mHealth and app delivery

<u>Staff delivery</u>

Potential options included having a specialist member of staff, such as a physical health therapist, nurse or personal trainer situated within the mental health service that they could access. Many UHR individuals claimed they would have more trust in a person who possesses sufficient expertise in physical health, such as an exercise therapist or dietician. This view was also supported by clinicians who claimed having someone within the service who could help with physical health would open up further opportunities for health promotion of this group. As the burden of mental health care provision increases, clinicians within the NHS are experiencing increased workload and pressure to meet targets and national standards. This pressure was expressed within interviews as clinicians often reported feeling frustrated as they knew physical health was important and wanted their clients to be able to access support for their physical health.

Clinician: "it could be a service that is offered by the NHS we would save ourselves billions and billions of pounds, if during therapy or through secondary care we were doing more for physical health as far as mental health goes. We spend too much time separating them, and it's… it's not difficult."

In line with previous research, (Knowles et al., 2016), UHR individuals expressed a need for someone to deliver the intervention who had an awareness of the mental health difficulties they experience. Individuals also held a favourable view for the involvement of someone they could identify with or someone who has had similar experiences to them within an intervention. Some suggestions included a physical health specialist who had previously worked within mental health settings, a clinician or therapist who had completed

additional physical health training and the inclusion of peer mentors or people with lived experience to assist professionals with running the intervention. This could be facilitated with the use of peer mentors to help out with groups, or take people to the gym. Attendees of the program could be offered the chance to become more involved with the delivery towards the end of the intervention, such as co-facilitating the groups, and help prepare for cooking sessions.

Service User: "I think maybe university students trying to find some kind of work experience really because I get on better with younger people, people around my age, erm, I feel less intimidated by them, I feel like they kind of understand what's happening in my life a bit better than if I had some, someone in their yanno late 30s early 40s telling me to do a spin class I'd be like –yeah just shut up."

Recommendation 4

To integrate physical health professionals within early intervention. From the interviews UHR individuals would trust a professional or an expert who has the knowledge of physical health, yet someone who also has experience working with mental health services. Some potential options would be to use:

- fully qualified dietitians, physiotherapists or physical health practitioners/nurses
- a potentially low cost option would be to use university students to run or deliver the sessions as part of one of their placements, supervised by fully qualified physical health practitioners
- someone trained in mental health such as a nurse or support worker, who has additional training in looking after physical health

mHealth

The use of mHealth approaches such as 'apps' was also highlighted as a popular method of intervention delivery for the UHR group and is a growing area of interest for mental and physical health provision (Firth et al., 2016d; Firth, Torous & Yung, 2016). Many individuals had previously used apps to

assist with their physical health. For example, one person used a diet app to log food intake throughout the day, and valued the ability to use a barcode scanner to keep track of what they had eaten that day, look up nutritional information and stay within a controlled calorie limit. Other uses for apps included monitoring functions such as step counters and activity trackers, where people aim towards a personalised goal. Apps could be used in addition to social support and may further encourage social engagement with other participants. Indeed apps facilitate the use of a wide range of behaviour change techniques such as self-monitoring, goal setting, social and practical support and behavioural prompts.

Service User: "it worked everything out for you, so you do your diary and then it would tell you what it is, what weight you are now, what your aim is and it would say you need to do this so, so many steps or so many hours of exercise to reach your goal and that was really good. I'd be looking at me phone and I would be thinking I can do that I can go for a run now and then I've done my exercise for the week."

One approach recommended by individuals would be to use apps to support a programme throughout the week, on the days where participants do not meet with a trainer, which would then encourage participants to engage in on-going physical activity (10,000 steps daily; Haskell et al., 2007). Psychoeducation modules are easily incorporated into apps, and can address barriers to living a healthy lifestyle, such as knowledge of healthy food, exercise and diet plans. Content from group sessions could be made available via an app or online platform so that participants can look back on information. Social support components could even be integrated within a mHealth intervention. For example, forums could be set up where individuals could (anonymously) discuss their progress throughout a physical health intervention. This could be monitored by a study team for risk issues or potential problems with the intervention.

Clinician: "Having an app to support an intervention would be absolutely brilliant. You know… an intervention having its own app. Where you can record your data on your phone rather than keeping old fashioned paper diaries, which we still use in CBT but actually having an app linked to your intervention that would be great"

Recommendation 5

The use of apps should be further explored in this group, but could serve as a useful adjunct to a face-to-face intervention. There is potential for a mobile phone app to aid the delivery and running of a programme. An app could have multiple functions; such as containing resources from sessions, and social interaction with other participants via anonymous forums. It could potentially be a low cost method to help young people meet their goals.

Format

People differed according to whether they would prefer a group setting or individualised one-on-one sessions. Some participants valued attending groups as it enabled them to meet new people and discuss shared experiences with others. This is in line with the findings of previous physical health interventions in youth with psychiatric diagnoses (Bradshaw et al., 2012; Curtis et al., 2016; Firth et al., 2015; Woodhead et al., 2017). Individuals who were more socially anxious claimed they would struggle attending groups, and would prefer instead to have one-on-one sessions. Other acceptable suggestions included being able to bring someone along with them who they trust, such as a therapist or friend, attending small groups of 2-3 initially and building up to larger groups and being offered taster sessions. Therefore, a combination of the two options may be more appropriate.

Service User: "I guarantee there will be some people doing it who will want to be in a group and some people will want to be on their own"

Recommendation 6

To aim for 10-12 weeks with approximately 2 sessions per week. A mixture of 1:1 and group sessions could run throughout the course of the program. This could take the form of having 2 sessions a week, alternating between healthy eating and exercise.

Location

A non-stigmatising setting, such as a community centre, college or local gym, as opposed to a specific mental health orientated location was preferred, in order to reduce further stigma from others (Carney et al., 2017a). UHR individuals also discussed how achieving the right balance of social support and attending the gym at quieter times (such as during the day) would help. Encouraging young people to attend services already available to them in the community could facilitate long-term change, as they would be able to continue making use of any opportunities available to them, in the absence of social support, for example when an intervention finishes.

Service User: "nobody knows why you are there. Like people don't know I am here for a mental health related thing, I think that would take the edge off it a bit… I don't know how many places like that there are. If there was a community where a lot of different stuff goes on, so it's all mixed and it feels a lot more normalised"

Recommendation 7

Exercise sessions could take place at a local community gym or in leisure facilities, but not within health services as UHR individuals felt that this would add to the stigma they experience and make them feel 'different' to their peers.

There is also evidence that green exercise or exercising outdoors is associated with positive mental health (Pretty et al., 2005; Lee & Maheswaran, 2011). Interviewees from Paper 6 reported that they would like to engage in some outdoor exercise, as it would allow them to leave if they were feeling too anxious. Some participants also reported that they enjoyed being physically active outdoors, for example walking in green spaces or parks, but avoided more formal exercise as they felt too self-conscious. The benefits of exercising outdoors included clearing their mind, relaxing, getting fresh air and feeling like they have achieved something. However, this was not the case for all people as in more deprived areas, issues with safety and access to green spaces was reduced.

Service User: "I usually just like to take walks, sometimes on my own, sometimes with my boyfriend. Erm, because it can be like a social thing as well, like if I'm with someone it's a good activity to like get me out of the house and do something... If I sort of need to just get away for a while I'll go for a walk in the woods or something, it's like a clear path to follow, and it is like always the same amount of time…"

Recommendation 8

To try and incorporate some form of outdoor activity into a programme, such as walking or small outdoor exercise groups, such as boot camps.

Behaviour change techniques

Paper 5 applies the COM-B (Capability, Opportunity and Motivation) model of behaviour to the issue of physical health in the UHR group (Carney et al., 2016a). Here potential techniques are proposed which can be used to help increase exercise and healthy eating in the UHR group. In the final qualitative interviews, a range of techniques to improve diet and physical activity were mentioned which individuals found had either worked for them in the past, or clinicians/parents had tried previously. These included goal setting, self-monitoring (for example using tracking apps, or food diaries), provision of feedback and tracking of progress, all of which can increase motivation and encourage long-term behaviour change (Michie et al., 2011; Michie, van Stralen & West, 2011).

Recommendation 9

Table 2 contains a summary of potentially useful behaviour change techniques which could be used in an intervention for this group:

Table 2: Behaviour change techniques which could be used in a health intervention for the UHR group

Target	Summary from Carney et al., (2017a)	Potential Behaviour Change Techniques (BCTs) taken from the Coventry, Aberdeen and London: Refined (CALORE) Taxonomy (Michie et al., 2011)	Example
Motivation	The UHR group had low motivation for activities and general disinterest in looking after their physical health. They would often rely on quick fixes such as convenience food and energy drinks. Yet many wanted the option to take control over their health and would like to be more motivated to do activities but it was not one of their priorities.	**CALORE 5.** Goal setting (Behaviour). *The person is encouraged to make a behavioural resolution (e.g. to take more exercise per week).* **CALORE 7.** Action planning. *Involves detailed planning of what the person will do including, as a minimum when, in which situation and/or where to act.* **CALORE 10.** Prompt review of behavioural goals. *Involves a review of the extent to which previously set behavioural goals were achieved, followed by a revision or readjustment of goals and/or means to attain them.*	Setting achievable goals with a trainer, e.g. small targets to be gradually increased. Ensuring there is a clear goal to reach and this goal is specific and measurable (daily step count) and this goal is reviewed throughout. Participants to work with a trainer to develop a plan of how they will achieve a set amount of exercise per week and how they plan to stick to a healthy diet.
		CALORE 16. Prompt self-monitoring of behaviour. *The person is asked to keep a record of specified behaviour as a method of changing behaviour.*	Monitoring progress using acceptable methods such as an app for step counting or food scanning, or a wearable device for overall activity.
Capability	Many struggled due to symptoms preventing them from activities such as going to the gym. Generally lacked confidence and felt like they did not know what to do in the gym and would feel self-conscious. Individuals wanted social support such as someone to help them go to the gym and improve their confidence. They also reported not	**CALORE 21.** Instructions on how to perform the behaviour. *Involves telling the person how to perform behaviour.* **CALORE 22.** Model or demonstrate the behaviour. *Involves showing the person how to perform behaviours through physical or visual demonstration.*	Trainers to tell individuals how to use gym equipment, what kinds of exercises are good to do at home, how they could improve their activity levels. They could also be told how to prepare certain foods. Trainers could also model the behaviour by going to the gym with individuals and showing them the exercise, then getting them to do it themselves. Video clips of exercises available to access on an app

	having sufficient skills to be able to cook healthy meals and would go for easy options which tended to be convenience foods.		could be used to demonstrate the behaviour and referred back to. Another example would be cooking classes where they are shown a healthy recipe which they then have to copy.
		CALORE 29. Plan social support/social change. *Involves prompting the person to plan how to elicit social support from others to help them achieve their target behaviour. This will include social support during interventions e buddy systems.*	Encouraging social support from other participants via group sessions, allowing people to bring a close friend or family member with them to sessions. Setting up an online forum or app chat facility so people can discuss the programme anonymously. Trainer to be on hand during gym sessions for social support.
Opportunity	Social opportunity reduced as young people engaged in a lot of unstructured activities, had difficulty planning their time and would avoid social situations due to symptoms such as anxiety and paranoia. Also believed there was a lack of physical opportunity as they did not know where to go for help with their physical health or access local facilities.	**CALORE 38.** Time management. *Any technique designed to teach a person how to manage their time in order to make time for their behaviour.*	Sitting with a trainer or the person delivering the intervention for 10 mins before or during a session and planning out when they will exercise that week or making a shopping list. Participants could be given a planner to chart in their activities and foods they will eat that week.
		CALORE 8. Barrier identification/ Problem solving. *This presumes having formed an initial plan to change behaviour. The person is then prompted to think about potential barriers and identify ways of overcoming them.*	Working with the UHR individual to identify ways they could access local facilities e.g. finding low cost exercise sessions which they would be interested in attending, attending gyms at quieter times, locating low cost supermarkets.

Potential outcomes

Initial outcomes should focus on assessing whether it is first feasible with the resources available and whether individuals find an intervention acceptable. Identifying methods of intervention delivery would be an important part of an initial feasibility study. For example, would participants find the use of activity trackers such as wearable devices, mobile phone apps or online activity logs an acceptable method to monitor activity levels? Also the level of adherence to each particular component would be necessary to inform the development of a full RCT. This would allow any aspect of the intervention to be modified prior to a full trial.

Recommendation 10

A feasibility study should be conducted to address the following questions:

- Do UHR individuals adhere to a physical health intervention offered within EDIT services?
- Can a physical health intervention help UHR individuals increase their physical activity levels and improve their diet?
- What methods are effective in bringing about a change in behaviour?
- What measures are acceptable as potential outcomes for a full trial, for example activity tracking, mental health assessments, quality of life, physical health monitoring?
- Are there any barriers to conducting a physical health intervention for this group?
- What are the opinions of participants regarding the acceptability of the intervention?

Future work

The recommendations suggested here can be used to guide future development around a physical health intervention for this group. However, further engagement with local communities and stakeholders is necessary

before the formal development of a protocol for this type of intervention. Potential options could include local PPI (patient and public involvement) events, liaison with services to assess current staff provisions and practice, meetings with universities to arrange for student placements to conduct the intervention, and meetings with local gyms and leisure facilities. To evaluate the impact of a physical health trial for the UHR group, both mental and physical health should be assessed, and the long-term impact of living a healthy lifestyle could be assessed using prospective studies.

Summary of Recommendations

A summary of recommendations is included in Table 3.

Table 3: Summary of Recommendations

Recommendation	Summary
Recommendation 1	To develop a structured lifestyle intervention for UHR individuals.
Recommendation 2	To address the main barriers to living a healthy lifestyle with an intervention including providing social support, motivational guidance and developing skills and knowledge.
Recommendation 3	To identify appropriate behavioural targets to increase physical activity and improve diet.
Recommendation 4	To integrate physical health practitioners within UHR services who have knowledge of mental health to work with the UHR group.
Recommendation 5	To explore the use of apps and mHealth as a mode of delivery and to accompany an intervention.
Recommendation 6	A structured lifestyle programme should aim to run for 10-12 weeks, with a mixture of 1:1 and group sessions.
Recommendation 7	Exercise and healthy eating sessions should take place in a non-stigmatising setting such as a community centre.
Recommendation 8	Aim to include some form of outdoor activity in an intervention.
Recommendation 9	A range of theoretically informed behaviour change techniques should be used to build the intervention.
Recommendation 10	A feasibility study should be conducted to inform the development of a full trial.

