The *Lancet Psychiatry* Commission: a blueprint for protecting physical health in people with mental illness

Joseph Firth, Najma Siddiqi, Ai Koyanagi*, Dan Siskind*, Simon Rosenbaum*, Cherrie Galletly*, Stephanie Allan, Constanza Caneo, Rebekah Carney, Andre F Carvalho, Mary Lou Chatterton, Christoph U Correll, Jackie Curtis, Fiona Gaughran, Adrian Heald, Erin Hoare, Sarah E Jackson, Steve Kisely, Karina Lovell, Mario Maj, Patrick D McGorry, Cathrine Mihalopoulos, Hannah Myles, Brian O'Donoghue, Toby Pillinger, Jerome Sarris, Felipe B Schuch, David Shiers, Lee Smith, Marco Solmi, Shuichi Suetani, Johanna Taylor, Scott B Teasdale, Graham Thornicroft, John Torous, Tim Usherwood, Davy Vancampfort, Nicola Veronese, Philip B Ward, Alison R Yung, Eoin Killackey†, Brendon Stubbs†*

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*Section lead authors

†Contributed equally

NICM Health Research Institute, Western Sydney University, Westmead, NSW, Australia (J Firth PhD, Prof J Sarris PhD); **Division of Psychology and Mental Health, School of Health Sciences** (J Firth, R Carney PhD, D Shiers MBChB, Prof A R Yung MD), **Division of Diabetes, Endocrinology and Gastroenterology** (A Heald DM), **and Division of Nursing, Midwifery and Social Work** (Prof K Lovell PhD), **Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK; Centre for Youth Mental Health** (J Firth, Prof P D McGorry MD, B O'Donoghue PhD, Prof A R Yung, Prof E Killackey DPsych), **Oxygen, The National Centre of Excellence in Youth Mental Health** (Prof P D McGorry, B O'Donoghue, Prof A R Yung, Prof E Killackey), **and Department of Psychiatry** (Prof J Sarris), **University of Melbourne, Melbourne, VIC, Australia; Department of Health Sciences, University of York, Hull York Medical School** (N Siddiqi PhD, J Taylor PhD); **Bradford District Care NHS Foundation Trust, Bradford, UK** (N Siddiqi); **Research and Development Unit, Parc Sanitari Sant Joan de Déu, Universitat de Barcelona, Fundació Sant Joan de Déu, Barcelona, Spain** (A Koyanagi MD); **Instituto de Salud Carlos III, Centro de Investigación Biomédica en Red de Salud Mental, Madrid,**

Executive summary

Background

The poor physical health of people with mental illness is a multifaceted, transdiagnostic, and global problem. People with mental illness have an increased risk of physical disease, as well as reduced access to adequate health care. As a result, physical health disparities are observed across the entire spectrum of mental illnesses in low-income, middle-income, and high-income countries. The high rate of physical comorbidity, which often has poor clinical management, drastically reduces life expectancy for people with mental illness, and also increases the personal, social, and economic burden of mental illness across the lifespan.

This Commission summarises advances in understanding on the topic of physical health in people with mental illness, and presents clear directions for health promotion, clinical care, and future research. The wide range and multifactorial nature of physical health disparities across the range of mental health diagnoses generate a vast number of potential considerations. Therefore, rather than attempting to discuss all possible combinations of physical and mental comorbidities individually, the aims of this Commission are to: (1) establish highly pertinent aspects of physical health-related morbidity and mortality that have transdiagnostic applications; (2) highlight the common modifiable factors that drive disparities in physical health; (3) present actions and initiatives for health policy and clinical services to address these issues; and (4) identify promising areas for future research that could identify novel solutions. These aims are addressed across the five parts of the Commission: in Parts 1 and 2 we describe the scope, priorities, and key targets for physical health improvement across multiple mental illnesses; in Parts 3, 4, and 5, we highlight emerging strategies and present recommendations for improving physical health outcomes in people with mental illness.

Part 1: Physical health disparities for people with mental illness

Part 1 summarises the findings of almost 100 systematic reviews and meta-analyses on the prevalence of physical comorbidities among people with mental illness. Around 70% of the meta-research focuses on cardiometabolic diseases, and consistently reports that mental illnesses are associated with a risk of obesity, diabetes, and cardiovascular diseases that is 1·4–2·0 times higher than in the general population. Although cardiometabolic diseases have mostly been studied in patients with severe mental illness (particularly psychotic disorders), the prevalence of cardiometabolic disease is also increased in individuals with a broad range of other diagnoses, including substance use disorders and so-called common mental disorders (such as depression and anxiety).

Part 2: Key modifiable factors in health-related behaviours and health services

Part 2 presents a hierarchical model of evidence synthesis to evaluate modifiable risk factors for physical diseases in mental illness. Most top-tier evidence has identified that smoking, excessive alcohol consumption, sleep disturbance, physical inactivity, and dietary risks are increased for a broad range of diagnoses, across various economic settings, and from illness onset. Additionally, parts 1 and 2 identify a scarcity of meta-research on the prevalence or risk factors of infectious diseases and physical multimorbidity in mental illness. We also highlight that increased attention on these areas will be particularly important in addressing the physical and mental comorbidities observed in low-income and middle-income settings.

Part 3: Interplay between psychiatric medications and physical health

Part 3 examines the interactions between psychotropic medications and physical health across a range of conditions. Antipsychotics remain the best evidence-based treatments for psychotic disorders and reduce mortality rates compared with no treatment, but they have adverse effects on many aspects of physical health. Although drugs for depression have a less immediate effect on cardiometabolic health than drugs for psychosis per individual, drugs for depression are prescribed much more commonly, and the number of prescriptions is increasing over time. Therefore, further research is required to establish the population burden of the cardiometabolic side-effects of drugs for depression, particularly from long-term use. Part 3 also discusses emerging pharmacological strategies for attenuating and managing physical health risks, and provides recommendations for improving prescribing practices.

Spain (A Koyanagi)**; Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain** (A Koyanagi)**; Metro South Addiction and Mental Health Service, Brisbane, QLD, Australia** (D Siskind PhD, S Suetani MD)**; School of Medicine** (D Siskind, Prof S Kisely DMedRes) **and Queensland Brain Institute** (S Suetani)**, University of Queensland, Brisbane, QLD, Australia; School of Psychiatry, Faculty of Medicine** (S Rosenbaum PhD, Prof J Curtis MBBS, S B Teasdale PhD, Prof P B Ward PhD) **and The George Institute for Global Health** (Prof T Usherwood MD)**, University of New South Wales, Sydney, NSW, Australia; Ramsay Health Care Mental Health, Adelaide, SA, Australia** (Prof C Galletly MD)**; Northern Adelaide Local Health Network, Adelaide, SA, Australia** (Prof C Galletly)**; Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK** (S Allan MA)**; Departamento de Psiquiatría, Pontificia Universidad Católica de Chile, Santiago, Chile** (C Caneo MD)**; Youth Mental Health Research Unit** (R Carney) **and Psychosis Research Unit** (D Shiers)**, Greater Manchester Mental Health NHS Foundation Trust, Manchester, UK; Centre for Addiction and Mental Health, Toronto, ON, Canada** (Prof A F Carvalho MD)**; Department of Psychiatry, University of Toronto, Toronto, ON, Canada** (Prof A F Carvalho)**; Deakin Health Economics, Institute for Health Transformation, Faculty of Health** (M L Chatterton PharmD, Prof C Mihalopoulos PhD) **and Food and Mood Centre** (E Hoare PhD)**, Deakin University, Melbourne, VIC, Australia; Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA** (Prof C U Correll MD)**; Department of Psychiatry, Zucker Hillside Hospital, Glen Oaks, NY, USA** (Prof C U Correll)**; Department of Child and Adolescent Psychiatry, Charité Universitätsmedizin, Berlin, Germany** (Prof C U Correll)**; South London and Maudsley NHS Foundation Trust, London, UK** (F Gaughran MD, T Pillinger MRCP, B Stubbs PhD);

Part 4: Multidisciplinary approaches to multimorbidity

Part 4 discusses multidisciplinary lifestyle interventions in mental health care. The Diabetes Prevention Program (DPP) is an example of a gold-standard lifestyle intervention that has broadly been successful in the general population. However, people with mental illness rarely have access to programmes based on the principles of the DPP, through either primary care or secondary care services. Based on the findings of large-scale clinical trials, we propose that future lifestyle interventions in mental health care must adopt the core principles of the DPP by partnering with appropriately trained physical health professionals, and by providing sufficient access to supervised exercise services. Prevention is a key focus of the DPP. Similarly, lifestyle interventions for people with mental illness should be available pre-emptively to protect metabolic health from the point of the first presentation of illness. Priorities for future initiatives and research include translating the principles of the DPP into interventions for people with mental illness across primary care, secondary services, and low-income and middle-income settings, and using implementation science and cost-effectiveness evaluations to develop a business case for integrating DPP-based interventions as the standard of care in mental health care.

Part 5: Innovations in integrating physical and mental health care

Part 5 focuses on the availability, content, and context of physical health care for people with mental illness. We summarise valuable new resources and guidelines from national and international health bodies that aim to address inequalities in both public health and clinical settings. National health strategies urgently need to give greater consideration to individuals with mental illness, who are often left behind from population gains in public health. The development of integrated care models for efficient management of physical and mental multimorbidity is an important step forwards, particularly in low-income and middle-income settings where health inequalities for people with mental illness are greatest. Similarly, taking a syndemic approach to the interaction between physical and mental comorbidities might improve the implementation of customised health interventions for a specific location or social setting. Continuing advances in digital health technologies also present new opportunities for addressing health inequalities on a global scale, although realising this potential will be dependent on further rigorous research. The Commission concludes with a discussion on the accountabilities and responsibilities of governments, health commissioners, health providers, and research funding bodies in implementing the recommendations of this Commission and protecting the physical health of people with mental illness.

Part 1: Physical health disparities for people with mental illness

Introduction

The premature mortality of people with mental illness has been recognised by the medical community for more than half a century.[1,2] Although premature mortality was initially shown in patients with severe mental illnesses such as schizophrenia and bipolar disorder,[3–5] there is now evidence that individuals who have diagnoses across the entire spectrum of mental disorders have a substantially reduced life expectancy compared with the general population.[3–11] Although suicide contributes to a considerable proportion of these premature deaths (with approximately 17% of mortality in people with mental illness attributed to unnatural causes),[12,13] the majority of years of life lost in people with mental illness relate to poor physical health, specifically due to comorbid non-communicable and infectious diseases.[11,14–19] The consequent poor physical health outcomes of people with mental illness have been alluded to as a human rights issue,[20] and the amount of research on this topic has increased substantially over the past two decades (appendix p 2).

Despite the increasing amount of research in this area and more general advancements in health care and medicine, the poor physical health outcomes (and the associated decrease in life expectancy) of people with mental illness have not improved.[3,12,21] In fact, the number of years of life lost due to physical health conditions in people with mental illness might be increasing.[3,21–23] The premature mortality of people with mental illness reflects a large number of health inequalities between people with and without mental illness throughout the life course. Although the psychiatric literature is largely unified on the consensus that physical comorbidities have a life-shortening effect for people with mental illness, the prevalence and specific effects of the physical comorbidities that can potentially affect individuals with diagnoses across the spectrum of mental disorders (not only severe mental illness) have not yet been widely examined.

Comorbidity of mental and physical diseases: a literature meta-review

To provide an overview of the literature in this field, we systematically identified all systematic reviews and meta-analyses of chronic physical disorders in people with common mental disorders, severe mental illnesses, alcohol and substance use disorders, and various other mental health disorders, published between Jan 1, 2000, and Oct 26, 2018. In particular, we sought to identify the top-tier evidence on the prevalence of chronic conditions in comparison with the general population (generally defined as individuals without mental illness). Further details on our search strategy and selection criteria are in the appendix (pp 2–5). We considered this body of meta-research and key recent reports from health-care and governmental bodies in developing the scope,

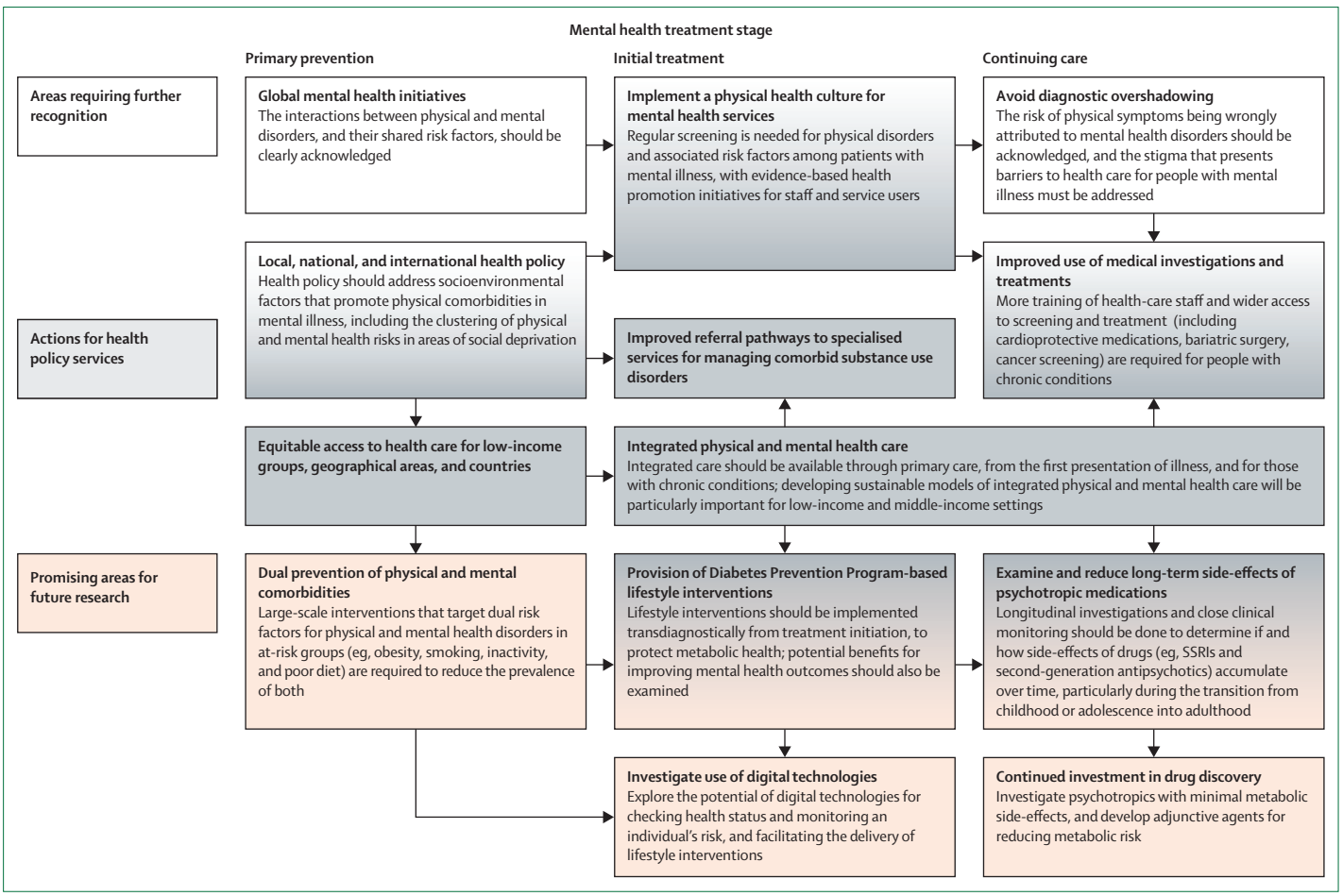

Figure 1: **Strategies to protect physical health in people with mental illness**
Strategies are applicable from the stage of mental illness indicated, and onwards. White boxes are areas that require further recognition. Grey boxes are actions for health policy and services. Orange boxes are promising areas for future research. Boxes that have a gradient of two colours are included in two of these categories.

priorities, and recommendations of this Commission (figure 1).

