identify the molecular and neural mechanisms that link genotype to phenotype.

The CNVs accounted for only 5–20% of the phenotypic variance in the study by Chawner and colleagues; most of the variance is attributable to other factors. Indeed, the authors report that age accounts for as much as a quarter of the variance in some phenotypes. This finding should not come as a surprise, because several of these phenotypes vary considerably with age and might be modified by interventions at crucial time periods.

The next step is to evaluate the association between developmental trajectories of these phenotypes and the CNV genotypes. Do developmental trajectories change with CNV genotype? Do specific interventions work equally well across the CNV genotypes? These are important issues that need to be investigated to provide better support to individuals with neurodevelopmental CNVs.

An inherent limitation of the study is the absence of whole-genome data. Evidence suggests that even in carriers of damaging mutations, common, inherited genetic variants might contribute to a proportion of the phenotypic variance, and, in some instances, might modify the penetrance of rare variants. Genetic variants across the allelic spectrum are associated with neuropsychiatric conditions. In light of this, will accounting for other genetic variants in CNV carriers help better delineate genotype-specific effects of these CNVs? Advances in sequencing technology and statistical methods coupled with larger sample sizes could help answer this.

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8 Satterstrom FK, Walters RK, Singh T, et al. ASD and ADHD have a similar burden of rare protein-truncating variants. bioRxiv 2018; published online March 6. DOI:10.1101/277707 (preprint).

Neighbourhood and mortality in severe mental illness

People with severe mental illness have higher mortality rates, culminating in about 20 years of lost life compared with that of the general population, and momentum is growing to reduce this inequality. In the general population, neighbourhood social context is related to mortality, but whether such patterns also exist for people with severe mental illness has received little attention. Understanding this relationship could allow us to tailor social interventions for this distinctive population. The study by Jayati Das-Munshi and colleagues in The Lancet Psychiatry represents a welcome step in that direction, linking higher neighbourhood ethnic density to lower mortality rates among people with severe mental illness from ethnic minority backgrounds. These results raise the intriguing possibility that factors associated with ethnic density might promote longevity among people with severe mental illness.

Their study was based on a large cohort of 18201 people with severe mental illness, identified and followed with use of electronic health registers for mortality outcomes for a median of 6.36 years in an ethnically heterogeneous location in south London, UK. Using these data, Das-Munshi and colleagues had previously observed that mortality rates were lower for some ethnic minority groups than for the white British population. In this study, they extend those findings to show that neighbourhood-level ethnic density, defined
as the proportion of the neighbourhood population who identified as ethnic minorities, modified this relationship. All-cause mortality was higher for ethnic minority groups in the least ethnically dense areas (adjusted relative risk 0.96, 95% CI 0.71–1.29) compared with that of ethnic minority groups in the most ethnically dense areas (0.52, 0.38–0.71), relative to the white British population rate. This difference appeared to be driven by natural rather than unnatural (eg, suicide) mortality.

These patterns were not confounded by neighbourhood-level urbanicity, social fragmentation, or deprivation, which were not associated with mortality in this cohort. This is somewhat surprising given that deprivation has been linked to higher mortality in the general population, but might reflect high levels of deprivation within the study region (all neighbourhoods were in the top 40% of most deprived areas in England), which could have attenuated these expected associations; this result echoes findings for risk of psychotic disorders, which appears higher in south London than in other, less deprived areas, but does not vary within this area by deprivation. Henceforth, we focus on the ethnic density result.

Ethnic density remains a somewhat elusive construct, the meaning of which and mechanisms through which it affects health are poorly understood. Ethnic density can be operationalised narrowly (own-group) or broadly (all ethnic minorities), and might have multiple meanings depending on other contextual factors, including migrant status, ethnic identity, and wider social contexts. Despite these caveats, robust associations with mental health, and occasionally with other health outcomes, have been reported, generally in a protective direction.