Discussion

Summary of PhD findings

The aim of this PhD was to investigate the physical health and lifestyle of individuals at ultra-high risk for psychosis (UHR). This is the first attempt to take a holistic look at both physical and mental health in this group. Several important findings have emerged from this PhD, which advance our understanding of UHR psychopathology. First was the finding that many UHR individuals display risk factors for cardiometabolic disease and that a large proportion of this risk is related to modifiable behaviours.

While the National Institute for Health and Care Excellence (NICE, 2014) and the NHS England Early Intervention in Psychosis Standard (NHS England, 2016) recommend that early intervention services address poor physical health in people with FEP, monitoring and management of physical health in the UHR population is not mentioned. However, this PhD summarises existing evidence and presents new data to suggest there is scope to intervene to promote healthy living even earlier than the first-episode. UHR individuals are at risk for poor physical health, largely due to behavioural risk factors such as physical inactivity, substance use and poor diet (Carney et al., 2016b, 2017b, c; Papers 1-3). Most existing studies compare the UHR group to controls. Yet there is evidence to suggest that even compared with psychiatric controls, UHR individuals are significantly more likely to use substances and partake in the use of multiple substances (Carney et al., 2017c; Paper 2). This suggests that the unhealthy profile observed may not be attributed to psychological distress and general psychopathology alone, but may be associated with the UHR group.

The findings are timely, and suggest that there has been a missed opportunity for early intervention. Prior to this research, most efforts were directed towards intervening during FEP. However, these studies show that even prior to the onset of psychosis, interventions to improve lifestyles are warranted. From the available data, we did not find evidence to suggest that UHR individuals have the same poor physical health as people with FEP (Paper 1; Carney et al., 2016b). However they are at a significant disadvantage for poor physical health due to high rates of modifiable risk factors (such as low physical activity, high tobacco, cannabis and alcohol use) and low rates of physical health monitoring

in services (Carney et al., 2015; Paper 4). I also found that engaging in unhealthy lifestyle behaviours can impact on mental health in this group, highlighted by the link between cannabis use and more severe symptoms (Carney et al., 2017b; Paper 3). Paper 6 also emphasises how mental health symptoms directly affect a young person's ability to live a healthy lifestyle. Numerous barriers to living a healthy lifestyle were reported which put UHR individuals at a significant health disadvantage, (Carney et al., 2017a; Paper 6). Thus there is a link between physical and mental health in this group.

Physical health promotion for people with mental health difficulties is a major area of research, including people with depression, early psychosis, and other schizophrenia spectrum disorders (Rosenbaum et al., 2014; Richardson et al., 2005; Schuch et al., 2016; Firth et al., 2015; Gorczynski & Faulkner, 2010). The findings of this PhD provide a foundation to inform the development of appropriate behavioural interventions for this group.

Recent research

Since the start of this PhD, several additional studies have been published which are relevant to our findings. Cordes et al., (2017) showed that UHR individuals were significantly more likely to have metabolic abnormalities such as increased blood pressure, increased fasting glucose (a precursor to type 2 diabetes) and a larger waist circumference. Prior to the Cordes et al., (2017) study and this PhD, there was limited research focusing on the metabolic health of the UHR cohort. Paper 1 included studies reporting BMI, and found no difference in the BMI of UHR individuals and controls (Carney et al., 2016b). However, BMI could potentially be a less sensitive measure than other determinants of body composition such as waist circumference, and central adiposity when quantifying risk for cardiovascular disease. For example, recent studies have shown waist circumference is a more valid predictor of mortality risk than BMI (Hamer et al., 2017). In the Cordes et al., (2017) study, metabolic abnormalities were not linked to side effects of medication as individuals were unmedicated and antipsychotic naive. Cordes et al., (2017) therefore, proposed that genetic factors may be a potential cause of poor physical health in this group. However, they did not account for lifestyle behaviours. Given the high

rates of unhealthy lifestyle behaviours in this group it is important to consider their potential role in the development of physical comorbidity. I make this point in a letter published in response to the Cordes et al., (2017) paper (see Carney et al., 2017d; Appendix B).

Another recently published study focused on assessing the rates of modifiable cardiometabolic risk factors such as physical activity and fitness in the UHR group, (Lederman et al., 2017). Similar to the conclusions of this PhD, Lederman et al., (2017) showed that UHR individuals had lower levels of physical activity than their peers. Sleep quality was also poor in this group. This is an important area of future research, given the link between sleep and metabolic health (Lederman, Carney & Kalucky, 2017). For example, poor sleep can result in physiological changes including impaired appetite regulation and reduced day-time energy levels (Sigurdson & Ayas, 2007).

The long-term effects of health behaviours have also recently been reported. Sormunen et al., (2017) found low levels of physical activity during childhood and adolescence independently predicted psychosis in adulthood (Sormunen et al., 2017). These findings provide an important contribution to the literature and further support our argument for promoting physical activity in this group. Therefore, all three recent studies are consistent with the findings of this PhD and add further weight to our conclusions that even prior to FEP, UHR individuals are at-risk for poor physical health. Regardless of what is causing low levels of physical activity, the inclusion of exercise and physical health promotion in early intervention is necessary to protect against future ill-health.

Potential mechanisms and reasons for poor lifestyles

Potential reasons for why UHR individuals may be more likely to engage in unhealthy behaviours are discussed within the individual papers. Paper 6 explores this issue further by highlighting some of the barriers to living a healthy lifestyle, reported from the perspectives of UHR individuals, their parents and their clinicians.

Effect of symptoms

Mental health symptoms such as low motivation, paranoia and social anxiety have an impact on the lifestyle behaviours of young people. As discussed in Paper 6, symptomatic barriers often prevent UHR individuals from attending local leisure facilities such as gyms and large shopping centres, due to feeling anxious or paranoid. Comfort eating junk food or using substances when their mood was low were common examples of how a person's mental health impacted on their lifestyle choices.

Low motivation is commonly experienced by UHR individuals, and was identified as a key barrier in Paper 6. This group often have difficulties with motivation to undertake regular activities, and often function poorly in day-to-day life (Cotter et al., 2014; 2016). Emerging symptoms of psychosis and psychological distress often overshadow any motivation to look after their physical health. Therefore, engaging in health promoting behaviours such as exercise or stopping smoking may not be a priority for this group. Indeed the qualitative study (Carney et al., 2017a; Paper 6) suggested that promoting autonomy would be beneficial, as many UHR individuals wanted the opportunity to take control and be motivated to improve their physical health. However, due to the high levels of psychological distress experienced in this group, seeking mental health care often takes priority. This is also the case for services, evident from the findings from the clinical audit (Paper 4) and the qualitative interviews with clinicians (Paper 6). Despite being aware that physical health is important and should be addressed, clinicians often reported their primary goal was to focus on mental health. As a result, physical health issues were largely neglected in services as they were not seen as an area of immediate concern (Carney et al., 2015; Paper 4).

The relationship between symptoms and health behaviours could be explored further, as it is unclear whether there is a causal relationship between symptoms and health behaviours. The recent longitudinal study by Sormunen et al., (2017) shows that engaging in higher levels of activity during adolescence is associated with better mental health in adulthood. This suggests exercise may protect against future mental health difficulties. There is also evidence that consuming a Mediterranean diet, rich in fruit, vegetables, olive oils, grains and

fish is linked to increased quality of life in adolescents (Muros et al., 2017). In Paper 6 (Carney et al., 2017a) many UHR individuals reported feeling worse about themselves when they do engage in unhealthy behaviours such as eating junk food or using substances. Some examples given were a lack of energy, low motivation and low mood. However, it is unclear what comes first; do young people experience changes to their mental health which then increases the likelihood of engaging in unhealthy behaviours, such as sedentary behaviour, poor diet and substance use? Alternatively, does engaging in unhealthy behaviours result in an exacerbation of poor mental health in this vulnerable group? It could potentially be a vicious cycle whereby mental health symptoms increase the tendency to engage in unhealthy lifestyle behaviours, which then further exacerbates symptoms (Figure 1).

Figure 1: Shared risk factors for poor mental and physical health and relationship with symptoms
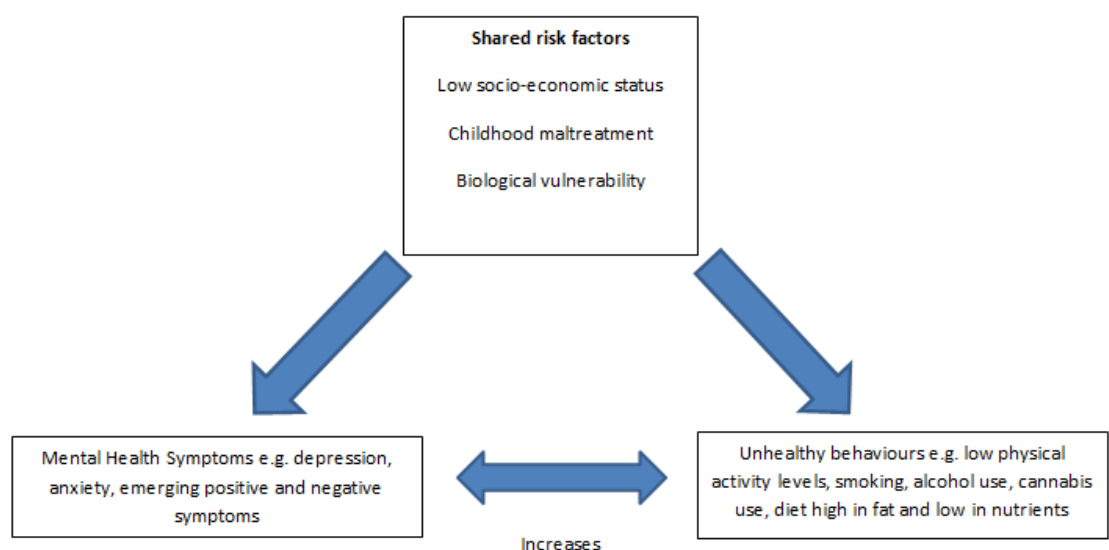
Paper 5 and 6 present a behavioural analysis considering some of the factors affecting health behaviours in the UHR group, such as, emerging psychotic symptoms, low motivation, lack of social support and lack of opportunities. However, we can only speculate about the aetiology of this unhealthy profile in the UHR group. Although we can see that mental and physical health are linked, it is unclear why this group are at-risk for both SMI and also at-risk for

poor physical health. A plausible explanation could be the presence of shared risk factors for both the development of poor mental health and the tendency to engage in unhealthy behaviours. This may include socio-economic factors, biological or genetic factors and childhood adversity.

Socio-economic factors

Environmental factors, such as socio-economic status, trauma, and adversity increase the risk of developing mental health problems and the likelihood of engaging in behaviours such as smoking, substance use and poor diet (Darmon & Drewnowski, 2008; Howes et al., 2004; Redonnet et al., 2012). UHR individuals are likely to come from a more deprived background, and live in areas of low socio-economic status, with high rates of social inequality and adversity (Brucato et al., 2017; Cotter et al., 2016; Davies et al., 2016). Low educational attainment and poor occupational functioning is common in this group (Cotter et al., 2016; Niemi et al., 2003). Therefore, a lack of knowledge, education and skill may occur as a result of persistent social inequalities. For example, some UHR individuals may not know how to cook and prepare a healthy meal, or how to use equipment in the gym.

The physical environment also impacts on a person's lifestyle. Access to leisure facilities and healthy food options, transport links, and opportunities to engage in healthy activities are all factors which affect lifestyle behaviours in this group. A higher density of fast food outlets, tobacco and alcohol suppliers and fewer opportunities to exercise are often observed in areas of high socio-economic deprivation compared with more affluent areas (Shortt et al., 2015; Vancampfort et al., 2013). A previous study found having the opportunity in the local environment to engage in activity, such as the provision of bike lanes or equipment significantly increased activity levels (Vancampfort et al., 2013). Indeed one of the main barriers to living a healthy lifestyle found in Paper 6 was a lack of opportunity to do so (Carney et al., 2017a). This study was conducted in the North-West of England, an area which suffers vast social inequalities in relation to allocation of resources and government investment in services. Yet, even when community leisure facilities are available for people to use, many UHR individuals struggle with practical issues such as costs due to a lack of

employment, reliance on parents, or financial implications of smoking or using other substances (Cotter et al., 2017). Therefore, the UHR group are at a significant disadvantage when it comes to looking after their physical health.

Biological factors

Biological or genetic factors may pose a significant risk factor for both the emergence of UHR symptoms and the propensity to engage in unhealthy behaviours. Having a first-degree relative with SMI significantly increases the risk of a person developing a psychotic disorder. Therefore a group of UHR individuals may possess a biological vulnerability which predisposes them to developing psychosis, and also poor physical health. For example, there is evidence of metabolic dysfunction in some first degree relatives of people with psychosis (Baptista et al., 2011; Darcin et al., 2015). Metabolic abnormalities are also observed in antipsychotic naive people with FEP suggesting there may be an inherent genetic vulnerability for poor physical health which precedes the use of antipsychotic medication (Vancampfort et al., 2013). It is therefore plausible that a subsample of people in the UHR group may also have metabolic abnormalities, particularly those who will go on to transition to psychosis. Future longitudinal studies of the metabolic health of this group may clarify this.

