A syndemic of psychiatric morbidity, substance misuse, violence, and poor physical health among young Scottish men with reduced life expectancy

Jeremy Coid [a,b,1,*], Yingzhe Zhang [a,c,1], Paul Bebbington [d], Simone Ullrich [b], Bianca de Stavola [d], Kamaldeep Bhui [e], Alexander C. Tsai [f,g]

[a] *Mental Health Center and Psychiatric Laboratory, The State Key Laboratory of Biotherapy, West China Hospital of Sichuan University, Chengdu, Sichuan, China*
[b] *Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK*
[c] *Harvard T.H. Chan School of Public Health, Boston, MA, USA*
[d] *Department of Mental Health Sciences, University College London, London, UK*
[e] *Department of Psychiatry & Nuffield Department of Primary Care Health Sciences Medical Sciences Division, University of Oxford, London, UK*
[f] *Center for Global Health and Mongan Institute, Massachusetts General Hospital, Boston, MA, USA*
[g] *Harvard Medical School, Boston, MA, USA*

ABSTRACT

Background: Scotland has the shortest life expectancy in Western Europe, driven by high rates of cancer, suicides, alcohol-related causes and drug-related poisonings. These disparities cannot be explained solely by socioeconomic deprivation. Our aim was to investigate whether a syndemic in a socioeconomically deprived area of Glasgow might account for premature mortality among men.
Methods: We analysed data from two cross-sectional population surveys: a national sample of 1916 British men and another of 765 men in Glasgow East. The survey included men aged 18–34, and was undertaken in 2011 to study correlates of violence. Questionnaires covered current physical health, psychiatric symptoms, substance misuse, and crime and violence. Syndemic components were identified using confirmatory factor analysis. Associations and synergistic interactions between these variables and health status were estimated using logistic regression.
Results: An aggregation of multiple health conditions and health-related behaviours was found in Glasgow East. A syndemic model of joint effects, adducing a four-component latent variable (violence, substance dependence, psychiatric morbidity and a diathesis of biological/behavioural risk) showed synergy between components and explained persistent disparities in poor physical health/chronic health conditions. Effect modification was found between the general syndemic factor and contextual variables at individual and social environmental level according to location.
Conclusions: Syndemic effects from synergistic interactions were confirmed between psychiatric morbidity, substance misuse, violence, and biological/behavioural risk for physical health. A hypothetical model was developed to explain how the syndemic leads to potentially life-threatening risks to young men, both currently and as precursors of physical health conditions which may shorten their lives in the future.

1. Introduction

Psychiatric morbidity, substance use and self-harm in early adulthood set in motion a range of socioeconomically patterned physical illnesses in later life, including liver and renal diseases, ischaemic heart disease, cerebral infarction, chronic obstructive bronchitis, lung cancer and dementia as a cascade of life-shortening health conditions (Kivimaki et al., 2020). The mechanisms involved remain unknown. Scotland has persistently endured the shortest life expectancy in Western Europe (Walsh et al., 2020). This is mainly due to premature mortality rates in the largest urban area, Glasgow, driven not only by higher rates of all cancers, but also suicide, alcohol-related causes, and drug-related poisonings referred to as "deaths of despair" (Schofield et al., 2016). Socio-economic deprivation is exceptionally high in certain parts of

---

Glasgow and some other Scottish cities. Men living in the poorest parts of Glasgow have a life expectancy fifteen years lower than those living a few miles apart, in the most wealthy areas, with men in the poorest areas having only a 53% chance of reaching their 65th birthday (Cowley et al., 2016). However, the excess mortality cannot all be explained by deprivation. In particular, Scottish mortality rates worsened between 1981 and 2011 compared with other UK countries, and despite a later relative improvement in levels of deprivation. Moreover, the "Scottish effect" persists after accounting for socioeconomic deprivation and health behaviours such as smoking, physical activity, and diet (Schofield et al., 2016).

Drug-related deaths in Scotland are currently more frequent than in the European Union and similar to those in the USA, particularly in Glasgow (National Records of Scotland, 2019). Lower life expectancy among young men in Scotland may reflect high levels of drug and alcohol misuse and their impact on both physical and mental health. At the end of the 20th century, Scotland had the highest homicide rates in western Europe (Leyland & Dundas, 2010) although rates of violence have more recently fallen among younger people (Scottish Government, 2019). Violence in some areas of Glasgow remains prevalent, being strongly associated with criminality and the distribution and sale of illicit drugs (Densley et al., 2018; McLean et al., 2018). People living in the most deprived areas of Scotland are also three times more likely to receive inpatient psychiatric care than those in the least deprived areas, particularly in Glasgow and Dundee (Scotland, 2019). Overall numbers for adults under 65 years are somewhat higher for men. The most common diagnoses are mental health and behavioural disorders due to psychoactive substance use (National Records of Scotland, 2019). Taken together, these findings indicate excess mental and physical health risks in parts of Scotland, particularly Glasgow.

1.1. Large-scale social forces in the Glasgow conurbation

Large-scale political, economic, and cultural forces such as changing political and economic conditions, shifting ecological and environmental conditions, and altering demographics and social behaviours may provide the context for clustered epidemics of various diseases (Singer et al., 2017). Glasgow became wealthy during the 19th century as a hub of industrial and economic development, particularly in textiles and shipbuilding, in tandem with large scale, inward migration for work from other parts of Scotland, Ireland and Europe. Along with other UK cities, Glasgow later experienced the economic and social consequences associated with the decline of empire and increasing international industrial competition. However, the social forces associated with poor health and the stalling of improvements in life expectancy relative to other parts of the UK and Europe began later, with progressive post-industrial decline in the latter half of the 20th century. By the 1950s, tenement slums were increasingly replaced by a new generation of post-war high-rise housing and large suburban housing estates. These were associated with the fracturing of long-established community relationships and social structures, resulting in concentrations of deprivation and criminality associated with loss of social capital. The 1970s and 1980s were a period of serious and accelerated decline in industry leading to mass unemployment and urban decay. Political policies and social changes outside the control of the local population in deprived areas of Glasgow included relocation of younger, skilled workers to "New Towns" away from the "declining city", continuing urban change, and slum clearance. People were displaced to poor quality peripheral housing estates, often surrounded by an equally impoverished physical environment, with vacant and derelict land. High-risk subgroups of people with histories of mental illness, substance use disorders, and homelessness were relocated to hostels and cheaper accommodation in these areas, encouraging a 'democratic deficit' with experiences of despondency, disempowerment, and lack of sense of control (Walsh et al., 2017).

Overall, social capital is thought to be lower in Glasgow than in other

British cities such as Manchester, Liverpool and Belfast that ostensibly share the experience of socioeconomic deprivation following post-industrialisation (Walsh et al., 2017). However, no single contributing factor appears to explain why Scotland, and Glasgow in particular, should have different mortality patterns compared with other UK cities experiencing comparable deprivation (Walsh et al., 2017). Thus, when comparing pooled cohort studies, only a quarter of the excess mortality among Scottish respondents could be explained by available baseline risk factors (McCartney et al., 2015). Many have attempted to explain the Scottish and Glasgow effects, with one report identifying forty possible hypotheses ranging from socioeconomic, cultural, political, genetic and environmental factors: however, none were linked to sufficiently robust evidence to support causal claims (Walsh et al., 2017). Most studies do conclude, however, that the excess of poor health outcomes is partially attributable to the cumulative effects of risk factors. An alternative, but previously untested explanation for these observed disparities in poor health is that the disparities of diseases and health conditions exhibit synergistic interactions, resulting in shortened life expectancy. If proven, this has significant implications for preventive policy and interventions in other cities facing marked deprivation and persistent health inequalities including premature mortality amongst men and those with psychiatric conditions.

