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

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Abstract

Urbanisation is on the rise across the globe, as are common mental disorders (CMDs; depressive, anxiety, and substance use disorders). Moreover, the world population faces continuing mental health challenges related to the impact of the COVID-19 pandemic. In this paper, we discuss how urbanicity and risk of CMDs relate to each other and call for a complexity science approach to advance our understanding of this interrelationship. First, we performed an ecological analysis using recent data on urbanicity and CMD burden in 191 countries, indicating a positive non-linear relationship, with a higher CMD prevalence in more urbanised countries, most prominently for anxiety disorders. We also performed a review of meta-analytic studies on the association between urban factors and CMD risk. Here, we identified factors relating to the ambient, physical, and social urban environment and revealed differences per diagnosis. We argue that factors in the urban environment likely operate as a complex system, interacting with each other and with individual city inhabitants (including their psychological and neurobiological characteristics), to shape mental health in an urban context. These interactions exhibit dynamics such as feedback loop mechanisms over various timescales, rendering temporal system behaviour characterised by non-linearity and limited predictability over time. Accordingly, we present a conceptual framework for future urban mental health research, adopting a complexity science approach. We conclude by discussing how complexity science methodology (e.g. network analyses, system-dynamic modelling, and agent-based modelling) could facilitate identification of actionable targets for treatment and policy, aimed at decreasing CMD burdens in an urban context.

The urgency of advancing urban mental health research

The beginning of the twenty-first century witnessed two major events that are expected to heavily impact human society. First, following an unprecedented increase in urbanisation over the past two centuries, humans have, for the first time in their existence, become a predominantly 'urban species'. 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] With the related higher risks of morbidity and mortality, CMDs pose an increasing societal and economic burden.[4,5] In addition, the world population's mental health faces continuous challenges by the ongoing COVID-19 pandemic.[6] City populations may experience specific stressors related to the urban environment, such as confinement in smaller living spaces and higher levels of crowding in public areas.[7] Many researchers in modern history have wondered whether being an 'urban species' and risk of mental disorders are interrelated. This resulted in a wealth of studies identifying risk factors for CMDs associated with cities (i.e. 'urban factors' such as air pollution or crime), or investigating the psychological and neurobiological impact of urban living.[8,9] Nonetheless, we have yet to reach a 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 impedes the development of more efficacious interventions that may lower the burden of CMDs in an urban context. Factors and interactions that altogether shape city inhabitants' mental health likely operate as a complex system.[10] In such a system, the interactions at play show dynamics like feedback loop mechanisms over multiple timescales.[11] Consequently, the resulting behaviour of the system at large is 'complex' , exhibiting features such as non-linearity, path dependency, and sudden transitions between states.[10–14]

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

The link between urbanicity and CMDs: recent international data

In order to explore the current relationship between levels of urbanicity and burden of CMDs on the global level, we performed an ecological analysis using data from 191 countries from the United Nations and the Global Burden of Disease (GBD) study from the year 2017.[1,15] The resulting plot shows a positive correlation between the degree of urbanisation and the prevalence of the different CMDs, with the respective trend lines indicating a positive non-linear relationship (Figure 1). It seems that the prevalence of CMDs is higher in countries where more than 50%-60% of the population lives in urban areas, especially with regard to 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 a non-parametric locally weighted scatterplot smoothing (LOWESS) technique, including bootstrapped 95% confidence intervals (n=191x0.5=95, k=500) that show the stability of the fit.[16] An additional plot indicated no correlation between country population size and CMD prevalence (appendix p. 24), so 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 may impact our results, we plotted the relative error of the prevalence estimates, calculated as ((upper bound – lower bound)/estimate), as 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 higher availability of data in more economically developed countries. While conclusions following from Figure 1 should be drawn with caution, the difference in relative error does not seem large enough to invalidate our general observation that higher levels of urbanicity are associated with a higher prevalence of CMDs. The results as represented in Figure 1 serve as a basis for further research. For example, it raises the question what factors and dynamic processes underlie the suggested non-linear association, and whether specific factors in urban areas drive the observed trends, for instance for anxiety disorders as compared to other CMDs.

