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Advancing urban mental health research: from complexity science to actionable targets for intervention

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Urbanisation and common mental disorders (CMDs; ie, depressive, anxiety, and substance use disorders) are increasing worldwide. In this Review, we discuss how urbanicity and risk of CMDs relate to each other and call for a complexity science approach to advance understanding of this interrelationship. We did an ecological analysis using data on urbanicity and CMD burden in 191 countries. We found a positive, non-linear relationship with a higher CMD prevalence in more urbanised countries, particularly for anxiety disorders. We also did a review of meta-analytic studies on the association between urban factors and CMD risk. We identified factors relating to the ambient, physical, and social urban environment and showed differences per diagnosis of CMDs. We argue that factors in the urban environment are likely to operate as a complex system and interact with each other and with individual city inhabitants (including their psychological and neurobiological characteristics) to shape mental health in an urban context. These interactions operate on various timescales and show feedback loop mechanisms, rendering system behaviour characterised by non-linearity that is hard to predict over time. We present a conceptual framework for future urban mental health research that uses a complexity science approach. We conclude by discussing how complexity science methodology (eg, network analyses, system-dynamic modelling, and agent-based modelling) could enable identification of actionable targets for treatment and policy, aimed at decreasing CMD burdens in an urban context.

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The urgency of advancing urban mental health research

At the beginning of the 21st century, two major events occurred that are expected to affect human society in a major way. First, following an unprecedented increase in urbanisation over the past two centuries, humans live in predominantly urban settings for the first time in their existence. More than 50% of the world population now lives in cities, with an expected rise to 70% in 2050.[1] Second, while the disability and mortality burdens of most diseases have decreased over the past three decades, the burden of mental disorders, including common mental disorders (CMDs) such as depressive, anxiety, and substance use disorders, has increased.[2] Depression currently ranks first in terms of the global burden of disability[2,3] and, with the related higher risks of morbidity and mortality, CMDs pose an increasing societal and economic burden.[4,5] Additionally, the mental health of the global population faces continuous challenges due to the COVID-19 pandemic.[6] City populations can experience specific stressors related to the urban environment, such as living in small spaces and being exposed to crowding in public areas.[7]

Many researchers in modern history have wondered whether living in an urban environment and risk of mental disorders are interrelated. Many studies have identified risk factors for CMDs associated with cities (ie, urban factors) such as air pollution or crime, or investigated the psychological and neurobiological effect of urban living.[8,9] Nonetheless, there is no comprehensive understanding of exactly how different urban factors interact over time, with each other, and with individual city inhabitants to contribute to the risk of CMDs. This knowledge gap impedes the development of efficacious interventions that could lower the burden of CMDs in urban settings. Factors and interactions that altogether shape city inhabitants' mental health are likely to operate as a complex system.[10] In such a system, the interactions show dynamics such as feedback loops over multiple timescales.[11] Consequently, the resulting behaviour of the system is multifaceted and has complex features such as non-linearity, path dependency, and sudden transitions between states.[10–14]

In this Review, we explore the relationship between urbanicity and CMD burden using data from 191 countries. We discuss epidemiological, psychological, and neurobiological studies on the association between urbanicity and CMDs and present the results of a rapid literature review on meta-analytic evidence linking urban factors to CMD outcomes. We introduce a conceptual framework that uses a complexity science approach to guide future urban mental health research. We conclude by discussing how complexity science methodology could identify actionable targets for intervention and policy regarding CMDs in an urban context.

Urbanicity and CMDs: recent international data

To explore the relationship between urbanicity and CMD burden on the global scale, we did an ecological analysis using data from 191 countries from the UN[1] and the 2017 Global Burden of Disease (GBD) study.[15] The resulting plot shows a positive correlation between the degree of urbanisation and the prevalence of the different CMDs, with the respective trend lines showing a positive non-linear relationship (figure 1). The prevalence of CMDs is higher in countries where more than 50–60% of the population lives in urban areas, particularly for anxiety disorders. Non-linearity was further suggested by the poor fit of ordinary least square regression lines (appendix p 23). The trend lines shown in figure 1 were fitted using

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For an **interactive version of figure 1** see https://chart-studio.plotly.com/~mhlees/21/#plot

See **Online** for appendix

a non-parametric locally weighted scatterplot smoothing (LOWESS) technique, including bootstrapped 95% confidence intervals (n=95, k=500) that show the stability of the fit.[16] An additional plot suggested no association between country population size and CMD prevalence (appendix p 24); therefore, confounding by country population size seems unlikely. A limitation of the analyses is the use of country-level data, with no distinction in CMD prevalence between urban and rural areas. Furthermore, prevalence in the GBD study is reported as an estimate (with an upper and lower bound), with different accuracy per country.[15] To investigate how this estimate could affect our results, we plotted the relative error of the prevalence estimates (calculated as upper bound–lower bound/estimate), as a function of degree of urbanisation (appendix p 25). We found that estimates for the prevalence of CMDs are slightly more accurate in more urbanised countries, possibly reflecting the high availability of data from high-income countries (HICs). Conclusions drawn from figure 1 should be made with caution: the difference in relative error does not seem large enough to invalidate our general observation that high degrees of urbanicity are associated with a higher prevalence of CMDs. The results presented in figure 1 serve as a basis for future research questions—eg, what factors and dynamic processes underlie the suggested non-linear association and do specific urban factors cause these observed trends?