1.2. Syndemic theory

A syndemic was proposed by Singer (1996) as an aggregation of two or more epidemics of diseases or other health conditions in a population whereby there is some level of deleterious biological or behavioural interface that exacerbates negative health effects of any or all of the diseases involved. Syndemics involve adverse interaction between epidemics of all types and are most likely to emerge under conditions of health inequality caused by poverty, stigmatisation, stress or structural violence, and where cultural and historical factors may have an effect (Coid et al., 2020). The synergistic interactions between epidemics can be on the additive or multiplicative scale. Only a minority of studies that purport to describe a syndemic have actually done so because most have not demonstrated synergistic interaction between the proposed components of the syndemic. (Tsai & Burns, 2015; Tsai et al., 2017). Through synergy, the disease burden attributable to health risks in combination exceeds the sum of the disease burden of the health risks when considered separately (Tsai et al., 2017).

To test the hypothesis that disparities in health conditions which potentially increase risk of premature mortality cluster in parts of Glasgow and constitute a syndemic, we conducted surveys of young adult men from a representative sample of the British population (including Scotland) and a Scottish sample in an urban area of Glasgow characterised by exceptionally high socioeconomic deprivation, economically inactive persons and shorter life expectancy. Our specific aims were to (a) compare the prevalence of mental health and behavioural problems, substance use disorders, and poor physical health, including long-term risks for shortened life expectancy, crime and violence in the British general population with those from a deprived area of Glasgow and investigate whether they clustered in the latter location; (b) when focusing on overall poor physical health as the outcome, investigate whether other domains of health conditions had synergistic interactions with each other in their associations with poor physical health; and (c) investigate contextual associations with the syndemic, according to location.

2. Method

We firstly compared the prevalence of health conditions and health risks in different domains in a representative National survey of men in England, Scotland and Wales with men in Glasgow East (GE). We adjusted for confounding to test whether differences were explained by higher levels of socioeconomic deprivation in GE. We then assessed the

extent to which disease clustering was present. We applied the same method to identify a syndemic which has previously explained excess psychotic illness among young Black men in inner London, UK (Coid et al., 2019). We validated the structure of different health domains using factor analysis. We carried out tests of interaction between domains (violence, physical health, mental health, substance use) specifying poor physical health/long-standing physical health condition as the outcome. We additionally wanted to investigate whether the burden of physical health outcome was partly explained by high-risk health behaviours and biological risk. We therefore carried out an analysis on the components of the syndemic to test our hypothesis that poor physical health/chronic conditions as our outcomes were potential precursors of conditions that would later shorten life. We used proxy measures of biological and behavioural risk for physical diseases as the fourth component of the syndemic to test for interactions with the other three components (violence, substance misuse, psychiatric morbidity). We used two items of physical health as the outcome: self-reported poor physical health and long-standing heath conditions. We finally tested whether the effects of contextual factors on the syndemic (at the individual level and capturing the social environment) were modified by residence in GE.

2.1. Study participants

We used data from the Second Men's Modern Lifestyles Survey carried out in 2011 using random location sampling, an advanced form of quota sampling shown to reduce biases introduced when interviewers are able to choose locations to sample from (see supplementary file). The statistical reliability of this approach depended both on strictly defining the selection of the sampling points and on setting representative quotas at each point, then meeting these quotas. Compliance with this procedure produced a fully representative data set for both the national survey and for GE. Informed consent was obtained from respondents. Pencil and paper self-report questionnaires were administered at home, with the respondent left to complete the questionnaire in their own time. The researcher either returned later that day or the next. Each questionnaire took approximately 45 min to complete. Participants were given £5 on completion of the questionnaire. The National survey derived a representative sample of young men aged 18–34 years from England, Scotland and Wales. We compared a boost survey of men of the same age range from GE for comparison purposes because of exceptionally high levels of recorded health, social problems, and reduced life expectancy in that location and to test the hypothesis that a syndemic may be operating in this location. Identical sampling principles were used for both surveys. This age range and a male sample were originally chosen to investigate risk factors for violence, substance misuse, and psychopathology at the population level as one component within a programme of research studies to improve risk management of violence (Coid et al., 2016). Additional boost samples included hard-to-reach participants, including those from areas with exceptional characteristics and known to have high levels of violence, which included GE.

2.2. Health-related and other measures

We evaluated 25 health-related measures from 4 different domains. These were treated as categorical variables. Where these were derived from standardised scales, we used cut-off scores: substance use, including alcohol, drug dependence, problem gambling; mental health, including psychosis, anxiety disorder, depressive disorder, antisocial personality disorder, suicide attempts; physical health risks, including short statue, high fat/low fibre diet, lack of exercise, and serious life-threatening injury; violence and criminality, including repeated fights, intimate partner violence (IPV), fear of violent victimisation, weapon carrying, gang fights, instrumental violence, friends encouraging criminal activity, convictions for ≥3 different types of crime, and imprisonment on ≥2 occasions.

For our outcome, we selected physical health fair or poor and long-standing physical health condition as our proxy measure of burden of disease and hypothetical precursors of life-shortening physical conditions in the future. One or both of these variables had to be present.

Positive screening for psychosis was recorded if ≥ 3 criteria were met using the Psychosis Screening Questionnaire (PSQ) (Bebbington & Nayani, 1995). The Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) defined anxiety and depression based on scores ≥11 in the past week. Scores ≥20 on the Alcohol Use Disorders Identification Test (Babor et al., 2001) and scores ≥25 on the Drug Use Identification Test (Berman et al., 2005) identified alcohol or drug dependence, respectively. The Structured Clinical Interview for DSM-IV Personality Disorders Screening Questionnaire (Ullrich et al., 2008) identified antisocial personality disorder.

High fat/low fibre diet was defined as 2 or more criteria met of eating vegetables and/or fresh fruit less than once a week, eating fatty or sugary foods, and food cooked in fat more than once a week.

The Standard Occupational Classification for the UK was used to measure social class (Office for Population Censuses and Surveys, 1991). Socioeconomic deprivation was measured using a ranking on the Index of Multiple Deprivation Ranking (IMDR) which measures the proportion of the population in an area experiencing deprivation according to domains of income, employment, health and disability, education skills and training, barriers to housing and services, crime, and living environment (Communities and Local Government., 2010).
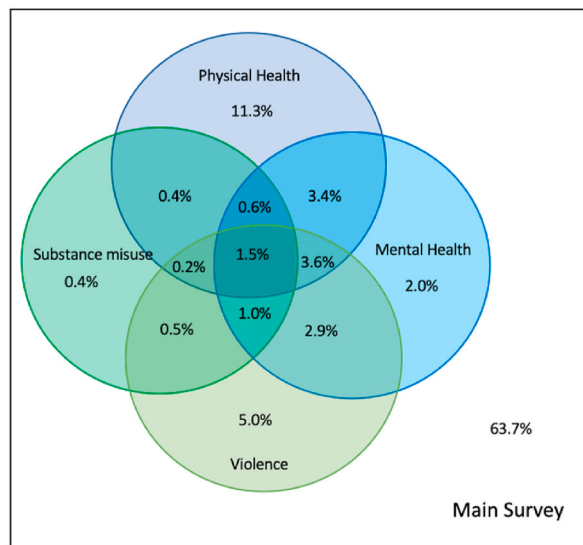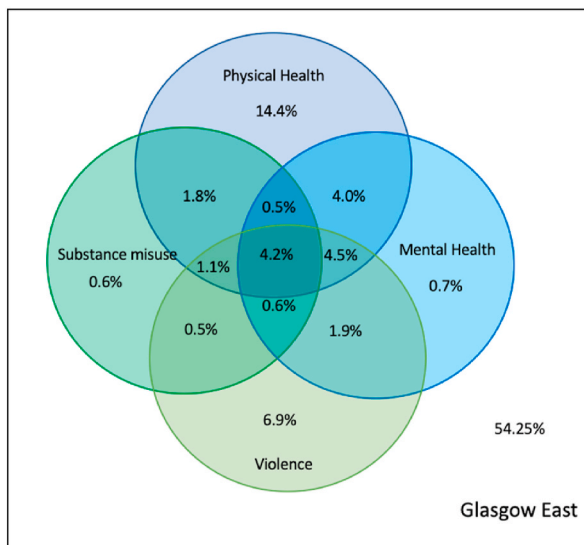
The social environment refers to relationships, groups and social processes that exist between individuals and groups who live and work in a neighbourhood context to interact positively but where such interactions may also interact negatively (Carroll-Scott et al., 2013). To investigate the social environment and its impact, we included two additional variables measuring social interactions: peers encouraging drug use and crime). Because unemployment is associated with mortality (Roelfs et al., 2011) and high in GE, we used a robust measure of economic inactivity: not in unemployment, education or training (NEET) (OECD, 2020; UCL Institute of Health Equity, 2014).