As detailed in table 1, since 2000, almost 100 systematic reviews and meta-analyses have been published on the physical health comorbidities associated with mental illness. The findings from the most recent systematic reviews and meta-analyses on the prevalence or risk of physical illness for each category of mental illness are shown in the appendix (pp 6–14). In common with another review,[121] we found a shortage of evidence from low-income and middle-income countries. Most meta-research on the physical health of individuals with mental disorders has focused on cardiovascular or metabolic diseases in high-income countries. Overall, the available evidence shows that for individuals with diagnoses across the entire spectrum of mental health disorders, the risk for cardiometabolic disease is increased by 1·4–2·0 times compared with individuals without mental illness (appendix pp 6–14). For instance, for patients with depression, the risk of developing cardiac disease, hypertension, stroke, diabetes, metabolic syndrome, or obesity is around 40% higher than in the general population. Similarly, 16 reviews of cardiovascular and metabolic health in patients with severe mental illness[14,54–58,77–80,91–95,100] showed clear evidence of an increase in risk of 1·4–2·0 times across all cardiovascular and metabolic diseases examined. Although fewer studies have been done for other mental disorders, the existing reviews of anxiety disorders,[46,76,87,98] substance use disorders,[81,96] attention-deficit hyperactivity disorder,[101] and personality disorders[104] consistently find evidence of poor cardiometabolic health in patients with these diagnoses, with substantially higher rates of obesity, diabetes, and metabolic syndrome than in the general population (appendix pp 6–14). The only inverse relationship that has been identified between cardiometabolic health and mental disorders is the reduced incidence of diabetes in patients with anorexia nervosa (odds ratio [OR] 0·71) compared with those without anorexia nervosa.[82] However, because of the

Centre for Global Mental Health (Prof G Thornicroft PhD) **and Psychosis Studies** (F Gaughran, T Pillinger, B Stubbs)**, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK; Manchester Academic Health Science Centre, University of Manchester, Manchester, UK** (A Heald)**; Department of Diabetes and Endocrinology, Salford Royal Hospital, Salford, UK** (A Heald)**; Department of Behavioural Science and Health, University College London, London, UK** (S E Jackson PhD)**; Department of Psychiatry, Dalhousie University, Halifax, NS, Canada** (Prof S Kisely)**; Greater Manchester Mental Health NHS Foundation Trust, Manchester, UK** (Prof K Lovell)**; Department**

	Common mental disorders (48 reviews)			Severe mental illnesses (30 reviews)			Alcohol and substance use disorders (6 reviews)		Other mental illnesses (8 reviews)				Mixed mental illness (7 reviews)	Total
	Depression	Anxiety	Mixed common mental disorder	Schizophrenia	Bipolar disorder	Mixed severe mental illness	Alcohol use disorder	Substance use disorder	Attention-deficit hyperactivity disorder	Autism spectrum disorder	Eating disorders	Personality disorders		
Number of reviews	33	12	3	15*	8	7*	5	1	4	1	2	1	7	99
Non-communicable diseases														
Asthma	2 reviews[24,25]	..	..	..	1 review[26]	..	..	..	1 review[27]	1 review[28]	..	..	..	5
Autoimmune disorders	..	..	..	..	..	1 review[29]	..	..	..	..	..	..	..	1
Cardiovascular disease	16 reviews[30–45]	6 reviews[46–51]	2 reviews[52,53]	2 reviews[54,55]	1 review[56]	3 reviews[14,57,58]	..	..	..	..	..	..	..	30
Cancer	4 reviews[59–62]	..	..	5 reviews[63–67]	..	..	..	..	..	..	..	..	1 review[68]	10
Diabetes	7 reviews[69–75]	1 review[76]	..	2 reviews[77,78]	2 reviews[79,80]	1 review[58]	1 review[81]	..	..	..	1 review[82]	..	2 reviews[83,84]	17
Metabolic syndrome	2 reviews[85,86]	3 reviews[87–89]	1 review[90]	3 reviews[78,91,92]	3 reviews[93–95]	1 review[58]	1 review[96]	..	..	..	..	..	1 review[97]	15
Obesity	..	2 reviews[98,99]	..	..	1 review[100]	..	..	..	3 reviews[101–103]	..	..	1 review[104]	2 reviews[97,105]	9
Osteoporosis or bone loss	1 review[106]	..	..	1 review[107]	..	..	..	..	..	..	1 review[108]	..	..	3
Parkinson's disease	1 review[109]	..	..	..	..	..	..	..	..	..	..	..	..	1
Rheumatoid arthritis	..	..	..	1 review[110]	..	1 review[29]	..	..	..	..	..	..	..	2
Infectious diseases														
Hepatitis B	..	..	..	..	..	3 reviews[111–113]	..	..	..	..	..	..	..	3
Hepatitis C	..	..	..	..	..	3 reviews[111–113]	1 review[114]	1 review[115]	..	..	..	..	..	5
HIV	..	..	..	..	..	3 reviews[111–113]	1 review[116]	..	..	..	..	..	1 review[117]	5
Syphilis	..	..	..	..	..	1 review[112]	..	..	..	..	..	..	..	1
Tuberculosis	..	..	..	..	..	..	1 review[118]	..	..	..	..	..	..	1
Other														
Mixed illnesses or comorbidities	..	..	..	2 reviews[119,120]	1 review[95]	1 review[58]	..	..	..	..	..	..	..	4

*Includes studies that examined several different mental illnesses.

Table 1: **Map of systematic reviews and meta-analyses that have examined physical comorbidities across different mental illnesses**

of Psychiatry, University of Campania Luigi Vanvitelli, Naples, Italy (Prof M Maj MD); **Discipline of Psychiatry, University of Adelaide, Adelaide, SA, Australia** (H Myles MBBS, Prof C Galletly); **Medical Research Council London Institute of Medical Sciences, London, UK** (T Pillinger); **Institute of Clinical Sciences, Faculty of Medicine, Imperial College London, London, UK** (T Pillinger); **The Melbourne Clinic, Melbourne, VIC, Australia** (Prof J Sarris); **Department of Sports Methods and Techniques, Federal University of Santa Maria, Santa Maria, Brazil** (Prof F B Schuch PhD); **Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University, Cambridge, UK** (L Smith PhD); **Neurosciences Department and Padua Neuroscience Centre, University of Padua, Padua, Italy** (M Solmi MD); **Queensland Centre for Mental Health Research, The Park Centre for Mental Health, Wacol, QLD, Australia** (S Suetani); **Keeping the Body in Mind Program, South Eastern Sydney Local Health District, Sydney, NSW, Australia** (Prof J Curtis, S B Teasdale); **Department of Psychiatry, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA** (J Torous MD); **Department of General Practice, Westmead Clinical School, University of Sydney, Westmead, NSW, Australia** (Prof T Usherwood); **Department of Rehabilitation Sciences, Katholieke Universiteit Leuven, Leuven, Belgium** (Prof D Vancampfort PhD); **University Psychiatric Centre, Katholieke Universiteit Leuven, Kortenberg, Belgium** (Prof D Vancampfort); **National Research Council, Neuroscience Institute, Aging Branch, Padova, Italy** (N Veronese MD); **and Schizophrenia Research Unit, Ingham Institute of Applied Medical Research, Liverpool, NSW, Australia** (Prof P B Ward)

Correspondence to:
Dr Joseph Firth, NICM Health Research Institute, Western Sydney University, Westmead, NSW 2145, Australia
j.firth@westernsydney.edu.au

	Alcohol	Tobacco use	Physical activity	Sedentary behaviour	Poor diet	Poor sleep
Major depression	SR: around 30% of patients have or have had alcohol use disorder[124]	SR: patients are more likely to smoke and be dependent on nicotine, are less likely to quit, and are more likely to relapse[125]	MA: around 60–70% of patients do not meet physical activity guidelines[126,127]	MA: patients are sedentary for 8·5 h per day[127]	ES: patients have significantly higher food intake and poorer diet quality than the general population[128]	ES: patients have significantly poorer continuity of sleep and reduced sleep depth compared with healthy controls[129]
Anxiety disorders	ES: 17·9% of patients have alcohol dependence or misuse[130]	MA: 41% increase in risk of regular smoking and 58% increase in risk of nicotine dependence[131]	ES: individuals with panic disorders, social phobia, and agoraphobia report significantly less activity[132]	SR: inconsistent evidence for increased sedentary time in people with anxiety[133]	Insufficient evidence	MA: anxiety disorders[129,134] and obsessive-compulsive disorder[135] are associated with reduced sleep quality
Bipolar disorder	MA: 1 in 3 patients have or have had alcohol use disorder[136]	MA: increased rates of current smoking (higher than in patients with major depression but lower than in patients with schizophrenia)[137]	MA: the majority of patients meet physical activity guidelines and are no different to the general population[81,126]	MA: patients are sedentary for more than 10 h per day[81,126]	MA: patients consume around 200 calories more than the general population per day[138]	MA: even between episodes, people with bipolar disorder have increased sleep-wake disturbance, similar to patients with insomnia[139]
Schizophrenia	MA: 1 in 5 patients have or have had alcohol use disorder[140]	MA: significantly higher rates of current smoking, heavy smoking, and nicotine dependence[141]	MA: the majority of patients do not meet physical activity guidelines[108,126]	MA: patients are sedentary for around 11 h per day[142]	MA: patients consume around 400 calories more than the general population per day[138]	MA: patients have significantly reduced sleep time and quality of sleep[129,134]
First-episode psychosis	MA: 27% of patients have or have had alcohol use disorder or alcohol dependence[143]	MA: 58% of patients use tobacco, which is a significantly higher prevalence than in matched controls[144]	MA: patients are less active than individuals with long-term schizophrenia[108]	Insufficient evidence	Insufficient evidence	MA: patients have significantly reduced sleep time and quality of sleep[134]
Post-traumatic stress disorder	SR: increased prevalence of comorbid alcohol misuse (10–61%) compared with the general population[145]	MA: patients are 22% more likely to be current smokers than the general population[98]	MA: patients are 9% less likely to be physically active than the general population[98]	Insufficient evidence	MA: patients are 5% less likely to have a healthy diet than the general population[98]	MA: significantly poorer continuity of sleep and reduced sleep depth compared with healthy controls[129]

Results described as significant had p<0·05. Comparisons are with the general population unless otherwise stated. SR=systematic review of case-control, clinical, or epidemiological research. MA=meta-analysis of multinational data. ES=large-scale epidemiological studies.

Table 2: **Prevalence of behavioural risk factors across different mental health diagnoses**

physically damaging behaviours that are inherent to the disorder, individuals with anorexia nervosa are at a much higher risk for other health issues, such as a 12 times greater incidence of osteoporosis,[108] and one of the highest rates of premature mortality across all mental disorders (all-cause standardised mortality ratio 5·9, 95% CI 4·2–8·3).[12] Furthermore, individuals with other eating disorders, such as bulimia, have a much higher risk of diabetes (OR 3·45) than people without eating disorders.[82]

The relationship between mental illnesses and cancer risk is uncertain. Although some reviews have found that mental illnesses are associated with a small increase in overall cancer risk,[59] other reviews have found no relationship, or a decreased cancer risk.[63,68] The risk of cancer associated with mental illness might vary for different cancer types. For instance, whereas patients with common or severe mental illnesses have an increased risk of lung cancer, the risk of colorectal cancer appears to be similar to (or even lower than) that in the general population.[59,63] Further research is required to understand these relationships, but a possible explanation is that people with mental illness have a reduced life expectancy, resulting in a reduced lifetime rate of cancer in this group. Another area requiring further investigation is the relationship between psychiatric and neurological disorders, because the tendency to separate these two types of illness into different categories, despite their overlapping characteristics, could result in underestimations of the true burden of mental illness on a global level.[122] A recent meta-analysis has shown that for people with depression, the risk of developing Parkinson's disease is doubled compared with people without depression,[109] but the relationships between other psychiatric and neurological disorders have yet to be established.

See **Online** for appendix

Gaps in the meta-research

Our meta-research showed an absence of meta-analyses on chronic obstructive pulmonary disease (COPD) in people with mental disorders, although individual health database studies[19,123] have found an increased prevalence of COPD in people with severe mental illness.

The harmful effects of infectious diseases on the physical health of people with mental disorders might also be underestimated, because they have largely been unexplored in mental health disorders other than severe mental illnesses (table 2). The reviews that we identified on infectious diseases in populations with severe mental illness found that the average prevalence (across multiple countries) for hepatitis B infection, hepatitis C infection, and HIV was 15·63%, 7·21%, and 7·59%, respectively,[111] and the prevalence of syphilis was 1·1–7·6%.[112] Within

specific settings or countries, prevalence data highlight that individuals with mental illness have an increased risk of infectious disease compared with the general population. For instance, in the USA, the prevalence of both hepatitis B and hepatitis C infections in patients with severe mental illness is around 20%, whereas the prevalence of these infectious diseases in the US population is estimated to be 0·3% and 1·0%, respectively.[146,147] Similarly, the median prevalence of HIV among people with severe mental illness in the USA is 1·8%, which is almost four times greater than the general US population.[146] In low-income and middle-income settings, infectious diseases are a major cause of mortality in people with severe mental illness. For example, in a 10-year follow-up study in Ethiopia,[148] individuals with severe mental illness died 30 years prematurely compared with the general population, and half of the deaths among individuals with severe mental illness were from infectious diseases. Further scientific and governmental attention is required for infectious diseases among people with mental illness in low-income and middle-income settings, particularly given that rates of infection are highest in these settings, and inequalities between people with and without mental illness are most pronounced.[149] Furthermore, despite the compelling evidence for increased risk of infectious diseases in adults with severe mental illness, the prevalence of infectious diseases in other mental disorders, and the extent to which this increased risk applies to young people with mental illness, is not well established. Future research should also aim to identify the underlying factors resulting in an increased rate of infectious diseases among people with mental illnesses so that more appropriate and targeted solutions can be developed (as discussed in Part 2).

Much of the published literature assessing physical health in mental illness to date has examined the prevalence of specific health outcomes or disorders in isolation. The prevalence and specific effects of physical multimorbidity (ie, the presence of more than one chronic physical disorder) in people with mental illness are not fully understood. Some large-scale, multinational studies have shown that people with severe mental illness,[123,150] common mental disorders,[151,152] and substance use disorders[18,153] are at a greatly increased risk of physical multimorbidity from the point of onset of the mental illness.[154] The average age of onset of multimorbidity is younger in people with mental illness compared with the general population.[123,154] Multimorbidity greatly increases the personal and economic burden associated with chronic conditions, and reduces life expectancy compared with a single morbidity.[155,156] Urgent attention is required to address the onset and accumulation of physical multimorbidity, particularly in low-income and middle-income settings, where physical multimorbidity is increased among people with mental illness compared with the general population,[81,83,151] but services do not have the resources to deal with the burden and complexity of these cases. Additionally, the development of cost-effective approaches that address the root causes of multimorbidity is needed to prevent long-term disability in people with mental illness.