Urbanicity and CMDs: epidemiological findings

The positive association between urbanicity and CMD burden agrees with most epidemiological studies in HICs, which show higher burdens of CMDs in urban areas than rural areas.[17–23] For example, a study in Denmark[17] (n=2 894 640) found higher incidence rates of CMDs for individuals born in urban areas than individuals born in rural areas; the study measured depressive disorders (incidence rate ratios 1·24, 95% CI 1·21–1·27), anxiety and stress-related disorders (1·57, 1·54–1·59), and mental or behavioural disorders due to alcohol (1·75, 1·69–1·80) or cannabis use (2·47, 2·34–2·60). Studies in Sweden[18,19] (n=4·4–4·5 million) revealed higher incidence rates for first hospitalisation due to depression in men (hazard ratio 1·12, 95% CI 1·03–1·23) and women (1·20, 1·11–1·30), alcohol use disorder in men (1·71, 1·60–1·82) and women (1·76, 1·58–1·96), or substance use disorder in men (2·38, 2·12–2·67) and women (1·89, 1·67–2·15) who live in areas with the highest degree of urbanisation compared with areas with a lower degree of urbanisation. A pooled analysis of eight Dutch cohort studies[20] (n=32 487) showed higher odds for prevalence of depression in more urbanised areas (odds ratio [OR] 1·05, 95% CI 1·01–1·10) than less urbanised areas.In North America, a meta-analysis of Canadian population surveys[21] done between 2000 and 2014 (n=477 449) revealed higher odds for major depressive episodes in urban areas than in rural areas (OR 1·18, 95% CI 1·12–1·25). By contrast, a meta-analysis of population surveys done in the USA[22] between 2009 and 2011 found no urban–rural differences for major depression in adolescents (n=55 583) and the highest risk of major depression in adults (n=116 459) in small metropolitan and semi-rural areas. A meta-analysis of 20 urban versus rural comparison studies in HICs[23] published between 1985 and 2008 (n=143 894) revealed higher odds for mood (OR 1·28, 95% CI 1·13–1·44) and anxiety disorders (1·13, 1·00–1·28), but not for substance use disorders, for individuals living in urban areas. Results for substance use disorders are mixed, partly because of the wide variety of substances and differences in availability or legal status.[13,23]

In low-income and middle-income countries (LMICs), where urbanisation typically occurs at a higher pace than in HICs, urban mental health is a topic of major importance.[24] Studies on urban–rural differences in CMDs in LMICs have more mixed findings than in HICs.[25–28] For example in China, a country with rapid urbanisation and economic growth, large studies showed no urban–rural differences in anxiety or alcohol use disorders,[26,29] but a higher prevalence of depression in rural areas.[30,31] These mixed results could have multiple origins, including differences in the phase of economic development in urban and rural areas, as this variation will affect risk factors (eg, poor housing) and protective factors (eg, availability of treatment) for mental health. Furthermore, several sociodemographic factors associated with rapid urbanisation (eg, megacities,[24] crowding in informal settlements,[32] and large-scale labour migration)[33,34] in LMICs deserve attention, given their presumed effect on mental health.

Considering mind and brain

An important focus in urban mental health research is the relationship between the urban environment and the mind and brain of city inhabitants. This concept relates to how an urban environment affects the development of internalising and externalising problems, including CMDs, through effects on psychological factors (eg, neuroticism), mechanisms (eg, cognitive beliefs and coping), and neurobiology (eg, brain development, neurobiological stress response, and epigenetics).[8,35]

For example, regarding psychological factors, frequent exposure to negative circumstances such as inequality or crime in disadvantaged urban areas can lead to maladaptive appraisal in the form of negative self-evaluation or heightened perceived threats, increasing the risk of internalising disorders.[36,37] By contrast, a positive appraisal style could increase mental resilience, which has been shown for the effect of stressors related to the COVID-19 pandemic.[38] Furthermore, social norms in particular areas could affect individual residents' behaviour, including (illicit) substance misuse.[39] Notably, many studies on CMDs use outcomes that rely on subjective evaluation, which can be distorted in the case