Substance use disorders are common in people with SMI, and in those at-risk for developing psychosis. Both substance use disorders and psychotic disorders have a high degree of heritability suggesting the potential role of shared biological vulnerability (Chambers, Krystal & Self, 2001). The underlying neural pathways may overlap for both types of disorders. One example of this could include common genes responsible for the regulation of the dopamine system. Dopamine is involved in the reward pathway of substances of abuse and also in the expression of positive symptoms (Volkow et al., 2009). The UHR group have altered dopamine function (Stone et al., 2010), and high rates of cannabis use disorders (Carney et al., 2017b; Paper 3). Cannabis abusers who display decreased dopamine reactivity have been shown to have lower reward sensitivity and motivation and increased levels of stress (Volkow et al., 2014). Therefore, an overlap in the neural pathways associated with cannabis abuse

and the development of UHR psychopathology could explain both the significant motivational deficits and high degree of comorbid substance use disorders observed in this group. A similar association may be found for tobacco use, as the UHR group are significantly more likely to smoke than their peers, (Carney et al., 2016b; Paper 1). This could be due to shared biological risk factors (de Leon & Diaz, 2005). An alternative reason is that tobacco may have a causative role in the development of positive symptoms in people who have a biological vulnerability for psychosis, which could be driven by dopamine dysregulation (Gurillo et al., 2015).

Childhood maltreatment

Childhood maltreatment and adversity is also a shared risk factor for both psychosis and unhealthy lifestyles. For example, childhood trauma increases the risk of developing psychosis and other serious mental illnesses (Gilbert et al., 2009; Hovens et al., 2012; Isvoranu et al., 2016). The UHR group have high rates of childhood trauma and adversity (Kraan et al., 2015 a, b). Furthermore, childhood trauma independently predicts long-term functioning in the UHR group (Yung et al., 2015), and individuals who experience early adversity are significantly more likely to become further victims of abuse and trauma during adulthood (Cotter, Drake & Yung, 2016). As well as having a negative impact on mental health, childhood trauma is also a risk factor for developing physical ill-health such as obesity during adolescence and in later adulthood (Danese & Tan, 2014; Hemmingsson, Johansson & Reynisdottir, 2014). A review of childhood sexual abuse also found trauma was associated with higher rates of poor general health outcomes, including gastrointestinal, reproductive, and cardiopulmonary health in later life (Irish, Kobayashi & Delahanty, 2010). Therefore, this could represent a further shared risk factor which increases the liability for developing mental and physical ill-health.

The impact of an unhealthy lifestyle on UHR individuals

Physical health

As UHR individuals face multiple barriers to living a healthy lifestyle, they are at-risk for future metabolic ill-health if they continue to engage in unhealthy behaviours. This is a particularly pertinent issue in those who go on to develop serious mental illness, given the high degree of comorbidity and premature mortality experienced at a later stage (De Hert et al., 2006; Mitchell et al., 2013; Shiers, Bradshaw & Campion, 2015). Even individuals who do not experience psychosis are at-risk for long-term physical ill-health problems as a result of high rates of unhealthy lifestyle behaviours. Tobacco use, for example is associated with significantly increased risk of developing CVD, lung disease, stroke and many types of cancer, independent of any other risk factor (Elders et al., 1997). Additionally, physical inactivity increases the risk of numerous non-communicable diseases and premature mortality (Lee et al., 2012). Therefore, encouraging this group to live a healthy lifestyle may protect against future metabolic problems, regardless of whether they transition to psychosis or not.

Although the detrimental effect of cannabis on mental health has been widely reported, the physical impact of using cannabis is unclear. General population studies suggest cannabis may exert a positive effect on cardiometabolic health, as cannabis users have a lower BMI, smaller waist circumference, lower levels of fasting glucose and insulin and lower rates of diabetes and high-density lipoproteins (Le Strat & Le Foll, 2011; Muniyappa et al., 2013; Penner, Buettner & Mittleman, 2013; Rajavashisth et al., 2012; Sophocleous et al., 2016). People with SMI are more than twice as likely to use cannabis compared with the general population, (Koskinen et al., 2009), and this PhD demonstrates that cannabis use is common even in those at UHR for psychosis (Carney et al., 2017b, c). Given the increased risk for CVD in people with and at-risk of SMI it is important to consider the impact cannabis can have on a person's overall health. Although modifiable risk factors for CVD in people with SMI have been a focal area of research, little attention has been given to the role of cannabis in developing metabolic syndrome, (Wattereus et al., 2016). Data from over 1800 patients with psychotic illness showed cannabis users had significantly lower levels of metabolic syndrome than non-users, and despite having a detrimental

effect on mental health, it may in fact protect against CVD (Wattereus et al., 2016). However, the relationship may be more complex. A separate study of Dutch patients found people who stopped using cannabis experienced significant increases in BMI, waist circumference, blood pressure and other metabolic risks, compared with non-users and continued users (Bruins et al., 2016). Frequent cannabis use is also associated with low bone density and increased risk of fractures (Sophocleous et al., 2016).

The seemingly apparent benefits of cannabis on a person's mental health can be explained in a number of ways. First, the beneficial effects could arise from the non-psychoactive components of cannabis. Cannabinoids such as cannabidiol, exert anti-inflammatory properties and have been assessed as novel treatments for inflammatory conditions such as rheumatoid arthritis, and gastrointestinal disorders including crohn's disease and ulcerative colitis (Esposito et al., 2013; Nagarkatti et al., 2009; Zuardi et al., 2008). An alternative explanation could be that cannabis has a causative role in the onset of UHR psychopathology and positive symptoms in this group, and without the use of cannabis some people may not have experienced mental ill-health. Therefore, the onset and trajectory of mental health could be different to other people meeting UHR criteria. This could represent a subgroup of people who are not predisposed to experiencing metabolic abnormalities. However, other confounding factors could be involved, for example cannabis is usually smoked with tobacco which increases the resting metabolic rate (Compher et al., 2006).

Mental health

Living an unhealthy lifestyle can have a negative impact on a young person's mental health. Given that this group is already vulnerable for SMI, the effects of unhealthy lifestyle behaviours such as substance use, excessive alcohol use and physical inactivity may be even more pronounced. There is already evidence to suggest a link between adolescent behaviours and later mental ill-health (Di Forti et al., 2014; Fusar-Poli et al., 2017; Koivukangas et al., 2010; Sormunen et al., 2017). Therefore, if UHR individuals continue to live a sedentary lifestyle they may be introducing further risk factors for poor mental health. Substance use also has a negative effect on a person's mental health.

Excessive alcohol use is associated with depression and impaired functioning (Conner, Pinquart & Gamble, 2009). Continued cannabis use after the onset of psychosis is associated with more severe positive symptoms, poorer functioning, lower adherence to medication and worse long-term outcome (Schoeler et al., 2017; Schoeler et al., 2016; Seddon et al., 2016). There is also evidence that heavy use of cannabis can exacerbate and even induce symptoms of psychosis in both the general population and in UHR individuals (Di Forti 2014; McHugh et al., 2017). A previous study found UHR individuals stopped using cannabis due to exacerbation of UHR symptoms (Valmaggia et al., 2014). Paper 3 of this PhD also found an association between cannabis use and more severe positive symptoms, thus highlighting the need for early intervention to address lifestyle behaviours in this group (Carney et al., 2017b; Paper 3).

The link between lifestyle behaviours and transition to psychosis is unclear as there have been relatively few cohort studies to date that have focused on lifestyle. However, as reported in Paper 1, several longitudinal studies do report a link between unhealthy lifestyle behaviours and transition. This includes smoking (Brewer et al., 2003; Howes et al., 2011; Labad et al., 2015), heavy alcohol use (Howes et al., 2011), physical inactivity (Koivukangas et al., 2010) and consuming more calories per day than controls (Labad et al., 2015). In a recent meta-analysis of psychosis risk, physical inactivity, tobacco use and alcohol abuse significantly increased the chance of an UHR individual developing psychosis (Fusar-Poli et al., 2017). Therefore, as these behaviours are common in the UHR group, this evidence can be used to strengthen the argument for the inclusion of structured lifestyle programmes in early intervention.

Implications for future research

Given the findings of this PhD, there is a need to intervene to address some the modifiable risk factors for future ill-health in the UHR group. Much of the cardiovascular risk observed occurs as a result of unhealthy lifestyle behaviours, which could, and indeed should, be targeted with early intervention. There should also be a shift in policy to reflect the growing concern for the

overall health of this group. There are two main areas for future work in the UHR group:

1. Development of an intervention informed by the findings of this PhD
2. Dissemination of findings and promotion of the fact physical health should be monitored and addressed in the UHR group

1. Intervention development

There is a need to further develop and evaluate physical health interventions in this group, given the poor long-term outcome of people with more established illness. The previous chapter describes potentially useful approaches informed by the findings of this PhD and makes recommendations for a physical health intervention. Future work should build on this. First, an intervention should be developed which is acceptable for the UHR cohort. This should focus on breaking down some of the barriers experienced and help motivate this group to take autonomy over their physical health, as reported in Paper 6 (Carney et al., 2017a). Adopting techniques such as goal-setting, self-monitoring, problem solving and motivational counselling could enable young people to make changes to their physical health. Increasing their capability to live a healthier lifestyle (focusing on exercise and consuming a healthy diet) may also open up further opportunities to engage in these behaviours on a long-term basis.

Individualised physical health interventions would be the gold standard intervention for this group. However, identifying the most cost-effective methods would be required to ensure that any attempt to support young people would be achievable and able to be implemented within services. There is also scope for this work to extend even further and focus on changing policy and practice, as discussed in Paper 4. Although it is necessary to establish the overall effectiveness of an intervention, developing and trialling a physical health program alone is insufficient. Future efforts should establish the most feasible way to implement support for UHR individuals within early detection and intervention services on a more permanent basis. An integrated lifestyle stream within services could be a potentially useful option to help promote physical health and wellbeing in this group. 'Exercise on referral' schemes could be a potential way to implement this support. This includes giving people access to

low cost gym facilities and guidance to increase their physical activity levels (Duda et al., 2014; Hanson et al., 2013; Pavey et al., 2011). This would ensure all UHR individuals have the option to access support to help with their physical health.

2. Monitoring and changes to policy

One of the main findings arising from this PhD is that the physical health and lifestyle behaviours of UHR individuals are not monitored routinely within mental health services, despite unhealthy behaviours being prevalent in this group (Carney et al., 2015; Paper 4). Additionally, there is a lack of support available for UHR individuals, evident from the findings of the qualitative study and clinical audit (Carney et al., 2015; 2017a). This is a failure of care. Since the studies of this PhD have been conducted, the new national standards for EIP have been developed (NHS England, 2016). All EI services are required to provide support to UHR individuals in an attempt to prevent the onset of psychosis and reduce distress of emerging psychological symptoms. It is necessary to assess the physical health of individuals meeting FEP but not for UHR. This is based on the assumption that the poor physical health associated with FEP is due to metabolic side effects of antipsychotic medication. However, despite not being on antipsychotic medication, many UHR individuals experience poor physical health as a result of unhealthy lifestyles such as poor diet and low levels of physical activity. Therefore physical health should be monitored in the UHR group. This should either be by staff within the EI services, or a more integrated system should occur where UHR individuals are sent to their GP for regular physical health screening.

Clinical implications

The studies conducted for this PhD have clinical implications. There is now evidence that the unhealthy profile experienced by people with FEP and SMI predates the onset of full psychotic symptoms. When it comes to living a healthy lifestyle, the UHR group are at a significant disadvantage compared with their peers. This is important for several reasons.

First, we are aware that the UHR group are at-risk for SMI, but they are also at-risk for poor physical health. This has important implications for service provision, as there is a need to assess physical health and offer support to help the UHR group live a healthy lifestyle. Second, if people transition to psychosis they will generally receive antipsychotic medication which has a detrimental effect on their physical health (Alvarez-Jiminez et al., 2006, 2008; De Hert et al., 2006; Foley & Morley, 2011; Perry et al., 2016). Therefore, if they are already engaging in high-risk behaviours such as physical inactivity, this may accelerate unwanted metabolic side-effects of medication, for example weight gain. Third, although many UHR individuals will not transition to psychosis, they will continue to experience difficulties with their mental health and are more likely to have non-psychotic co-morbid mental disorders and poor functioning (Cotter et al., 2015; Lin et al., 2015; Michel et al., 2017; Rutigliano et al., 2016). For example, a recent 6 year follow up of UHR individuals found 56.8% of people who did not transition developed co-morbid disorders, mainly depressive and anxiety disorders (Rutigliano et al., 2016). Additionally, continued substance use is associated with poor health and long-term outcome (Hides et al., 2006; Lambert et al., 2005). Therefore, even in apparent 'false positives' promoting a healthy lifestyle may be of benefit.

Finally, unhealthy lifestyle behaviours are modifiable. Just as early intervention for mental health can benefit long-term psychological outcome, intervening at the earliest possible stage to prevent future physical health may ameliorate the risk of later cardiovascular disease and ill-health. There is undoubtedly a caveat within the research, and interventions addressing overall health including physical activity, diet, substance use and general life skills should be developed for this group. The studies conducted here highlight a link between physical and mental health, which raises questions for future research including:

- Are the UHR group metabolically different to controls and youth with other non-specific mental health difficulties?
- What is the long-term impact of living an unhealthy lifestyle on mental and physical health?
- Are there any differences in the physical health and lifestyle behaviours of UHR individuals who transition compared with those who do not?

- Does promoting healthy behaviours such as exercise in the UHR group have an effect on the development of psychosis?
- What is an appropriate and feasible way to encourage UHR individuals to live a healthier lifestyle?
- Can a structured lifestyle intervention be implemented within EI services to improve the health of UHR individuals and is it useful?

Strengths and limitations

Strengths

This PhD is the first series of studies to draw attention to this area which has previously been neglected and provides findings which could influence policy and practice. There are many strengths of this series of research including:

- The initial review was the first to address physical health and lifestyle in the UHR group. It covers a range of topics which takes a holistic look at the health in this group, including exercise, substance use, diet and measures of physical health, and contributes to ongoing UHR research.
- The conclusions of this PhD are drawn from different methods, selected to answer specific questions. For example, quantitative methods and systematic reviews were used to show that UHR individuals had higher levels of unhealthy lifestyle behaviours (Carney et al., 2015; 2016b; 2017b,c). Meta-analyses were used to draw conclusions from the existing literature, and when the data was too heterogeneous to combine, a narrative synthesis was conducted. Qualitative methods were used in Paper 6 to gain an understanding of the factors affecting lifestyle behaviours in this group, in an attempt to identify potential targets for an intervention (Carney et al., 2017a).
- The studies containing original data were conducted in different services across the world; two in greater Manchester (Carney et al., 2015; Carney et al., 2017a), and one in multiple sites across Australia (Carney et al., 2017b). The meta-analyses also synthesised data from many different countries, therefore widening the generalisability of the findings.