Further considerations

Although the impact of physical comorbidities on the life expectancy of individuals with mental illnesses is well established,[13,14] further research is needed to examine whether the psychological distress associated with mental illness is compounded by the additional burden of these chronic conditions. For instance, in the general population, diabetes is commonly associated with distress, which can have a considerable effect on the person's quality of life and their ability to manage their overall health.[157] Diabetes-related distress also affects people with common mental disorders,[157] severe mental illness,[158] and substance use disorders.[159] The prevalence of obesity is considerably increased across most classes of mental disorder compared with the general population (appendix pp 6–14). Weight gain can be distressing and negatively affect an individual's quality of life and self-esteem, and might impede treatment-seeking behaviour because an individual is concerned about further weight gain.[160] Similarly, obesity can perpetuate lifestyle behaviours, such as social withdrawal[161] and sedentary behaviour,[126] that are characteristic of many mental disorders, and are also key risk factors for poor cardiometabolic health.[162] Emerging evidence suggests that obesity and metabolic syndrome are independent predictors of relapse and rehospitalisation for those with severe mental illness.[163,164] This relationship could be explained by the inflammatory effects of abdominal obesity; inflammation has also been associated with worse mental health[165] and increased suicidality.[166] In addition to the personal burden, physical comorbidities in people with mental illness result in an increased financial cost, the extent of which requires further research (panel 1).

To address physical health inequalities in people with mental illness compared with those without mental illness, we must focus on both reducing the prevalence of chronic health conditions, and lessening their effects across the life course. In particular, cardiometabolic diseases are a relevant and transdiagnostic target for improving physical health outcomes across a broad spectrum of mental illnesses. Although schizophrenia is typically associated with the greatest degree of cardiovascular risk (partly due to the side-effects of drugs for psychosis), there is compelling evidence that the risk of obesity, metabolic syndrome, diabetes, and cardiometabolic disease is similarly increased in other mental disorders, including common mental disorders.[46,76,83,85,87,97,98,175–177] Given the high prevalence of these mental disorders, developing strategies for improving health outcomes that can be applied across many different mental health diagnoses (including severe mental illness) could considerably reduce premature mortality and the lifelong burden of poor physical health for people with mental illness. The effects and prevalence

of other non-communicable diseases and infectious diseases in low-income, middle-income, and high-income countries cannot be neglected. As such, understanding the epidemiology of mental and physical comorbidities in low-income and middle-income countries,[178] and developing evidence-based interventions that integrate mental and physical health care in these settings,[179] is increasingly recognised as a major research priority for global health. The following parts of the Commission discuss key modifiable factors that drive mental and physical health comorbidities, describe strategies for improving the management and prevention of these conditions, and present directions for both immediate clinical action and future research to reduce physical health inequalities for people with mental illness (figure 1).

Part 2: Key modifiable factors in health-related behaviours and health services

Introduction

Part 1 identified cardiometabolic diseases as a category of physical comorbidities that is particularly pervasive and has profound effects on patient wellbeing, morbidity, and mortality, across many mental disorder diagnoses.[46,76,81,83,85,87,96–98,157–159,175–177,180] In addition to the side-effects of psychotropic medications (described in Part 3), the reasons for increased cardiometabolic morbidity and mortality in people with mental illness can be separated into patient-related factors and provider-level or system-level factors.[121]

Lifestyle risk factors, such as smoking, poor diet, and inactivity, are modifiable, patient-related factors that are known to be associated with cardiometabolic disease,[108,128,138,141] as well as affecting many other aspects of physical health.[46,76,81,83,85,87,96–98,175–177] However, the extent to which lifestyle risk factors in patients with various mental disorders differ from the general population is not fully established. As a result, current lifestyle interventions for people with mental illness could be imprecise, or could focus too much on one behavioural modification at the expense of other important risk factors (eg, increasing physical exercise without considering the impact of diet, or focusing on smoking over alcohol intake).

We applied a systematic hierarchical approach (appendix pp 15, 16) to identify top-tier evidence on lifestyle risk factors for non-communicable diseases in people with mental illness. We focused on behavioural risk factors in affective and psychotic disorders, rather than on mental health illnesses that are characterised by physically damaging behaviours, such as eating disorders and substance or alcohol use disorders (in which the greatest behavioural risks to physical health are the behaviours that define the conditions). Table 2 summarises findings from meta-analyses, systematic reviews, and population-scale studies, published since 2000, on lifestyle risk factors in various mental health populations.

***Panel 1*: Adding up the costs of physical comorbidities in people with mental illness**

Cost-of-illness studies, which assess the economic burden of a diagnosis or group of diagnoses, have found that people with combined physical and psychiatric comorbidity have higher hospital costs, increased readmission rates, and higher total health sector costs compared with people without psychiatric diagnoses.[163,167–171]

Although cost-of-illness studies are important for describing economic burden, only economic evaluations can estimate the cost-effectiveness of interventions to support decision making on the investment of limited health-care (and other sector) resources. Economic evaluations are used to assess pharmaceuticals and health technologies in many countries. Evidence regarding the cost-effectiveness of referral programmes and lifestyle interventions for people with mental illness and increased cardiovascular disease risk factors is mostly positive, but little evidence is available.[172–174] Further economic evaluations that collect cost and outcome data, and that are done alongside clinical trials, will be needed to provide convincing evidence of the economic benefits of these programmes in people with mental health diagnoses.

Challenges to trial-based economic evaluations include excessive respondent burden and respondent bias in collecting cost information, although these might be overcome by using administrative data systems. Fragmentation of information and poor availability of data for some populations present additional challenges. Trial-based evaluations, which often use intermediate efficacy endpoints (eg, LDL cholesterol levels), will be an important source of data for modelled economic evaluations. Modelled evaluations will be crucial to establish the long-term cost-savings and improvements in outcomes (eg, quality of life and mortality) through the avoidance of future health consequences, such as metabolic syndrome and cardiovascular disease events. As this area of research develops, both trial-based and modelled economic evaluations will need to adhere to published methodology standards, including presenting health-care and societal perspectives to assist policy makers.

Lifestyle risk factors across various diagnoses

Although the initial aim of our hierarchical evidence synthesis was to determine key lifestyle risk factors that are associated with individual mental disorders, most of the published literature showed that all psychiatric diagnoses are associated with a wide spectrum of lifestyle risk factors (table 2). People with mental illness tend to have more unhealthy lifestyles compared with the general population, and among people with mental illness, those with schizophrenia have a particularly high risk of smoking, sedentary behaviour, and poor diet.[128,137,138] Socioeconomic factors could partly mediate this trend, because the incidence of schizophrenia is higher in low-income communities,[181] and such communities also have higher rates of behavioural risk factors compared with

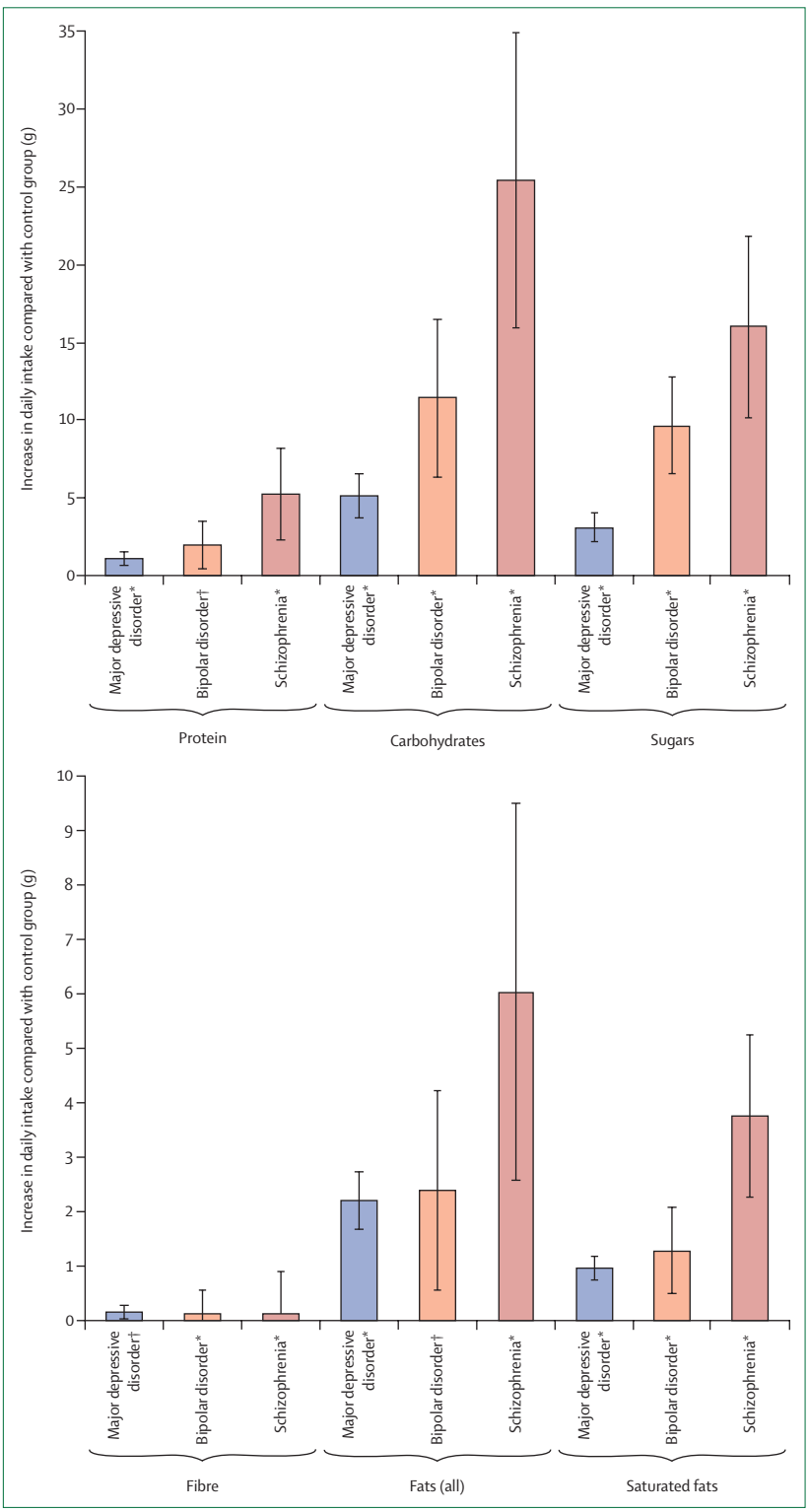

Figure 2: **Dietary intake by food group in patients with major depressive disorder (n=14 619), bipolar disorder (n=952), and schizophrenia (n=262)**

Bar heights represent the age-adjusted and sex-adjusted mean differences. Error bars represent 95% CIs of adjusted means. Data are based on the UK Biobank study and reproduced from Firth and colleagues.[128] *p<0·05 compared with healthy controls. †p<0·001 compared with healthy controls.

high-income communities.[182] However, lifestyle risk factors are still greater in patients with schizophrenia than those with other mental health disorders, even when controlling for socioeconomic factors. For instance, a population-scale study from 2018 that used data from the UK Biobank[128] found that individuals with severe mental illness ate more obesogenic food than the general population, particularly those with schizophrenia (figure 2), and the differences in diet persisted after adjusting for social deprivation and education.[128] The use of second-generation antipsychotics (SGAs) could contribute to changes in diet, because trials in healthy volunteers found that SGAs such as olanzapine can reduce satiety, increase appetite[183] and lethargy, and have sedative effects.[184–186] Although some SGAs, such as olanzapine, have the most obvious cardiometabolic side-effects, other more widely prescribed psychotropic medications also have cardiometabolic side-effects that accumulate over time. Thus, early intervention strategies for managing lifestyle and cardiometabolic risk for patients treated with psychotropic medications are important for preventing cardiometabolic diseases from arising (panel 2) The side-effects of SGAs and other psychotropic medications (such as drugs for depression) are discussed further in Part 3.

Lifestyle risk factors in low-income and middle-income settings

Although most of the data presented in table 2 are from high-income countries, similar trends have been found in low-income and middle-income countries.[137,141,194–199] For instance, data from the WHO Study on Global Ageing and Adult Health and the WHO World Health Survey show that individuals with depression in low-income and middle-income countries are more likely to smoke (OR 1·41),[194] to not meet physical activity guidelines (OR 1·42),[195] and to have sedentary behaviour for 8 h or more per day (OR 1·94)[196] than individuals without depression. Similarly, low levels of physical activity are found in individuals with anxiety and psychotic disorders in low-income and middle-income countries.[137,141,197–199] Despite the differences in sociocultural factors in low-income and middle-income countries compared with high-income countries, people with mental illness in both settings have more lifestyle risk factors compared with the general population. In low-income and middle-income countries, there are new challenges to maintaining a healthy lifestyle caused by the spread of fast-food restaurants, new technologies that allow for reduced physical inactivity, and tobacco promotion and legislation.[200–202] Because lifestyle risk factors, such as physical inactivity and poor diet, are elevated in people with mental illness (table 2), further efforts are needed to develop lifestyle interventions that address these factors appropriately for those with mental illness living in low-income and middle-income settings (see Part 5).

In addition to non-communicable diseases, other behavioural risk factors, such as intravenous drug use and high-risk sexual behaviours, are also over-represented in people with severe mental illness in low-income, middle-income, and high-income settings (see Part 1), and can lead to infectious disease. Most available data are for adults with severe mental illness, so the prevalence in other age groups and for other diagnoses might be underestimated. For instance, a recent meta-analysis[203] of 3029 adolescents with a range of psychiatric diagnoses showed a 15% (95% CI 3–50) lifetime prevalence of sexually transmitted illnesses, and found that 40% (95% CI 23–78) of the adolescents had shown high-risk sexual behaviour during their most recent sexual encounter. Furthermore, recent alcohol use increased the likelihood of having unprotected sex (OR 1·66, 95% CI 1·09–2·52).[203] The interactions between risk factors for non-communicable diseases and infectious diseases should not be overlooked, and suggest that screening for multiple lifestyle factors, rather than single factors or biological markers alone, will be the most efficient method for improving health outcomes for people with mental illness.

Interventions for multiple lifestyle risk factors in mental illness

In summary, although our evidence synthesis process aimed to identify key behavioural risk factors for specific mental disorders, the evidence suggests that simultaneously considering multiple lifestyle factors is more appropriate in understanding and managing risk factors across all mental health diagnoses. However, such transdiagnostic, multifactorial approaches are not widely reflected in the published literature, which generally focuses on specific factors for individual disorders. Furthermore, no suitable tools are available for clinicians to comprehensively assess lifestyle factors as part of standard care. The sole use of biological markers for physical health assessment (such as >7% increase in bodyweight, high blood pressure, and an abnormal lipid profile) could mean that interventions are applied only when it is too late to protect metabolic health or pre-empt obesity (panel 2). Clinical guidelines are increasingly recommending that assessments of diet, physical activity, and health risk behaviours are done alongside assessments of anthropomorphic parameters and blood markers of metabolic status,[204] to more accurately assess current physical health and future risk.

To comprehensively promote the physical health of people with mental illness, a positive first step would be developing quick and widely applicable tools for lifestyle screening. These tools could be used across different diagnoses, settings, and services, to assess a range of behavioural risk factors (eg, exercise, diet, substance use, and sleep) at once, and thus identify key drivers of poor physical health on a case-by-case basis. A comprehensive lifestyle assessment would give patients more actionable physical health information than that which is typically provided from screening for biological markers, because patients will be informed of specific lifestyle changes they could make to protect their physical health. Self-report questionnaires are often burdensome and inaccurate, reducing their suitability for capturing lifestyle factors in people with mental illness.[205] Thus, a priority for future research is to examine if digital technologies (including smartphones and wearable technologies) could provide feasible and accurate methods of broad lifestyle assessment.[205,206]

In addition, more efficient care pathways are needed to help people with mental illness minimise behavioural risk factors (see Part 4). For instance, multidisciplinary referral pathways (available through both primary and secondary care) could provide access to specialised physical activity, smoking cessation, dietetics, and other allied health services, depending on the individual's specific behavioural profile and health goals. The dissemination of risk behaviour interventions in low-income and middle-income countries is an urgent challenge, because individuals with mental illness in these countries are disproportionately affected by an increased risk for infectious diseases and non-communicable diseases.