2.3. Statistical analysis

We estimated the associations between socio-demographic characteristics among men in the National and GE surveys by fitting multivariable logistic regression models to the data. We next explored associations with psychiatric morbidity, violence, physical health, substance misuse and health service utilization between young men in the national survey and GE. To test whether associations between young men in GE (versus the national survey) and health-related risk factors are explained by the socioeconomic deprivation levels that were higher in GE (McLennan et al., 2019), we fitted two logistic regression models for each variable, with one adjusted for age, and the other adjusted for age and IMDR.

We conducted a confirmatory factor analysis (CFA) to validate the structure of health-related domains among young men in both the National survey and GE to provide a more parsimonious understanding of the covariation in a set of indicators in factor scores. We constructed the CFA model consisting of violence, psychiatric morbidity, substance misuse and physical health risks (excluding our 2 physical health outcomes) as four latent factors within a total of 23 health-related variables (Fig. 1). To achieve an appropriate structure of these health-related risks, we sought to obtain a good model fit in the CFA model with reasonable structure domains. To accommodate the binary indicators, a weighted least squares mean- and variance-adjusted estimator was used to account for bias in estimates. The model was standardised by fixing factor variances at 1. For identification of the CFA model, item variances were allowed to be estimated freely. Model fit was assessed using the root-mean-square error of approximation (RMSEA), the comparative fit index (CFI) and the Tucker–Lewis index (TLI). Values ≤ 0.05 for RMSEA, and ≥0.95 for CFI and TLI, were interpreted as suggesting very good

>=1items per factor
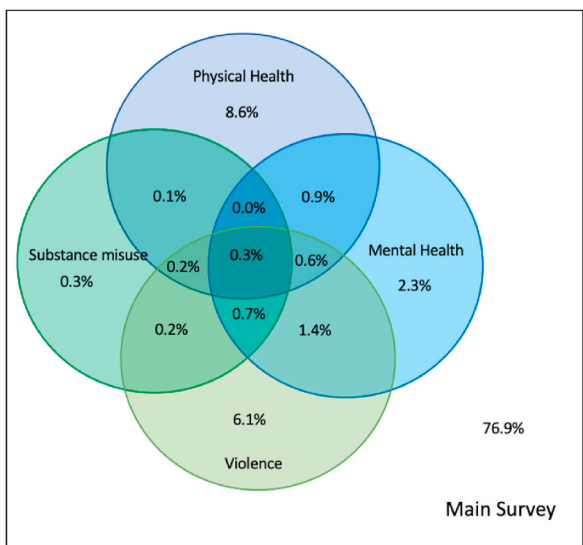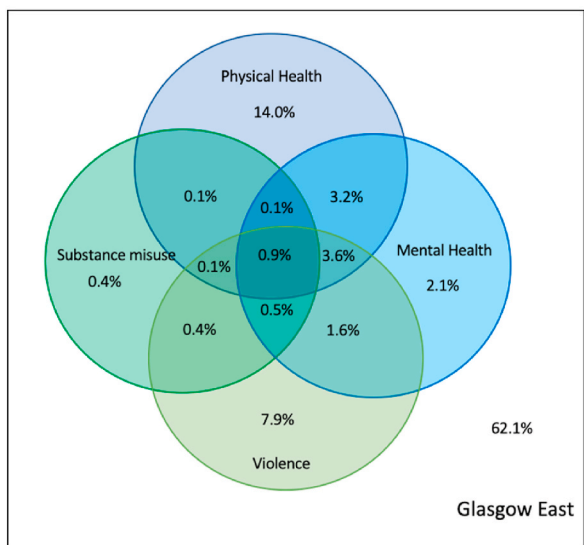

>=2 items per factor

Fig. 1. Comparing clustering of mental health, substance misuse, violence, and physical health items among men in the National (n = 1916) and Glasgow East (n = 765) surveys.

model fit (Hu & Bentler, 1999).

Factor scores for violence, psychiatric morbidity and substance misuse were derived from CFA to estimate associations with indicators of physical health, setting a clinically robust cut-off of ≥2 of 4 physical health-related variables to indicate a cluster, including high fat/low fibre diet, lack of exercise, short stature, serious life-threatening injury. In order to test for syndemic effects between violence, psychiatric morbidity and substance misuse, and physical health risks on poor physical health/long-standing conditions (outcome), we estimated interaction terms using logistic regression. Because of high correlations between violence, mental health and substance misuse (pearson coefficient between violence and mental health, 0.78; between violence and substance misuse, 0.95; between substance misuse and mental health, 0.93), we estimated interactions using two factors at a time.

To investigate potential overall syndemic effects, the model was extended to a second-order factor model to establish a high-order latent variable representing a general syndemic construct. The general syndemic factor derived from the second-order factor model can represent

the clustering effect of risk factors within a sub-population so that we can compare the clustered health-related risks between different sub-populations by demographic factors (i.e., age, single, non-UK born, no educational qualifications, social class and ethnicity) and different social environments (i.e. peers encouraged crime, peers encourage drug use). The general syndemic factor was measured as a continuous score based on the second order factor analysis in Fig. 2. Associations between the contextual factor variables and general syndemic factor were estimated by comparing each subgroup (men with characteristics in national survey, other men in GE, and men with characteristics in GE) with the reference group (other men in national survey) using linear regression. We also contrasted the differences between men with characteristic factors in GE and men with characteristic factors in national survey for each variable.