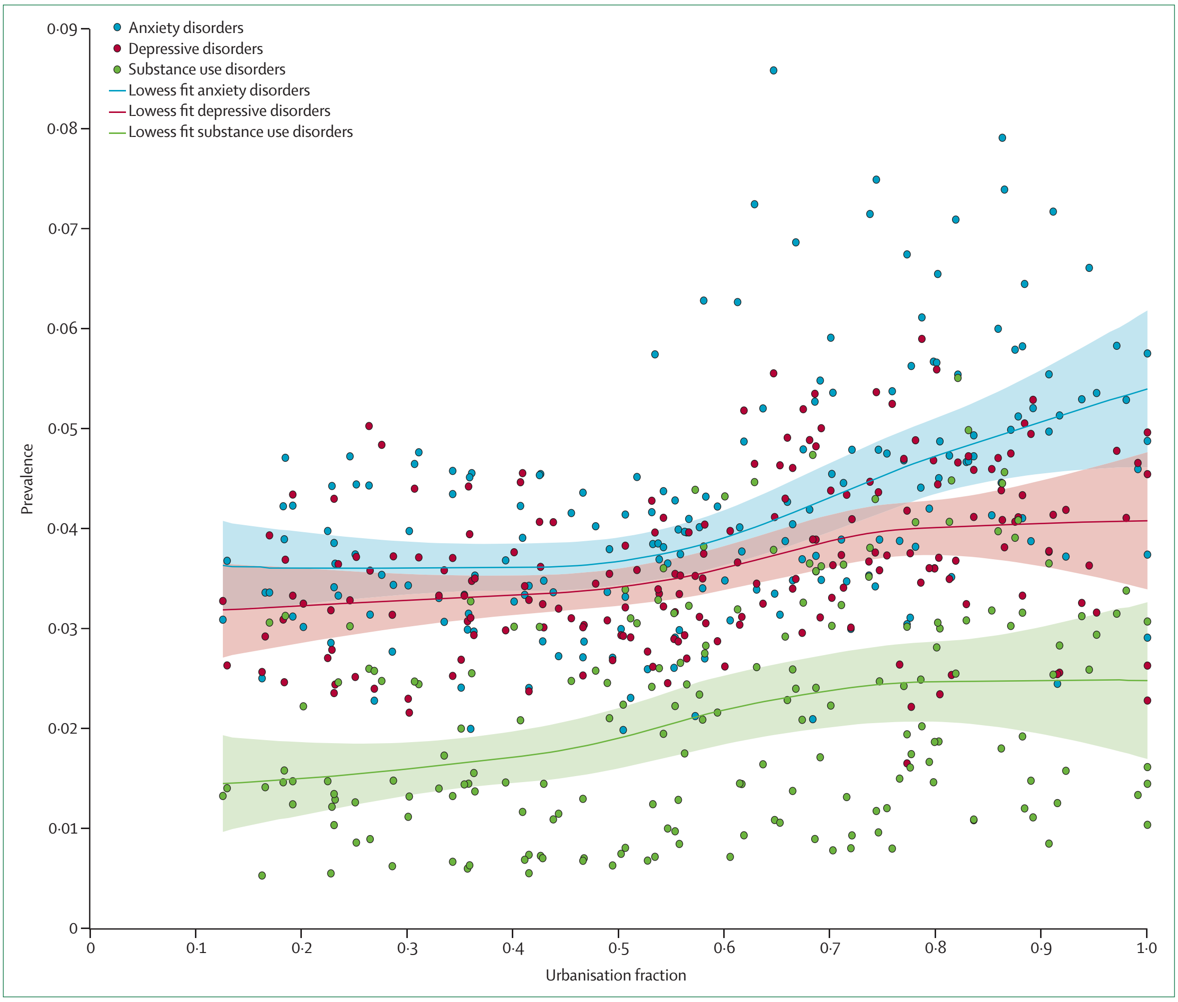

Figure 1: **Relationship between urbanisation and prevalence of common mental disorders**
The x-axis shows the proportion of a country's population living in urban areas, and the y-axis represents the prevalence of the common mental disorders. The dots represent countries, with each country included three times, once for each of the disorders, as shown by the three different colours. The countries and diagnostic codes included in the plot are shown in the appendix (pp 18–22). Trend lines were produced using a locally weighted scatterplot smoothing (LOWESS) technique; the shaded areas represent bootstrapped 95% CIs.

of CMDs. Hence, negative circumstances such as perceived threat, adverse neighbourhood aesthetic, or availability of substances might be overrated by comparison with objective measures. This weighted perception can further increase maladaptive behaviours, such as social isolation or illicit substance use, which will feed back to the urban environment (eg, by affecting neighbourhood social cohesion or crime).[39] Psychological factors and mechanisms operate in the context of neurobiological and genetic characteristics, which can render individuals susceptible to CMDs when exposed to specific environmental urban stressors. Several leading theories on the causes of CMDs, such as the diathesis-stress theory,[40] Belsky's theory of differential susceptibility,[41] or Beck's unified model of depression,[42] propose integrated mechanisms. These theories state that the accumulation of stressors throughout life results in different mental health outcomes due to individual differences in developmental, psychological, and neurobiological factors.