Panel 2: Why wait for weight? Tipping the scales towards prevention

Clinical guidelines for metabolic screening upon initiation or continuation of second-generation antipsychotics recommend that blood pressure, body-mass index, blood glucose, and lipid profile should be checked at least every 6 months.[187-189] This is a positive example of considering physical health outcomes for people with severe mental illness. However, a large body of research in the general population has shown that preventing conditions such as obesity and metabolic syndrome from arising is considerably more efficient than attempting to reverse their long-term consequences.[190] Thus, proactive lifestyle interventions in mental illness might not have their maximal effect if the interventions are only provided after large changes in biological or clinical markers of adverse metabolic health are found during screening.

Individuals with first-episode psychosis are at considerable lifestyle risk from illness onset (table 2), because they tend to be less physically active and have a higher rate of alcohol use disorders than those with long-term schizophrenia, and also have nutrient deficits and a high rate of smoking (around 60% for both first-episode psychosis and schizophrenia, which is much higher than in the general population). Many other behavioural risk factors also seem to precede, rather than accompany, the onset of psychotic disorders,[191] and metabolic disturbance might be present from illness onset.[192]

Although treatment with second-generation antipsychotics (SGAs) can be important for stabilising mental health, taking these drugs can further increase metabolic risk (see Part 3). Given the high likelihood of physical health deterioration while taking SGAs, clinicians who prescribe them to patients have a duty of care to ensure that the patients are given access to evidence-based lifestyle interventions (as detailed in Part 4) from the start of treatment. Lifestyle interventions should be made available even to those with intact metabolic health. Although health screening should continue, more timely and effective strategies for improving health outcomes will require intervening on the basis of lifestyle plus pharmacological risk, rather than waiting for visible weight gain or metabolic dysfunction to happen.[193]

Health provider-level and system-level factors

Lifestyle-related factors are unlikely to be the only explanations for poor physical health outcomes in people with mental illness.[121] For severe mental illness in particular, mortality remains high even after adjusting for behavioural risk factors such as smoking, physical activity, and body-mass index.[207] Increasingly, evidence suggests that the poor physical health outcomes of people with mental illness are partly driven by differences in the availability and quality of health care that they receive. For instance, people with severe mental illness are less able to access adequate health care than the general population. In the USA, people with severe mental illness are twice as likely as those without mental disorders to have been denied medical insurance because of a pre-existing condition.[208] These disparities exist at all levels of health services. In primary care, people with severe mental illness are less likely to have a physical examination (eg, weight and blood pressure),[209] or to be assessed and treated for hyperlipidaemia, than people without mental illness.[210,211] People with mental illness also have more emergency department visits and more avoidable admissions to hospital for physical conditions that with appropriate primary care should not require inpatient treatment.[212] Patients with a range of psychiatric diagnoses, including depression, anxiety, substance use disorder, and severe mental illness, have reduced access to oral health care.[213,214]

In secondary health services, physical health might also be poorly managed for people with mental illness.[215] In particular, people with mental illness are less likely to receive medical or surgical interventions that are commonly given in the general population. For example, people who have had prior contact with mental health services are less likely to receive cardiac catheterisations and coronary artery bypass grafting than people who have no prior contact, which contributes to the higher mortality for circulatory disease among people with a history of mental illness.[216–218] People with mental illness are also less likely to receive appropriate medications, such as β blockers and statins, at discharge after myocardial infarction.[219] The incidence of many cancer types (including common types, such as breast, colorectal, and prostate cancer and melanoma) among patients with psychiatric illness is only slightly higher than that of the general population (see Part 1), but mortality is markedly higher.[220,221] Disparities at the health-service level are thought to be responsible for increased cancer mortality, because people with mental illness are less likely to be offered cancer screening,[222] have a reduced likelihood of surgery for all types of cancer, and wait longer for surgery.[223]

A possible explanation for disparities in care for people with mental illness is that clinicians attribute emerging somatic symptoms to the patient's underlying psychiatric disorder, resulting in missed diagnoses (sometimes known as diagnostic overshadowing).[224,225] In addition, people with mental illness can have difficulties with reporting medical problems, distinguishing physical symptoms from the symptoms of mental illness, and engaging with health services (ie, attending follow-up appointments), particularly if the services are non-inclusive, or perceived as non-inclusive, of people with mental illness.[224,226]

Physicians might be reluctant to offer some medical procedures to people with mental illness because of the ensuing psychological stress, difficulties with obtaining informed consent or compliance with postoperative care, or contraindications, such as substance misuse and smoking.[226] However, contraindications to specialised interventions, such as smoking or problems with informed consent, are not relevant to the prescription of vascular drugs, such as angiotensin-converting enzyme inhibitors, β blockers, or statins, that are known to reduce morbidity and mortality.[227] Furthermore, people with schizophrenia are as adherent to diabetes medication as the general population.[228] Access to secondary health care for people with mental illness might be restricted by financial costs, fragmentation of care, and social stigma.[224,226,229] Although health-care providers should recognise that challenging behaviour can be a symptom of illness, evidence shows that some health-care providers have stigmatised views towards people with mental illness.[224,225] Nonetheless, health services should routinely offer health screening and lifestyle interventions for people with psychiatric disorders, in the same way as for patients with chronic physical conditions.[230]

In conclusion, people with mental illness are likely to receive a poorer standard of health care compared with people without mental illness who have the same physical health problems. To address this discrepancy, changes need to be made in the training of health providers and to the overall health system (see Part 5). Greater integration of physical and mental health care in primary care settings is a key recommendation for improving the management of physical comorbidities in people with mental illness. Mental health clinicians should be wary of attributing emerging somatic symptoms solely to an underlying mental illness, and refresher training on the detection, management, and prevention of chronic medical conditions needs to be available to mental health staff.[229] Furthermore, developing clinical tools for comprehensive lifestyle assessment, and improving referral pathways to targeted interventions, will enable practitioners to identify and manage cardiometabolic risk factors in a timely manner. At the service level, screening procedures need to be improved to support prevention initiatives, alongside investment in the integration of physical health within mental health services, and vice versa.

Part 3: Interplay between psychiatric medications and physical health

Introduction

As discussed in Part 1, a broad range of psychiatric diagnoses are associated with high comorbidity for physical conditions (particularly cardiometabolic diseases). Although lifestyle risk factors for chronic illness seem to be consistent across a wide range of mental illnesses (Part 2), the physical health risks associated with individual mental health diagnoses are modified by the types of psychotropic medications that are given to treat each condition. In this section, we present research on the interactions between psychotropic medications and physical health, and discuss pharmacological strategies for managing the physical health risks associated with mental illness and avoiding psychotropic adverse drug reactions (ADRs).

ADRs associated with psychotropic medications

Antipsychotic medications are a key component of treatment for psychotic disorders, because they reduce acute symptoms,[231] and reduce the risk of relapses,[232] emergency hospital admissions,[233] rehospitalisation,[234,235] and mortality.[21,236] Antipsychotic medications are also used for bipolar affective disorder.[237,238] However, the long-term effects of ADRs related to physical health are a major concern, and can be broadly divided into the following categories: cardiometabolic, endocrine, neuromotor, and other ADRs. The ADRs associated with specific antipsychotics are described in the appendix (p 17).

Cardiometabolic ADRs

Weight gain is an important ADR because it mediates other cardiometabolic outcomes, such as type 2 diabetes and cardiovascular diseases. Weight gain is the most distressing side-effect reported by callers to mental health helplines,[188] and is associated with poorer quality of life[239–241] and barriers to social engagement.[242] As a result, patients who gain weight have a reduced adherence to treatment, which can lead to relapse and poor mental health outcomes.[163,164] Although most antipsychotic medications lead to weight gain, clozapine and olanzapine have the highest propensity, and haloperidol, lurasidone, and ziprasidone have the lowest propensity.[243,244] Weight gain pathways induced by antipsychotic medication include those involving histamine H1 receptors, D2 dopamine receptors, blockade of 5-hydroxytryptamine receptor 2C, and dysregulation of glucagon-like peptide-1.[243,245] Meta-analyses (table 1) have found that the risk of metabolic syndrome and type 2 diabetes is at least twice as high in people with schizophrenia, bipolar affective disorder, and major depressive disorder compared with the general population (appendix pp 6–13).

Endocrine ADRs

Antipsychotic-induced hyperprolactinaemia is the most common endocrine ADR.[246] Antipsychotic medications block dopamine in the tuberoinfundibular pathway, leading to reduced inhibition of prolactin synthesis and secretion. Hyperprolactinaemia is most commonly found with first-generation antipsychotics, as well as risperidone, paliperidone, and amisulpride.[247] Hyperprolactinaemia can be asymptomatic, or can lead to complications, such as menstrual disturbance and sexual dysfunction (including reduced libido, erectile dysfunction, vaginal dryness, and orgasmic dysfunction[248]) in the short-term,[247] and osteopenia in the long-term.[249]

Neuromotor ADRs

Extrapyramidal side-effects are the most common neuromotor ADRs of antipsychotics. These side-effects can be socially stigmatising and are associated with poor quality of life, treatment dissatisfaction, and non-adherence to treatment.[239,240] Extrapyramidal side-effects include dystonia (muscle spasm), Parkinsonism (tremor, rigidity, and bradykinesia), akathisia (subjective restlessness), and tardive dyskinesia (abnormal involuntary movements). The detailed mechanisms of these side-effects are unknown, but they are likely to be related to blockade of dopamine receptors in the nigrostriatal pathway.[250] The annual incidence of tardive dyskinesia is lower among patients taking SGAs compared with those taking first-generation antipsychotic medications.[251] Neuroleptic malignant syndrome is a rare but serious condition (incidence of one to two cases per 10 000 people per year) that can be life-threatening.[252] It is characterised by fever, severe rigidity, autonomic disturbances, and confusion.[252] The incidence of neuroleptic malignant syndrome has reduced since SGAs became more widely used.[252]

Other ADRs

Antipsychotics are associated with varying degrees of cardiac conduction delay, indicated by a prolonged QTc interval, that can predispose the patient to torsade de pointes and lead to sudden death.[253] Therefore, cardiac conduction should be monitored in patients at risk.

Anticholinergic effects are common side-effects of antipsychotic medications, particularly chlorpromazine, clozapine, and olanzapine.[254] Anticholinergic effects are mediated by antagonism of acetylcholine by inhibition of the muscarinic receptors. They can be either central (eg, impairment of cognition, memory, and concentration, and sedation) or peripheral (eg, constipation, dry eyes, mouth, and skin, blurred vision, tachycardia, and urinary retention). These effects are particularly burdensome in the older population and can have cumulative effects when multiple anticholinergic agents are used.[254]

Somnolence, sedation, and hypersomnia are also common side-effects of antipsychotics.[244] Although sedation might have short-term benefits for an acutely exacerbated or agitated patient, in the long term, somnolence and sedation can affect physical activity,

bodyweight, concentration, and the ability to participate in daily activities or psychosocial rehabilitation, and could lead to medication non-adherence.[239]

Most antipsychotic medications can reduce the seizure threshold. The greatest dose-related risk for seizures is associated with clozapine.[253]

Clozapine

Clozapine is the only approved antipsychotic medication for people with treatment-resistant schizophrenia.[255] It is the most effective antipsychotic medication for reducing positive symptoms[256] and hospitalisations.[257] However, clozapine is associated with severe neutropenia (agranulocytosis; incidence 0·9%; 95% CI 0·7–1·1), usually in the first month after commencement, that can rarely cause death (0·013%; 0·010–0·017).[258] Cardiac ADRs can be life-threatening and include myocarditis (incidence of 0·03–1·00%, usually within the first month)[259,260] and cardiomyopathy (incidence of 0·06–0·12%, usually after the first year).[259,261] Other ADRs of clozapine include weight gain, type 2 diabetes, sedation, sialorrhoea, constipation, tachycardia, postural hypotension, gastro-oesophageal reflux, nocturnal enuresis, seizures, and obsessive-compulsive symptoms.[262]

Mood stabilisers

Mood stabilisers are prescribed for bipolar affective disorder[263] and adjunctively for refractory schizophrenia.[264,265] Individuals who are prescribed lithium have a mean weight gain of 4 kg over 2 years.[266] Lithium is also associated with thyroid disease,[267] including development of goitre (in up to 50% of patients[268]), hypothyroidism,[269] or hyperthyroidism.[270] Lithium is also associated with polydipsia, polyuria, diabetes insipidus, and other forms of renal dysfunction.[269] Sodium valproate is associated with metabolic effects, with at least half of individuals gaining weight in the first 3 months after initiation,[271] with a mean weight gain of 6·4 kg over 3 months.[272] It is also associated with insulin resistance, which increases the risk of developing type 2 diabetes.[273]

Antipsychotic medications are often prescribed concurrently with mood stabilisers; additional caution is required in this situation because the metabolic effects of the two classes of medication could be additive.[93] Although lithium and sodium valproate are the two most widely prescribed mood stabilisers, other mood stabilisers have a lower propensity for weight gain (eg, carbamazepine)[271] or have no effect on weight (eg, lamotrigine).[274] All mood stabilisers are associated with teratogenic effects and should be avoided in pregnancy and lactation (appendix p 18).

Drugs for depression

Common ADRs with newer-generation drugs for depression include headache, nausea, agitation, sedation, dizziness, sexual dysfunction, hyponatraemia, weight gain, and metabolic abnormalities.[275] Gastrointestinal side-effects, headache, and sexual side-effects are associated with all proserotonergic drugs for depression, whereas sedation, weight gain, and metabolic effects vary across agents. Antihistaminergic agents (eg, mirtazapine) are more associated with cardiometabolic effects and sedation. Less commonly, drugs for depression can have cardiac (eg, arrhythmias), neurological (eg, seizures), and hepatic ADRs.[275] Treatment with tricyclic antidepressants is associated with anticholinergic effects, including dry mouth, sedation, blurred vision, constipation, and urinary retention, as well as increased appetite, weight gain, and hyponatraemia (especially in older patients).[276] Furthermore, tricyclic antidepressants are associated with a risk of orthostatic hypotension and falls.[277] They also have a known arrhythmogenic effect; electrocardiogram (ECG) changes can include prolongation of PR interval, QRS interval, and PT (appendix p 19).

Pharmacological management of ADRs and physical health comorbidities

For the physical comorbidities associated with serious mental illness that are also commonly seen in the general population (eg, cardiovascular disease), national and international prescribing guidelines developed for the general population should be followed. By contrast, conditions that are secondary to psychiatric pharmacological treatment (eg, extrapyramidal side-effects) require a specialised approach. Close monitoring of physical health parameters is required for people taking antipsychotic medications, and evidence-based pharmacological treatments are needed.[278] If it is safe and feasible, modifying psychiatric medications that are associated with an ADR (eg, by reducing doses or switching medications) should be considered, in consultation with the patient. Here, we provide a targeted, evidence-based approach to addressing commonly observed physical health ADRs in patients with severe mental illness.