The link between urbanicity and CMDs: epidemiological findings

The aforementioned results suggestive of a positive association between higher levels of urbanicity and burden of CMDs are in line with most epidemiological studies in high-income countries (HICs), which show higher burdens of CMDs in urban versus rural areas.[17–23] For example, a study in Denmark (N=2 894 640) found higher incidence rates (incidence rate ratios; 95% confidence interval, CI) for individuals born in urban versus rural areas, for depressive disorders (1·24; 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).[17] Studies in Sweden (N=4·4 - 4·5 million) revealed higher incidence rates (hazard ratios; 95% CI) for first hospitalisation due to depression (men: 1·12; 1.03-1.23 / women: 1·20; 1.11-1.30), alcohol use disorder (men: 1·71; 1·60-1·82 / women: 1·76; 1.58-1.96) or substance use disorder (men: 2·38; 2·12-2·67 / women: 1·89; 1·67-2·15), for people living in the most urbanised areas.[18,19] A pooled analysis of eight Dutch cohort studies (N=32 487) showed higher odds (odds ratio, OR; 95% CI) for prevalence of depression in more urbanised areas (1·05; 1·01-1·10).[20] In North-America, a meta-analysis of Canadian population surveys (2000-2014, N=477 449) revealed higher odds for major depressive episodes in urban versus rural areas (OR: 1·18; 1·12-1·25).[21] In contrast, a meta-analysis of populations surveys in the United States (2009-2011) 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.[22] A meta-analysis compiling 20 urban-rural comparison studies in HICs published between 1985 and 2008 (N=143 894 participants), revealed higher odds for mood- (OR: 1·28; 1·13-1·44) and anxiety disorders (OR: 1·13; 1.00-1.28), but not substance use disorders, for individuals living in urban areas.[23] Results for substance use disorders are more mixed, in part due to the wide variety of substances and (perceived) availability in relation to their legal status.[13,23]

In lower- 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] Notably, studies in LMICs on urban-rural differences in CMDs are more mixed than in HICs.[25–28] For example in China, a country witnessing rapid urbanisation and economic growth, large studies showed no urban-rural differences in anxiety or alcohol use disorders[26,29], and a higher prevalence of depression in rural areas.[30,31] While these mixed results may have multiple origins, they possibly reflect differences in the phase of economic development (both in urban and rural areas), as this will impact both risk factors (e.g. pour housing) and protective factors (e.g. availability of treatment) for mental health. Furthermore, several sociodemographic developments associated with rapid urbanisation in LMICs deserve our attention, given their presumed impact on mental health. These include the rise of megacities[24], (crowding in) informal settlements[32], and large-scale labour migration.[33,34]

The link between urbanicity and CMDs: 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 relates to how an urban environment influences the development of internalising and externalising problems including CMDs through effects on psychological factors (e.g. neuroticism), mechanisms (e.g. cognitive beliefs, coping), and on neurobiology (e.g. brain development, neurobiological stress response, epigenetics).[8,35]

Taking psychological factors, frequent exposure to phenomena such as inequality or crime in disadvantaged urban areas may foster maladaptive appraisal in the form of negative self-evaluation or heightened perceived threats, increasing the risk of internalising disorders.[36,37] In contrast, a positive appraisal style may increase mental resilience, such as recently shown for the impact of stressors related to the COVID-19 pandemic.[38] Furthermore, social norms in certain areas may impact individual residents' behaviour, including (illicit) substance use.[39] Notably, many studies on CMDs use outcomes that rely on subjective evaluation, which may be distorted in the case of CMDs. Hence, phenomena like perceived threat, adverse neighbourhood aesthetics, or availability of substances may be overrated compared to objective measures. This may further increase (mal)adaptive behaviours, such as social isolation or illicit substance use, which will give feedback to the urban environment at large (e.g. by the impact on neighbourhood social cohesion or crime).[39] Moreover, psychological factors and mechanisms operate against the backdrop of neurobiological and genetic characteristics, which may render individuals vulnerable to CMDs in the context of specific environmental (urban) stressors. Several leading theories on CMD aetiology, 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. Here, the (accumulations of) stressors throughout life results in different mental health outcomes, due to individual differences in developmental, psychological, and neurobiological vulnerabilities.