Appropriate non-response weights were used throughout. We used cluster-correlated robust standard errors to account for correlations within survey areas due to clustering within postcodes. A significance level of 0.05 was adopted throughout.
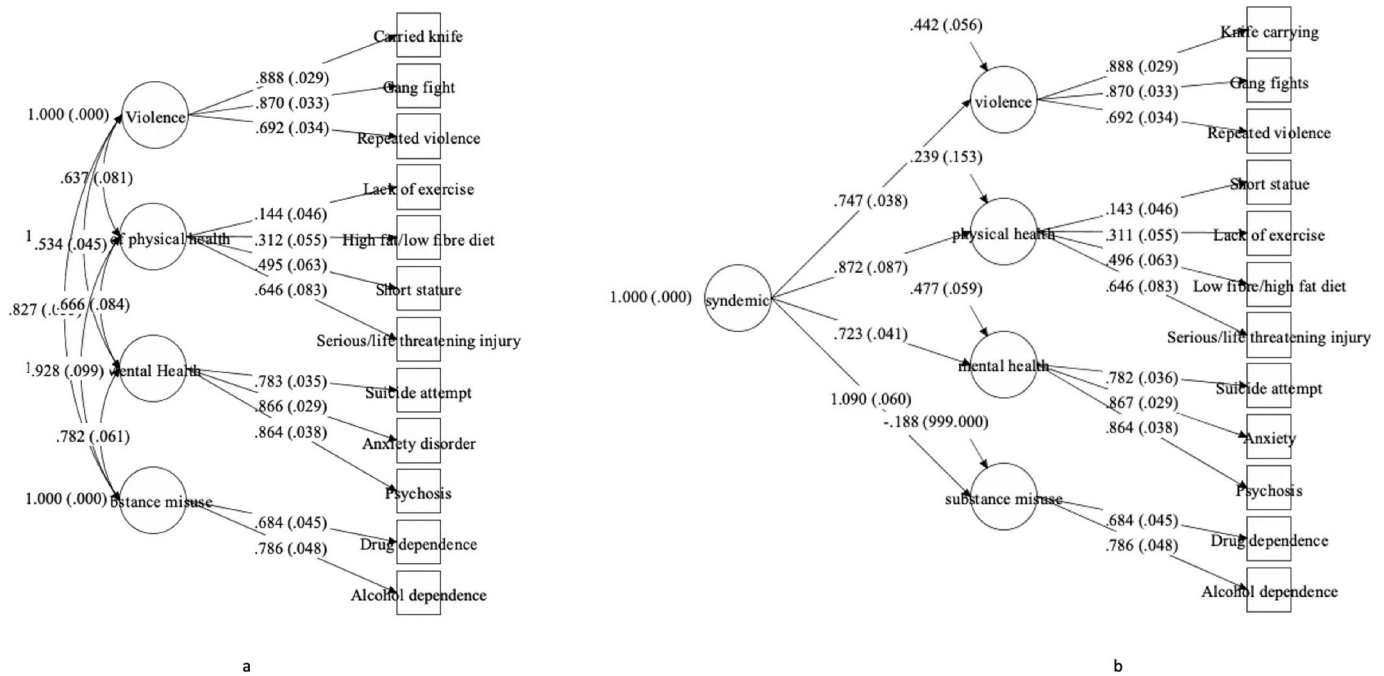
Fig. 2. Confirmatory factor model for psychiatric morbidity, substance misuse, violence, and physical health/risks (a), and a second-order general syndemic factor model(b).

Statistical analyses were conducted using Stata version 15 for Windows and Mplus version 8.3 for Windows (Muthén & Muthén, 2017).

3. Results

The unweighted sample included 2681 men, aged 18–34 years; 1916 (71.5%) were from the representative survey, and 765 (28.5%) were from GE. Table 1 shows differences in demographic characteristics between young men in GE and the National survey. GE men were more likely to be single, few were non-UK born, had educational qualifications, or were of black and minority ethnic background (BME), Table 1

Table 1
Sample characteristics of national and Glasgow East young men (n = 2681).

Demographics	National survey	Glasgow East survey
	N (%)	N (%)
Sample size	1916 (71.5)	765 (28.5)
Age, years		
18–24	710 (37.1)	292 (38.2)
25–34	1206 (62.9)	473 (61.8)
Single	1122 (58.6)	546 (71.4)***
Non-UK born	173 (9.0)	12 (1.6)***
No educational qualifications	201 (10.5)	171 (22.4)***
Social Class		
I and II [a]	267 (13.9)	40 (5.2)
III	597 (31.2)	170 (22.2)*
IV and V	335 (17.5)	161 (21.0)**
Unemployed	609 (31.8)	392 (51.2)***
Ethnicity		
White	1694 (88.4)	752 (98.3)
BME	222 (11.6)	13 (1.7)***
NEET	206 (10.8)	172 (22.5)***
	Mean (SD)	Mean (SD)
IMDR	12,454 (9883)	1296 (1443)***

All data are weighted frequencies and percentages (row %).
a. Association test based on multinomial logistic regression with social classes I and II as base level.
*P < 0.05, **P < 0.01, ***P < 0.001.
BME: black and minority ethnic background, NEET: not in employment, education, or training, IMDR:the Index of Multiple deprivation ranking.

shows a social class gradient whereby significantly more were of lower social class, below level III. More than twice as many men in GE were not in employment, education, or training (NEET). The mean level of socioeconomic deprivation measured by ranking on the IMDR was considerably higher for GE men than for men in the national survey. There were no differences in age.

Table 2 Compares health outcomes among men in the national survey with those in GE. Men in GE showed higher prevalence of psychiatric conditions of psychosis and anxiety; substance use disorders, including drug and alcohol dependence, and problem gambling; all measured items of violence except IPV; all measured conditions indicating poor physical health and physical health risks except lack of exercise and obesity. The table also compares the two surveys following adjustment for socioeconomic deprivation measured at the small-area level. Following adjustment, the odds of association for psychiatric morbidity were attenuated and no longer statistically significant. Increased odds of association were still observed between men in GE and drug and alcohol dependence. All measured items of violence previously observed before adjustment for IMDR were statistically significant except repeated violence. All measured items of physical health/risks except high fat/low fibre diet remained statistically significant.

The co-occurrence of items from four domains of psychiatric morbidity, substance misuse, violence, and poor physical health and physical health risks are compared between men in the national survey and GE in Fig. 1. The Venn diagram shows that 36.3% men in the national survey had one or more of any items compared with 45.8% in GE. For GE men, 19.1% showed co-occurrence of an item from one domain with an item of another domain, compared with 14.1% in the national survey. When two or more items were examined, 23.1% in the national survey had two or more items from any domain compared to 37.9% in GE. For GE men, 10.5% showed co-occurrence of two or more items with one domain with two or more from another domain, compared with 4.4% in the national survey. There were 33.8% men in the national survey and 42.3% in GE with three or more items from any domain.

CFA was used to develop a syndemic model including four factors of violence, physical health risks (excluding poor physical health and longstanding conditions), mental health and substance misuse (Fig. 2). The first step identified first order syndemic variables by domain,

Table 2
Effects on health outcomes comparing National Survey and Glasgow East young men (n = 2681).

	National		Glasgow east		National cf Glasgow east			
					Model 1		Model 2	
Mental Health	n	%	n	%	OR	95%CI	OR	95%CI
Psychosis (PSQ3+)	38	2.0	26	3.5	1.77*	1.07–2.94	1.11	0.95–1.29
Anxiety disorder	202	10.7	106	14.0	1.34*	1.04–1.73	1.07	0.99–1.15
Depressive disorder	134	7.5	65	8.9	1.22	0.89–1.66	0.99	0.90–1.08
Antisocial personality disorder	367	20.3	173	23.2	1.18	0.96–1.45	0.99	0.93–1.05
Suicide attempt	114	6.1	48	6.2	1.02	0.72–1.44	0.94	0.85–1.04
Substance Use								
Alcohol dependence	132	7.0	84	11.4	1.71***	1.28–2.27	1.10*	1.01–1.19
Drug dependence	41	2.2	47	6.3	2.95***	1.92–4.52	1.20**	1.06–1.37
Problem gambling	112	6.5	69	9.9	1.61**	1.17–2.20	1.07	0.98–1.17
Violence and criminality								
Repeated violence ≥4	252	13.6	132	18.1	1.43**	1.13–1.80	1.06	0.99–1.13
IPV	63	3.3	28	3.7	1.10	0.70–1.74	0.95	0.84–1.08
Fear violent victimisation	280	15.3	175	24.2	1.79***	1.44–2.21	1.15***	1.08–1.22
Carried knife	106	5.5	84	11.0	2.13***	1.58–2.88	1.11*	1.02–1.22
Gang fights	56	2.9	67	8.8	3.32***	2.29–4.80	1.27***	1.14–1.43
Peers encourage crime	161	9.0	102	14.0	1.67***	1.28–2.18	1.11*	1.03–1.20
In prison ≥2 times	38	2.0	61	8.0	4.06***	2.68–6.17	1.35***	1.18–1.54
Instrumental violence	143	7.6	120	15.8	2.27***	1.75–2.94	1.17***	1.08–1.26
Criminal versatility ≥3	63	3.3	57	7.5	2.32***	1.60–3.36	1.12*	1.01–1.25
Physical health/risks								
Physical health poor/fair	212	11.2	165	21.7	2.15***	1.71–2.69	1.15***	1.08–1.24
Longstanding physical condition	161	8.4	109	14.3	1.72***	1.32–2.24	1.09*	1.01–1.18
Serious/life threatening injury	52	2.7	36	4.7	1.70*	1.10–2.64	1.18*	1.03–1.35
High fat/low fibre diet	121	6.3	75	9.8	1.63**	1.20–2.20	0.96	0.87–1.05
Lack of exercise	186	9.7	94	12.2	1.28	0.98–1.66	1.03	0.95–1.11
Smoking ≥ 15/day	271	14.1	146	19.1	1.43***	1.15–1.79	1.13***	1.06–1.22
Short stature ≤160.5 cm	40	2.4	35	5.0	2.12***	1.34–3.36	1.21**	1.05–1.41
Obesity (BMI>30)	208	12.7	84	12.4	0.92	0.70–1.21	0.95	0.88–1.03