- The initial substance use paper contained data from the Transitions Study, one of the largest help-seeking cohorts currently available (Purcell et al., 2015 a, b). Over 700 individuals were included in this analysis and a range of confounding variables were accounted for, thus making it an important resource to be analysed (Carney et al. 2017c).

- The studies have implications for policy; particularly the clinical audit which showed physical health was not monitored in early detection services (Carney et al., 2015). As a result of these findings, the service was awarded a small grant to purchase physical health monitoring equipment to encourage staff to assess physical health in their service users.

- The qualitative study is the first study to be conducted which takes into account the experiences of multiple groups of people; UHR individuals, their parents/carers and clinicians. This is a novel approach to capture the experiences of one clinical group from a range of different viewpoints, rather than just their own subjective reporting. Clinicians and parents were able to discuss implications and difficulties they had encountered when attempting to look after the health of the UHR group. This helps to understand the complex issues affecting the lifestyles of UHR individuals.

- The qualitative interviews and intervention development was guided by a theoretical model (the COM-B Model; Michie et al., 2011). Using a theoretical framework to guide intervention development is recommended by the MRC to ensure rigour (Craig et al., 2008).

Weaknesses

Despite this PhD making a contribution to the area of UHR research, there are some limitations and challenges with the studies of this PhD which should be considered:

- Although the studies benefit from being conducted in different countries (UK and Australia), the degree to which the findings can be applied cross-culturally is limited as both are Westernised societies. Relatively little research has been conducted in non-westernised settings in the UHR group looking at lifestyle. Therefore the overall findings may lack

cultural generalisability. Additionally, the qualitative study was made up of a predominantly white British sample, thereby limiting the cross-cultural validity of the findings.

- Some of the data come from existing sources (for example, studies included in both meta-analyses) and physical health was not independently assessed in UHR individuals in the UK. The initial review and clinical audit showed that there was relatively little data on physical health available in the existing literature and in the case notes of UHR individuals (Carney et al., 2015; 2016b). Yet information was available regarding the health behaviours and lifestyle of this group, as many studies included information on behaviours such as smoking or cannabis use as confounding variables. The final qualitative study (Carney et al., 2017a) did not record the physical health of the UHR group and instead was focused on gaining the subjective experiences of living a healthy lifestyle. Despite having a relatively large sample size for a qualitative study (n=31), any metabolic screening would have been underpowered and insufficient to detect any significant differences between UHR individuals and controls. Given that relatively little was known about the physical health of this group, an exploratory qualitative approach was taken in order to inform intervention development. However, the metabolic health of the UHR cohort should be a priority for future research.

- All research concerning substance use is challenging and suffers methodological limitations. Many studies are confounded by differences in quantifying and classifying cannabis use, and the varying degree of legality of cannabis across cultures introduces additional response bias. The financial implications of urine or blood testing for substances often means researchers use more subjective self-report questionnaires and interviews to establish data on cannabis use. It is also difficult to control for the type and potency of cannabis in research. In Paper 3 (Carney et al., 2017b) other substances such as alcohol and tobacco were taken into account, yet the strength of cannabis was not, and would be difficult to do so given that many users are unaware themselves of the strength of the cannabis they are using. Higher potency cannabis, or 'skunk' has the most detrimental impact on a person's mental and physical health (Di

Forti et al., 2009; 2014), yet in both studies on cannabis this could not be controlled for. In the UK, there is currently a growing issue with synthetic cannabinoids or legal highs such as 'spice' (Pierre, 2011; Seeley et al., 2012; Van Amsterdam et al., 2015). It is unclear whether cannabis users were also using these substances. The cannabis use meta-analysis suffered from these challenges as controlling for other factors such as strength, quantity and polysubstance use was not possible (Carney et al., 2017b). The age of onset of cannabis use is also an important factor that could not be accounted for, as earlier age of onset is associated with poorer long-term outcome and increased risk of psychosis (Dragt et al., 2010).

- Sample bias within Paper 6 is a further potential issue. Participation in the interview was voluntary, which limits the extent to which the responses can be applied to the wider UHR cohort. This arises from the fact that individuals who took part will have had sufficient social functioning to engage with the study. However, even in a subgroup of more highly functioning individuals, issues with social anxiety and poor functioning were present and a degree of social support is still warranted to overcome symptomatic barriers (Carney et al., 2017a).

- Whilst we can speculate about the reasons for unhealthy lifestyles, it is difficult to disentangle the multiple factors which affect the choices people make, such as environment, genetic predisposition, biological mechanisms and psychological symptoms. Identifying an individual cause for unhealthy lifestyles in the UHR group is unlikely and there are many factors which have not been taken into account in the PhD studies here, such as the biological mechanisms discussed above. Future research should seek to fully assess issues around physical health and the effect of living a healthy lifestyle in this vulnerable group.

Summary of future work

There is a need for more long-term investigations of metabolic health in this group, examining lifestyle behaviours prospectively and the impact they have on physical and mental health. There is also a need to develop lifestyle

interventions to address the high rates of physical inactivity, poor diet and substance use comorbidity in this group, informed by the recommendations presented in the previous chapter and the findings of the qualitative study. The long-term impact of changing behaviour should be assessed to identify whether behavioural interventions such as exercise and healthy diet have a positive effect on physical and mental health, using feasibility studies and, more long-term prospective studies of metabolic health.

Conclusions

This PhD shows for the first time that cardiometabolic risk factors precede the onset of full psychotic symptoms. UHR individuals are significantly more likely to engage in health behaviours that are detrimental to both their physical and mental health. This includes substance use (mainly tobacco, cannabis and alcohol), physical inactivity and poor diet. Through the use of qualitative methods we now know more about the barriers UHR individuals face to living a healthy lifestyle and some potential facilitators to helping them improve their physical health. We are also aware that the UHR group are at a significant disadvantage for living a healthy lifestyle. There is potential for early intervention services to target this group with structured lifestyle interventions to help them to live a healthier lifestyle. Recommendations for the development of such an intervention are made in this thesis. Such an intervention would potentially benefit both the mental and physical health of UHR individuals.

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Appendix A:

Physical health promotion in people with schizophrenia: why we should consider the ultra-high risk state

Author Contributions:

Rebekah Carney conceived the original idea for the paper and created the first draft of the manuscript. Professor Alison Yung and Dr Tim Bradshaw provided clinical input and all critically reviewed and agreed on the submitted manuscript for publication.

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Physical health promotion in people with schizophrenia: why we should consider the ultra high-risk state

In the August issue of *Acta Psychiatrica Scandinavica* 2015 (1), the guest editors Alex Mitchell and Marc De Hert focused on the important issue of improving the physical health of people with schizophrenia. They rightly ask the question 'Can we prevent cardiometabolic problems before they begin?' We propose that there is scope for the research to extend even further, prior to the onset of psychosis, during the At Risk Mental State (or Ultra High-Risk (UHR) stage). This refers to the putatively prodromal phase, which can now be identified prospectively using operationalised criteria (2, 3).

There is evidence that individuals in the UHR group have an unhealthy profile (4). We recently conducted a review and meta-analysis on the available literature which supported this, showing that UHR individuals have high rates of smoking, alcohol abuse, cannabis use and low levels of physical activity. Further longitudinal analysis of UHR cohorts will enable us to investigate fully the impact of such lifestyle factors on physical health including cardiometabolic problems. UHR individuals who 'transition' to develop a psychotic disorder are especially at risk of poor physical health as they are likely to receive antipsychotic treatment. Thus, additional cardiometabolic risks, such as weight gain and glucose and lipid dysregulation, may well be imposed on people with pre-existing risk factors for poor physical health.

Therefore, if there is an indication that premorbid cardiometabolic risk factors are present in UHR individuals, such as physical inactivity and smoking; these should be addressed at the earliest possible stage. Yet to date, there is no evidence that cardiometabolic risk factors such as obesity, physical activity and smoking status are even being monitored routinely in UHR services (5), nor has any attempt has been made to apply healthy living interventions to this group. This is a substantial failure of care.

Interventions to improve physical health, similar to those used for people with schizophrenia and early psychosis, should be investigated in people who are first identified by services as at risk for psychosis. It is feasible to suggest action to prevent cardiometabolic risk factors could at least in some cases, begin prior to the onset of psychosis. Interventions could include programs to improve physical activity, decrease sedentary behaviour and promote smoking cessation. Physical health problems could therefore be prevented or at least minimised.

Even if individuals do not develop psychosis, benefits to future health are still important and can reduce later cardiovascular risk associated with tobacco use and other lifestyle factors.

There is a paucity of research which looks at the physical health and cardiometabolic risk factors in the UHR cohort. However, we should be investigating this area more to establish when the physical health disparities of people with schizophrenia begin, and if they do in fact, have a more insidious onset extending prior to the development of psychosis. Of course, we are aware that not all people who are ultimately diagnosed with a schizophrenia spectrum disorder present to early detection settings and not everyone who is UHR will develop schizophrenia. However, there is no doubt that this is a phase where early intervention may have significant benefits to the long-term physical and mental wellbeing of young people. Echoing the words of Mitchell and De Hert, there is certainly much more we can do to help reduce the physical health disparities of people with schizophrenia, by intervening at the first possible stage.

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Reply

We thank Dr Carney, Bradshaw and Yung for their useful insights into our question 'can we prevent cardiometabolic problems before they begin?' We welcome their research suggesting individuals with prodromal schizophrenia or even those at ultra high risk (UHR)may have high rates of smoking, substance misuse and low levels of physical activity and/or fitness (1). What is not clear, however, is if such individuals have abnormal cardiometabolic markers. We have recently documented that in early psychosis unmedicated patients have only slight evidence of metabolic change. In this group, the overall rate of metabolic syndrome was 9.8% using standardized criteria, whilst diabetes was found in 2.1% and hyperglycaemia (>100 mg/dl) in 6.4% (2, 3). Only hypertension (31.6%) appeared significantly elevated. This suggests that although individuals in prodromal and early stages are at risk due to smoking, low fitness and inactivity that frank abnormalities take longer to develop. Further, a significant part of metabolic change appears to arise due to long-term side effects of most types of antipsychotic medication. This itself prompts caution if clinicians are considering prescribing long-term antipsychotics to high-risk individuals who have not yet met criteria for psychosis (4). That said, we agree that UHR individuals should receive physical health screening with the assumption that they are at high risk of physical complications as well as psychosis (unless proven otherwise). We also agree that health disparities should be actively studied in this group and at the same time proactively minimized by healthcare professionals. Overall the research of Dr Carney et al. on UHR individuals is very timely as it will also help to answer the question of when do physical health complications first arise and when is the best time to intervene? If and when UHR individuals present to

clinicians, clinicians may be understandably hesitant to prescribe long-term antipsychotic medication but there is no reason not to focus on physical health and lifestyle not just by monitoring but active health promotion (5).

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Appendix B:

Lifestyle factors may be linked to symptoms of metabolic syndrome in people at risk for psychosis

Published as:

Author Contributions:

Letter to the Editor

Lifestyle factors may be linked to symptoms of metabolic syndrome in people at risk for psychosis

A recent article by Cordes and colleagues reported the prevalence of metabolic syndrome (MetS) in individuals at clinical-high risk of psychosis (CHR) (Cordes et al. 2017). The authors add to the growing evidence that physical health abnormalities may occur even prior to the onset of psychosis. In their study, the CHR group had higher rates of individual MetS criteria than a general population sample; specifically higher blood pressure, waist circumference, fasting blood glucose and reduced HDL concentration. This carries important clinical implications, and strengthens our recommendation that physical health should be monitored in this group (Carney et al., 2015).

While we know that the metabolic side effects of antipsychotic medication, poor lifestyle and inadequate monitoring of physical health contribute to physical morbidity in people with schizophrenia (De Hert et al., 2011), it is unclear why CHR individuals also have poor physical health. In their paper, Cordes et al. (2017) state that it is unlikely that lifestyle factors could account for this. However, in a previous review and meta-analysis, we found that CHR individuals display high rates of cardiometabolic risk factors such as smoking, and physical inactivity (Carney et al., 2016). There is also evidence to suggest this group experience more barriers to living a healthy lifestyle than those not at-risk (Deighton and Addington, 2015). Therefore, sedentary behaviour could have a negative impact on metabolic health in this group.

We also suggest that the differences observed in metabolic health may be related to other psychiatric conditions, not just schizophrenia. A large proportion of CHR individuals have depression, anxiety and substance use disorders at baseline and are at high risk of developing these disorders over time (Lin et al., 2015). They also have poor socio-occupational functioning (Cotter et al., 2014). These comorbidities may influence physical health. For example, there is evidence for a bidirectional relationship between cardiovascular risk and depression (Pan et al., 2012). CHR individuals also frequently present to mental health services with high levels of psychological distress, which can be associated with high blood pressure (Pruessner et al., 2013).

We agree that the CHR phase presents an ideal opportunity to intervene and prevent future mental and physical ill-health. However, there are several unanswered questions: what factors affect the development of poor physical health in CHR populations? Is the physical health of CHR individuals who ultimately transition to psychosis worse than those who do not? Perhaps most importantly, how can we reduce the physical health disparities of people experiencing poor mental health? Future longitudinal studies assessing metabolic health and associated risk factors, including genetic, proteomic and lifestyle factors may enable these important questions to be answered.