The impact of the urban environment on the brain ranges from neurodevelopmental changes around (pre)conception and fetal development to structural and functional alterations throughout life in response to environmental exposures.[8,9] Cities are generally associated with higher social stress levels, which can alter the stress response.[43] Accumulation of stressors has a negative effect on neurobiological stress resilience (allostasis), modifying the risk to develop CMDs throughout life.[44,45] This is illustrated by a neuroimaging study, showing that urban living is associated with increased amygdala activity during social stress exposure, and that urban upbringing is associated with differential activity of the perigenual anterior cingulate cortex (pACC) and decreased connectivity between the amygdala and the pACC (i.e. key regions for regulating negative affect and stress).[46] Furthermore, exposure to air pollution seems related to disruption of white matter development in childhood and higher brain atrophy levels in later life.[47,48] Moreover, the gut microbiome has recently been shown to influence brain function and possibly contribute to the pathophysiology of mental disorders as well.[49] In addition, transgenerational effects may induce neurodevelopmental changes that alter stress response and resilience to mental disorders in offspring, for example 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 greenspace can positively impact stress recovery and cognitive and affective brain functioning.[53]

Altogether, the interrelationship between urban surroundings and psychological and neurobiological factors and mechanisms is important to consider in urban mental health research. This relationship is unlikely to be a one-way street from the city to the individual, as the mental health of city inhabitants will feedback and influence the urban environment as well.

Urban factors and CMDs: a rapid review of the literature

While the literature reports many factors in the urban environment related to CMD risk, meta-analytic evidence on the association between these factors and CMD outcomes is scattered. Therefore, we conducted a rapid literature review of meta-analyses studying the associations between urban factors and CMD risk. For the methods, see the textbox 'Search strategy and selection criteria rapid review'. We included 13 meta-analyses on urban-rural differences in CMD burden and 45 meta-analyses on 18 urban factors (for all factors and references, see appendix p. 1-14).

Factors for which we identified meta-analyses could be categorised as pertaining to the ambient environment (e.g. air pollution or noise), physical environment (e.g. urban design or greenspace), or social environment (e.g. social cohesion, crime, or socioeconomic status). We found notable differences in terms of the meta-analytic evidence between the three CMDs and the associated urban factors. For instance, ambient environmental factors were mostly studied in relation to depression, mainly reporting mixed results, but leaning towards a positive association between higher exposure to air pollution or noise and risk of depression.[54–59] Meta-analyses on noise and anxiety disorders reported no significant effects[57–60], and these factors have not been studied meta-analytically in 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 (i.e. urban heat islands).[61,62] Regarding social factors, economic stressors such as low socioeconomic status or economic inequality have been studied more in relation to depression and substance use, and less often in anxiety disorders. For anxiety disorders, meta-analyses in this domain mostly focus on social stressors such as ethnic discrimination, sexual minority status, or crime (appendix p. 1). Whether these findings reflect actual differences in what urban factors are relevant for the respective CMDs, or whether they expose a gap in research, requires further investigation. Such knowledge may also help to explain the differences in CMD burden between countries with different levels of urbanisation, as suggested by our results in Figure 1.

We only found one meta-analysis that suggested a protective effect, which was on exposure to greenspace and depressive mood.[63] Hence, factors that may promote mental health in cities (e.g. through urban design, economic opportunities, or better access to health services) require further research. In addition, there is a need for more robust evidence on the impact of phenomena such as rapid urbanisation and migration on CMDs, especially in LMIC settings (e.g. informal settlements and crowding).[25,64]

A call for a complexity science approach in urban mental health research

As outlined above, past research efforts have identified numerous urban factors that show an association with CMD outcomes. Notwithstanding the significance, most of these findings represent univariate explanations for phenomena that are most likely shaped by a multitude of dynamical interactions and feedback processes over time. Consequently, there is a considerable gap in our knowledge of how the urban environment shapes mental health.[10,12–14] For example, neighbourhood deprivation, low socioeconomic status, and crime, have all been reported to influence mental health negatively.[20,39] However, it remains unclear how these factors reciprocally interact over time in their impact on mental health, or how they are influenced by feedback from poor mental health outcomes in the local population. Evidently, the sole identification of risk (or protective) factors for CMDs does not provide a comprehensive explanation per se of how living in cities influences the risk of developing CMDs. Instead, the involved factors are part of dynamical 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 and processes of circular causality occurring 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 policymaking, aimed at reducing the burden of CMDs in urban populations. Therefore, we call for a complexity science approach as a novel avenue for urban mental health research.