The effect of the urban environment on the brain ranges from neurodevelopmental changes during fetal development to structural and functional alterations throughout life in response to environmental exposures.[8,9] Cities are generally associated with prolonged exposure to social stress, which can alter the stress response.[43] Accumulation of stressors has a negative effect on neurobiological stress resilience (ie, allostasis), modifying the risk to develop CMDs throughout life.[44,45] For example, one neuroimaging study[46] showed that urban living was associated with increased amygdala activity during social stress exposure and that urban upbringing was associated with differential activity of the perigenual anterior cingulate cortex and decreased connectivity between the amygdala and the perigenual anterior cingulate cortex (ie, key regions for regulating negative affect and stress). Furthermore, exposure to air pollution could be related to disruptions in white matter development in childhood and increased brain atrophy in later life.[47,48] Moreover, the gut microbiome has been shown to affect brain function and possibly contribute to the pathophysiology of mental disorders.[49] Additionally, transgenerational effects could induce neurodevelopmental changes that alter the stress response and resilience to mental disorders in offspring—eg, through maternal use of substances or serotonin reuptake inhibitors during pregnancy, or suboptimal parenting.[50–52] Regarding protective factors, neuroimaging studies have shown that exposure to green space can positively affect stress recovery and cognitive and affective brain functioning.[53]

Altogether, the interrelationship between urban surroundings and psychological and neurobiological factors is important to consider in urban mental health research. This relationship is unlikely to be linear (ie, from the city to the individual), as the mental health of city inhabitants will feed back and affect the urban environment.

Urban factors and CMDs

We did a rapid review of meta-analyses studying the associations between urban factors and CMD risk. We included 13 meta-analyses on urban–rural differences in CMD burden and 45 meta-analyses on 18 urban factors (appendix pp 1–14).

Studies were categorised as pertaining to the ambient environment (eg, air pollution or noise), physical environment (eg, urban design or green space), or social environment (eg, social cohesion, crime, or socioeconomic status). We found notable differences in terms of the meta-analytic evidence between the three CMDs and associated urban factors. For instance, ambient environmental factors were mostly studied in relation to depression, mainly reporting mixed results but with some studies reporting a positive association between exposure to air pollution or noise and risk of depression.[54–59] Meta-analyses on noise and anxiety disorders reported no relationship,[57–60] and these factors have not been studied meta-analytically for substance use disorder. Ambient factors that have been less extensively studied, but have been associated with CMDs, are artificial light at night and the occurrence of higher ambient temperatures in cities (ie, urban heat islands).[61,62] Regarding social factors, economic stressors such as low socioeconomic status or economic inequality have been studied for depression and substance use disorder and, less often, for anxiety disorders. Meta-analyses of anxiety studies mostly focus on social stressors such as ethnic discrimination, sexual minority status, or crime (appendix p 1). Whether these findings reflect actual differences in which urban factors are relevant for the respective CMDs, or whether they expose a gap in research, requires further investigation. Such knowledge could help to explain the differences in CMD burden between countries with different degrees of urbanisation.

We only found one meta-analysis that suggested a protective effect, which was on exposure to green space and depressive mood.[63] Hence, factors that could promote mental health in cities (eg, improving urban design, economic opportunities, or access to health services) require further research. There is also a need for robust evidence on the effect of rapid urbanisation and migration on CMDs, especially in LMICs (eg, informal settlements and crowding).[24,64]

Complexity science for urban mental health research

Although numerous urban factors have been associated with CMD outcomes, most of these findings represent univariate explanations for urban mental health problems and disorders, which are most likely to be shaped by a multitude of dynamic interactions and feedback processes over time. Consequently, there is a considerable gap in our knowledge of how the urban environment affects mental health.[10,12–14] For example, neighbourhood deprivation, low socioeconomic status, and crime, have all been reported to impair mental health.[20,39] However, it is unclear how these factors interact over time or how they are affected by feedback from poor mental health outcomes in the local population. The identification of risk (or protective) factors for CMDs does not provide a comprehensive explanation of how living in cities affects the risk of developing CMDs. Instead, the involved factors are part of dynamic processes, spanning from the city to the individual and back, shaping mental health in an urban context.[10,12–14] We argue that these factors operate within a complex system, meaning that their interactions are characterised by feedback loop mechanisms occuring over different timescales, resulting in a complex network of dynamical interactions that renders non-linear behaviour of the system at large.[10,12] Accounting for this notion is an important step forward in gaining a better understanding of the interplay between the urban environment and mental health. This step is essential to uncover new targets for interventions and policy making, aimed at reducing the burden of CMDs in urban populations. Therefore, we call for a complexity science approach to be applied to future urban mental health research.