Type 2 diabetes

Pharmacological management of type 2 diabetes for patients with severe mental illness should follow guidelines for the general population (appendix p 20). The first-line pharmacological therapy is metformin monotherapy, and second-line therapies are listed in the appendix (p 20). The relative risks and benefits of different type 2 diabetes treatments for patients with severe mental illness are presented in table 3. Metformin reduces the risk of transition from prediabetes to type 2 diabetes,[283,284] and should be considered for individuals with severe mental illness and prediabetes. Glucagon-like peptide 1 receptor agonists also reduce the transition from prediabetes or non-diabetes to type 2 diabetes, as well as leading to clinically significant weight loss.[282]

Weight gain

When behavioural interventions are ineffective, pharmacological methods for attenuating weight gain in patients

	Mechanism	Risks	Benefits	Evidence base in severe mental illness
Biguanide (metformin)	Increases insulin sensitivity; reduces hepatic synthesis and release of glucose; increases peripheral glucose uptake	Lactic acidosis; B12 deficiency; gastrointestinal effects (a modified release formulation can be tried if these occur); contraindicated in patients with estimated glomerular filtration rate <30 mL/min per 1·73 m^2	Weight loss (3 kg); low risk of hypoglycaemia	Good evidence for use in patients with severe mental illness, and should be considered a first-line treatment;[279] consider use in patients with pre-diabetes who are receiving olanzapine and clozapine[280]
DPP4 inhibitor (eg, sitagliptin)	Inhibits action of DPP4 that acts to break down incretins (eg, GLP-1), resulting in increased incretin effect, as seen with GLP-1 receptor agonists	Possible increase in hospitalisations for heart failure with alogliptin and saxagliptin; possible increased risk of pancreatitis	No effect on weight; low risk of hypoglycaemia	Insufficient trial data in patients with severe mental illness
GLP-1 receptor agonist (eg, exenatide)	Incretin mimetic: stimulates release of insulin; reduces glucagon release; delays gastric emptying; reduces appetite	Nausea or vomiting; possible increased risk of pancreatitis; subcutaneous administration	Weight loss (3·0–4·5 kg); low risk of hypoglycaemia; liraglutide is approved by the FDA for prevention of major cardiac events	Current evidence base suggests it should be considered a second-line therapy in patients with severe mental illness; some evidence for the use of exenatide in patients treated with clozapine;[281] GLP-1 receptor agonists have been shown to reduce the transition to type 2 diabetes[282]
Sulfonylurea (eg, gliclazide)	Increases endogenous production of insulin	Weight gain; hypoglycaemia	None established	Insufficient trial data in patients with severe mental illness
SGLT2 inhibitor (eg, dapagliflozin)	Inhibits SGLT2 in the proximal renal tubule, thereby reducing reabsorption of glucose and promoting glucosuria	Polyuria; postural hypotension; urinary tract infection; diabetic ketoacidosis can occur in stress settings; mild fracture risk	Weight loss (2–3 kg); low risk of hypoglycaemia; empagliflozin is approved by the FDA to reduce cardiovascular mortality; canagliflozin reduces cardiac events	Insufficient trial data in patients with severe mental illness
Thiazolidinedione (eg, pioglitazone)	Improves insulin sensitivity by promoting adipogenesis and reducing circulating fatty acid and lipid availability	Weight gain; heart failure; oedema; bone fractures	Might reduce stroke risk; low risk of hypoglycaemia	Insufficient trial data in patients with severe mental illness
Insulin	Supplements the insufficient endogenous production of insulin	Weight gain; hypoglycaemia	In acute settings or in poorly controlled type 2 diabetes, it might be the only effective treatment for stabilising sugars	Insufficient trial data in patients with severe mental illness

DPP4=dipeptidyl peptidase 4. GLP-1=glucagon-like peptide 1. FDA=US Food and Drug Administration. SGLT2=sodium-glucose cotransporter 2.

Table 3: **Risks and benefits of different drug classes for diabetes treatment and the evidence base for their use in patients with severe mental illness**

with severe mental illness should be considered. Pharmacological agents are described in detail in the appendix (p 21); the most evidence in individuals treated with drugs for psychosis is for metformin and topiramate.[285] Bariatric surgery can also be considered as a last-resort treatment if both behavioural and pharmacological interventions are not effective. Weight gain associated with drugs for psychosis is not usually dose-dependent, so dose reduction will not be effective in reducing weight.[286]

Arterial hypertension

Pharmacological management of hypertension in patients with severe mental illness should follow guidelines used for the general population (appendix p 20).

Dyslipidaemia

Data on dyslipidaemia treatments that are specific for people with mental illness are scarce. Therefore, the best guidance available comes from general population studies. Statins reduce the risk of coronary heart disease events by 20–30%.[287–289] Cardiovascular risk calculators that incorporate factors such as age, hypertension, and type 2 diabetes diagnosis, and particularly those that include diagnosis of severe mental illness and use of drugs for psychosis (eg, QRISK3 calculator),[290] inform decisions about the initiation of statin therapy.[291] The pharmacological management of dyslipidaemia in patients with severe mental illness should follow guidelines used in the general population (panel 3). No strong evidence is available to support targeting hypertriglyceridaemia therapeutically to decrease cardiovascular risk.

Sinus tachycardia

Sinus tachycardia in patients with severe mental illness could be a feature of the illness, of drug withdrawal, or of an acute drug reaction (eg, serotonin syndrome or neuroleptic malignant syndrome). Psychotropic-related tachycardia is persistent, and usually dose-related.[295] If dose reduction or switching medication is not feasible, and inappropriate sinus tachycardia has been confirmed (including a 24-h ECG), the first-line treatment is a cardioselective β blocker (eg, atenolol 25–100 mg per day) with uptitration until the heart rate normalises (60–100 beats per min). If β blockers are not tolerated (eg, in patients with postural hypotension), or are ineffective, then ivabradine (5·0–7·5 mg twice a day) can be introduced.[296] Ivabradine has been shown to be effective and tolerated in clozapine-induced tachycardia.[297]

Panel 3: **General principles for prescribing antihypertensives and statins to people with severe mental illness**

Antihypertensives

- If the patient has no indications for a specific medication, then any of the following four medication classes can be used as first-line treatment:[292] thiazide diuretics, long-acting calcium-channel blockers (eg, amlodipine), angiotensin-converting enzyme inhibitors, and angiotensin II receptor antagonists
- A thiazide-like diuretic or long-acting dihydropyridine calcium-channel blocker should be used as the initial monotherapy for black patients[293]

Statins

- Consider using a cardiovascular disease risk assessment tool (eg, QRISK3 calculator)[290] to guide whether statins should be used; measure total and HDL cholesterol to achieve the best estimate of cardiovascular disease risk[294]
- Before offering statins to the patient for primary prevention of cardiovascular disease, discuss the benefits of lifestyle modification, and optimise the management of other modifiable cardiovascular disease risk factors, if possible
- Offer statin therapy (eg, atorvastatin 20 mg once a day) for primary prevention of cardiovascular disease if the QRISK3 assessment tool shows that the individual has a 10-year risk of developing cardiovascular disease of 10% or higher[294]

Postural hypotension

In addition to the causes of postural hypotension that exist in the general population, it can be related to taking psychotropic medication, notably clozapine and quetiapine.[298] If increased fluid intake and salt consumption are ineffective, a dose adjustment or switch of the responsible psychiatric medication should be considered if safe to do so. If dose adjustment or medication switch is not feasible, non-pharmacological therapy (appendix p 22) with regular blood pressure monitoring should be undertaken.

Extrapyramidal side-effects

Around 10% of individuals who are taking antipsychotic medications have acute dystonia.[299] It is more common in antipsychotic-naive individuals, and can occur rapidly after the initiation of the drug for psychosis. Acute dystonia can be treated with an anticholinergic medication (eg, benzatropine), which is given orally, intramuscularly, or intravenously, depending on urgency. Parkinsonism is seen in approximately 20% of individuals taking antipsychotic medications.[300] If changing medication or reducing the dose is not effective or feasible, patients can be given an anticholinergic medication. The risk of akathisia varies for different drugs for psychosis, but is estimated to occur in 25% of individuals taking first-generation antipsychotics.[301] If dose reduction of the causative medication is unsuccessful, a switch to quetiapine, olanzapine, or clozapine can be considered.[302,303] Other treatments include β blockers (eg, propranolol 30–90 mg per day),[304] 5-hydroxytryptamine receptor 2 antagonists (eg, mirtazapine 15 mg per day, mianserin 30 mg per day, or cyproheptadine 16 mg per day),[304–306] antimuscarinics (eg, benzatropine 6 mg per day),[307] and benzodiazepines (eg, clonazepam 0·5–3·0 mg per day).[304] Tardive dyskinesia occurs in 5% of patients per year of exposure to drugs for psychosis.[251] If tardive dyskinesia occurs, it is recommended that anticholinergics are stopped and treatment is rationalised (ie, stopping the causative drug or reducing the dose), with clozapine most likely to provide symptomatic relief.[308] Adjunctive treatments include tetrabenazine,[309] and novel vesicle monoamine transporter type 2 inhibitors that have been approved by the US Food and Drug Administration, such as valbenazine and deutetrabenazine.[310]

Anticholinergic effects

The first-line management of anticholinergic ADRs of drugs for psychosis is dose reduction, if it is feasible.[298] For constipation caused by an anticholinergic-related reduction in gastric motility,[311] stool softeners (eg, macrogols or docusates) and a stimulant laxative (eg, senna) might be effective.[312] For patients taking clozapine, sialorrhoea is common. Augmentation with diphenhydramine or benzamide antipsychotics (eg, amisulpride) can ameliorate sialorrhoea.[313]

Sexual side-effects

Sexual side-effects can include reduced libido, delayed or blocked ejaculation, erectile dysfunction, decreased orgasm, persistent genital arousal, lactation, and numbness of the vagina or nipples. Patients with sexual side-effects should be assessed by examining prolactin concentration, concomitant medications, and comorbid causes (which can be psychological or physical—eg, diabetes or cardiometabolic disease).[298] If prolactin is elevated, the antipsychotic dose might need to be reduced or the drug might need to be switched. Alternatively, low-dose aripiprazole could be prescribed.[298] Patients who are taking SSRIs and have sexual dysfunction could be switched to another drug for depression, or given a trial of bupropion or sildenafil, if appropriate.[314]

Thyroid disease

In patients with hyperthyroidism who are taking lithium, a pertechnetate scan might be required to determine the cause of the thyroid disorder. Graves' hyperthyroidism or toxic multinodular goitre can be treated with thionamides, radioiodine, or surgery, whereas if the patient has lithium-induced thyroiditis, cessation of lithium should be considered.[267] Lithium-induced hypothyroidism can occur in the presence or absence of goitre. When lithium-induced

hypothyroidism is present, treatment with levothyroxine is indicated, according to general guidelines for the management of primary hypothyroidism.[315] Lithium-induced goitre requires an ultrasound examination to assess for diffuse versus nodular enlargement, and where appropriate, fine needle aspiration should be done to guide diagnosis. Levothyroxine might stabilise or reduce lithium-induced goitre.[316] Because of the high incidence of thyroid disease in patients who are taking lithium, baseline clinical thyroid examination and serological assessment of thyroid function is recommended, with at least annual monitoring during treatment. The development of thyroid dysfunction while taking lithium does not usually require lithium therapy to be stopped; the risks and benefits of continuing treatment should always be considered.

Renal disease

Lithium-induced nephrogenic diabetes insipidus, with associated polyuria and polydipsia, can affect a patient's quality of life. It is usually at least partially reversible with cessation of lithium, although it can be permanent after prolonged therapy.[317] If ongoing lithium treatment is required and the patient only has a mild-to-moderate renal-concentrating defect, the introduction of amiloride (which is thought to reduce the accumulation of lithium in collecting tubule cells) can reduce urine volume, increase urine osmolality, and improve responsiveness to antidiuretic hormone.[318] Thiazide diuretics with a low-sodium diet have also been found to have a paradoxical effect of reducing urinary output in nephrogenic diabetes insipidus.[319] For patients with chronic kidney disease secondary to chronic interstitial nephritis, lithium cessation might be indicated if renal insufficiency progresses. Some renal function might be recovered after discontinuation of lithium, although progressive renal failure can occur.[320] Regular monitoring of renal function is required, and monitoring of other risk factors for renal failure (eg, hypertension and diabetes) is also important.

Nicotine and smoking cessation

Smoking, and its associated physical morbidity, is a key contributor to the excess mortality of individuals with mental illness.[321,322] Therefore, reducing smoking rates is a priority. However, clinicians should be aware that abrupt smoking cessation can change the pharmacokinetics and pharmacodynamics of many psychotropic medications (eg, increasing blood concentrations of clozapine, and to a lesser extent olanzapine and fluvoxamine). Patients who are planning to stop smoking should be followed up closely; plasma concentrations of medications should be monitored, if possible, and appropriate dose adjustments should be made.

In the general population, nicotine replacement therapy increases the odds of successful smoking cessation by 1·5–2·0 times, with good evidence of efficacy in patients with mental illness.[323] Nicotine replacement therapies should be used for approximately 8–12 weeks. Different preparations are available, including sublingual tablets, gum, patches, nasal spray, inhalators, lozenges, and electronic cigarettes (e-cigarettes). Bupropion and varenicline can increase the likelihood of successful smoking cessation without increasing the risk of neuropsychiatric events in people with severe mental illness.[324]

In conclusion, the burden of ADRs associated with psychotropic medications is important to consider in the context of treatment effectiveness and patient acceptability. Drugs for psychosis (or antipsychotics) are the best evidence-based treatments for psychotic disorders, and lead to lower all-cause mortality in schizophrenia than giving no treatment.[325] Mood stabilisers are the most effective treatment for bipolar affective disorder,[263] and drugs for depression (or antidepressants) have an important role in the treatment of depression.[326] Careful and regular monitoring of laboratory and clinical parameters could help to identify ADRs early, and prevent the development of iatrogenic comorbidities. We would advise against ceasing or switching psychotropic treatments to modalities that are less effective without careful consideration of the risk of relapse. Involvement of the patient in treatment decisions is important when balancing the effectiveness of a medication against its ADRs.[327]

Part 4: Multidisciplinary approaches to multimorbidity

Lifestyle interventions: what works?

Modifiable lifestyle factors, such as physical activity, diet, and smoking, are increasingly recognised as being fundamental to both physical and mental health. Interventions targeting these modifiable risk factors, delivered by practitioners with specific expertise, are referred to as multidisciplinary lifestyle interventions. The efficacy of such multidisciplinary lifestyle interventions in reducing the risk of cardiometabolic-related morbidity in the general population is well established.[283] Accordingly, the 2018 WHO guidelines[328] recommend that lifestyle interventions are considered as first-line strategies for the management of physical health (including weight management, cardiovascular disease and cardiovascular risk reduction, and diabetes treatment and prevention) in adults with severe mental illness. However, a broad spectrum of mental disorders, not only severe mental illness, are associated with high rates of cardiometabolic diseases (Part 1) and lifestyle risk factors (Part 2) that are compounded by the medications that are commonly used to treat mental illnesses (Part 3). Thus, a first step in reducing physical health disparities for people with mental illness is the adoption, translation, and routine provision of evidence-based lifestyle interventions as a standard component of mental health care. However, not all lifestyle interventions are equally useful. The efficacy

Panel 4: Key components of lifestyle interventions

Smoking cessation

Challenge: general population approaches have not worked for people with mental illness

- Although smoking rates have substantially decreased for the general population since the mid-1990s, they have remained high for people with mental illness;[329] as a result, people with mental illness now consume around half of all cigarettes sold in the USA, Australia, and the UK[321,330]
- People with mental illness are as motivated to stop smoking as people without mental illness, but they are more nicotine-dependent and less likely to seek out and receive appropriate interventions tailored to their needs[331,332]
- Smoking-related deaths disproportionally affect people with mental illness, and smoking is a leading cause of the premature mortality observed in this population[321,322]

Emerging solution: specialised cessation interventions

- Evidence on pharmacological interventions shows that they could be effective; for instance, a 2016 meta-analysis[324] showed that bupropion and varenicline were the most effective interventions for smoking cessation for people with severe mental illness, and both resulted in a five times increase in smoking cessation compared with placebo treatments
- For non-pharmacological interventions to be effective, they must account for the additional barriers to treatment that people with mental illness can have (eg, cognitive impairments);[333] for instance, the SCIMITAR+ programme is a candidate model of a bespoke smoking cessation intervention for people with severe mental illness, which was developed with service users to address the needs of this population[334]
- Policy-level interventions can also be implemented; for instance, in 2016 NHS England announced that all mental health services would become smoke free, which included a ban on smoking on mental health wards and hospital premises, and the dissemination of smoking cessation interventions throughout community care.[335] Initial data suggest that smoking bans and bespoke smoking cessation programmes are well received in inpatient settings, and they could have broader benefits by supporting a culture of physical health and wellbeing within mental health services[336]

Future research priorities: improve the accessibility and timing of cessation interventions

- Training on smoking cessation is now freely available online for health-care professionals, which could increase access to evidence-based interventions for people with mental illness; for instance, a concise e-learning tool on smoking from the National Centre for Smoking Cessation and Training[330] could help front-line mental health staff to deliver smoking cessation advice
- Electronic cigarettes (e-cigarettes) are already widely used among people with a range of mental health disorders,[337] and are a potentially useful tool for reducing smoking-related deaths. The UK Science and Technology Committee has advised mental health trusts to allow e-cigarette use on their premises; however, e-cigarettes are not authorised or available in many countries, and further research is required to establish the health outcomes of using e-cigarettes as a smoking harm-reduction intervention[338]
- Early intervention for smoking is feasible,[339] and could improve cessation rates and long-term physical-health outcomes[340]

(Continues on next page)

and effectiveness of multidisciplinary lifestyle interventions are impacted by both their content and timing of delivery. Some key considerations for the individual components of multidisciplinary interventions are presented in panel 4.