The hallmark of complexity science is the notion that phenomena can be characterised as 'systems' constituted by individual lower-level 'elements' that, by virtue of their dynamical interactions, can give rise to emergent higher-level phenomena and patterns of self-organising (often non-linear) behaviour.[11]

Both cities and CMDs exhibit defining features of a complex system. First, cities constitute many elements that only in concert, and not in isolation, account for the palpable dynamics that emerge in the urban landscape.[65] Such elements range from city-level factors like urban design, to social factors like neighbourhood segregation, down to city inhabitants' individual characteristics. In mental health research, adopting a complexity science approach has become increasingly popular as well, both with regard to the conceptualisation of mental disorders as a disease entity and in the study of their aetiology.[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, which can give rise to a pathological state of the system resembling a psychiatric phenotype.[66] To illustrate 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 (2006-2007) of the Survey of Health, Ageing and Retirement in Europe study (SHARE, n=4,970).[68,69] The resulting network visualises the interwoven and multivariate nature of associations between urban factors and depression symptoms (Figure 2). In this regression-based network, estimated using the package *mgm* in R, green nodes represent urban factors and red nodes represent depression symptoms.[70] Connections between nodes signify group-level conditional dependencies between the variables, with thickness of the connections reflecting the strength of the positive or negative association. Since the network serves an illustrative purpose, we show it without the corresponding regression weights.

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 loops and processes of circular causality over different timescales, resulting in system behaviour that is non-linear and shows limited temporal predictability.[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 socalled superlinear scaling properties are proposed to result from an increasing 'return to scale', as opportunities for social interaction and (coupled) feedback loops are higher in larger cities.[71] In this light, it would be interesting to investigate how the burden of CMDs scales with city population size, especially given our findings suggestive of a positive association between levels of urbanicity and CMD burden (Figure 1).

Complex system behaviour in CMDs can be found in the occurrence of sudden deterioration of symptoms, characterised as (path-dependent) sudden transitions around tipping points from a healthy to a pathological state, such as shown in computational models and human time-series data on depression.[72,73] Here, underlying dynamics could consist of reinforcing symptom-level feedback loops (e.g. rumination and sleep) or aetiological drivers (e.g. diet and physical exercise) of mental disorders.[67,72] In addition, CMD outcomes can also feedback to explanatory factors, including some that impact urban surroundings. For example, depression may cause a decreased ability to maintain household duties,[74] which could result in neglect of one's physical surroundings. Ultimately, this could negatively impact neighbourhood aesthetics, as has also been suggested by other authors.[75] Such feedback could result in circular causality, where outcomes (i.e. CMDs) feedback and amplify the explanatory factors (e.g. neighbourhood aesthetics) that contributed to the onset of the disorder in the first place.

A conceptual framework for urban mental health research

To guide future urban mental health research, we present a conceptual framework (Figure 3) that lays out four important principles when theorising on the impact of the urban environment on mental health (and vice-versa) from a complexity science perspective. These principles are: (I) the factors and outcomes involved operate as dynamically interacting elements within a complex system, (II) factors are influenced by meta-level factors such as (changes in) city size, urbanisation, migration, and stage of economic development, (III) interactions between explanatory factors and CMD symptoms occur over different timescales, and (IV) CMD outcomes can influence explanatory factors (feedback loops). We will briefly discuss these principles below, before illustrating them with an example.

First, urban mental health phenomena are characterised as emerging properties within a complex system in which 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 (I) the (ambient or physical) urban environment, (II) the social environment, or (III) to individual city inhabitants (e.g. gender and age, but also neuroticism, neurobiological factors, or daily functioning). These elements can be both risk or protective factors for CMDs. CMDs are represented as symptom clusters that can be influenced by external elements, but symptoms may also influence each other, in line with the network theory of mental disorders.[66] CMDs in our framework are connected through 'bridge symptoms', as at least some symptoms are transdiagnostic.[76] Second, certain 'meta factors', listed in the vertical column on the left of the framework, have a profound impact on the urban environment at large. These include changes in city and population size, the process of urbanisation, migration (internal or international, e.g. for economic, political, or educational purposes), and stage of economic development (e.g. housing quality or availability of treatment).[24,64,71] Third, we account for the fact that interactions between explanatory factors and CMD outcomes occur over different timescales. 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 impact 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] Fourth, since CMDs are known to feedback to explanatory factors over multiple timescales, this is accounted for by the oscillating arrows from CMDs back to other elements in the system.