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6 November 2016

Appendix C:

MRC framework for developing and evaluating complex interventions

Taken from:

Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I. and Petticrew, M., 2008. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ, 337*, a1655.
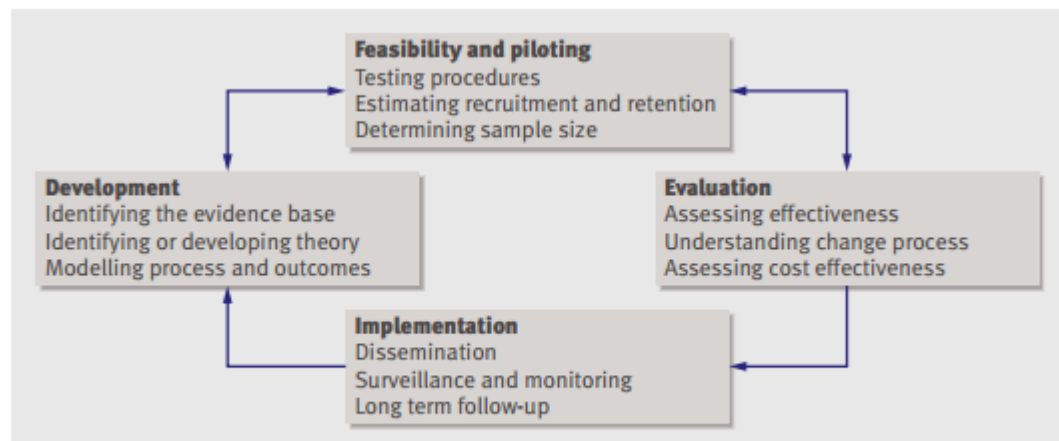

Fig 1 | Key elements of the development and evaluation process

Appendix D:

The Behaviour Change Wheel

Taken from:

Michie, S., van Stralen, M.M. & West, R. (2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implementation Science. 6* (1), p.42.
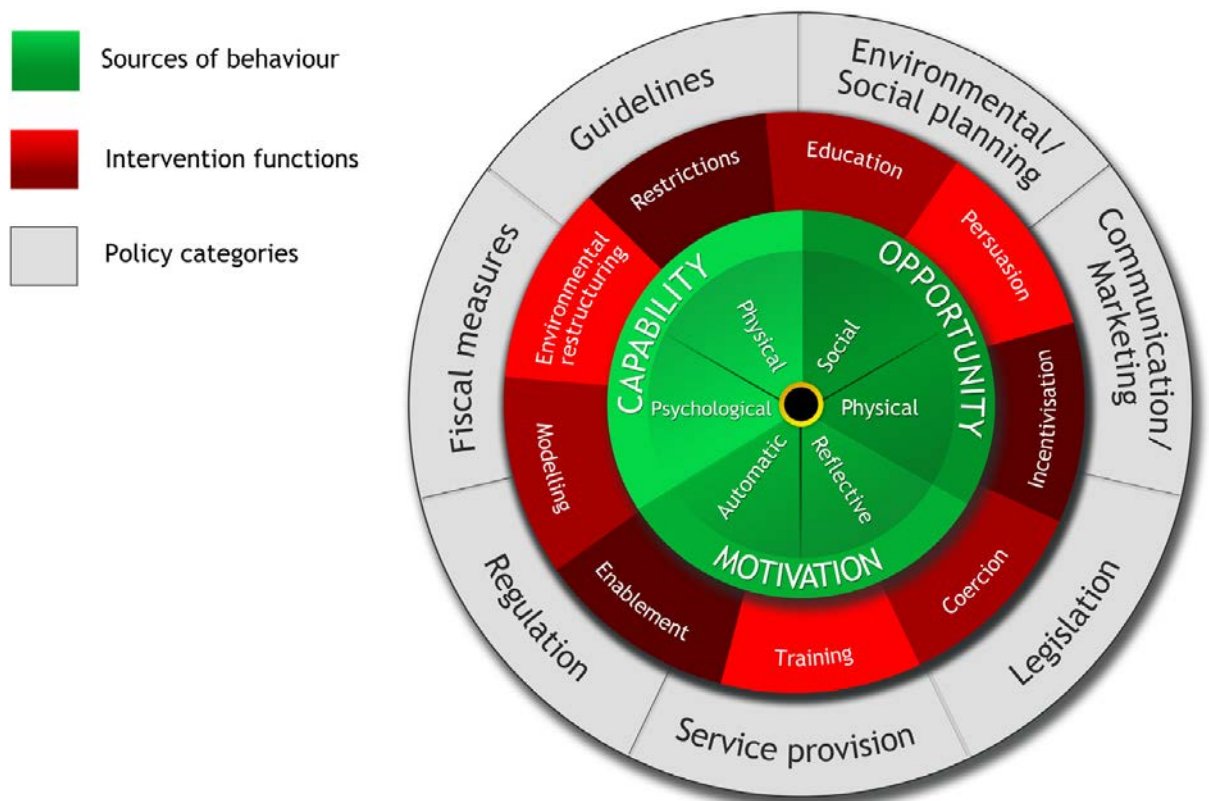
Appendix E:

Data extraction form (Paper 4; Carney et al., 2015)

The data extraction form used to assess whether physical health and lifestyle behaviours were monitored in early detection services in Greater Manchester, (Paper 4). Results reported in:

Carney, R., Bradshaw, T., & Yung, A.R. (2015). Monitoring of physical health in services for young people at ultra-high risk of psychosis. *Early Intervention in Psychiatry.* In press: https://dx.doi.org/10.1111/eeip.12288.

Audit of physical health in At Risk Mental State patients attending EDIT.

How well is physical health being measured in the EDIT teams?

<u>Section A: Smoking</u>

	Yes	No
Smoking Status (Y/N)		
Frequency		
Quantity		

YRBS 2003

(1) During the past 30 days, on how many days did you smoke cigarettes?

A.   0 days

B.   1 or 2 days

C.   3 to 5 days

D.   6 to 9 days

E.   10 to 19 days

F.   20 to 29 days

G.   All 30 days

(2) During the past 30 days, on the days you smoked, how many cigarettes did you smoke per day?

A.   I did not smoke cigarettes during the past 30 days

B.   Less than 1 cigarette per day

C.   1 cigarette per day

D.   2 to 5 cigarettes per day

E.   6 to 10 cigarettes per day

F.   11 to 20 cigarettes per day

G.   More than 20 cigarettes per day

<u>Section B: Alcohol</u>

	Yes	No
Alcohol Use (Y/N)		
Frequency		

Quantity		

YRBS 2003

(1) During the past 30 days, on how many days did you have at least one drink of alcohol?

A.   0 days

B.   1 or 2 days

C.   3 to 5 days

D.   6 to 9 days

E.   10 to 19 days

F.   20 to 29 days

G.   All 30 days

(2) During the past 30 days, on average how many units of alcohol per week did you consume? (ibeep FFQ)

_____ Units

(3) Alcohol Use Status

Use	
Abuse	
Dependence	

Section C: Other Substances

	Yes	No
Other Substance Use (Y/N)		
Name of Substance		
Frequency		
Quantity		

(1) Substance use

Use	
Abuse	
Dependence	

(2) Any other substance use

Cannabis	Amphetamines	Cocaine	LSD
Heroin	Ketamine	Ecstasy	Solvents
Other:	None		

(3) During the past 30 days, on how many days did you use the substance?

A. 0 days

B. 1 or 2 days

C. 3 to 5 days

D. 6 to 9 days

E. 10 to 19 days

F. 20 to 29 days

G. All 30 days

[If no information about current use, indicate how many times used ever _____

_____]

If Cannabis….

(4) During the past 30 days, on the days you used cannabis, how many times did you use it per day?

A. I did not use cannabis during the past 30 days

B. Less than once per day

C. once per day

D. 2 to 5 times per day

E. 6 to 10 times per day

F. 11 to 20 times per day

G. More than 20 times per day

Section D: Physical Activity

	Yes	No
Physical Activity Level		

Total physical activity level per week (mins) _____

<u>Section E: Physical Measures</u>

	Yes	No
Height		
Weight		
BMI		

    (1) Height _____

    (2) Weight _____

    (3) BMI _____

<u>Section F: Other</u>

Age at time of acceptance:

Yes	No

Transition to FEP:

Location (delete as appropriate): Wigan/Salford

Date:

Conducted by:

Appendix F:

Protocol for Lifestyle Study

Protocol (v1.1) used for Paper 6:

Carney, R., Cotter, J.C., Bradshaw, T., & Yung, A.R. (2017a). Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: a qualitative study involving service users, parents and clinicians. *Psychiatry Research.* 255, 87-93.

Title: Lifestyle – Developing a healthy lifestyle intervention for young people at-risk of psychosis

Research Team

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Lay Summary

People with psychosis have poor physical health and are at risk of developing cardiovascular disease and long term physical health conditions. This comes from side effects of antipsychotic medication, such as weight gain, and living an unhealthy lifestyle, including high rates of smoking, alcohol and drug use, low levels of physical activity and poor diet. People in the initial stages of psychosis, who present with symptoms for the first time, often display signs of poor physical health. Recent evidence suggests people have an unhealthy lifestyle even before they develop psychosis.

There are specialist services set up to help identify and provide support to young people who are at risk for psychosis. These young people present with emerging psychotic symptoms, such as feeling like they are being watched, but they may not be as severe or long-lasting as people with psychosis will experience. There has not been much research looking at physical health

and unhealthy lifestyle factors in young people at-risk for psychosis. However, the studies which have been done suggest they also have high rates of unhealthy lifestyle factors, such as smoking and low physical activity. We would like to explore this further in this group, as living an unhealthy lifestyle contributes to future ill-health, and increases the risk of cardiovascular disease. If an individual does go on to develop psychosis, they will most likely receive antipsychotic medication, further contributing to long term health complaints. So far, there has been no attempt to address lifestyle factors in this group, despite potential benefits to mental and physical health.

We aim to explore service users' views about their lifestyle, including any barriers and facilitators of healthy living to establish what might be acceptable as a healthy living intervention. This will cover factors such as content, setting, and delivery of an intervention. The interview should last approximately 1 hour. We will also be conducting individual interviews with staff members from the at-risk service and parents or carers of the young people attending the service to see what they think might be acceptable as an intervention for this group.

Background

The physical health of people with schizophrenia is poor. They are at 2.5 times the risk of premature mortality and their life expectancy is 10 to 30 years lower than the general population (1-3). Low levels of physical inactivity (4, 5), poor diet (6), and high rates of substance use including smoking, alcohol and cannabis use (6-8), increases the risk of later cardiovascular disease. Together with the metabolic side effects of antipsychotic medication, these unhealthy lifestyle factors contribute to the increased morbidity and premature mortality of this population, (1-3).

However, these risk factors are believed to be present prior to antipsychotic medication (9, 10). Furthermore, high rates of substance use are observed early in the illness course, including in individuals with first-episode psychosis (FEP) (11-13), with some evidence to suggest this unhealthy profile may be present prior to experiencing a first-episode of psychosis, during the prodromal phase (14, 15). This can be studied further by looking at the UHR cohort. The ultra-high risk (UHR) state allows the identification of people in the putative prodrome for psychosis. Criteria have been developed to identify individuals vulnerable to developing a psychotic disorder (16-18). These have been referred to as the prodromal, ultra-high risk (UHR), clinical high-risk (CHR) and at-risk mental state (ARMS) criteria (19). In order to meet UHR status a patient must exhibit one or more of the following characteristics: attenuated psychotic symptoms, brief limited intermittent psychotic symptoms which

spontaneously resolve, or genetic-risk combined with a recent decline in functioning (20). Approximately one third of UHR individuals transition to full-threshold psychotic disorders within three years (21). These criteria have important implications for early intervention and allow us to apply physical and psychological interventions prior to the development of psychosis.

Emerging evidence suggests individuals at ultra-high risk (UHR) for developing psychosis present with cardiometabolic risk factors, prior to the onset of FEP (15). This includes high rates of smoking, cannabis use and alcohol abuse, and low levels of physical activity, (14, 15). However, this is not currently monitored on a routine basis within services in the UK (22), and little is known about the barriers and facilitators young people face to living a healthy lifestyle.

Healthy living interventions have frequently been explored in people with schizophrenia, often showing a beneficial effect on physical and mental health (23-25). Yet this has not yet been done in the UHR group. Therefore, it is necessary to understand more about physical health and unhealthy lifestyle factors in the UHR group, to be able to inform the development of an appropriate intervention. Recent research has highlighted the role of the environment in determining overall physical activity levels in people with schizophrenia (26, 27). However, this has not yet been assessed in the UHR group. Barriers and facilitators to living a healthy lifestyle should be explored in UHR individuals, as well as establishing what may be an acceptable healthy living intervention for this group.

Research Questions

(1) What barriers and facilitators affect whether a person engages in unhealthy lifestyle factors, such as smoking, alcohol use, substance use, poor diet and low physical activity levels?

(2) What are the preferences of UHR individuals for a healthy living intervention?

(3) What do health professionals and parents or carers of UHR individuals attending at-risk services believe to be an acceptable and feasible healthy living intervention?

Purpose

The main purpose of this study is to develop a healthy lifestyle intervention for the UHR group. This involves identifying barriers to living a healthy lifestyle and factors which influence unhealthy lifestyle factors in the UHR group. We are also interested in what might be acceptable way to help young people improve their lifestyle.

Method

Objectives

The main objective is to explore the reasons why young people do, or do not, engage in unhealthy lifestyle factors, and what factors may prevent people from living a healthy lifestyle. We then want to explore what may be an acceptable way to improve physical health in UHR, and use this information to contribute to the development of an appropriate intervention.

Aims

The main aim of the qualitative study is to inform the development of an acceptable healthy living intervention for the UHR group. We therefore aim to: (1) qualitatively explore barriers and facilitators of healthy lifestyles; (2) establish the preferences of UHR individuals for a healthy living intervention (content, setting, delivery); (3) establish what health professionals and parents or carers think is an acceptable lifestyle intervention.

Design

A qualitative design will be used. This will provide us with knowledge about why young people at-risk for psychosis engage in unhealthy lifestyle factors, and enable us to use this knowledge to inform a development of a healthy living intervention.

Participants

Participants will be recruited from Wigan and Salford.

UHR

Inclusion

- Aged 18-25
- Current service user of the EDIT Salford or Wigan service, and meeting criteria on the CAARMS assessment for Ultra-High Risk for Psychosis (UHR)

Exclusion

- Inability to provide informed consent
- Insufficient English to understand and complete assessment
- Intellectual disability which impacts on the ability to complete assessments
- Above threshold on CAARMS assessment, (meets criteria for first-episode psychosis)

The inclusion criteria require that an individual is receiving help or support from Salford or Wigan EDIT at Greater Manchester West Mental Health NHS Foundation Trust, and meets the criteria for UHR as defined by the Comprehensive Assessment for At-Risk Mental States. This is the standard assessment provided to young people presenting at the EDIT service. Care co-ordinators will be consulted to confirm if the individual meets criteria. Individuals who are above threshold on the CAARMS and are thus judged as experiencing a first-episode of psychosis will be excluded, as we are interested in assessing people prior to psychosis onset.