Although it might seem counterintuitive to dedicate intensive resources to individuals with relatively good metabolic health, focusing on cardiometabolic protection in at-risk populations could be the optimal approach for lifestyle interventions (panel 2). The Diabetes Prevention Program (DPP),[283] developed and evaluated in the USA, is an example of a gold-standard lifestyle intervention (panel 5). The key features of DPP include individual case managers; frequent face-to-face contact with participants; a structured educational component that includes behavioural self-management strategies; supervised physical activity sessions; a maintenance intervention that combines group and individual approaches, motivational strategies, and individualisation through a so-called toolbox of adherence strategies; tailoring of materials and strategies to address ethnic diversity; and an extensive network of training, feedback, and clinical support.[283]

The primary study on DPP[284] recruited 3234 adults without diabetes who were at risk of developing type 2 diabetes (established via multiple risk factors); patients were assigned to receive placebo, metformin, or a lifestyle intervention that involved at least 150 min of physical activity per week with the goal of at least a 7% weight loss. The lifestyle intervention resulted in a 58% reduction in the development of type 2 diabetes over the 3-year study, with 4·8 cases of diabetes per 100 person-years observed in the lifestyle intervention group, compared with 11·0 cases in the placebo group (incidence in the metformin group was 7·8 cases per 100 person-years).[283,284] Furthermore, both the clinical benefits and cost-effectiveness of the DPP lifestyle intervention were maintained over a 10-year follow-up, as compared with metformin as the control condition.[361,362] These results show that lifestyle interventions with beneficial

(Panel 4 continued from previous page)

Physical activity

Challenge: patients find it difficult to stay motivated

- Weight loss is often a primary motivation factor for physical activity,[341] but exercise alone in the absence of dietary modification will not reliably reduce a patient's bodyweight, particularly in the short term;[342] exercise can attenuate further weight gain, but weight maintenance might not be a strong motivator for people with mental illness, particularly if they were overweight before the onset of mental illness, which can result in disengagement with exercise

Emerging solution: fitness goals designed by fitness professionals

- Rather than focusing on weight loss, improving fitness might be a more motivating[341] and achieveable[343,344] goal for exercise interventions for people with mental illness; improving fitness can also have important health benefits, because even a modest improvement is associated with a 15% decrease in mortality in the general population[345]
- Exercise interventions delivered by qualified exercise professionals (with a university qualification in exercise prescription, such as physiotherapists or exercise physiologists) have significantly greater physical and psychological benefits and adherence compared with interventions delivered by non-specialised practitioners.[346–348] In addition, the integration of qualified exercise professionals into mental health services could ensure that mental health staff have the knowledge and training to give clear advice on exercise

Future research priorities: varied and personalised exercise programmes

- Although most research on physical activity has focused on aerobic exercise, evidence from the general population increasingly shows that strength and resistance training or so-called high-intensity interval training can have beneficial effects for both metabolic and mental health[349–351]
- Given that enjoyment and satisfaction are key factors in determining exercise adherence,[352] offering a range of exercise options that accommodate patient preferences and goals will be important for establishing sustainable and engaging exercise routines

Diet

Challenge: additive effect of medication and diet

- Dietary risks are a leading risk factor for cardiometabolic disease identified by the Global Burden of Disease Study;[353] for people with mental illness, the risk is exacerbated[128,138] because of the side-effects of psychotropic medications (eg, excessive or insatiable hunger, cravings for high-calorie, low-nutrient foods),[183,354] an insensitive reward system and poor cognitive control,[355] and food insecurity and financial constraints[356]

Emerging solution: dietary support

- Improved diet quality[357] and reduced bodyweight[358] are both associated with decreased mortality in the general population
- Dietary interventions in people with mental illness are more effective if they are delivered by specialist clinicians, such as dietitians, and at an early stage of treatment;[359] cardiometabolic care and subsequent dietary intervention should be implemented within a multidisciplinary framework[360]

Future research priorities: personalised pathways to health and fitness

- As with exercise, the most effective dietary regime for people with mental illness will be one that is sustainable; future research might identify strategies that alleviate the obesogenic effects of psychotropic medications, and that address the insensitive reward system and poor cognitive control of some people with mental illness
- Links between dietary intake, the microbiome, inflammation, and obesity are increasingly becoming clear, and could provide new ways to improve physical outcomes for people with mental illness

components (panel 5) can reduce the incidence and burden of cardiometabolic diseases when used as a preventive strategy in at-risk populations. Notably, the DPP has also been adapted and successfully delivered in primary-care settings.[363]

Considering the increased metabolic and lifestyle risk observed across multiple classes of mental health disorder (Parts 1 and 2), the DPP could be adapted for people with mental illness and made available through primary care, on a referral basis. The use of such transdiagnostic, evidence-based, and cost-effective lifestyle interventions could help to protect the cardiometabolic health of people with mental illness who are treated in primary care settings. Furthermore, evidence increasingly shows that supervised exercise training (a key component of the DPP) can improve psychiatric symptoms, cognition, and functioning across a range of mental health diagnoses.[346,364,365] Therefore, integrating the DPP principles into mental health care could improve overall recovery, not only metabolic health. However, the majority of DPP studies to date have excluded individuals with a "major psychiatric disorder which, in opinion of clinic staff, would impede conduct of the DPP".[284] The DPP needs to be analysed as a transdiagnostic lifestyle intervention for people with mental illness through primary care services and specialised mental health

Panel 5: **Lifestyle intervention guidelines adapted from the Diabetes Prevention Program[283]**

Measurable and specific goals
- Maintain bodyweight or reduce by between 5% and 7% of total bodyweight
- Reduce calorie intake (500–1000 kcal less than the calorie intake needed for weight maintenance per day, and a maximum of 25% of calories from fat), and improve diet quality
- Increase the number of minutes of physical activity (meet recommendations of 150 min per week of moderate-to-vigorous physical activity)
- Replace sedentary behaviour with light intensity activity as often as possible
- Increase cardiorespiratory fitness
- Cessation of smoking

Case managers or lifestyle coaches with university (or equivalent) training in nutrition and dietetics, exercise prescription, or behavioural change
- Allow for individualised programme design and delivery
- Offer a combination of group sessions and one-on-one sessions
- Provide supervised exercise and nutrition sessions at least two times per week (eg, community centre sessions, neighbourhood group walks, or one-on-one personal training)
- Do relevant assessments at regular intervals
- Ensure lifestyle coaches have training in psychopathology and the basic principles of working with people with mental illness

Frequent contact and ongoing intervention
- Deliver core curriculum on topics including nutrition (modifying energy intake), physical activity (and sedentary behaviour), and behavioural self-management (barrier identification and problem solving)
- Provide a flexible maintenance programme with supplemental group classes
- Provide motivation campaigns and restart opportunities

Individualisation through a toolbox of adherence strategies
- Self-monitoring of outcomes and behaviours, such as weight, physical activity, sedentary behaviour, and dietary intake (fat and calorie intake)
- Barriers to treatment are identified and addressed with simple, individualised resources (eg, a cookbook might be given to a patient trying to improve their diet)

Strategies that are adapted for culturally and ethnically diverse groups
- Translation of documentation to local languages
- Identification of culturally appropriate resources and intervention approaches
- Cooking groups that allow for dietary restrictions or religious requirements

Local and national network of training, feedback, and clinical support
- Appropriate training of existing and emerging mental health staff
- Clear referral pathways and the integration of lifestyle coaches into a standard multidisciplinary mental health team
- Monitoring and evaluation of effectiveness and adherence

services. Although the core principles of the DPP are crucial to its design and delivery, more support is likely to be required by people with severe mental illness compared with the amount needed to effect change in the general population. A randomised controlled trial of an adapted version of the DPP for people with severe mental illness found significant reductions in obesity and other metabolic risk markers associated with antipsychotic treatment compared with usual care.[366] Conversely, in some situations, adaptation of evidence-based programmes for people with mental illness can threaten their effectiveness. For instance, reducing the amount or frequency of interventional components, because of conflicting demands on the priorities and workload of mental health staff and diagnostic overshadowing,[20] could mean the programme is insufficient to effect change for those patients. The challenge for policy makers, clinicians, and service providers is to apply established, effective principles of behaviour change to people with mental illness, particularly with regards to adopting a framework of early intervention and prevention.[13]

Implementing lifestyle interventions for severe mental illness

A 2019 meta-review[285] aggregated data from 27 meta-analyses of physical health interventions for people with schizophrenia. Exercise, diet, and broader lifestyle interventions (eg, sleep hygiene, smoking cessation strategies, motivational interviewing) had significant benefits for multiple cardiometabolic outcomes (including bodyweight, waist circumference, blood pressure, and glucose and lipid markers), with a similar efficacy to pharmacological management of metabolic health.[285] However, the clinical trials from which these efficacy data were predominantly derived could reduce the generalisability and external validity of the findings, because trials are rarely done under real-world conditions and are typically resourced differently to routine clinical care.[367]

Few studies have been done on the effectiveness, pragmatic implementation, or sustainability of lifestyle interventions in people with mental illness.[368] Furthermore, several large-scale clinical trials in people with mental illness have had null findings. To provide guidance on effective implementation of lifestyle interventions within mental health services, the interventions that are associated with negative and positive outcomes in trials should be considered. Trials of lifestyle interventions in mental health care often do not meet all the principles of programmes such as the DPP (appendix p 23). Specific aspects of the DPP that have been poorly implemented in trials are: (1) using qualified exercise professionals and dietitians to deliver lifestyle interventions, (2) providing sufficient access to supervised exercise services, and (3) ensuring that existing mental health staff are familiar with the lifestyle interventions. Large-scale clinical trials of lifestyle interventions addressing multiple risk factors in people with mental illness are described in the appendix (pp 24–30).

The high acceptability of lifestyle interventions among patients[365,366,369,370] means that they are a novel route to reach typically disengaged service users in more traditional mental health treatment. For example, providing gym-based resistance exercise is a potential clinical pathway to care for young people with early psychosis,[369] or veterans

with post-traumatic stress disorder.[371] However, an important consideration is how such programmes are applied across different clinical and broader public health settings. Flexibility in delivery, a focus on practical exercise and dietary advice, and provision of support to integrate the lifestyle measures into daily life are highly recommended.[372,373] Further research is needed on how interventions are delivered; a mixed model that involves both online and face-to-face delivery is a potentially balanced and cost-effective way forward (appendix pp 31–34).[206,193]

Training health professionals for a culture shift

Multidisciplinary teams in mental health settings are rapidly evolving to include allied health professionals with expertise in nutrition, physical activity, behaviour change, and other aspects of mental health, such as psychoeducation and mindfulness training. For this transition to be successful, allied health practitioners should receive at least introductory training in psychopathology and in the principles of working with patients with mental illness. Accordingly, the curriculum for health professionals, including dietitians, physiotherapists, and exercise physiologists should be updated to reflect the increasing role for such professionals within mental health teams.[374]

In addition, medical and mental health professionals should receive training on working with allied health professionals in an integrated manner, and understanding the principles of lifestyle interventions. The importance of training medical students in so-called lifestyle medicine is increasingly being recognised globally.[375] Efforts towards integrating lifestyle interventions within routine mental health care should avoid an isolated focus on individual-level behavioural changes, and should also include broader changes to service structure, delivery, and culture (see Part 5). For instance, evidence suggests that medical and nursing practitioners who have healthy lifestyle behaviours are more likely to recommend such behaviours to patients.[376] Advances in implementation science could also provide ways to ensure that lifestyle interventions have meaningful benefits for patient outcomes.[368]

Barriers, opportunities, and future research

Some of the issues, emerging solutions, and research priorities for smoking cessation, physical activity, and dietary interventions for people with mental illness are presented in panel 4. For all types of lifestyle intervention, a gradient of intervention intensity, or so-called stepped care, needs to be considered. For example, intervention intensity might vary between individuals, treatment settings, and cultures, and could depend on the readiness to provide lifestyle interventions, particularly in low-resource settings.

Even in high-resource settings, only providing intensive lifestyle interventions through mental health services could cause issues for individuals who do not attend mental health centres frequently; those who have been discharged might find it difficult to stay engaged with lifestyle changes. One strategy for sustaining engagement with health behaviour interventions is the use of primary care referral schemes. For example, exercise referral schemes for people with mental illness typically involve health-care providers referring individuals to community-based organisations to provide free (or discounted) access to a wide range of fitness activities, facilities, and expertise through community leisure centres and services. Community-based interventions might also be a non-resource-intensive strategy for maintaining physical activity behaviour in a way that complements and supports clinician-led strategies. Exercise referral has already been introduced through multiple large-scale implementation projects for sedentary adults in primary care in the UK, although only small beneficial effects have been found to date.[172,377] However, preliminary data show that community exercise can be beneficial and engaging for young people with mental illness, including for those with severe conditions.[378,379] Community-based diet programmes, such as Weight Watchers, are cost-effective weight-loss interventions when delivered via primary care to obese individuals.[370,380] Research is now warranted to determine the suitability and effectiveness of such programmes for psychiatric populations.

Mobile device health (or mHealth) technologies could provide new routes for applying adapted versions of programmes such as the DPP in patients with mental illness. For example, a pilot study[381] found that FitBit activity trackers could potentially be used alongside fitness applications (apps) in people with schizophrenia to deliver DPP-based interventions, with features such as daily prompts, motivational messages, and self-determined step-count goals. Participants found the technology to be engaging, motivating, and empowering,[381] but a small sample size (n=25) makes it difficult to determine efficacy. Although they have only been evaluated in small-scale pilot studies to date, mHealth technologies present potential opportunities to deliver a wide range of novel, scalable, and sustainable lifestyle interventions for people with mental illness. mHealth interventions could also be disseminated easily, even in low-resource settings. Therefore, further development and evaluation of evidence-based mHealth interventions for improving physical health in people with mental illness is warranted.