How do these caveats affect the interpretation of the ethnic density results in this study? The main findings of Das-Munshi and colleagues were based on overall ethnic density for anyone whose self-ascribed ethnicity was black Caribbean, black African, south Asian, or Irish. Similar trends were observed independently in all groups except the Irish, possibly because this group’s minority status was less visible. Such results provide a crucial signal for future investigations but, as the authors acknowledged, they are not fine-grained enough to identify the objective or the perceived sociocultural experiences aligned to ethnic density and identity that might shape mortality risk by ethnicity. It is also possible that these results partly reflect higher absolute mortality in white British people living in high ethnic density areas, perhaps driven by selection into such neighbourhoods or by perceived social isolation.

Studies that have tried to assess which dimensions of ethnic density are related to health outcomes have produced inconsistent results, and the mechanism might not be the same for all populations or outcomes. As with the authors, we think it is plausible that protection from social isolation is involved, as it has been associated with higher mortality in the general population and is particularly salient in people with severe mental illness. This theory would also offer opportunities to investigate how other neighbourhood contexts—including social fragmentation, ethnic diversity, and ethnic segregation—are linked to social isolation and mortality in people with severe mental illness. We recommend that future longitudinal studies include such measures, both objective and, importantly, as perceived by the residents, as well as individual characteristics that could confound or interact with this social context. The rigorous study by Das-Munshi and colleagues paves the way for us to better understand how these complex contextual influences can shape mortality risk in people with severe mental illness from different ethnic groups.

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Parenting groups can be effective across the social spectrum: the next step is access

In the 1990s, there was no evidence of effectiveness for interventions for conduct disorder and many child and adolescent psychiatrists considered the disorder untreatable. Then a seminal randomised controlled trial (RCT) of the Incredible Years group parenting programme showed that conduct disorder was treatable, even in real-world settings.

The importance of this finding cannot be overstated. Conduct disorder is a massive public health problem with a population effect that expands across the life-course. In the Dunedin study, a small group of boys with stable conduct problems in early childhood went on to have more than half of the adult convictions for crime in the group overall. By not addressing conduct disorder, we all suffer: the children themselves whose criminal convictions lead to poor employability and social isolation, their families and friends who are affected by their aggression, and the rest of us, who fear violent streets and pay dearly through our taxes to keep violent offenders off them.

The role of parenting is crucial. So-called callous-unemotional traits are identifiable in children as young as 4 years old and predict severe and chronic antisocial behaviour, but callous-unemotional traits seem to develop only if positive parenting is rated by observers as low. Because the Incredible Years intervention uses tried and tested behavioural methods that are theory driven to improve parenting, we should not be surprised that the intervention can effectively reduce symptoms of conduct disorder.

Poor parenting can occur right across the social spectrum and children from every social class can develop conduct disorder, but conduct disorder prevalence is much higher in socially disadvantaged groups than it is in advantaged groups, which is a challenge for parenting interventions. At a population level, evidence exists that families from more materially deprived areas might struggle to engage in parenting interventions, despite the best efforts of staff. Therefore, even if the intervention is effective, this poor engagement could still increase health inequalities—and wider health inequality in populations is associated with a higher prevalence of antisocial behaviour.

This international effort in The Lancet Psychiatry by Frances Gardner and colleagues to find out whether Incredible Years is as effective across all social strata is important. The meta-analysis of individual participant data from 13 of the 15 RCTs of Incredible Years in Europe was a laudable achievement. The trials themselves should be commended for recruiting such a high proportion of families (nearly 60%) on low-income. Thanks to this study, we now know that Incredible Years can work just as well for families at a social disadvantage (eg, poverty, lone or teenage parenthood, joblessness, or low education) as it does for families with greater social advantage.

There is, however, one important limitation: the RCTs involved in the meta-analysis did not assess data on variation in access to parenting services across socioeconomic groups. Socially disadvantaged families were probably recruited at lower rates than were less socially disadvantaged families in the trials, but no data are available on this. If such differential recruitment rates exist, then even though Incredible Years is just as effective for socially disadvantaged families as it is for advantaged families, roll-out across populations could still result in social inequalities.

A proportion of socially disadvantaged families can be hard to reach. We did a study of psychiatric problems associated with maltreatment in young