Complexity science is the study of systems that are constituted by individual lower-level elements that, by virtue of their dynamical interactions, can give rise to emergent higher-level effects and patterns of self-organising (often non-linear) behaviour.[11]

Both cities and CMDs have defining features of a complex system. Cities have many factors that, when taken together, account for the dynamics of the urban landscape—eg, infrastructure factors such as urban design, social factors such as neighbourhood segregation, and city inhabitants' individual characteristics.[65] In mental health research, the complexity science approach has become increasingly popular, particularly with regard to the conceptualisation of mental disorders as a disease entity and in the study of their causes.[35,66,67] A notable example is the network theory of mental disorders, which conceptualises psychopathology as an emerging property within a complex system consisting of causally interacting symptoms, potentially giving rise to a pathological state of the system resembling a psychiatric phenotype.[66]

To show that cities and mental disorders can be considered as systems of interacting elements, we uncovered the network structure of data on urban surroundings and depression symptoms, from the second wave (2006–07) of the Survey of Health, Ageing and Retirement in Europe study (SHARE; n=4970).[68,69] The resulting network visualises the interwoven and multivariate nature of associations between urban factors and depression symptoms (figure 2).

However, interacting elements alone do not automatically comprise a complex system. A quintessential feature of complex systems is that the relationships between elements are subject to feedback loop mechanism over different timescales, resulting in system behaviour that is non-linear and hard to predict in the long term.[11] For example, in cities, this is seen in the non-linear relationship between population size and metrics such as economic output or crime rates.[71] These so-called superlinear scaling properties are proposed to result from an increasing return to scale, as there are more opportunities for social interaction and feedback loops in larger cities.[71] Future studies should investigate how the burden of CMDs relates to city population size, especially given our findings that suggest a positive association between urbanisation and CMD burden (figure 1).

Complex system behaviour in CMDs can be found in the occurrence of sudden deterioration of symptoms, characterised as sudden transitions around tipping points from a healthy to a pathological state, which has been shown in computational models and human time-series data on depression.[72,73]

Underlying dynamics could consist of reinforcing symptom feedback loops (eg, rumination and sleep) or contributors to mental disorders (eg, poor diet and insufficient physical exercise).[67,72] Additionally, CMD outcomes can also feed back to explanatory factors, including some that affect urban surroundings. For example, depression might decrease the ability to maintain household duties,[74] which could result in neglect of the physical surroundings and, ultimately, negatively affect neighbourhood aesthetics.[75] Such feedback could result in circular causality, by which outcomes (ie, CMDs) feed back and amplify the explanatory factors (eg, neighbourhood aesthetics) that contributed to the onset of the disorder in the first place.