All participants must be aged between 18 and 25. This is the approximate age most UHR individuals will first present at a service. The lower age limit of 18 is set as participants will be asked about alcohol and tobacco consumption. The exclusion criteria also exclude patients unable to give informed consent, insufficient command of the English language and intellectual disability which makes completing the assessments difficult.

Health Professionals

Staff at the Wigan and Salford EDIT services will be approached to take part in individual interviews. All health professionals who come into contact with UHR individuals will be approached.

Parents/Carers

Parents or carers of UHR individuals currently receiving help from either Wigan or Salford EDIT will be invited to take part in individual interviews.

Sample Size

We aim to recruit up to 20 UHR participants over a period of 6 to 9 months for individual interviews (or until the qualitative data reaches saturation). Wherever possible, we will endeavour to conduct the interview in one session. Therefore, drop outs should be minimal. UHR participants will be recruited from EDIT; a specialised early detection service for young people at-risk for psychosis. Posters and leaflets will be left in waiting rooms and staff members who are in contact with young people in these centres will be approached as potential referrers. We also aim to recruit up to 6 health professionals and 8 parents or carers for individual interviews (or until qualitative data reaches saturation).

Research Methods

Procedure

RC will be responsible for recruitment of participants.

Part 1:

Recruitment of UHR participants will be done through liaison with care co-ordinators at the EDIT service in Salford and Wigan. Information sheets and leaflets will be left within the service and posters put up in the waiting room. Potential UHR participants will discuss taking part in the study with their care co-ordinator, who will inform a research assistant to contact them with further information. Therefore, there is no obligation to take part, and researchers will only be made aware of the participant if they express an interest. Participants from EDIT may also self-refer and contact the research assistant via details included on liaison materials.

Potential participants will be contacted by the researcher to discuss the study and establish eligibility. All eligible individuals will be sent out an information sheet in the post, or via email. Only limited personal identifiable information will be collected at this stage (name, address etc). Potential participants will have the information for a minimum of 24 hours prior to meeting with the researcher to discuss the study. Ability to provide informed consent will be established by the researcher at time of assessment. Assessments and interviews will be conducted at the EDIT service, or another mutually agreed location, (such as college, or GP surgery). Relevant lone worker policies will be adopted to ensure safety of the researcher. If necessary, the interview can be conducted over more than one session. Participants will be assigned a case ID number to maintain anonymity and permit withdrawal of data if consent is withdrawn. The participant will be informed that this confidentiality agreement will only be broken if they reveal information to suggest they themselves, or somebody else, is at immediate risk of harm. In this case a relevant professional body will be informed, (care co-ordinator, social worker).

The qualitative interview will be conducted by the research assistant and participants will be asked to discuss their current lifestyle and factors which they think may influence the choices they make. They will also be asked about what barriers and facilitators they face to living a healthy lifestyle and what kind of intervention may be appropriate. Interviews will be recorded on an encrypted dictaphone and participants will be assigned pseudonyms to maintain anonymity.

Participants are under no obligation to complete the study, and are free to withdraw at any time. As a token of gratitude, UHR participants will be given a £10 voucher for a high-street retailer of their choice. This is a reasonable reimbursement without acting as a monetary incentive.

Part 2:

Recruitment of health professionals and parents/carers will be conducted at Wigan and Salford EDIT. Staff members will be approached during their team meeting for their participation in individual interviews. Health professionals at Wigan and Salford EDIT will also be asked when they make a referral if they wish to take part. They will be asked to provide written consent, and will be informed of the aims of the study before taking part. Parents/carers will be recruited through posters in the waiting room of Wigan and Salford EDIT, and also through liaison with staff members at the service. UHR individuals who take part in the individual interviews in Part 1 of the study will be asked if they think their parent/carer may be interested in taking part in a qualitative interview and to pass on a leaflet. If so the same consent process will be conducted. Similar procedures will be followed as described above for the qualitative interviews with UHR individuals. The interviews will be recorded and transcribed as detailed above. Professionals and parents/carers will be entered into a draw to receive a £25 gift voucher.

Consent

Researchers seeking consent are trained in Good Clinical Practice and have experience gaining informed consent from young people presenting with mental health difficulties. The clinical staff have many years' experience (AY, TB) and will provide regular supervision to ensure capacity to consent is being assessed appropriately. The issues that will be covered in assessing capacity will be to ensure that the person: understands the purpose and nature of the research; understands what the research involves; the possible benefits, risks and burdens; and is able to retain and recall this information in order to be able to make a rational decision. All potential participants will be asked to consent for themselves. Individuals will be made aware that they do not have to consent to take part, and are able to make the free choice to withdraw at any time before, during or after the study has taken place.

Qualitative Measures

Qualitative interviews will follow a topic guide and consist of semi-structured questions. This will cover:

1. Current experiences of unhealthy lifestyle factors, such as smoking, alcohol, physical activity and diet.
2. Barriers and facilitating factors for these behaviours.
3. Preferences for a healthy living intervention (content, delivery, setting, duration)

Reimbursement

UHR participants will receive a £10 voucher for taking part in the study, which will be paid after the qualitative interview is complete. Professionals and carers will be entered into a draw to receive a £25 voucher.

Transcription

Audio recordings will be listened to carefully and transcribed verbatim into NVivo qualitative software for coding and data analysis. Transcripts will be stored on secure university servers with password protected access. A selection of transcriptions will be proof read against the audio file by a member of the supervisory team in order to check for accuracy.

Data Analysis

The qualitative analysis will be conducted with the help of NVivo software. I have chosen to use thematic analysis for the qualitative data, due to the flexibility of the method to identify themes across the data to answer my initial research questions. As there is little existing research within this area, I will be adopting an 'inductive' or 'bottom-up' framework approach to analysis, (28). The data analysis will begin during the transcription stage. Data will be coded by reading the transcripts line by line and identifying concepts, meaning and themes. The transcripts will be constantly re-read to identify any underlying themes and whether those established sit within the larger context. As coding develops and different themes emerge, these will be grouped into overarching concepts and constructs. Field notes will be kept throughout the coding process and memos will be made to describe the rationale behind the constructs. I aim to identify common themes relating to the influencing factors which underpin lifestyle choices described in the quantitative component, and develop an understanding of the experiences of young people in relation to lifestyle factors.

Confidentiality

All participants will be allocated a unique study number which will be used to identify participant information. Participant information will be kept in a locked filing cabinet or on a password protected university computer (depending on the format), to which only the research team will have access. Participants will be assigned pseudonyms for the qualitative

interview. Person identifiable information will be stored in a separate locked cabinet at the same site, to enable responses to be removed if participants chose to withdraw their data. The data will be destroyed 10 years after study completion. Prior to the interview being conducted participants will be informed that all responses will be confidential, except for when the participant discloses information indicating they themselves, or somebody else, is at immediate risk of harm. In the event that this occurs, the care co-ordinator of UHR participants or relevant professional body (e.g GP, social services) will be contacted.

Burden

Undertaking the qualitative interview should last approximately 60 minutes, however this may vary according to participant responses. Depending on what the participant prefers, they may complete this over more than one session, or in one sitting, and researchers will be flexible with participants.

Benefits

The benefits to taking part in the study include providing an important contribution to new information in the area of mental health. The information will enable us to target healthy living interventions to help young people improve their physical health. We will be able to understand the barriers young people face to living a healthy lifestyle.

Information Governance

The study will be conducted in-line with Good Clinical Practice (GCP) guidelines. All personal identifiable information will be stored separate to participant data, and only named researchers will have access to this information. Participants will be assigned a case ID numbers, or pseudonyms. Interviews will be stored on encrypted devices such as a USB or Dictaphone then transferred to secure university servers which are password protected to be transcribed.

Conflict of Interest

There is no conflict of interest in the study. At the end of the study a summary of the de-identified results will be given back to participants if they are interested.

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Appendix G:

Confirmation of ethical approval

Favourable opinion letter to conduct the 'Lifestyle' qualitative study following ethical review by the Health Research Authority.

East Midlands - Derby Research Ethics Committee

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09 December 2015

Miss Rebekah Carney
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University of Manchester
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M13 9PL

Dear Miss Carney

Study title:	Lifestyle - Developing a healthy lifestyle intervention for young people at-risk of psychosis
REC reference:	15/EM/0559
Protocol number:	1
IRAS project ID:	184852

Thank you for your letter of 07 December 2015, responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager Miss Vic Strutt, NRESCommittee.EastMidlands-Derby@nhs.net. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Conditions of the favourable opinion

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers.   The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA Approval (England)/ NHS permission for research is available in the Integrated Research Application System, www.hra.nhs.uk or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of management permissions from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from the HRA. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	Version	Date
Copies of advertisement materials for research participants [Leaflet EDIT]	1.1	
Response to Provisional Opinion Letter		07 December 2015
Copies of advertisement materials for research participants [Poster EDIT]	1.1	
Copies of advertisement materials for research participants [Poster Parents]	1.1	
Copies of advertisement materials for research participants [Referrer Leaflet]	1.1	
Covering letter on headed paper [Cover Letter]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)		
GP/consultant information sheets or letters [CC Letter v1]	1	07 December 2015
Interview schedules or topic guides for participants [Topic guide EDIT]	1.1	
Interview schedules or topic guides for participants [Topic guide Parents]	1.1	
Interview schedules or topic guides for participants [Topic guide Prof]	1.1	
IRAS Checklist XML [Checklist_08122015]		08 December 2015
Letter from sponsor		
Other [TB CV supervisor]		
Participant consent form [Consent form EDIT]	1.1	
Participant consent form [Consent form Prof_Parent]	1.1	
Participant information sheet (PIS)	2	07 December 2015
Participant information sheet (PIS)	2	07 December 2015
Participant information sheet (PIS)	2	07 December 2015
REC Application Form [REC_Form_26112015]		26 November 2015
Research protocol or project proposal	1.1	15 October 2015
Summary CV for Chief Investigator (CI)		
Summary CV for supervisor (student research)		

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

<u>Reporting requirements</u>

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

<u>Feedback</u>

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
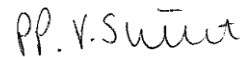http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

15/EM/0559	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

pp. V. Swift

Mrs Janet Mallett
Chair

Email: NRESCommittee.EastMidlands-Derby@nhs.net

Enclosures: *"After ethical review – guidance for researchers"*

Copy to: Lynne MacRae
                    Dr Kathryn   Harney, Greater Manchester West Mental Health NHS
                    Foundation Trust

Appendix I

Participant information sheets

Three separate participant information sheets (v3) are included for EDIT service users, their parents/carers and clinicians used in Paper 6:

Carney, R., Cotter, J.C., Bradshaw, T., & Yung, A.R. (2017a). Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: a qualitative study involving service users, parents and clinicians. *Psychiatry Research.* 255, 87-93.

EDIT service users

Lifestyle

The University of Manchester

Greater Manchester West NHS
Mental Health NHS Foundation Trust

Participant Information Sheet

Thank you for your interest in the Lifestyle study. This information sheet is designed to explain why we are doing the study and what is involved. Take as much time as you need to read this information and feel free to ask any questions.

What is the purpose of the study?

We want to explore physical health and lifestyle factors in young people who are experiencing psychological difficulties. We want to get a better understanding of the barriers young people face to living a healthy lifestyle and identify what could help improve physical health by developing a healthy living intervention.

Who is being asked to take part?

We are inviting young people to take part who receive support from the Early Detection and Intervention Team in Salford or Wigan, and who may be experiencing psychological difficulties. This is so we can develop an intervention targeted to this group. You do not have to take part if in the study if you do not want to, and your care at EDIT will not be affected.

What does the study involve?

If you are interested, a researcher will meet with you to discuss the study and check whether the study is right for you. You will sign a consent form and have the opportunity to ask any questions. You may have been referred by your care co-ordinator, or you may have found out about the study elsewhere, but we will give your care co-ordinator a call to let them know you are taking part. The study consists of an interview lasting approximately one hour.

Interview: Here you will discuss your current lifestyle and physical health. We will ask you to tell us what may prevent you from living a healthy lifestyle and what affects

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whether you smoke, drink alcohol and exercise. We will ask about your preferences for a healthy living intervention and what things might help you be healthier.

The interview can be conducted at a place that is convenient for you. This can be at the EDIT service, local GP or college. You can complete the interview in one go or over more than one session. The interview will be audio recorded on an encrypted dictaphone and transferred onto a secure university computer. It will then be transcribed by a member of the research team in anonymous format for analysis.

How long will it take and do you get reimbursed for your time?

We estimate that the interview will take approximately 60 minutes. You will be reimbursed with a £10 voucher after the interview is complete, as compensation for your time.

What are the risks and benefits of taking part?

Risks: Some people might feel embarrassed revealing information about physical health; however, researchers have been trained to administer interview questions in a sensitive, non-judgemental and professional manner. All responses will be anonymised and you are free to discuss any worries with your care co-ordinator.

Benefits: It is unlikely that this study will benefit you directly, however the information obtained from this interview will help us to target appropriate interventions to help young people improve their physical health and live a healthy lifestyle. You will also be contributing to new research looking at helping young people with emerging psychological difficulties.

Are responses confidential?

Yes, all information will be stored in locked filing cabinets and secure IT systems at the University which are all password protected. The information will not contain your name or any information which could be used to identify you. Responses will be stored securely on IT systems at the university or in locked cabinets for 10 years after the completion of the study and then destroyed. Only members of the research team will have access to your information. Please note if during the course of the study we

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become aware that you or another person is at imminent risk of harm we have a duty of care to inform a relevant professional and we will discuss this with you at the time.

The only other time someone might need to look at the study information is during an audit or monitoring visit. This is when people from the University of Manchester, NHS Trust or regulatory authorities review all the data to make sure the study is being carried out as planned. They will include your identifiable data when doing the checks (they will see it belongs to you). Anyone that does look at the data will have a duty to keep it confidential.

What happens if you change your mind?

You can change your mind at any time before, during or after the study and do not have to give a reason to withdraw. This will not affect the standard of care you receive from EDIT.

Who has approved the study?

The University of Manchester has agreed to be the sponsor of the study. The study has also been reviewed and approved by the East Midlands- Derby Research Ethics Committee (15/EM/0559).