To illustrate our framework's use, we present a tentative example of an urban mental health scenario (appendix p. 26). Our example concerns Jane, an inhabitant of a neighbourhood with little greenspace (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] Furthermore, chronic exposure to air pollutants (urban factor) may negatively impact brain structures and functioning,[48] further increasing her risk of developing a CMD. Insomnia may increase financial distress by a negative impact on work performance, creating a reinforcing feedback loop.[79] Depending on Jane's (psychological) coping and neurobiological vulnerability, this may be enough to trigger, for example, a depressive disorder.[79] However, Jane's municipality is investing in sustainable urban development (meta factor) and build a park (protective urban factor) between her apartment building and the busy road. This intervention may improve Jane's mental health by reducing stress (individual factor)[63], and mitigating traffic noise (urban factors) in the short term[80], and eventually also by increasing neighbourhood social cohesion (social factor) [81] or perhaps even by mitigating air pollution (urban factor).[82] This tentative example showcases how a multiplex of interactions, crossing down from the urban to the individual level, triggering CMD symptomatology, feeding back and reinforcing distress, altogether shaped Jane's mental health. It also exemplifies how interventions in the system may impact multiple pathways over different timescales.

From a conceptual framework to theoretical and quantitative models

As illustrated above, our conceptual framework serves as a starting point to approach 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 draw maps of dynamical interactions and presumed cause and effect within the system as a whole. Network analyses and machine learning approaches can further advance theoretical causal maps by (data-driven) estimations of the multivariate statistical associations between a set of variables, such as shown in 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 at large.[83] Methods like 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 of interest, including those that transcend the individual level, such as the consequences of the current COVID-19 pandemic.[84] An example of an agent-based modelling study would be to investigate the mental health effect of repercussions of the COVID-19 restrictions in urban areas, such as psychological effects of large families in small living spaces, crowding in informal settlements, and increased risk of domestic violence.[7,85]

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

Future prospects: from complexity to actionable targets for intervention

The urban environment is becoming the main habitat of the world population,[1] a demographic shift that is accompanied by an increase in exposure to urban stressors that have been associated with higher risk of CMDs. This shift takes place amidst the ongoing COVID-19 pandemic, which poses additional mental health challenges on urban residents.[7] In this paper, we have argued that a complexity science approach should guide future urban mental health research. Complexity science methodologies can help to identify actionable targets for CMD interventions and policy. They can do so by pinpointing which leverage points in the real-world networks of elements that make up the urban system at large should be targeted, to have a meaningful impact on mental health outcomes. Notably, the most effective targets may not always be the ones most centrally located in a complex network, but may instead be (a combination of) the ones that are more peripherally connected.[90] In addition, innovative interventions should be developed for high-risk populations that are currently underserved by healthcare 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 both HICs and LMICs, including in urban populations with low socioeconomic status.[91–94]

In conclusion, answering the question of which actionable targets within urban systems should be addressed to improve the mental health of city inhabitants, represents one of the major challenges in the field. Adopting a complexity science approach may help to formulate answers to this question. We therefore presented a conceptual framework that can serve as a starting point for future urban mental health research. Novel insights from this approach could provide input for new treatment interventions and urban policies addressing CMDs in our ongoing urbanising world.