In conclusion, the principles of existing gold-standard prevention programmes, such as the DPP, can be used as a benchmark for the implementation and maintenance of lifestyle interventions as an integrated, routine component of mental health care (panel 5). However, programmes might need to be adapted to specific care settings, and for particular patient needs. Efforts are required to translate the DPP principles into both (1) preventive, transdiagnostic lifestyle interventions

available through primary care, and (2) intensive interventions for specialist services. If these efforts are successful, effective programmes for protecting the cardiometabolic health of people living with mental illness could be implemented.

Part 5: Innovations in integrating physical and mental health care

Introduction

Social determinants, including poverty, poor education, unemployment, homelessness, and childhood abuse,

	Directions and rationale	Actioned by
Treating syndemics	Examining how broader societal factors affect the interaction between physical and mental health conditions within a given region can provide insight into these comorbidities and their risk factors; in turn, this can inform the development and implementation of preventive strategies and interventions for chronic health conditions within a given socioeconomic setting	Led by public health; developed and implemented by national and local health-care providers
Preventing multimorbidity	Evidence-based integrated care should be provided from the onset of mental illness; changes are needed at the primary, secondary, and tertiary levels of care to reduce the prevalence and impact of physical health conditions in people with mental illness (panel 5)	Led by public health; delivered by primary, secondary, and tertiary care, and community groups
Primary and parallel care	Primary care is the first point of contact for most patients, and is an important part of care after discharge from specialist services. Implementing integrated models of mental and physical health care through primary care services could be effective for efficient management of physical health comorbidities in people with mental illness; however, the management of comorbid substance use disorders might depend on improving accessibility, referral pathways, and quality of dedicated parallel services	Led by commissioners of health-care organisations; developed via culturally sensitive integrated care models designed by local health professionals; and implemented by health-care practitioners
Implementation in low-income and middle-income countries	Incorporating integrated care models within the emerging mental health services of low-income and middle-income countries is important for reducing physical health inequalities for people with mental illness, and might also provide a more cost-effective approach to health-care provision in these settings	Led by commissioners of health-care organisations; developed via culturally sensitive integrated care models designed by local health professionals; and implemented by health-care practitioners
mHealth technology solutions	mHealth technology and other digital technologies provide many novel methods for promoting physical health and delivering interventions remotely. The low cost, scalability, and global accessibility of such approaches are highly appealing, particularly in low-income and middle-income settings; while the evidence-base is still nascent, this can be considered a high-priority area for future research	Led by mental health commissioners; developed with communities, researchers, and industry; and implemented by health-care practitioners

mHealth=mobile device health.

Table 4: **Considerations and directions for integrating health care**

	Year	Organisation	Illness	Outcomes
Management of physical health conditions in adults with severe mental disorders: WHO guidelines[328]	2018	WHO	Severe mental illness	Morbidity, premature mortality
Health matters: reducing health inequalities in mental illness[330]	2018	Public Health England	Severe mental illness	Morbidity, premature mortality
Bringing together physical and mental health: a new frontier for integrated care[386]	2016	King's Fund, London, UK	All mental illness	Cardiometabolic health
Improving physical healthcare for people living with severe mental illness in primary care: guidance for CCGs[387]	2018	NHS England	Severe mental illness	Premature mortality
The physical health of people with mental health conditions and/or addiction[388]	2017	Te Pou, Auckland, New Zealand	Severe mental illness	Mortality, morbidity
Excess mortality in persons with severe mental disorders: a multilevel intervention framework and priorities for clinical practice, policy, and research agendas[121]	2017	World Psychiatric Association	Severe mental illness	Premature mortality
Helping people with severe mental disorders live longer and healthier lives[149]	2017	WHO	Severe mental illness	Premature mortality
Improving the physical health of adults with severe mental illness: essential actions[389]	2016	Royal College of Psychiatrists	Severe mental illness	Premature mortality

CCG=clinical commissioning group.

Table 5: **Key resources on the integration of physical and mental health**

increase the risk for both mental and physical illnesses.[182,382] The relationships between adversity, physical health, and mental health are complex, and risk factors can act synergistically to reinforce disadvantage and disability.[182] For instance, people with mental illness are more likely to be in poverty and to have cardiometabolic and infectious diseases (see Parts 1 and 2), and conversely, chronic physical health conditions and social deprivation are key risk factors for mental illness.[182,383,384] A 2017 *Lancet* Series[385] on the co-occurrence of chronic health conditions described how syndemic frameworks could be used to understand how health risks and comorbidities interact with one another within the broader environmental context. For instance, epidemiological research has applied syndemic frameworks to characterise the complex relationships between poverty, diabetes, mental illness, and infectious diseases in low-income settings.[178] This syndemic approach highlights that national and local conditions affect the interplay between physical and mental health, and shows the importance of taking social, political, and economic factors into account when designing public health interventions, or implementing changes to health services (table 4).[179]

Numerous national and international health-care and advisory bodies are now focusing on health inequalities in people with mental illnesses. Resources from these organisations (table 5, appendix pp 35–42) present new ideas and best practice approaches for improving the integration of physical and mental health care at the individual, health service, and societal levels. Several key health organisation guidelines[149,330,386] and academic articles[179] have included case studies of new local and national initiatives that account for the surrounding environmental conditions and improve the integration of physical and mental health care. As well as detailing required improvements to health care for existing patients, some sets of guidelines discuss approaches to prevention of chronic physical and mental health conditions.[330,386] Wide-scale adoption and implementation of strategies that aim to prevent chronic conditions (physical or mental), multimorbidity, and risk of premature mortality are required to reduce health inequalities for patients with mental illness in the future. Some examples and considerations for prevention at the primary, secondary, and tertiary levels are presented in panel 6.

Panel 6: Prevention of physical health morbidity and mortality in individuals with mental illness

Primary prevention

Primary preventive strategies aim to provide people with the tools needed to live a healthy lifestyle[190] by avoiding smoking, alcohol and substance misuse, poor diet, and physical inactivity. Among those with mental illness, a healthy lifestyle should ideally be adopted in the early stages of illness to build healthy habits, and to protect physical health as much as possible. Primary prevention strategies need to be adapted for people with mental illness, because public health strategies that are effective in the general population are not always as effective for those with mental illness. Separation of patients into diagnostic categories (eg, depression, anxiety, and schizophrenia) is not an effective way of determining the best primary prevention strategies for physical health. Instead, transdiagnostic approaches that account for individual-level differences (eg, gender, cultural and ethnic identity, lifestyle risk factors, medication use, and social circumstances) will be more effective (see Part 2).

Secondary prevention

Secondary preventive strategies, such as screening and preventive treatments, are often underused in people with mental illness.[216–218,222] Many people with mental illness are affected by comorbid physical diseases, which can be present from illness onset (see Part 1). Population-scale data from NHS England[390] indicate that physical health intervention is required even from childhood for those with mental illness. At the age of 11–19 years, children with mental illness are three times as likely to be obese as children without mental illness.

Tertiary prevention

Tertiary preventive strategies involve improving treatment and recovery from disease. To be engaging and responsive, integrated care services require flexibility from individual clinicians and service planners. For example, cardiac mortality among patients with severe mental illness is significantly reduced by efficient administration of cardioprotective medications after first cardiac events.[227] This supports the claim made in new guidelines[328,387] that tertiary preventive measures for people with mental illness are underused, despite their potential to improve health and reduce premature mortality.

Improving integrated care for people with mental illness

Effective management of multimorbidity requires integrated care to be provided in a holistic manner,[391] so that common risk factors and the bidirectional interaction between physical and mental health disorders, and the treatments for each, can be addressed together.[386] Internationally, health organisations agree that primary care is the optimal setting for addressing and coordinating the management of multimorbity.[392,393] In many countries, most people with mental illness first present to the health system through primary care, and most mental health care is delivered in primary care.[179] Patients requiring specialist mental health services still need ongoing engagement with primary care to deliver and coordinate other aspects of their health care, including prevention and management of comorbid physical illness. The aim of primary care is to provide equitable, accessible, safe, effective, comprehensive, person-centred care that meets the needs of individuals, families, and communities throughout life.[394] Therefore, primary care is ideal for managing multimorbidity,

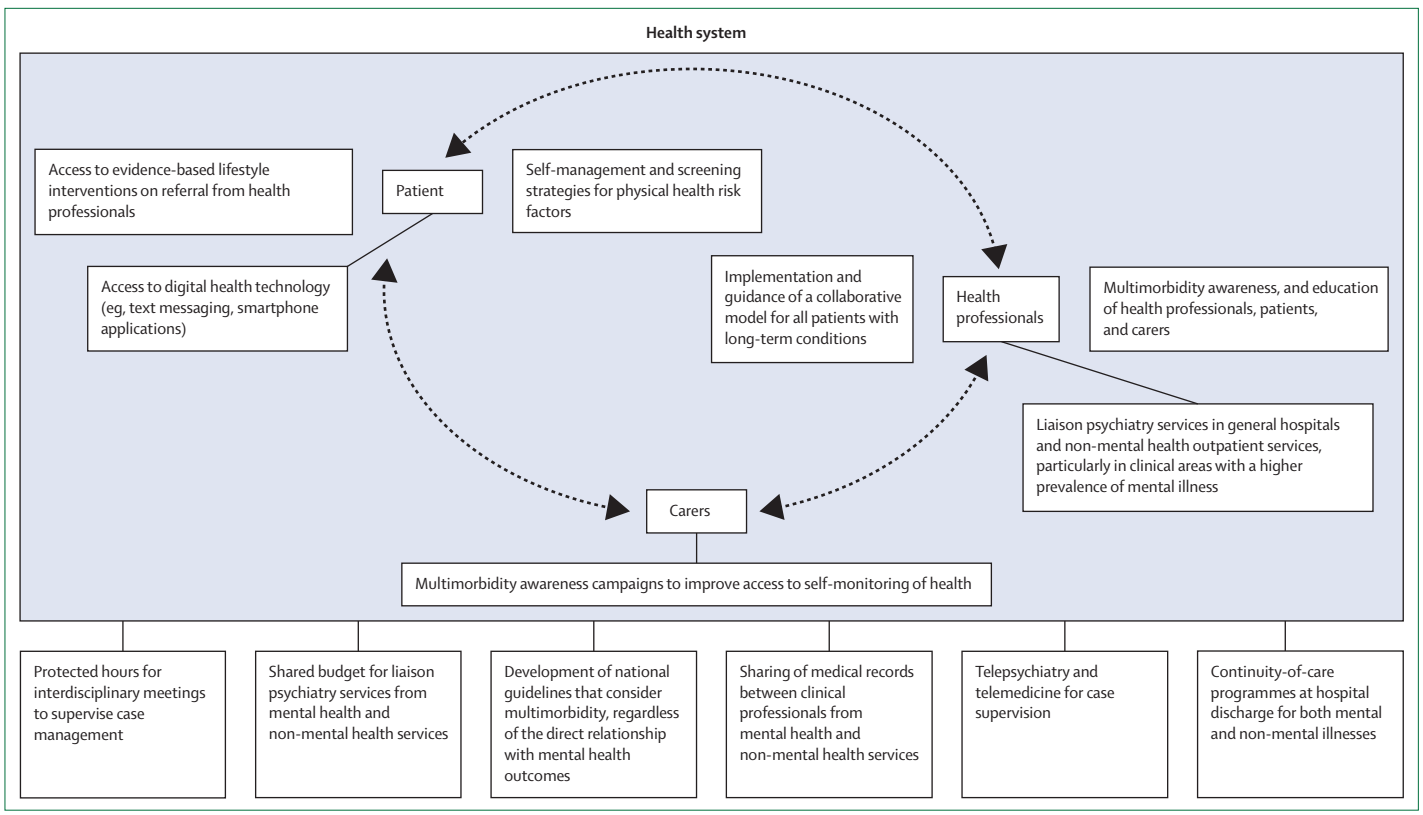

Figure 3: **Proposed model of collaborative care for people with physical and mental comorbidities**

which requires an individualised approach that not only addresses the increased burden of multimorbidity, but also manages competing or conflicting treatment needs by accounting for individual preferences and treatment priorities.[392] Further discussion on how primary care settings should provide physical health care for people with mental illness is presented in the 2018 guidelines from NHS England[387] (appendix p 38).

As a minimum level of integration, health providers should communicate with each other frequently to ensure the safety and effectiveness of treatment. Ideally, services should take further steps towards integration, aiming for multidisciplinary care that is structured, comprehensive, and proactive. However, integration of this type usually involves overcoming bureaucratic barriers at the service level, such as difficulties in sharing medical records. Governance and funding issues can also restrict the provision of coordinated health care (figure 3). A 2016 report[386] from the King's Fund in the UK presents an aspirational approach towards improving integrated care across a range of physical and mental health conditions, with advice on overcoming common barriers to implementation. For instance, the report recommends a curriculum redesign to give all health professionals a common foundation in mental and physical health and encourage a whole-person approach, and creating opportunities for skills transfer between professionals (appendix p 35). Some examples of integrated care models, and their evaluated outcomes, are described in panel 7.

Managing substance comorbidity and promoting smoking cessation

Across many mental illnesses, the use of alcohol, tobacco, and illicit drugs is more prevalent than in the general population, and is associated with worse physical and mental health outcomes (table 2).[405–407] A bidirectional relationship exists between substance misuse and mental illnesses, because substance misuse can cause and exacerbate mental illness, yet it is often used by patients as a way of reducing anxiety, dysphoria, and other symptoms.[408] Genetic risk factors for schizophrenia also appear to predispose individuals towards illicit drug use.[409]

Addressing substance misuse within mental health services should be a high priority.[408] However, many services have no standardised screening for substance use, and mental health clinicians are often not trained to treat substance misuse.[410] For example, in high-income countries, people with severe mental illness report wanting to quit smoking as much as the general population, but are unlikely to be supported to do so.[331,332] Furthermore, patients are sometimes excluded from drug treatment programmes or mental health

services if they have comorbid drug or alcohol use disorder.[411]

Because of the complexity of comorbid mental health and substance use disorders, patients need individualised treatment that has an emphasis on overcoming the barriers associated with mental illness and enhancing engagement with evidence-based treatments. Readiness for change, cognitive ability, and cognitive distortions resulting from mental illness need to be taken into account. Evidence-based treatments include motivational interviewing, cognitive behavioural therapy, and family interventions (also known as family therapy).[408]

Evidence-based interventions can be a challenge to implement in mental health services that are already struggling to meet demand. Notably, little evidence is available to recommend integrated interventions as compared with sequential or parallel treatment programmes, particularly in alcohol use disorders.[412] Each approach has advantages and disadvantages. One advantage of an integrated approach is that the patient does not need to receive care from two services, whereas a disadvantage is that it requires substantial resources and investment from within the mental health system to train mental health clinicians in the treatment of substance use disorder. An advantage of sequential or parallel treatments is that the interventions are delivered within a highly specialised substance use programme. However, the approach requires coordination and sharing of information between agencies. A clear referral policy between mental health and substance misuse treatment services (including those in primary care) should be developed so that a programme of patient care is delivered consistently and in full.