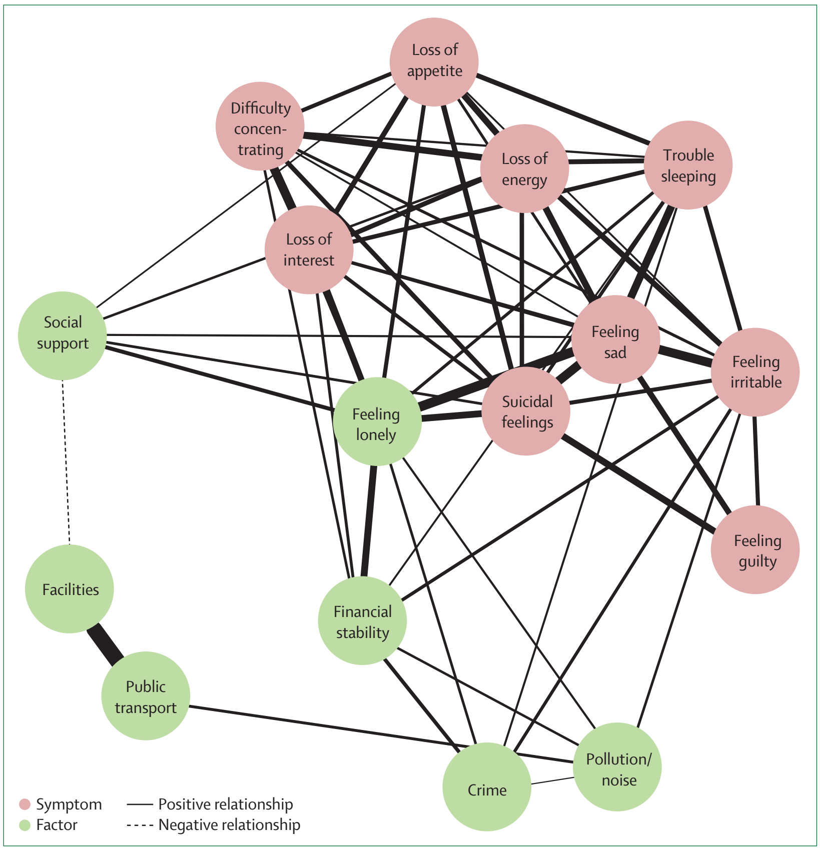

Figure 2: **Network of urban factors and symptoms of depression**
Information is based on a regression-based mixed-graphical model (mgm package in R). Green nodes represent urban factors. Red nodes represent depression symptoms.[70] The thickness of the lines represents the strength of the positive (straight line) or negative (dotted line) association. Because the network serves an illustrative purpose, regression weights for the corresponding associations are not shown.

A conceptual framework for urban mental health research

To guide future urban mental health research, we present a conceptual framework (figure 3) that is based on four important principles and can be used for theorising the effect of the urban environment on mental health (and vice-versa) from a complexity science perspective. These principles are: (1) the factors and outcomes involved operate as dynamically interacting elements within a complex system, (2) factors are affected by meta-factors such as changes in city size, urbanisation, migration, and stage of economic development, (3) interactions between explanatory factors and CMD symptoms occur over different timescales, and (4) CMD outcomes can affect explanatory factors (feedback loops).

First, urban mental health problems and disorders are characterised as emerging properties within a complex system whereby the elements dynamically interact across the different domains of the conceptual framework, as visualised by the arrows between the elements (figure 3). The horizontal strata on the left of the framework categorise elements other than CMDs as pertaining to the urban environment, social environment, or individual