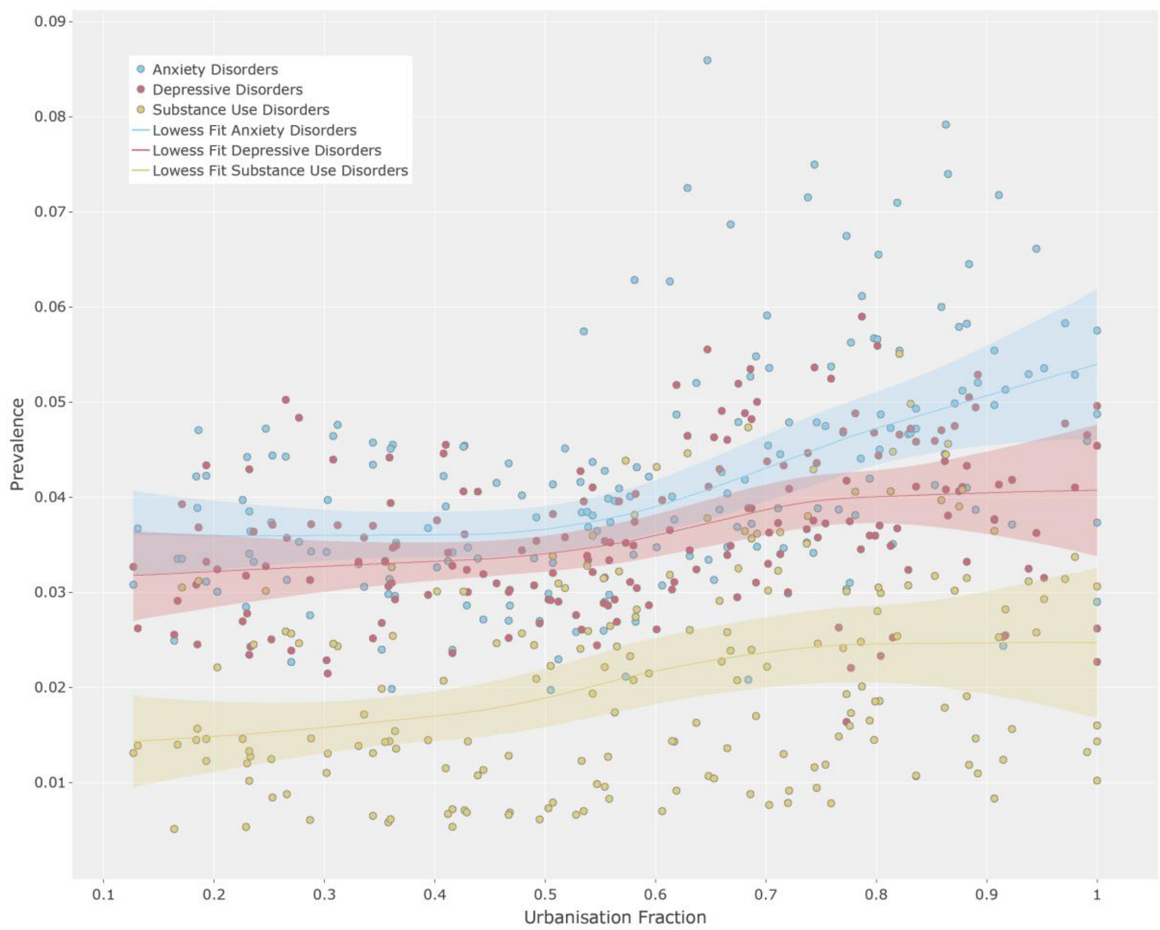

Figure 1: Relationship between level of urbanisation and prevalence of common mental disorders
The x-axis shows the proportion of a country's population living in urban areas, and the y-axis represents the prevalence of the common mental disorders. The dots represent countries, with each country included three times, once for each of the disorders, as indicated by the three different colours. An overview of the countries and diagnostic codes included in the plot are shown in the appendix (p. 18-22). Trend lines were produced using a locally weighted scatterplot smoothing (LOWESS) technique, the shaded areas represent bootstrapped 95% confidence intervals (n=191x0.5=95, k=500). An interactive version of this plot, specifying country, disorder, and data per dot, can be found at: https://chart-studio.plotly.com/~mhlees/21/#plot. The code and data sources used to produce this plot can be found at: https://github.com/mhlees/UMH-Plots