Regardless of how interventions are provided, investment in screening within mental health services is a priority. Mental health clinicians should be trained to do regular assessments of comorbid substance use, to assess patients' readiness for change, and to provide motivational interviewing. An emphasis on a so-called no wrong door policy for accessing substance misuse treatments, in which everyone is accepted and offered treatment wherever they present, and the development of clear referral policies between mental health and substance misuse treatment services should be a priority.[330]

If cessation of substance misuse is not possible, harm-minimisation strategies should be adopted. For instance, patients might be able to switch to alternative, safer forms of the drug (eg, e-cigarettes, methadone, or buprenorphine and naloxone) or access could be provided to safe injecting facilities. The challenges and innovations regarding smoking cessation interventions for people with mental illness are presented in panel 4. The Royal College of Physicians published a report in 2016 on harm minimisation for those who are unable or find it difficult to quit, which recommended e-cigarettes, nicotine replacement therapy, and other non-tobacco nicotine products.[413]

***Panel 7:* Examples of integrated care for physical and mental illness**

Within the broad category of integrated care, collaborative care models are emerging as effective approaches that can simultaneously reduce costs and improve clinical outcomes and treatment adherence in the management of both mental illness and chronic physical conditions.[395-398] A core component of collaborative care models is the involvement of several health-care professionals working as a team, including a physician, a case manager, and a mental health clinician.[395,396] Although the specific actions vary between models, all collaborative care approaches use structured management plans, scheduled patient follow-ups, and extensive interprofessional communication.[395] Figure 3 shows the potential components of a collaborative care model for improving health management in people with physical and mental comorbidities.

The TEAMcare intervention[399,400] in 14 primary care clinics in Washington, USA, is an example of a collaborative care approach within primary care. TEAMcare was designed for adults with depression plus diabetes, heart disease, or both, and comprised pharmacological care management with integrated behavioural change support delivered by a nurse. Compared with usual care, the TEAMcare intervention resulted in significant improvements in metabolic health over 12 months, with a decrease in the percentage of glycated haemoglobin of –0·56% (95% CI –0·85 to –0·27), a decrease in LDL cholesterol of –9·1 mg/dL (–17·5 to –0·8), and a decrease in systolic blood pressure of –3·4 mm Hg (–6·9 to 0·1). A reduction in Symptom Checklist Depressive Scale score of more than 50% was found in more than three times as many patients in the TEAMcare group compared with usual care (odds ratio 3·37, 95% CI 1·84 to 6·17), as well as improved perceived self-efficacy, and greater patient satisfaction with medical care.[399-401]

The COINCIDE trial[397] tested a psychological intervention for people with depression and comorbid diabetes or cardiovascular disease that addressed behavioural activation, healthy lifestyle, exercise, and diet. This integrated approach resulted in significant improvements in depression and patient satisfaction at 4 months.[173] Health benefits were sustained at a 24-month follow-up, and the intervention was found to be cost-effective.[173] Additionally, evidence from the RAINBOW trial, published in 2019, supports the use of collaborative care models for improving both physical and mental health outcomes in people with common mental disorders and cardiometabolic comorbidities.[402] However, these evaluations of collaborative care models have all been done in high-income settings; similar evaluations in low-income and middle-income settings are needed (see Part 5).

Although collaborative care models have been shown to be effective for people with common mental disorders, the evidence for their use in people with long-standing severe mental illness is conflicting,[174,403,404] and optimal models of integrated care in this group are yet to be found. The PRIMROSE study[174] compared integrated primary care with usual care in 327 people with severe mental illness, and found no significant benefits for HDL cholesterol over 12 months. However, integrated care did have a 12-month mean cost difference of –£824 (95% CI –568 to 1079) compared with usual care, and was found to be cost-effective because of fewer hospital readmissions over a 12-month period.[174]

Innovations in integration for low-income and middle-income countries

In most low-income and middle-income countries, less than 1% of the health budget is spent on mental health,[414] including mental health care within specialist mental health services, general health services, and social care services.[414] As a result, mental health services are poorly resourced; 90% of people who need treatment do not receive any care.[415] Mental health services in low-income and middle-income countries predominantly rely on expensive psychotropic drugs, which are seldom

available, and are associated with various side-effects that require close management (see Part 3).[416] Previously, little attention has been given to the complex bidirectional relationship between physical and mental health, and the relevance of screening, in low-income and middle-income settings.[416,417]

WHO guidelines from 2018 state that health inequalities for people with severe mental illness could be worse in low-income and middle-income countries than high-income countries, because "the resources are inadequate, the institutions are not well managed and access to quality mental health care and physical care is limited".[328] The largest gaps in life expectancy for people with severe mental illness compared with the general population are observed in low-income settings.[5,149] Mental health care systems in low-income and middle-income countries need to be reoriented towards integrated models. However, many low-income and middle-income countries do not have integrated physical health and mental health services, and have poorly developed community-based services, resulting in over-reliance on institutional psychiatric care.[416] In many countries, mental health legislation and policies are outdated.[417] Specific barriers to the development and implementation of integrated mental and physical health policies include: insufficient coordination across different government levels; a shortage of trained staff at all levels of care; a need for commitment from health services; governmental bureaucracy; and shortage of funding. In addition, funding for health services is provided by several different sources, which makes the sharing of decisions and responsibility challenging.[179] As a consequence, in daily clinical practice, mental health providers in community settings do not generally ask about or test for physical health issues because they are not considered to be a priority, and time and resources are limited.[418]

In low-income and middle-income countries, there is an urgent need to increase awareness that patients with mental health illness could have physical health needs, and vice versa.[416] For example, public health campaigns could increase awareness of the links between chronic physical and mental disorders. In a 2016 review[419] of interventions for mental disorders at the population and community levels in low-income and middle-income countries, mass public awareness campaigns and school-based awareness programmes were considered to be good practice, with limited but promising evidence to support their use.

At the system level, the physical health of people with mental illness could be improved by increasing the competencies of existing staff at all levels of care. Although education campaigns on the links between chronic physical and mental health conditions are important tools, bringing about changes to skills and behaviour will require a long-term approach. Multiple training sessions and subsequent top-ups will usually be required, with rolling programmes to support staff turnover.[420] In addition, mental health policies in low-income and middle-income countries need to be changed to make an integrated care model the central focus of mental health care action plans. A review across high-income, middle-income, and lower-income settings[179] presents clear evidence for the rationale and effectiveness of integrated care. The Practical Approach to Care Kit (PACK), which comprises a guide, a training strategy, a health system strengthening intervention, and monitoring and evaluation, is an example of a best-practice approach towards providing universal integrated primary health care.[421] PACK has been successfully implemented in several low-income and middle-income countries, including Botswana, Brazil, Ethiopia, Nigeria, and South Africa.[422] Development of clinical practice guidelines that build on best-practice examples such as PACK and consider the local context, including staff attitudes and available resources, will be crucial in encouraging policy uptake in low-income and middle-income countries. The local context, including prevalent knowledge, behaviours, and attitudes towards mental health conditions, is a good predictor for the success of implementing changes to clinical practice.[420]

Clinical practice guidelines should also incorporate strategies for collaboration between formal primary care and mental health services, and community-based providers, such as traditional healers. Approximately half of individuals seeking formal health care for mental disorders in low-income and middle-income countries choose traditional and religious healers as their first care provider, and this choice is associated with delays in accessing formal mental health services.[423] Based on research into collaboration between traditional healer and biomedical health systems in Uganda,[424] strategies should involve improving clinicians' understanding of traditional healers' explanatory models for illness, and vice versa. Trust between the two types of health-care providers needs to be improved so that they can interact, rather than operating in isolation. In particular, negative attitudes of clinicians towards traditional healers need to be addressed. The quality of care provided by traditional healers needs to be enhanced by improving hygiene practices and eliminating unethical practices.

Task sharing with key community-based providers is a potentially effective implementation strategy in low-resource settings. Task sharing is the process of transferring a task usually delivered by a scarce resource, such as a physician, to a rapidly trained and less scarce resource, such as a health-care worker.[425,426] Research on the implementation of task-sharing collaborative-care models is being done,[427–429] and the findings could improve our understanding of the quality, safety, effectiveness, and acceptability of such strategies for mental health disorders in low-income and middle-income countries. Case studies from non-governmental organisations show that inefficient health system structures can present

barriers to successful task sharing,[427] indicating a need for more collaborative care services. However, whether such approaches will be successful in reducing premature mortality, improving wellbeing, and achieving better social outcomes in low-income and middle-income settings has yet to be fully established.[427]

Digital technologies for people with mental illness

Digital technology plays an increasing role in promoting health, addressing risk factors, and managing physical disease, with growing evidence for its effectiveness. Mobile phones provide a particularly convenient platform for digital health-care delivery (also known as mHealth). WHO estimates that 95% of the global population lives in an area covered by mobile networks, and over 7 billion mobile contracts have been issued, which is one for almost every person on the planet.[430] Smartphone technologies are closing the so-called digital divide (ie, between those who have easy access to computers and the internet, and those who do not) that was previously present in low-income and middle-income countries.[431] Unlike traditional health services that require attendance at a specific time and location, digital technology is available at a time and place that suits the patient.

Technologies as simple as text messaging have been shown to support lifestyle improvement. For example, in the TEXT ME trial of 710 patients with coronary heart disease,[432] patients in the intervention group received four personalised text messages per week for 6 months that provided advice, motivation, and support to change lifestyle behaviours. After 6 months, levels of LDL cholesterol were significantly lower in intervention participants compared with patients who received usual care, with concurrent reductions in systolic blood pressure and body-mass index, significant increases in physical activity, and a significant reduction in self-reported smoking. Further studies to assess the sustainability of these positive changes, and the effectiveness of text messaging in participants who have not yet experienced a cardiovascular event, are underway.[433] Text messaging can also support other important health behaviours, such as medication adherence for people with chronic conditions.[434]

Smartphone apps might promote healthy lifestyle change, but they vary in quality, and the quality of reported evaluation research is also inconsistent.[435] To date, few studies have examined clinical effectiveness or cost-effectiveness.[436] In addition, user engagement could be lower in everyday clinical practice than in trial settings.[437,438] Key strategies for effective user engagement include designing interventions in collaboration with patients, personalisation of interventions, and just-in-time adaptation (in which an intervention supports an individual's changing behaviours and contexts over time).[439] An example is the Australian FoodSwitch app, which uses a smartphone camera to scan the barcode of a food item, and recommends healthier alternatives from a crowd-sourced database of nutritional information.[440]

Several smartphone functionalities could be valuable for improving health, including the recording and analysis of data from sensors measuring activity or biological variables; access to health information via the internet; and the ability to engage with social media campaigns on lifestyle change.[441] Increasingly, people can access elements of their electronic health records via their smartphone or other portable device, providing an important opportunity for partnership between patients and health professionals, and for empowerment of patients to be more involved in decisions about their health care. However, because smartphones are more expensive than basic mobile phones and require an internet or data connection, text messaging might be required to reach the wider population in some low-income settings.[442]

To date, most studies using mHealth to promote healthy behaviours have recruited from the general population. Increasing numbers of individuals with severe mental illness also want to use technology to manage their health.[443] Although few evaluations of mHealth for physical health in mental illness have been done, emerging evidence indicates that online peer-support platforms, smartphone apps, and fitness trackers can successfully increase walking and physical activity in people with severe mental illness.[381,444,445] Furthermore, a review of digital health technologies for people with depression[446] found that online lifestyle interventions can have positive effects on various health behaviours, including alcohol use, sleep, and physical activity. Although the evidence is only preliminary, mHealth is a promising route towards reducing physical health disparities for people with mental illness globally, and further research is warranted (figure 1). Widespread adoption of mHealth will depend not only on technological advances, but also on rigorous evaluation of digital health interventions and overcoming of common limitations, such as consumer perceptions (particularly around safety, reliability, and trustworthiness) and ethical risks, such as the potential for intrusion, coercion, and data privacy breaches.[408,447]

Who is responsible?

To turn ideas into actions, governments, health commissioners, and care providers must acknowledge their respective responsibilities for improving physical health for people with mental illness, and clear accountabilities must be established. For instance, primary prevention is often regarded as the duty of governments, rather than health services.[448] The increased risk for physical disease among people with mental illness, which can be present even before the first diagnosis of mental illness, could represent a failure at the public health level, and perhaps even wilful abandonment of educational and health promotion

initiatives to reach this marginalised group. However, socioenvironmental factors that contribute to poor physical health, such as a shortage of green spaces and walking routes, the affordability and accessibility of fast foods compared with healthy foods, and tobacco and alcohol advertising (and associated legislation), are all areas that could feasibly be targeted by local and national health policy to improve the physical health of people with mental illness.

Furthermore, increasing evidence suggests that obesity,[449,450] smoking,[451,452] and physical inactivity[453,454] are dual risk factors for both chronic physical conditions and mental illnesses. Because these risk factors are also associated with social deprivation,[182,455] greater investment in public health schemes and policy to proactively address them in at-risk groups, particularly in young people, could potentially reduce the incidence of both physical and mental illnesses. However, the effectiveness of such schemes has yet to be demonstrated, and should be considered a promising area for future research (figure 1).

The risk of physical disease in people with mental illness is further compounded by barriers to health care at the personal, service, and social levels for this population. As a priority action, governments must address the inequalities in health insurance and access to care for people with mental illness, to provide a suitable environment for effective medical and lifestyle interventions. Additionally, health commissioners must acknowledge the shortage of resources allocated to the protection of cardiometabolic health in mental health services, and the broad neglect of physical health risks in the treatment of mental illness.

Clinical staff should also reflect on the duty of care that they have to people with mental illness, both at an individual level and through their national associations. Given the foreseeable nature of poor physical health outcomes, protecting the physical health of people receiving treatment for mental illness should be regarded as within the scope of clinical duty of care. Within sufficiently resourced settings, this duty of care must include: (1) measuring and addressing the physical health of the patient; (2) clearly explaining the risks associated with treatment; and (3) taking appropriate action to mitigate those risks and protect the physical health of the patient. As demonstrated in this Commission, and evidenced in guidelines (appendix pp 35–42), good clinical practice in mental health care is increasingly considered to include monitoring the physical health of service users.

The allocation of research funding is another pathway through which systemic discrimination affects the health and wellbeing of people with mental illness. Major research councils must aim to provide more funding to address the physical health disparities that affect people with mental illness. As a solely economic justification, the allocation of resources should at least correspond with the demonstrated financial cost of physical and mental comorbidities (see panel 2). This economic burden must also be considered alongside the unresolved (and worsening[3,21–23]) personal burden of comorbid physical diseases that disproportionately affect people with mental illness across the entire life course. Substantial research investment in this area is now required to eliminate physical health inequalities, and to develop novel methods that will prevent these disparities from arising in future generations.

Conclusion

Large disparities in physical health for those with mental illness are an ongoing health issue, and might even be worsening in some regions. Although this inequity is increasingly gaining attention, further investment, intervention, and research are urgently required to address the premature mortality and lifelong burden of poor physical health associated with mental illness.

Nonetheless, our Commission takes an optimistic approach, and describes how disparities could be reduced through evidence-based prescribing and better integration of physical and mental health care. Our priority actions for health policy, clinical services, and future research are presented in figure 1. Promisingly, multiple national and international guidelines now present feasible actions for improving the integration of physical and mental health, across various health and social care settings. Broader implementation of lifestyle interventions for mental illness is also required to reduce elevated cardiometabolic risk and attenuate medication side-effects. Whenever possible, interventions should maintain the core principles of evidence-based lifestyle programmes (such as the DPP) and be made accessible to those who do not have current physical comorbidities, with the aim of protecting cardiometabolic health from the earliest stages of mental health treatment. From a public health perspective, further exploration of population-scale strategies for primary prevention of co-occurring physical and mental disorders is warranted. Additionally, more government action is required to prevent discrimination and ensure equitable access to all aspects of health care for those with mental illness. Overall, protecting the physical health of people with mental illness should be considered an international priority for reducing the personal, social, and economic burden of mental health conditions.

Contributors

The Commission consisted of five independent parts to which authors were assigned as lead authors or co-authors. NS was the lead author for Part 1. AK was the lead author for Part 2. DSi was the lead author for Part 3. SR was the lead author for Part 4. CG was the lead author for Part 5. Co-authors for each part are detailed in the appendix, and all authors contributed equally to the writing of their respective sections. All authors have approved the final versions.

Declaration of interests

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