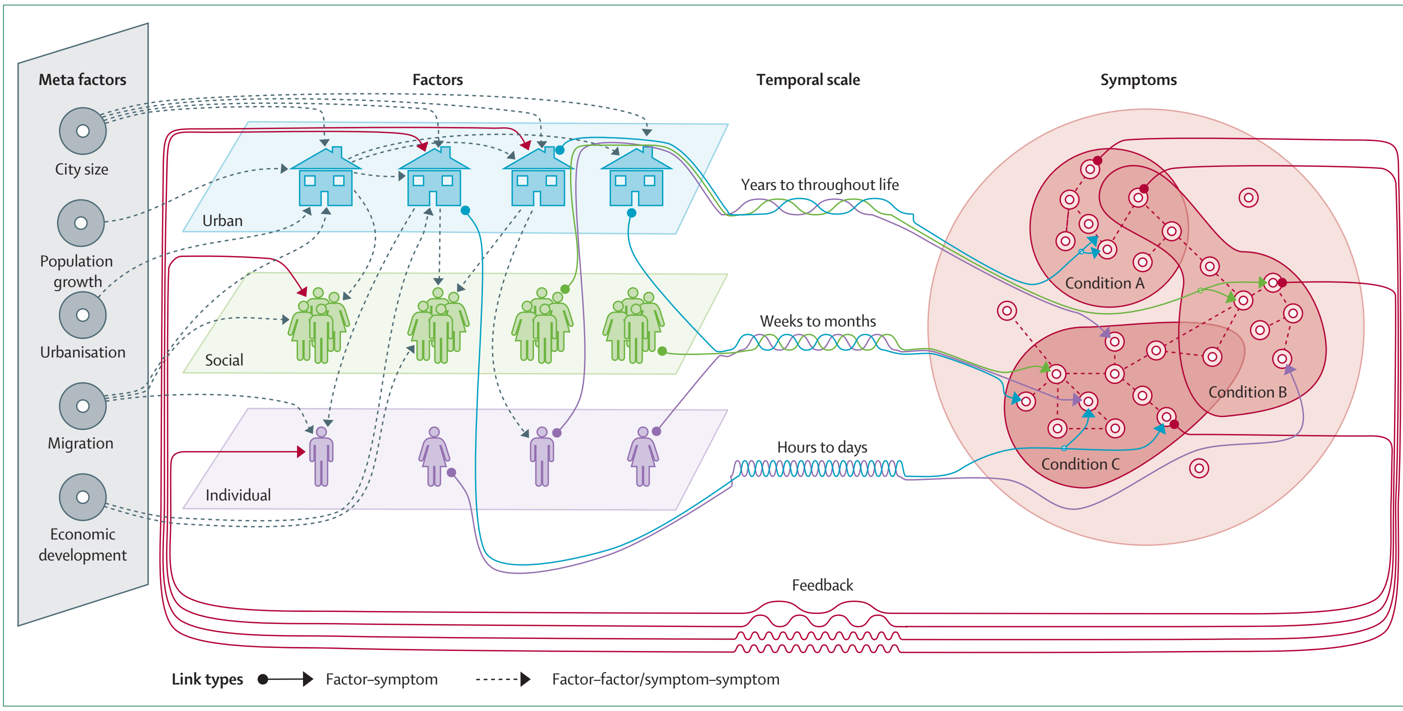

Figure 3: **Conceptual framework of the relationship between factors in the urban environment and CMD outcomes**
This framework conceptualises urban mental health from a complex systems perspective. Meta factors (grey box) are considered to have a dynamic effect on the urban environment and its inhabitants. Factors are categorised as urban factors (eg, air pollution or built environment), social factors (eg, social cohesion), or individual factors (eg, individual demographic, psychological, or neurobiological characteristics). Arrows between the factors and CMD symptoms represent the different temporal scales across which factors can assert their effect. CMDs are represented as symptom clusters connected by overlapping symptoms. Feedback arrows represent the possibility of feedback from CMD symptoms to explanatory factors, which can also occur over different timescales. CMD=common mental disorder.

city inhabitants (eg, gender and age, but also neuroticism, neurobiological factors, or daily functioning). These elements can be risk or protective factors for CMDs. CMDs are represented as symptom clusters that can be affected by external elements, but symptoms can also affect each other, in line with the network theory of mental disorders.[66] Symptom clusters in our framework overlap, as at least some symptoms overlap between CMDs.[76] Second, particular meta factors (ie, city size, population growth, urbanisation, migration, and economic development) have a profound effect on the urban environment. These effects include changes in city and population size and the process of urbanisation (eg, rapid urbanisation in LMICs), internal or international migration (eg, for economic, political, or educational purposes), and stage of economic development (eg, housing quality or availability of health-care services).[24,64,71] Third, different timescales in our framework, ranging from over hours to over the life course, are depicted by differences in the oscillation magnitude of the arrows that represent the effect on CMD symptoms. When processes operate on similar timescales, the possibility for reciprocal interactions is assumed to be higher. However, when one of the processes occurs at a vastly different pace, their effects on each other will be attenuated.[77] Finally, because CMDs are known to feed back to explanatory factors over multiple timescales, this process is accounted for by the oscillating arrows from CMDs back to other elements in the system.

To show the framework in practice, we present a hypothetical example of an urban mental health scenario (appendix p 26). Our example concerns Jane, an inhabitant of a neighbourhood with little green space (urban factor), in her country's largest city (meta factor). Her apartment is located close to a busy road. Jane has a low income, which often causes financial distress (individual factor). The constant traffic noise (urban factor) disturbs her sleep, causing insomnia.[78] Chronic exposure to air pollutants (urban factor) could negatively affect brain structures and functioning,[48] increasing her risk of developing a CMD. Insomnia could increase financial distress by negatively affecting work performance, creating a reinforcing feedback loop.[79] Depending on Jane's psychological coping and neurobiological susceptibility, these factors could trigger, for example, a depressive disorder.[79] However, her municipality is investing in sustainable urban development (meta factor) and building a park (protective urban factor) between her apartment building and the busy road. This intervention could improve Jane's mental health by reducing stress (individual factor)[63] and mitigating traffic noise (urban factors) in the short term,[80] and eventually by increasing neighbourhood social cohesion (social factor)[81] or perhaps even by mitigating air pollution (urban factor).[82] This hypothetical example shows how multiple interactions, from the urban to the individual level, can trigger CMD symptoms, create feedback loops, and reinforce distress. It also exemplifies how interventions can affect multiple pathways over different timescales.

Theoretical and quantitative models

Our conceptual framework can guide future urban mental health research from a complexity science perspective. Informed by existing studies, expert knowledge, and lived experience, the framework can be used to map and assess dynamical interactions between the urban environment and mental health. Network analyses and machine learning approaches can advance theoretical causal maps by using data-driven estimations of the multivariate statistical associations between a set of variables (figure 2) and by approximating weights of the presumed causal links. The next step is to translate such theoretical maps into quantitative models that approximate the interactions within the system of interest and thereby allow us to study the temporal behaviour of the system.[83] Methods such as agent-based modelling and system-dynamic modelling can use real-world data to study the temporal behaviour of the system of interest.[83] For example, agent-based models are able to study the interactions between multiple variables, including those that transcend the individual level, such as the consequences of the COVID-19 pandemic.[84] An example of an agent-based modelling study would be an investigation of the mental health effect of repercussions of the COVID-19 restrictions in urban areas, such as the psychological effects of large families living in small spaces, crowding in informal settlements, and increased risk of domestic violence.[7,85]

An important methodological development in mental health research is the use of ecological momentary assessment studies, bolstered by the widespread availability of mobile devices. Ecological momentary assessment studies allow for the collection of intensive longitudinal data, which can be used to infer interactions over time of variables of interest—eg, through temporal network analyses.[70,86] This information could be used to identify early warning signals before the onset of CMD symptoms,[73] to elucidate the underlying psychological mechanism of mental health interventions,[87] or to personalise treatment by providing insight into symptom dynamics.[88] Furthermore, including urban factors in ecological momentary assessment studies could provide new insights into the effect of the urban environment on CMDs.[89]