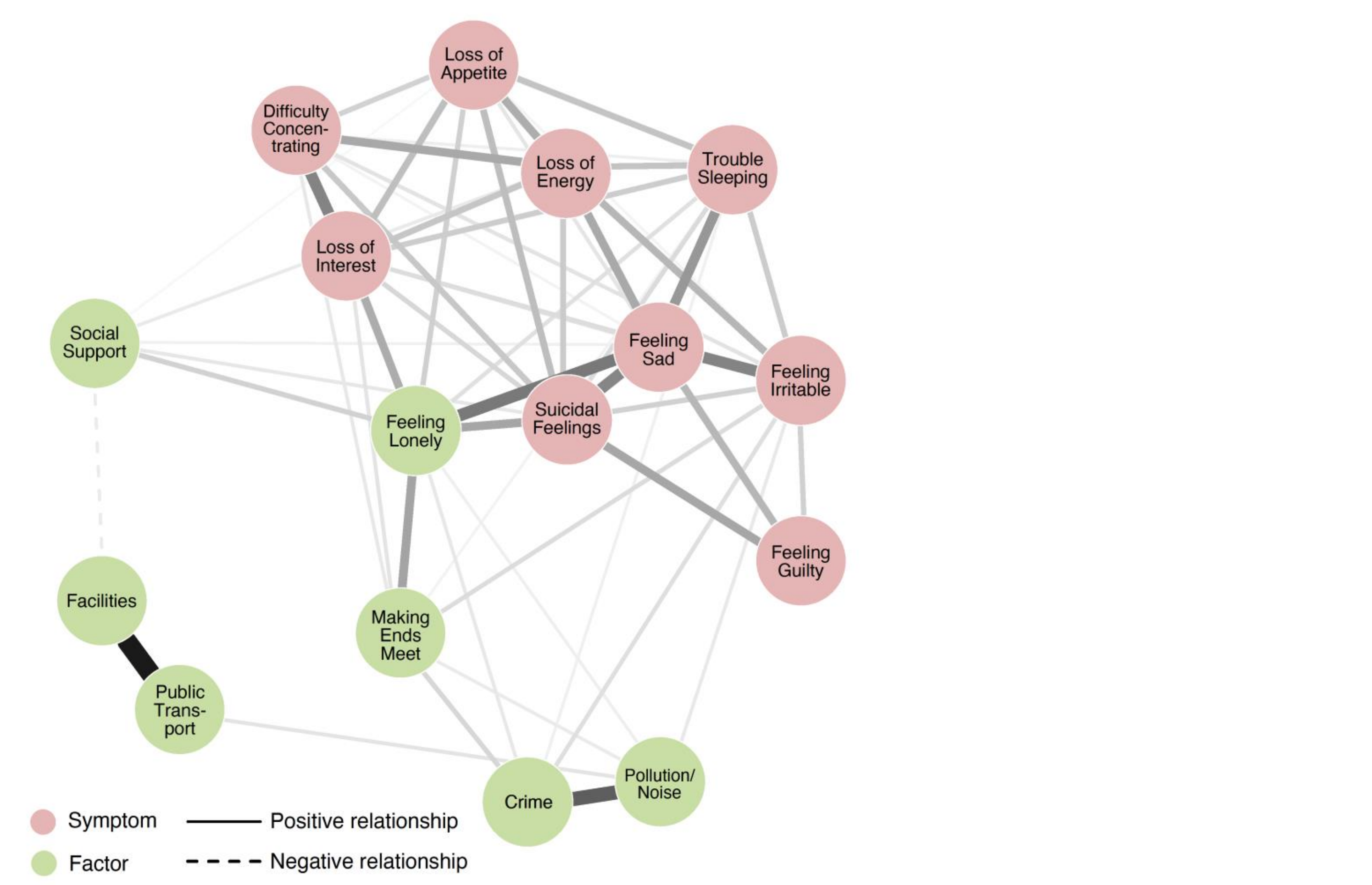

Figure 2: Network of urban factors and symptoms of depression
The network depicted is based on a regression-based mixed-graphical model, with nodes representing questionnaire scales and lines between nodes representing conditional dependence between the corresponding variables. The thickness of the lines reflects 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. Green nodes represent factors relating to the urban environment and red dots represent symptoms of depression.