Model 1: adjusted for age. Model 2: adjusted for age and IMDR.
*P < 0.05, **P < 0.01, ***P < 0.001.
PSQ: Psychosis Screening Questionnaire. IPV: intimate partner violence.

excluding items which did not load highly. Short stature showed moderate loading but would have worsened the model fit if excluded and was therefore included in the final model. Three variables of criminal behaviour were excluded due to poor convergence. Model fit indices were excellent: RMSEA = 0.029 [95% CI: 0.024–0.033], CFI = 0.967, TLI = 0.958.

Due to high correlations between the first order syndemic constructs, a second order CFA was then developed following standard SEM modelling practice to generate a general syndemic construct that linked first order health factor domains. Fig. 2 confirms that a second order syndemic construct should be included in the model (fit indices: RMSEA

Table 3
Associations and synergy between violence (V), mental health (MH), physical health risk factors (PHR)[a] and substance misuse (SM) with outcome [b].

Factor	Direct associations with outcome [b]	Synergy between factors in associations with outcome [b]
	OR (95% CI)	OR (95% CI)
Violence	1.16***(1.13–1.19)	
Physical health risk factors	3.94***(3.31, 4.68)	
Mental health	1.28***(1.24, 1.33)	
Substance misuse	1.30***(1.26–1.34)	
Interactions		
V by MH		1.05 (0.99–1.11)
V by PHR		1.22 (0.92–1.62)
V by SM		1.06*(1.00–1.12)
PHR by MH		1.56**(1.11–2.17)
PHR by SM		2.03***(1.44–2.86)
MH by SM		1.12***(1.05–1.20)

OR, odds ratio.
*P < 0.05, **P < 0.01, ***P < 0.001.
[a] High fat/low fibre diet, lack of exercise, short stature, serious injury.
[b] Poor/fair physical health and/or chronic physical condition.

= 0.034 [95% CI: 0.030–0.038], CFI = 0.953, TLI = 0.941).

Table 3 shows evidence of multiplicative interaction between violence and substance misuse, physical health risks and mental health problems, physical health risks and substance misuse, and mental health problems and substance misuse. All interactions had poor physical health/longstanding conditions as their outcome.

The second order syndemic factor in the factor analysis was finally used to obtain a score for each participant in both surveys. Table 4 shows the effect modification of disease context associations on the general syndemic factor according to survey location. Disease context associations at the individual level in the national survey, including single marital status, no educational qualifications, unemployment and NEET status, were significantly higher on the general syndemic factor. However, in addition to these same context associations showing significantly higher scores on the general syndemic factor among the men who resided in GE, we found non-UK born men showed significantly lower scores. When comparing location differences, all men with contextual associations shown in Table 4 showed significantly higher scores on the general syndemic factor except non-UK born and BME men, where there was no significant difference. In addition, we included two measures aimed to capture the social environment of the men. In the National survey 162 (9.1%) compared to 101 (14%) in GE reported they were encouraged by friends to engage in crime (OR 1.67, 95% CI 1.28–2.18); 410 (21.6%) in the national compared to 228 (30.0%) were encouraged by friends to use drugs (OR 1.59, 95% CI 1.31–1.92). GE men showed significantly higher scores than men reporting these two social environmental associations.

4. Discussion

Previous research has been unable to explain excess premature deaths among men in Glasgow on the basis of either cumulative risk

Table 4
Test of effect modification of contextual factor associations by survey location on the general syndemic factor.

Contextual association.	National survey		Glasgow East		Location differences[a]
	Other Men	Contextual factor	Other Men	Contextual factor	
	Ref.	β	β	β	Contrast. (β)
Age >24 years old (vs ≤ 24 years old)	Ref	−0.105***	0.044	0.156***	0.261***
Single	Ref.	0.134***	0.157**	0.308***	0.178***
Non-UK born	Ref.	−0.059	0.175***	−0.250	−0.191
No educational qualifications	Ref.	0.330***	0.084**	0.602***	0.272**
Unemployed	Ref.	0.196***	−0.011	0.484***	0.288***
Ethnicity, BME (vsWhite)	Ref.	−0.075	0.170***	−0.371	−0.296
NEET	Ref.	0.399***	−0.007	0.599***	0.201**
Peers encourage crime	Ref.	0.582***	0.120***	0.944***	0.262*
Peers encourage drugs	Ref.	−0.027	0.165***	0.163***	0.190***

Reference: national survey other men. *P < 0.05, **P < 0.01, ***P < 0.001.
BME: black and minority ethnic background, NEET: not in employment, education, or training, IMDR:the Index of Multiple deprivation.
[a] Location contrasts for contextual associations differences in coefficient.

factors or socioeconomic deprivation. To summarise, we firstly observed clustering of health conditions among young adult men in GE which were not entirely explained by higher levels of socioeconomic deprivation in this location. Secondly, we demonstrated a syndemic of psychiatric morbidity, substance misuse, violence, and a diathesis of behavioural/biological physical health risks, with synergistic interactions that increased the prevalence of generalised physical ill-health and chronic conditions among our participants. Among contextual factors, the syndemic factor was associated with being single, no educational qualifications, low social class, NEET, older age (25–34 years) (suggesting persistence of effects over time), and friends in their social environment who encouraged them to take drugs or become involved in crime.

4.1. Social inequality, social environment and contagion

Social inequality is crucial in the clustering of syndemic factors (Oldenburg et al., 2014). However, neighbourhood deprivation did not attenuate most disparities in the cluster of health conditions and health-related behaviours. This questioned whether low social status, indicated by unemployment, and particularly NEET, was an explanation (Roelfs et al., 2011). However, despite prevalence of NEET in GE twice that in the national sample, the syndemic cannot simply be explained by a high prevalence of NEET in GE. Other men in the same location showed area-level syndemic effects.

Future investigations of syndemics should measure a wider range of factors in the social environment. Neighbourhoods in which residents interact positively by forming social ties and engage in collective behaviour to establish norms, reciprocity, trust, and collective action can provide a safe, healthy environment (Sampson et al., 1997, 1999) in which neighbourhood social order is established and children's behaviour supported and corrected. Measures should include social cohesion, trust of neighbours, and social capital, as well as the built environment, which may all impact on the syndemic we have described. Social and neighbourhood determinants have been found associated with our four components of physical health: including healthier diet and more exercise among children (Carroll-Scott et al., 2013), injuries (Zhang et al., 2020), and a range of positive health outcomes (Xue et al., 2020); Violence and gangs (Kim, 2019; Sampson et al., 1999; Scorgie et al., 2017); Mental Health (Almedom, 2005; Lofors & Sundquist, 2007); and Alcohol and Drug misuse (Bryden et al., 2013; Ford et al., 2017; Jesmin & Amin, 2020). Our measures of encouragement by friends to become involved in crime and to take drugs were therefore limited. However, they indicate another important area for future syndemic study in terms of social contagion of health-related behaviours and non-communicable disease outcomes determined by social environment (Sauzet & Leyland, 2017; Susser, 1994).