Who do I speak to if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. You can also speak to your care co-ordinator at the EDIT service or your local GP.

What if I want to make a complaint?

If you want to make a complaint please follow the procedures below:

For minor complaints please contact the researcher in the first instance on **0161 306 7914** or **Rebekah.carney@postgrad.manchester.ac.uk.**

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance the please contact the Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL by emailing;

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research.complaints@manchester.ac.uk or by telephoning 0161 275 2674 or 275 2046.

What will the results be used for?

The results will be used to get a better understanding of the barriers to living a healthy lifestyle and inform the development of a healthy living intervention for young people with emerging psychological difficulties. This interview is being carried out as part of the student's PhD from the North West Doctoral Training Centre and funded by the Economic and Social Research Council. The findings from this study may be used to support other research in the future, and may be shared anonymously with other researchers. The results will be written up for publication in health professional journals and may be presented at conferences.

Who do I contact for more information?

For more information, please contact:

Rebekah Carney
Researcher
Rebekah.carney@postgrad.manchester.ac.uk
0161 306 7914

Parent/Carer

Lifestyle

Participant Information Sheet

Thank you for your interest in the Lifestyle study. This information sheet is designed to explain why we are doing the study and what is involved. Take as much time as you need to read this information and feel free to ask any questions.

What is the purpose of the study?

We want to get a better understanding of the barriers young people with emerging psychological difficulties face to living a healthy lifestyle and identify what could help improve physical health by developing a healthy living intervention for this group.

Who is being asked to take part?

We are inviting parents/carers of young people who receive support from the Early Detection and Intervention Team (EDIT) in Salford or Wigan to take part. This is so we can develop an intervention targeted to this group and use your lived experience to inform this. You do not have to take part if in the study if you do not want to.

What does the study involve?

If you are interested, a researcher will discuss the study with you in more detail. You will sign a consent form and have the opportunity to ask any questions. The study consists of a short interview with one of the researchers. This will be a discussion of what might be an appropriate intervention to help improve the physical health of young people receiving help from EDIT and how to encourage them to live a healthy lifestyle. Here we will aim to capture

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your opinions and suggestions. The interview will be audio recorded on an encrypted dictaphone and transferred onto a secure university computer. It will then be transcribed by a member of the research team in anonymous format for analysis.

How long will it take and do you get reimbursed for your time?

We estimate that the interview may take up to 60 minutes, depending on responses. You will be entered into a draw to receive a £25 voucher as a thank you.

What are the risks and benefits of taking part?

Risks: There is potential from any interview to cause stress, however, researchers are trained to conduct interviews in a non-judgemental and sensitive manner.

Benefits: It is unlikely that this study will benefit you directly, however the information obtained from this interview will help us to target appropriate interventions to help young people improve their physical health and live a healthy lifestyle. You will also be contributing to new research looking at helping young people with emerging psychological difficulties.

Are responses confidential?

Yes, all information will be stored in locked filing cabinets and secure IT systems at the University which are all password protected. The information will not contain your name or any information which could be used to identify you. Responses will be stored securely on IT systems at the university or in locked cabinets for 10 years after the completion of the study and then destroyed. Only members of the research team will have access to your information. Please note if during the course of the study we become aware that you or another person is at imminent risk of harm we have a duty of care to inform a relevant professional and we will discuss this with you at the time.

The only other time someone might need to look at the study information is during an audit or monitoring visit. This is when people from the University of Manchester, NHS Trust or regulatory authorities review all the data to make sure the study is being carried out as planned. They will include your identifiable data when doing the checks (they will see it belongs to you). Anyone that does look at the data will have a duty to keep it confidential.

What happens if you change your mind?

You can change your mind at any time before, during or after the study and do not have to give a reason to withdraw.

Who has approved the study?

The University of Manchester has agreed to be the sponsor of the study. The study has also been reviewed and approved by the East Midlands- Derby Research Ethics Committee (15/EM/0559).

Who do I speak to if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions.

What if I want to make a complaint?

If you want to make a complaint please follow the procedures below:

For minor complaints please contact the researcher in the first instance on **0161 306 7914** or **Rebekah.carney@postgrad.manchester.ac.uk.**

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance the please contact the Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL by emailing; research.complaints@manchester.ac.uk or by telephoning 0161 275 2674 or 275 2046.

What will the results be used for?

The results will be used to get a better understanding of the reasons behind the barriers to living a healthy lifestyle and inform the development of a healthy living intervention for people with emerging psychological difficulties. We hope that we will be able to design a healthy living intervention which can later be trialled in this group. This study is being carried out as part of the student' PhD from the North West Doctoral Training Centre and funded by the Economic and Social Research Council. The findings from this study may be used to support other research in the future, and may be shared anonymously with other researchers. The results will be written up for publication in health professional journals and may be presented at conferences in anonymised form.

Who do I contact for more information?

For more information, please contact:

Rebekah Carney
Researcher
Rebekah.carney@postgrad.manchester.ac.uk
0161 306 7914

Clinician

Lifestyle

Greater Manchester West
Mental Health NHS Foundation Trust

MANCHESTER 1824
The University of Manchester

Participant Information Sheet

Thank you for your interest in the Lifestyle study. This information sheet is designed to explain why we are doing the study and what is involved. Take as much time as you need to read this information and feel free to ask any questions.

What is the purpose of the study?

We want to get a better understanding of the barriers young people with emerging psychological difficulties face to living a healthy lifestyle and identify what could help improve physical health by developing a healthy living intervention for this group.

Who is being asked to take part?

We are inviting health professionals from the Early Detection and Intervention Team in Salford or Wigan to take part in an interview. This is so we can develop an intervention targeted to this group and use your professional experience to inform this. You do not have to take part if in the study if you do not want to.

What does the study involve?

If you are interested, a researcher will discuss the study with you in more detail. You will sign a consent form and have the opportunity to ask any questions. The study consists of an interview lasting approximately one hour with one of our researchers. This will be a discussion of what might be an appropriate intervention to help improve the physical health of young people receiving help from EDIT and how to encourage them to live a healthy

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lifestyle. The interview will be audio recorded on an encrypted dictaphone and transferred onto a secure university computer. It will then be transcribed by a member of the research team in anonymous format for analysis.

How long will it take and do you get reimbursed for your time?

We estimate that individual interviews will last approximately 60 minutes, depending on responses. You will be entered into a draw to receive a £25 voucher as a thank you.

What are the risks and benefits of taking part?

Risks: There is potential from any interview to cause stress, however, researchers are trained to conduct interviews in a non-judgemental and sensitive manner.

Benefits: It is unlikely that the study will benefit you directly, however, the information obtained from this interview will help us to target appropriate interventions to help young people improve their physical health and live a healthy lifestyle. You will also be contributing to new research looking at helping young people with emerging psychological difficulties.

Are responses confidential?

Yes, all information will be stored in locked filing cabinets and secure IT systems at the University which are all password protected. The information will not contain your name or any information which could be used to identify you. Responses will be stored securely on IT systems at the university or in locked cabinets for 10 years after the completion of the study and then destroyed. Only members of the research team will have access to your information. Please note if during the course of the study we become aware that you or another person is at imminent risk of harm we have a duty of care to inform a relevant professional and we will discuss this with you at the time.

The only other time someone might need to look at the study information is during an audit or monitoring visit. This is when people from the University of Manchester, NHS Trust or regulatory authorities review all the data to make sure the study is being carried out as planned. They will include your identifiable data when doing the checks (they will see it belongs to you). Anyone that does look at the data will have a duty to keep it confidential.

What happens if you change your mind?

You can change your mind at any time before, during or after the study and do not have to give a reason to withdraw.

Who has approved the study?

The University of Manchester has agreed to be the sponsor of the study. The study has also been reviewed and approved by the East Midlands- Derby Research Ethics Committee (15/EM/0559).

Who do I speak to if something goes wrong?

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions.

What if I want to make a complaint?

If you want to make a complaint please follow the procedures below:

For minor complaints please contact the researcher in the first instance on **0161 306 7914** or **Rebekah.carney@postgrad.manchester.ac.uk**.

If you wish to make a formal complaint or if you are not satisfied with the response you have gained from the researchers in the first instance the please contact the Research Governance and Integrity Manager, Research Office, Christie Building, University of Manchester, Oxford Road, Manchester, M13 9PL by emailing; research.complaints@manchester.ac.uk or by telephoning 0161 275 2674 or 275 2046.

What will the results be used for?

The results will be used to get a better understanding of the reasons behind the barriers to living a healthy lifestyle and inform the development of a healthy living intervention for people with emerging psychological difficulties. We hope that we will be able to design a healthy living intervention which can later be trialled in this group. This study is being carried out as part of the student's PhD from the North West Doctoral Training Centre and funded by the Economic and Social Research Council. The findings from this study may be used to support other research in the future, and may be shared anonymously with other researchers. The results will be written up for publication in health professional journals and may be presented at conferences in anonymised form.

Who do I contact for more information?

For more information, please contact:

Rebekah Carney
Researcher
Rebekah.carney@postgrad.manchester.ac.uk
0161 306 7914

Appendix I:

Recruitment leaflets

Recruitment leaflets (V4) for EDIT service users for Paper 6:

Carney, R., Cotter, J.C., Bradshaw, T., & Yung, A.R. (2017a). Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: a qualitative study involving service users, parents and clinicians. *Psychiatry Research.* 255, 87-93.

What happens if I want to take part?

We can give you a call to discuss whether the study is right for you. We will then send you out an information pack by post or email. If you are still happy we can meet at a time and place that works for you to complete the study. This can be at the EDIT service, GP service or local college. There's no pressure, you can change your mind at anytime!

How can you contact us?

If you want more information, would like to take part, or know someone who may be interested feel free to contact us using the details below!

Rebekah Carney
rebekah.carney@postgrad.manchester.ac.uk
0161 306 7914

Professor Alison Yung
alison.yung@manchester.ac.uk

Dr Tim Bradshaw
t.bradshaw@manchester.ac.uk

Address:
Room 3.306, Jean McFarlane Building, University of Manchester, Oxford Road, Manchester, M13 9PL

Greater Manchester West **NHS**
Mental Health NHS Foundation Trust

MANCHESTER
1824
The University of Manchester

Lifestyle Study

Participant Leaflet

0161 306 7914
Rebekah.carney
@postgrad.manchester.ac.uk

Why are we doing this study?

Evidence suggests young people who are experiencing emerging psychological difficulties may have high rates of unhealthy lifestyle factors such as smoking, substance use and low physical activity. This contributes to later physical ill-health. However, the reasons why have not been assessed.

We are interested in gaining a better understanding of the barriers young people face to living a healthy lifestyle and finding out ways we can help them to improve their health.

What is involved?

The study involves:

An **interview** with one of our researchers to discuss your current lifestyle choices and physical health. This will include things like exercise and diet. We will ask you about what factors affect your lifestyle and discuss what might be a helpful way to becoming more healthy. We will also ask you about what you think might be a good way to help young people improve their lifestyle and be more active. Doing this will help us to develop a new healthy lifestyle intervention.

Who can take part?

We are looking for people;
1. Aged 18-25.
2. Receiving support from EDIT Salford or Wigan and meeting CAARMS criteria.

How long does it take?

The study should last around **1 hour**, and you can do this over more than one session if you like. If you complete the study you will receive £10 for your time.

Appendix J:

Consent forms

Two separate forms were used to obtain consent (v1.1); one for EDIT service users and one for parents/clinicians in Paper 6:

Carney, R., Cotter, J.C., Bradshaw, T., & Yung, A.R. (2017a). Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: a qualitative study involving service users, parents and clinicians. *Psychiatry Research.* 255, 87-93.

Lifestyle Study
Room 3.306
Jean McFarlane Building
University of Manchester
Oxford Road
Manchester
M13 9PL
0161 306
7914

Lifestyle Study - **Consent Form EDIT**

Please initial box

1. I confirm that I have read the information sheet dated....................
   (version............) for the above study. I have had the opportunity to
   consider the information, ask questions and have had these
   answered.

2. I understand that my participation is voluntary and that I am free to
   withdraw at any time without giving any reason, without my medical
   care or legal rights being affected.

3. I understand that relevant sections of my data collected during the
   study may be looked at by individuals from the University of
   Manchester, regulatory   authorities, or from the NHS trust
   where it is relevant to my taking part in this research.   I give
   permission for these individuals to have access to my data.

4. I understand that the information collected about me will be used to
   support other research in the future, and may be shared anonymously
   with other researchers.

5. I agree to my care co-ordinator being informed of my participation in
   the study.

6. I understand interviews will be audio recorded so that what I say will
   be accurately recorded. I understand the interview is confidential and
   I will not be identified in any way in the report.

7. I agree for anonymised quotes from the interviews to be used in
   publications and the project report.

8. I agree to take part in the above study.

<div style="border:1px solid black; width:60px; height:60px; float:right;"></div>

_____	_____	_____
Name of Participant	Date	Signature

_____	_____	_____
Name of Researcher	Date	Signature

When completed: 1 copy for participant; 1 original for researcher site file.

Lifestyle Study
Room 3.306
Jean McFarlane Building
University of Manchester
Oxford Road
Manchester
M13 9PL
0161 306
7914

Lifestyle Study - **Consent Form Professionals and Parents**

Please initial box

1. I confirm that I have read the information sheet dated....................
   (version.............) for the above study. I have had the opportunity to
   consider the information, ask questions and have had these answered.

2. I understand that my participation is voluntary and that I am free to
   withdraw at any time without giving any reason.

3. I understand that relevant sections of my data collected during the
   study may be looked at by individuals from the University of
   Manchester, regulatory   authorities, or from the NHS trust
   where it is relevant to my taking part in this research.   I give
   permission for these individuals to have access to my data.

4. I understand that the information collected about me will be used to
   support other research in the future, and may be shared anonymously
   with other researchers.

5. I understand interviews will be audio recorded so that what I say will
   be accurately recorded. I understand the interview is confidential and
   I will not be identified in any way in the report.

6. I agree for anonymised quotes from the interviews to be used in
   publications.

7. I agree to take part in the above study.

Name of Participant   Date   Signature

_____   _____   _____

Name of Researcher   Date   Signature

When completed: 1 copy for participant; 1 original for researcher site file.