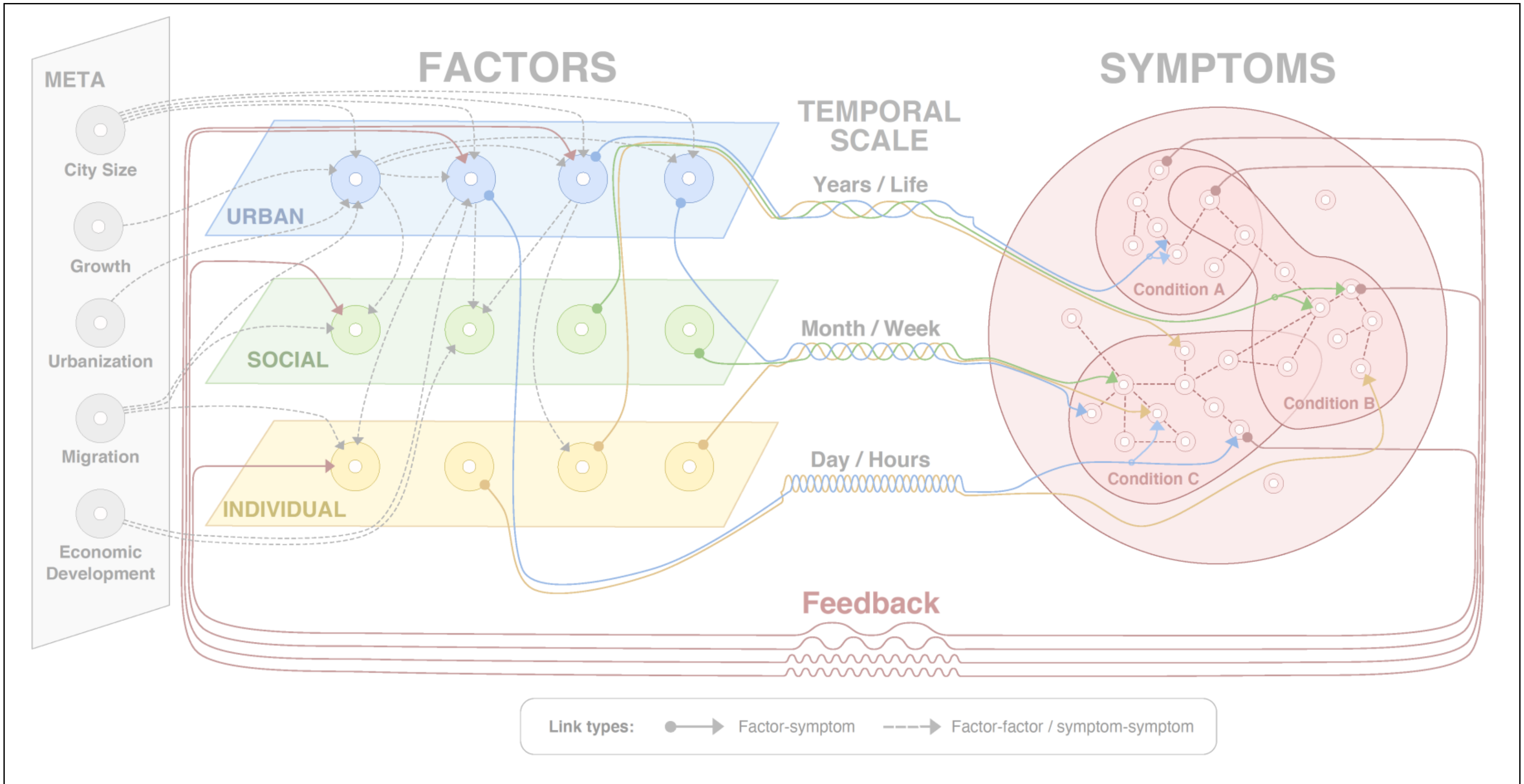

Figure 3: Conceptual framework of the relationship between factors in the urban environment and common mental disorder outcomes
This framework conceptualises urban mental health phenomena from a complex systems perspective. Meta factors (grey box) listed on the left are considered to have a dynamic impact on the urban environment and its inhabitants at large. Factors are categorized as urban factors (blue box; e.g. air pollution or built environment), social factors (green box; e.g. social cohesion) or individual factors (yellow box; e.g. individual demographic, psychological, or neurobiological characteristics). Oscillating arrows between the factors and common mental disorder (CMD) symptoms signify the different temporal scales across which factors can assert their effect. CMDs are represented as symptom clusters (red circle) connected by bridge symptoms. Feedback arrows represent the possibility of feedback from CMD symptoms to explanatory factors, which can also occur over different timescales.

Search strategy and selection criteria rapid review
For the rapid review, we performed 34 systematic searches on PubMed between April 22nd 2020 and June 5th 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 (p. 15-17). Both MeSH-terms and search terms in title or abstract were used to identify relevant studies. Results were filtered to only show meta-analyses published after 1990. We included meta-analyses that: studied the association between exposure to at least one urban-related factor and CMD outcome (diagnosis or symptomatology of a disorder classified as depressive-, anxiety- or substance use disorder in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders), included only studies in humans (of any age), had full-text availability, and were written in the English or Dutch language. We excluded meta-analyses that: studied participants with any comorbidity other than comorbid CMDs, only included studies in an occupational setting. Altogether, searches for depressive disorder yielded 96829 hits of which 599 were meta-analyses (503 remained after removing duplicates), searches for anxiety disorders yielded 48166 hits of which 287 were meta-analyses (105 remained after removing duplicates), and searches for substance use disorders yielded 91366 hits of which 502 were meta-analyses (392 remained after removing duplicates). Twelve additional meta-analyses were identified through hand-searching. Screening was primarily performed by JMvdW, with consultation of JJFB in case of uncertainty about inclusion. Furthermore, JJFB performed a crosscheck of a subset of the included and excluded papers. After screening, a total of 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 (19), wrong study design (19), CMD diagnosis or symptomatology not included as outcome (7), no full-text access (4), not in the English or Dutch language (2), or inclusion of participants with neuropsychiatric comorbidity other than comorbid CMDs (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 (p. 1-14).

Author contributions:

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 interest:

The authors declare no conflicts of interest.

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