4.2. Syndemic interactions

Studies typically find increased morbidity and disability in individuals who are socially disadvantaged (Dalstra et al., 2005; Hughes et al., 2017) and disease burden in this group increases with increasing age (Hughes et al., 2017; Kivimaki et al., 2020; Mackenbach et al., 2008). Our study contributes to evidence that psychiatric morbidity, substance misuse and behavioural disorders cannot be considered as a dimension of morbidity that can be separated from physical health conditions and that there are bi-directional relationships (Kivimaki et al., 2020). Mental disorders are shown to increase risk of physical diseases, both communicable and non-communicable, through higher prevalence of high-risk behaviours, reduced self-care, and reduced likelihood of help-seeking, together with increasing risk of substance misuse (Firth et al., 2019; Prince et al., 2007). This corresponds to synergistic effects between violence and substance misuse, and between substance misuse, poor mental health and a diathesis of biological/behavioural risk on our physical health outcomes. The diathesis, consisting of poor diet, lack of exercise, short stature, and previous trauma, assumes constitutional predisposition to physical disease, or group of diseases, through possible genetic predisposition, developmental factors, but also health behaviours learned during childhood and adolescence. A diathesis-stress model implies a pathway of disease progression where a stable, healthy state of an underlying regulatory physiological network undergoes pathophysiological changes to an unstable but initially reversible disease state, most often associated with stress. However, the network can then undergo transition to disease state when reaching a "tipping point" (Arnau-Soler et al., 2019; Stapelberg et al., 2019). Our mental health component of anxiety and psychotic symptoms constitutes severe psychological stress. Substance misuse which interacts with violence is likely to have further exacerbated the negative effects of poor diet, lack of exercise, and biological vulnerability to future poor health. Short stature within this component lends further support to an underlying biological component. Height variation is thought under genetic control (McEvoy & Visscher, 2009). However, developmental effects of stunted growth due to poor nutrition could be even more important with short stature as a marker of biological vulnerability to physical disease due to exposures in utero and infancy (World Health Organization, 2015).

4.3. A hypothetical model of shortened life expectancy

Fig. 3 shows a hypothetical model to explain how the syndemic drives risks of premature death through two theoretical pathways: Firstly, through immediate, increased risks of suicide, drugs-related and alcohol-related poisonings, trauma/accidents, and violence. Poor access to healthcare increase mortality risk in geographically isolated communities such as GE, with distance from emergency rooms, coupled with
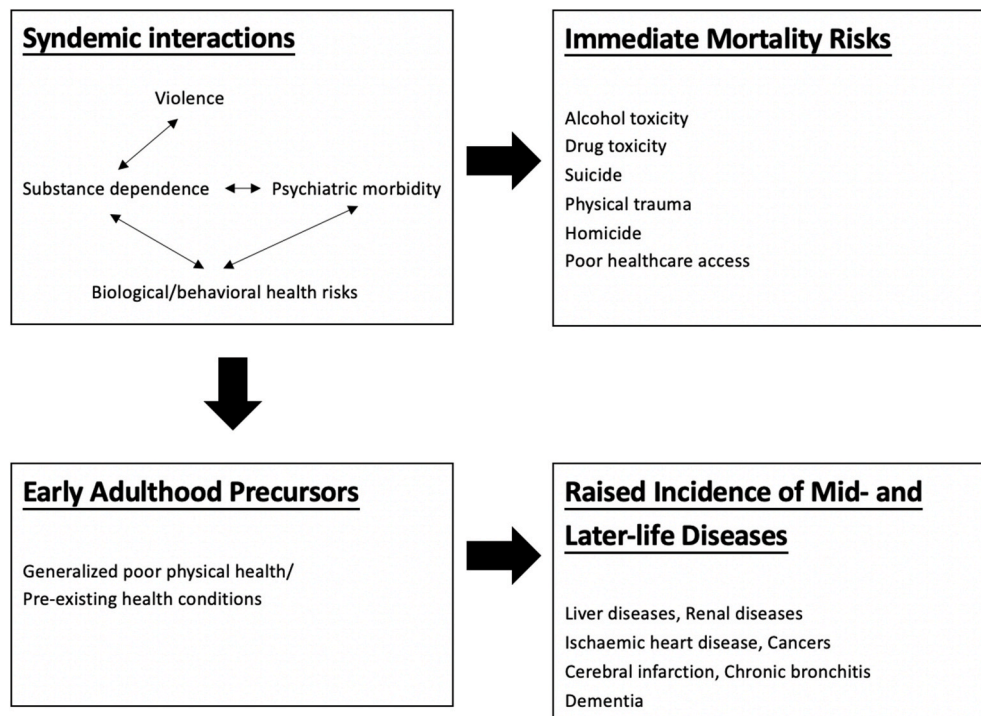
Fig. 3. Hypothetical model of pathways from the syndemic to premature mortality in Glasgow, Scotland.

poor transport links. Secondly, through an intermediary stage of "pre-diseases," or early adult precursors of the more severe physical conditions which will result in mortality later (Atukorala et al., 2014; Viera, 2011; Wilson et al., 2005). In this second pathway, syndemic interactions between multiple morbidities of poor mental health, substance misuse, violence, and a diathesis of biological/behavioural risk lead to this intermediary stage along the pathway consisting of early adult precursors of what will become a range of diseases in mid- and later-life. This second pathway increases mid-/later-life mortality through two hypothetical mechanisms: firstly, an overall increased incidence of a range of diseases which shorten life. Secondly, by bringing forward in time presentations of diseases which usually occur later among more advantaged populations (Seaman et al., 2019).

4.4. Limitations

Our study has several limitations. First, our hypothesis that a multi-component syndemic explains reduced life expectancy is based on results from a single geographical location (Glasgow East). However, there are other Scottish inner-urban areas with similar levels of socioeconomic deprivation in which our findings may be replicated. Second, shortened life expectancy is expected in multiple morbidity, and is based on assumptions from previous research and national statistics for Scotland. This outcome cannot be demonstrated in a cross-sectional study. However, there is no indication that subsequent improvements in socioeconomic deprivation have had an impact on life expectancy (Schofield et al., 2016). Third, our survey was originally designed to measure associations at the population level with violence and with a primary focus on mental health measures. This means we had few measures of physical health and our risk factors for physical health were limited. We did not have data on specific diseases in our study. The measures we have described as a biological and behavioural risk diathesis do not conform to a known syndrome or established biological measures and must therefore be considered as putative and preliminary measures for future research. Fourth, our survey was restricted to young adult men and our findings question whether there was an equivalent or corresponding syndemic among women in GE. Previous US studies of syndemics have

emphasised importance of substance misuse, HIV risk behaviour and violence, but where violence involved victimisation (Singer et al., 2006). IPV was no more prevalent among men in GE but it was noticeable that many lived alone without intimate partners, questioning whether other factors within the syndemic, resulting in heavy substance misuse, failure to find any occupation, criminality and imprisonment had impacted on their ability to sustain relationships. Fifth, we did not have a standardised measure of the social environment to study the impact of neighbourhood contextual factors on the syndemic. Only two variables measuring encouragement by peers to use drugs and commit crimes specifically measured negative behaviours of others in the same social environment. Sixth, random location sampling does not provide detailed information on numbers who declined to participate. However, the method is based on the National Census, participants were identified and included according to representative strata and their actual frequency in the population (see Supplementary file). Because young adult men of lower social class are more likely to decline participation in adult household surveys, this method has considerable advantages for investigating health-related behaviours such as violence and substance misuse.