Appendix K:

Qualitative interview schedules

Qualitative interview schedules (v1.1) were developed based on previous literature, and the COM-B model of behaviour. The topic guides were modified for each participant group; EDIT service users, their parents/carers and clinicians. Results reported in Paper 6:

Carney, R., Cotter, J.C., Bradshaw, T., & Yung, A.R. (2017a). Examining the physical health and lifestyle of young people at ultra-high risk for psychosis: a qualitative study involving service users, parents and clinicians. *Psychiatry Research.* 255, 87-93.

Study Title: Lifestyle – Developing a healthy lifestyle intervention for young people at-risk of psychosis

<u>Qualitative Interview Topic Guide – UHR individuals</u>

Thank you for agreeing to take part in this study. We are trying to find out how we might be able to help young people who use services like EDIT to stay fit and healthy and we would really value your opinions regarding the type of support that might help? *("How does that sound to you?")*.

So the aim of this interview is to find out about your current lifestyle and whether you would like to make any changes? We also wish to find out how we might be able to offer support in a way that would be acceptable and effective in helping to promote health and wellbeing *("how does that sound to you?")* The interview should take no longer than 60 minutes, if you need a break or wish to stop at any time please let me know. Is there anything you would like to ask me before we begin?

1. **Lifestyle (Capability)**
- Tell me a bit about how you spend your day and the type of activities you participate in.
- Tell me a bit about your current lifestyle
    - o [Prompts] diet, physical activity, tobacco use, alcohol use
- Do you have any concerns about your physical health or lifestyle?
    - o [Prompts] explore any concerns they have and the reasons for these concerns e.g. being inactive may make their mental health worse; lifestyle factors may adversely affect future physical health and wellbeing; increased demands on service, poor diet and low energy etc.
- How long have you had these concerns?
    - o [Prompts] any changes in lifestyle, raise in awareness of poor health
- Does anyone share these concerns?
    - o [Prompts] parents, staff at EDIT, friends, teachers
- What sort of things do you think are important in order to maintain a healthy lifestyle?
    - o [Prompts] eat a balanced diet, lose weight, stop smoking, be more physically active, look after teeth better etc.
- What do you think are the benefits of maintaining a healthy active lifestyle?
    - o [Prompts] better physical health, better mental health, weight control etc.
- What do you think about the support you receive to help with your lifestyle?
    - O [Prompts] explore what support they get, and how it could be improved.

- Would you like to work towards developing a healthier, more active lifestyle if help were available? Why/why not?

2. Environment (Opportunity)

- Tell me a bit about your environment and the area where you live
  - [Prompts] green spaces, gyms, fast food places, safe lit areas
- How does the area where you live affect the lifestyle choices you make?
  - [Prompts] explore positive or negative impact of the environment
- What would you change about the area where you live to make it easier for you to live a more active, healthy lifestyle?

3. Interventions (Opportunity)

- Is there anything that you are doing now to try and stay fit and healthy?
  - [Prompts] how well is this going? Is there anything that gets in the way?
- What type of help / support might help you maintain a healthy lifestyle?
  - [Prompts] dietary advice, personal trainer, cooking lessons, smoking cessation, free gym, hiking, football, rewards when meet targets etc.
- Any other things which might help that you yourself could do?
  - Use mobile phone apps, track steps per day, keep diary
- What would not help?
- Would you be interested in participating in activities to promote a healthy lifestyle if they were available? Why? Why not?
- Do you think there is anything that the EDIT service could do that might make it more likely that you would participate?
  - [Prompts] calling to picking them up from home, making activities free of charge, joining in the activities with them etc.
- Would you be more likely to engage in activities delivered on a group or one-on-one basis or both?
- What do you think is the most important thing to focus on and why?
  - [Prompts] diet, physical activity, weight, smoking, wellbeing.

3. Delivery (Opportunity)

- Who do you think would be the best person to deliver healthy living activities?
  - [Prompts] STR worker, personal trainer, nurse, youth worker, peer support worker other
- Where do you think would be the best place for it to be offered?
  - [Prompts] the EDIT service, local gym, in schools/colleges etc.
- How should activities be delivered?
  - [Prompts] Duration, frequency, time of day, planned in advance.
- How long do you think the intervention should last?

- o [Prompts] indefinitely, time limited with attempt promote independent participation in the longer term
- What should happen when the intervention finishes?

4. Potential barriers to success (Motivation)
- Do you think there would be anything that would get in the way of you trying to develop a healthy lifestyle if extra help was available?
  - o [Prompts] motivation, withdrawal, poor self-confidence, anxiety, low mood, time of day, physical fitness etc.
- How do you think these barriers could be overcome?
  - o [Prompts] combined psychological and health living support, persistent attempts to help (not taking no for an answer)

5. Recruitment
- How do you think we should approach young people to take part?
  - o [Prompts] posters, letters, via EDIT staff, facebook etc.
- Do you think people will want to take part? Why/Why not?
- What will stop people wanting to take part?
- Do you have any ideas how we might make their participation more likely to happen?
- Do you have any other suggestions or comments about how we might design and offer a healthy living intervention for young people like yourself?

That is all the questions I have to ask you today, would you like to ask me anything? Thank you for meeting with me today, your responses are very helpful.

End of Interview.

Study Title: Lifestyle – Developing a healthy lifestyle intervention for young people at-risk of psychosis

<u>Qualitative Interview Topic Guide – Parents</u>

Thank you for agreeing to take part in this study. The research we have been conducting has shown that young people who use services like EDIT sometimes have less active and healthy lifestyles than others their own age. We are trying to find out how we might be able to help young people like (name of son / daughter) to stay fit and healthy and we would really value your opinions regarding the type of support that might help them? *("How does that sound to you?")*.

So the aim of this interview is to find out your views about (name of son / daughter) current lifestyle and whether you would like them to make any changes? We also wish to find out from you how we might be able to offer support to (name of son / daughter) in a way that would be acceptable to them and might be effective in helping to promote their health and wellbeing *("how does that sound to you?")* The interview should take no longer than 60 minutes, if you need a break or wish to stop at any time please let me know. Is there anything you would like to ask me before we begin?

4. Lifestyle (Capability)

- Tell me a bit about how (name of son / daughter) spends their day and the types of activities they participate in.
- Do you currently have any concerns about (name of son / daughter) physical health or their lifestyle?
    - o [Prompts] explore any concerns they have and the reasons for these concerns e.g. being inactive may make their mental health worse; lifestyle factors may adversely affect future physical health and wellbeing etc.

- How long have you had these concerns?
    - o [Prompts] has there been a recent change in the young person's lifestyle? Did this coincide with the family member being concerned about their mental health?
- What sort of things do you think are important for (name of son / daughter) to do in order to maintain a healthy lifestyle?
    - o [Prompts] eat a balanced diet, lose weight, stop smoking, be more physically active, look after their teeth better etc.
- What do you think are the benefits of maintaining a healthy active lifestyle?
    - o [Prompts] better physical health, better mental health, weight control etc.

- Do you think (name of son / daughter) shares your concerns about his/her physical health / lifestyle?

- Do you think (name of son / daughter) would like to work towards developing a healthier more active lifestyle if help were available?

5. **Interventions (Opportunity)**

- Is there anything that you or anyone else is currently doing for (name of son / daughter) to try to help them stay fit and healthy?
    - [Prompts] – how well is this going? Is there anything that gets in the way of the help they are providing?
- What type of help / support do you think the EDIT service might be able to provide to help (name of son / daughter) to maintain a healthier lifestyle?
    - [Prompts] dietary advice, personal trainer, cooking lessons, smoking cessation, free gym, hiking, football etc.
- Do you think (name of son / daughter) would be interested in participating in these activities if they were available? Why? Why not?
- Do you think there anything that the EDIT service could do that might make it more likely that (name of son / daughter) would participate?
    - [Prompts] calling to picking them up from home, making activities free of charge, joining in the activities with them etc.
- Do you think (name of son / daughter) would be most likely to engage in activities delivered on a group or one-on-one basis or both?
- What do you think is the most important thing to focus on and why?
    - [Prompts] diet, physical activity, weight, smoking, wellbeing.

3. **Delivery (Opportunity)**

- Who do you think would be the best person to deliver healthy living activities?
    - [Prompts] STR worker, personal trainer, nurse, youth worker, peer support worker other
- Where do you think would be the best place for it to be offered?
    - [Prompts] the EDIT service, local gym, in schools/colleges etc.
- How should activities be delivered?
    - [Prompts] Duration, frequency, time of day, planned in advance.
- How long do you think the intervention should last?
    - [Prompts] indefinitely, time limited with attempt promote independent participation in the longer term
- What should happen when the intervention finishes?

6. **Potential barriers to success (Motivation)**

- Do you think there would be anything that would get in the way of (name of son / daughter) trying to develop a healthy lifestyle if extra help was available?
    [Prompts] motivation, withdrawal, poor self-confidence, anxiety, low mood, time of day, physical fitness etc.
- How do you think these barriers could be overcome?

- o [Prompts] combined psychological and health living support, persistent attempts to help (not taking no for an answer)

7. Recruitment
- How do you think we should approach young people like (name of son / daughter) to take part?
  - o [Prompts] posters, letters, via EDIT staff, facebook etc.
- Do you think people will want to take part? Why/Why not?
- Do you have any ideas how we might make their participation more likely to happen?
- Do you have any other suggestions or comments about how we might design and offer a healthy living intervention for young people like (name of son / daughter)?

That is all the questions I have to ask you today, would you like to ask me anything? Thank you for meeting with me today, your responses are very helpful.

End of Interview.

Study Title: Lifestyle – Developing a healthy lifestyle intervention for young people at-risk of psychosis

<u>Qualitative Interview Topic Guide – Clinicians</u>

Thank you for agreeing to take part in this study. The research we have been conducting has shown that young people who use services like EDIT sometimes have less active and healthy lifestyles than others their own age. We are trying to find out how we might be able to help young people who use your service at EDIT to stay fit and healthy and we would really value your opinions regarding the type of support that might help them? *("How does that sound to you?")*.

So the aim of this interview is to find out your views about the current lifestyle of your service users and whether you would like them to make any changes? We also wish to find out from you how we might be able to offer support in a way that would be acceptable to them and might be effective in helping to promote their health and wellbeing *("how does that sound to you?")* The interview should take no longer than 60 minutes, if you need a break or wish to stop at any time please let me know. Is there anything you would like to ask me before we begin?

6. **Lifestyle (Capability)**
- Tell me a bit about the EDIT service and the young people you see.
- What is the physical health like of the young people who receive help from EDIT?
- Do you have any concerns about their physical health or their lifestyle?
    - [Prompts] explore any concerns they have and the reasons for these concerns e.g. being inactive may make their mental health worse; lifestyle factors may adversely affect future physical health and wellbeing; increased demands on service etc.
- How long have you had these concerns?
    - [Prompts] recent research, become more aware of guidelines
- What sort of things do you think are important for young people to do in order to maintain a healthy lifestyle?
    - [Prompts] eat a balanced diet, lose weight, stop smoking, more physically active, look after teeth better etc.
- What do you think are the benefits of maintaining a healthy active lifestyle?
    - [Prompts] better physical health, better mental health, weight control etc.
- Do you think young people at EDIT share your concerns about their physical health / lifestyle?
- How do you think the other staff at EDIT feel about physical health and lifestyle of young people you see?

- What do you think about the support young people receive to help with their lifestyle?
    - [Prompts] explore what support they think young people get, and how it could be improved.
- Do you think they would like to work towards developing a healthier more active lifestyle if help were available?

7. Interventions (Opportunity)

- Is there anything that you or anyone else is currently doing for the young people at EDIT to try to help them stay fit and healthy?
    - [Prompts] – how well is this going? Is there anything that gets in the way of the help you provide? Anything which stops you from helping?
- What type of help / support do you think might enable young people to maintain a healthier lifestyle?
    - [Prompts] dietary advice, personal trainer, cooking lessons, smoking cessation, free gym, hiking, football etc.
- Who do you think should be responsible for providing this help? Why?
    - [Prompts] mental health service, GP, colleges, researchers
- Do you think young people would be interested in participating in these health promoting activities if they were available? Why? Why not?
- Do you think there is anything that the EDIT service could do that might make it more likely that young people would participate?
    - [Prompts] calling to remind, making activities free of charge, joining in the activities with them etc.
- Do you think young people would be most likely to engage in activities delivered on a group or one-on-one basis or both?
- What (if anything) would not be helpful to encourage young people to maintain a healthy lifestyle?

3. Delivery (Opportunity)

- Who do you think would be the best person to deliver healthy living activities?
    - [Prompts] STR worker, personal trainer, nurse, youth worker, peer support worker other
- Where do you think would be the best place for it to be offered?
    - [Prompts] the EDIT service, local gym, in schools/colleges etc.
- How should activities be delivered?
    - [Prompts] Duration, frequency, time of day, planned in advance.
- How long do you think the intervention should last?
    - [Prompts] indefinitely, time limited with attempt promote independent participation in the longer term

- What do you think is the most important thing to target with a healthy living intervention and why?
  - [Prompts] Physical activity, sedentary behaviour, diet, wellbeing, smoking
- What should happen when the intervention finishes?
- How do you think services like EDIT, could be encouraged to help young people improve their physical health and lifestyle?

8. Potential barriers to success (Motivation)

- Do you think there would be anything that would get in the way of young people you see at EDIT trying to develop a healthy lifestyle if extra help was available?

   [Prompts] motivation, withdrawal, poor self-confidence, anxiety, low mood, time of day, physical fitness etc.

- How do you think these barriers could be overcome?
  - [Prompts] combined psychological and health living support, persistent attempts to help (not taking no for an answer)

9. Recruitment

- How do you think we should approach young people to take part?
  - [Prompts] posters, letters, via EDIT staff, Facebook etc.
- Do you think people will want to take part? Why/Why not?
- Do you have any ideas how we might make their participation more likely to happen?
- Do you have any other suggestions or comments about how we might design and offer a healthy living intervention for young people receiving help from services like EDIT?

That is all the questions I have to ask you today, would you like to ask me anything? Thank you for meeting with me today, your responses are very helpful.

End of Interview