Future prospects

The global population is increasingly living in urban environments.[1] This demographic shift means there is an increase in exposure to urban stressors that have been associated with higher risk of CMDs. Since 2020, this shift has occurred during the COVID-19 pandemic, which poses additional mental health challenges on urban residents.[7] In this Review, we have argued that a complexity science approach should guide future urban mental health research. Complexity science can help to identify factors for CMD interventions and policy. Complexity science can also identify which factors in urban systems should be targeted to have a meaningful

Search strategy and selection criteria

We did 34 systematic searches on PubMed between April 22, 2020, and June 5, 2020, combining search terms of each of the three common mental disorders (CMDs) and search terms on factors associated with an urban environment. A list of all search terms can be found in the appendix (pp 15–17). Medical subject headings and search terms in the title or abstract were used to identify relevant studies. Results were filtered to show only meta-analyses published from Jan 1, 1990, up to the date the specific search was performed.

We included meta-analyses that studied the association between exposure to at least one urban-related factor and CMD outcome (diagnosis or symptoms classed as depressive, anxiety, or substance use disorder in DSM-5), included only studies in people (of any age), had full-text availability, and were written in English or Dutch. We excluded meta-analyses that studied participants with any comorbidity other than comorbid CMDs or only included studies in an occupational setting.

Searches for depressive disorder yielded 96 829 hits, of which 599 were meta-analyses; 503 remained after removing duplicates. Searches for anxiety disorders yielded 48 166 hits, of which 287 were meta-analyses; 105 remained after removing duplicates. Searches for substance use disorders yielded 91 366 hits, of which 502 were meta-analyses; 392 remained after removing duplicates. 12 additional meta-analyses were identified through manual searches.

Screening was primarily done by JMvdW, with consultation of JJFB in case of uncertainty about inclusion. Furthermore, JJFB did a crosscheck of a subset of the included and excluded papers. After screening, 58 meta-analyses were included: 44 meta-analyses reported on depressive disorders, 16 meta-analyses reported on anxiety disorders, and 14 meta-analyses reported on substance use disorder. Reasons for exclusion after full-text screening were the factor studied did not match the search terms (n=19), study design was not relevant to our search (n=19), CMD diagnosis or symptomatology was not included as outcome (n=7), no full-text access (n=4), not being in English or Dutch (n=2), or inclusion of participants with neuropsychiatric comorbidity other than comorbid CMDs (n=1). Result extraction was led by JMvdW, under supervision of JJFB. A comprehensive overview of these results, including the reference list, is presented in the appendix (pp 1–14).

effect on mental health outcomes. Notably, the most effective targets in a complex network might not always be the ones most centrally located, but may instead be (a combination of) the ones that are more peripherally connected, for example in the case of product recommendation in social networks.[90] Additionally, innovative interventions should be developed for high-risk populations that are currently underserved by health-care facilities or do not seek help themselves. Examples include increasing accessibility through the use of digital or mobile platforms or guidance by lay counsellors, which can be effective in treating CMDs in HICs and LMICs, including in urban populations with low socioeconomic status.[91–94]

Conclusions

Identifying actionable targets within urban systems is key to improving the mental health of city inhabitants and represents a major challenge in urban mental health research. Adopting a complexity science approach could identify relevant urban factors. In this Review, we presented a conceptual framework that can guide future urban mental health research. Novel insights from this approach could provide input for new treatment interventions and urban policies addressing CMDs in the increasingly urban world.

Contributors

CLB, RWW, PMAS, JMvdW, CDvB, JJFB, and MKD conceptualised this Review. JMvdW wrote the first draft of this paper. CDvB drafted the first versions of the conceptual framework. CLB, RWW, JMvdW, CDvB, JJFB, and MKD further developed the manuscript and, together with CL and PMAS, further developed the conceptual framework. JCL created the figures, with input from CDvB and JMvdW. ML, PMAS, CLB and RWW initiated the UN and WHO data analyses. The analyses were done by ML and results were interpreted by PMAS, ML, CLB, RWW, and JMvdW. JMvdW did the rapid review and results were extracted by JMvdW under supervision of JJFB. The Survey of Health, Ageing and Retirement in Europe network analysis was done by MKD and CDvB and interpreted together with JMvdW. PJL, MS, and RvH contributed to the section on neurobiology. KS, JCMvW, DB, and DD commented on the manuscript throughout the writing process. All authors reviewed the final version of the manuscript before submission.

Declaration of interests

We declare no competing interests.

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For the **Survey of Health, Ageing and Retirement in Europe** see www.share-project.org

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