5. Conclusion

This syndemic is likely to have arisen in the context of large-scale social forces that progressed in Scotland, particularly Glasgow, from the mid-20th century (McCartney et al., 2012) and were underway when our sample were children. Public health researchers in Glasgow have described multiple social determinants over a prolonged period that may have led to the clusters of health conditions we have observed. These impact most powerfully on persons living in areas of highest socioeconomic deprivation in Glasgow and in other Scottish cities which have experienced post-industrialisation, unemployment, and the adverse effects of certain economic and social policies (McCartney et al., 2012; Walsh et al., 2020). However, why Glasgow has shown little improvement over time and has been affected worse than other UK cities which faced similar hardships has remained unclear. We have put forward a potential new hypothesis and explanatory model to explain this among

young men.

Unlike common medical approaches based on comorbidity and multimorbidity, a syndemic framework explores the health effects of identifiable disease interactions and the social, environmental, or economic factors that promote such interaction and worsen disease (Singer, 1996; Tsai et al., 2017). The syndemic of violence, substance misuse, psychiatric morbidity and biological/behavioural diathesis observed in Glasgow East showed co-dynamics of synergistic interaction (Tsai et al., 2017). Each component presented potentially life-threatening risks, either currently or as precursors of conditions which would shorten life in the future, although confirmation would require longitudinal study. Public Health interventions to improve diet, reduce alcohol consumption and smoking, increase physical activity, and police interventions to reduce gang activity and violence have had varying degrees of success but no impact on overall life expectancy or drug misuse. Changes in health policy are needed which take into account the impact of social forces on the complex and contextually situated emergence of disease among impoverished populations such as Glasgow East. Dynamic interactions between components of the syndemic suggest need for multi-component and multi-agency interventions which are complimentary, although evidence that this approach would be effective is currently lacking. However, the syndemic framework suggests it is important not to target single disease or health-related behaviours or to prioritise one over others in future interventions.

Authors contributions

JC designed the study, directed the implementation and drafted the manuscript; YZ analysed the data and drafted the manuscript; PB contributed to the drafting of the manuscript and revised drafts; SU designed the study and questionnaire and revised drafts; BdeS designed the study's analytical strategy and provided statistical supervision; KB contributed to drafting the manuscript and revised drafts; ACT helped with the literature review and contributed to the study's analytical strategy.

Funding

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2021.100858.

Ethical statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by Queen Mary University London Ethics Committee.

References

Almedom, A. M. (2005). Social capital and mental health: An interdisciplinary review of primary evidence. *Social Science & Medicine, 61*, 943–964.

Arnau-Soler, A., Adams, M. J., Clarke, T.-K., MacIntyre, D. J., Milburn, K., Navrady, L., Hayward, C., McIntosh, A., Thomson, P. A., Generation, S. & major depressive disorder working group of the psychiatric genomics, C. (2019). A validation of the diathesis-stress model for depression in generation scotland. Translational Psychiatry 9, 25.

Atukorala, I., Kwoh, C., Guermazi, A., Roemer, F., Boudreau, R., Hannon, M., & Hunter, D. (2014). Synovitis in knee osteoarthritis: A precursor of disease? *Annals of the Rheumatic Diseases, 75*.

Babor, T., Higgings-Biddle, J., Saunders, J., & Monteiro, M. (2001). *The alcohol use disorders identification test* (2nd ed.). World Health Organization.

Bebbington, P., & Nayani, T. (1995). The psychosis screening questionnaire. *International Journal of Methods in Psychiatric Research, 5*, 11–19.

Berman, A. H., Bergman, H., Palmstierna, T., & Schlyter, F. (2005). Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. *European Addiction Research, 11*, 22–31.

Bryden, A., Roberts, B., Petticrew, M., & McKee, M. (2013). A systematic review of the influence of community level social factors on alcohol use. *Health & Place, 21*, 70–85.

Carroll-Scott, A., Gilstad-Hayden, K., Rosenthal, L., Peters, S. M., McCaslin, C., Joyce, R., & Ickovics, J. R. (2013). Disentangling neighborhood contextual associations with child body mass index, diet, and physical activity: The role of built, socioeconomic, and social environments. *Social Science & Medicine, 95*, 106–114.

Coid, J., Gonzalez Rodriguez, R., Kallis, C., Zhang, Y., Bhui, K., De Stavola, B., Bebbington, P., & Ullrich, S. (2019). Ethnic disparities in psychotic experiences explained by area-level syndemic effects. *British Journal of Psychiatry*, 1–7.

Coid, J., Gonzalez Rodriguez, R., Kallis, C., Zhang, Y., Bhui, K., De Stavola, B., Bebbington, P., & Ullrich, S. (2020). Ethnic disparities in psychotic experiences explained by area-level syndemic effects. *British Journal of Psychiatry, 217*, 555–561.

Coid, J. W., Ullrich, S., Bebbington, P., Fazel, S., & Keers, R. (2016). Paranoid ideation and violence: Meta-analysis of individual subject data of 7 population surveys. *Schizophrenia Bulletin, 42*, 907–915.

Communities and Local Government. (2010). *Department for communities and local government.* publishes 2010 to 2011 annual report and accounts.

Cowley, J., Kiely, J., & Collins, D. (2016). Unravelling the Glasgow effect: The relationship between accumulative bio- psychosocial stress, stress reactivity and Scotland's health problems. *Preventive medicine reports, 4*, 370–375.

Dalstra, J. A., Kunst, A. E., Borrell, C., Breeze, E., Cambois, E., Costa, G., Geurts, J. J., Lahelma, E., Van Oyen, H., Rasmussen, N. K., Regidor, E., Spadea, T., & Mackenbach, J. P. (2005). Socioeconomic differences in the prevalence of common chronic diseases: An overview of eight European countries. *International Jounal of Epidemiology, 34*, 316–326.

Densley, J., McLean, R., Deuchar, R., & Harding, S. (2018). An altered state? Emergent changes to illicit drug markets and distribution networks in scotland. *International Journal of Drug Policy, 58*, 113–120.

Firth, J., Siddiqi, N., Koyanagi, A., Siskind, D., Rosenbaum, S., Galletly, C., Allan, S., Caneo, C., Carney, R., Carvalho, A. F., Chatterton, M. L., Correll, C. U., Curtis, J., Gaughran, F., Heald, A., Hoare, E., Jackson, S. E., Kisely, S., Lovell, K., … Stubbs, B. (2019). The lancet psychiatry commission: A blueprint for protecting physical health in people with mental illness. *Lancet Psychiatry, 6*, 675–712.

Ford, J. A., Sacra, S. A., & Yohros, A. (2017). Neighborhood characteristics and prescription drug misuse among adolescents: The importance of social disorganization and social capital. *International Journal of Drug Policy, 46*, 47–53.

Hu, L., & Bentler, P. (1999). Cutoff criteria in fit indexes in covariance structure analysis: Conventional criteria versus new alternatives. *Structural Equation Modeling, 6*, 1–55.

Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., Jones, L., & Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: A systematic review and meta-analysis. *Lancet Public Health, 2*, e356–e366.

Jesmin, S. S., & Amin, I. (2020). Diseases of despair and social capital: Findings from a population-based survey on opioid misuse among adolescents. *Substance Use & Misuse, 55*, 1993–2001.

Kim, D. (2019). Social determinants of health in relation to firearm-related homicides in the United States: A nationwide multilevel cross-sectional study. *PLoS Medicine, 16*, Article e1002978.

Kivimaki, M., Batty, G. D., Pentti, J., Shipley, M. J., Sipila, P. N., Nyberg, S. T., Suominen, S. B., Oksanen, T., Stenholm, S., Virtanen, M., Marmot, M. G., Singh-Manoux, A., Brunner, E. J., Lindbohm, J. V., Ferrie, J. E., & Vahtera, J. (2020). Association between socioeconomic status and the development of mental and physical health conditions in adulthood: A multi-cohort study. *Lancet Public Health, 5*, e140–e149.

Leyland, A., & Dundas, R. (2010). The social patterning of deaths due to assault in scotland, 1980-2005: Population-based study. *Journal of Epidemiology & Community Health, 64*, 432–439.

Lofors, J., & Sundquist, K. (2007). Low-linking social capital as a predictor of mental disorders: A cohort study of 4.5 million Swedes. *Social Science & Medicine, 64*, 21–34.

Mackenbach, J. P., Stirbu, I., Roskam, A. J., Schaap, M. M., Menvielle, G., Leinsalu, M., Kunst, A. E. & **European union working group on socioeconomic inequalities in, H.** (2008). Socioeconomic inequalities in health in 22 European countries. New England Journal of Medicine 358, 2468-2481.

McCartney, G., Russ, T. C., Walsh, D., Lewsey, J., Smith, M., Smith, G. D., Stamatakis, E., & Batty, G. D. (2015). Explaining the excess mortality in scotland compared with England: Pooling of 18 cohort studies. *Journal of Epidemiology & Community Health, 69*, 20–27.

McCartney, G., Walsh, D., Whyte, B., & Collins, C. (2012). Has scotland always been the 'sick man' of Europe? An observational study from 1855 to 2006. *The European Journal of Public Health, 22*, 756–760.

McEvoy, B. P., & Visscher, P. M. (2009). Genetics of human height. *Economics and Human Biology, 7*, 294–306.

McLean, R., Densley, J. A., & Deuchar, R. (2018). Situating gangs within Scotland's illegal drugs market(s). *Trends in Organized Crime, 21*, 147–171.

McLennan, D., Noble, S., Noble, M., Plunkett, E., Wright, G., & Gutacker, N. (2019). In *The English indices of deprivation 2019*. D. f. c. a. L. Government.

Muthén, L., & Muthén, B. (2017). *Mplus user's guide* (8th ed.). Muthén & Muthén.

National Records of Scotland. (2019). *Drug related deaths in Scotland*.

Oecd. (2020). *Youth not in employment, education or training (NEET) Indicators*.

Office for Population Censuses and Surveys. (1991). Standard occupational classification. In *Social classifications and coding methodology* (Vol. 3). London: HMSO.

Oldenburg, C. E., Perez-Brumer, A. G., & Reisner, S. L. (2014). Poverty matters: Contextualizing the syndemic condition of psychological factors and newly diagnosed HIV infection in the United States. *AIDS, 28*, 2763–2769.

Prince, M., Patel, V., Saxena, S., & al, e. (2007). No health without mental health. *Lancet, 370*, 859–877.

Roelfs, D. J., Shor, E., Davidson, K. W., & Schwartz, J. E. (2011). Losing life and livelihood: A systematic review and meta-analysis of unemployment and all-cause mortality. *Social Science & Medicine, 72*, 840–854.

Sampson, R. J., Morenoff, J. D., & Earls, F. (1999). Beyond social capital: Spatial dynamics of collective efficacy for children. *American Sociological Review, 64*, 633–660.

Sampson, R. J., Raudenbush, S. W., & Earls, F. (1997). Neighborhoods and violent crime: A multilevel study of collective efficacy. *Science, 277*, 918.

Sauzet, O., & Leyland, A. H. (2017). Contextual effects on health inequalities: A research agenda. *The European Journal of Public Health, 27*, 587–588.

Schofield, L., Walsh, D., Munoz-Arroyo, R., McCartney, G., Buchanan, D., Lawder, R., Armstrong, M., Dundas, R., & Leyland, A. H. (2016). Dying younger in scotland: Trends in mortality and deprivation relative to England and Wales, 1981-2011. *Health & Place, 40*, 106–115.

Scorgie, F., Baron, D., Stadler, J., Venables, E., Brahmbhatt, H., Mmari, K., & Delany-Moretlwe, S. (2017). From fear to resilience: Adolescents' experiences of violence in inner-city johannesburg, South Africa. *BMC Public Health, 17*, 441.

Scotland. (2019). *Mental health inpatient Activity*. Scotland: ISD.

Scottish Government. (2019). In S. G. Justice (Ed.), *Recorded crime in Scotland: Attempted murder and serious assault, 2008-09 and 2017-18*. Analytical Services.

Seaman, R., Riffe, T., Leyland, A. H., Popham, F., & van Raalte, A. (2019). The increasing lifespan variation gradient by area-level deprivation: A decomposition analysis of scotland 1981-2011. *Social Science & Medicine, 230*, 147–157.

Singer, M. (1996). A dose of drugs, a touch of violence, a case of AIDS: Conceptualizing the SAVA syndemic. *Free Inquiry in Creative Sociology, 24*, 99–110.

Singer, M., Bulled, N., Ostrach, B., & Mendenhall, E. (2017). Syndemics and the biosocial conception of health. *Lancet, 389*, 941–950.

Singer, M. C., Erickson, P. I., Badiane, L., Diaz, R., Ortiz, D., Abraham, T., & Nicolaysen, A. M. (2006). Syndemics, sex and the city: Understanding sexually transmitted diseases in social and cultural context. *Social Science & Medicine, 63*, 2010–2021.

Stapelberg, N. J. C., Neumann, D. L., Shum, D., & Headrick, J. P. (2019). Health, pre-disease and critical transition to disease in the psycho-immune-neuroendocrine network: Are there distinct states in the progression from health to major depressive disorder? *Physiology & Behavior, 198*, 108–119.

Susser, M. (1994). The logic in ecological: I. The logic of analysis. *American Journal of Public Health, 84*, 825–829.

Tsai, A. C., & Burns, B. F. (2015). Syndemics of psychosocial problems and HIV risk: A systematic review of empirical tests of the disease interaction concept. *Social Science & Medicine, 139*, 26–35.

Tsai, A. C., Mendenhall, E., Trostle, J. A., & Kawachi, I. (2017). Co-occurring epidemics, syndemics, and population health. *Lancet, 389*, 978–982.

UCL Institute of Health Equity. (2014). Local action on health inequalities: Reducing the number of young people not in employment, education or training. In P. H. England (Ed.), *Health equity evidence review 3*. London.

Ullrich, S., Deasy, D., Smith, J., Johnson, B., Clarke, M., Broughton, N., & Coid, J. (2008). Detecting personality disorders in the prison population of England and Wales: Comparing case identification using the SCID-II screen and the SCID-II clinical interview. *Journal of Forensic Psychiatry and Psychology, 19*, 301–322.

Viera, A. J. (2011). Predisease: When does it make sense? *Epidemiologic Reviews, 33*, 122–134.

Walsh, D., McCartney, G., Collins, C., Taulbut, M., & Batty, G. D. (2017). History, politics and vulnerability: Explaining excess mortality in scotland and Glasgow. *Public Health, 151*, 1–12.

Walsh, D., McCartney, G., Collins, C., Taulbut, M., & Batty, D. H. (2020). In G. C. f. P. Health (Ed.), *History, politics and vulnerability: Explaining excess mortality in Scotland and Glasgow*. www.gcph.co.uk.

Wilson, P. W., D'Agostino, R. B., Parise, H., Sullivan, L., & Meigs, J. B. (2005). Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. *Circulation, 112*, 3066–3072.

World Health Organization. (2015). *Stunting in a nutshell*. https://www.who.int/news /item/19-11-2015-stunting-in-a-nutshell.

Xue, X., Reed, W. R., & Menclova, A. (2020). Social capital and health: A meta-analysis. *Journal of Health Economics, 72*, 102317.

Zhang, J., Zhai, H., Meng, X., Wang, W., & Zhou, L. (2020). Influence of social safety capital on safety citizenship behavior: The mediation of autonomous safety motivation. *International Journal of Environmental Research and Public Health, 17*.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*, 361–370.