

Comment

that would require many years of an antiresorptive drug treatment alone.^{16,17} In a direct comparator trial¹⁸ of romosozumab or alendronate for 1 year, followed by alendronate for 2 years more in women with prevalent vertebral fractures, the incidence of new vertebral fractures was reduced by 37% at 1 year and 48% at 2 years in participants who received romosozumab first, whereas the incidence of clinical and non-vertebral fractures was significantly reduced in this group compared with alendronate alone by the end of the analysis (median 33 months).

Ultimately, these studies should lead clinicians to reconsider the most efficient sequence of therapy in patients at high risk of fracture: namely, a bone-forming drug first, rather than one too late, or not at all.

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- 1 Gehlbach S, Saag KG, Adachi JD, et al. Previous fractures at multiple sites increase the risk for subsequent fractures: the Global Longitudinal Study of Osteoporosis in Women. *J Bone Miner Res* 2012; **27**: 645–53.
- 2 Yusuf AA, Matlon TJ, Grauer A, Barron R, Chandler D, Peng Y. Utilization of osteoporosis medication after a fragility fracture among elderly Medicare beneficiaries. *Arch Osteoporos* 2016; **11**: 31.
- 3 Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. *Ann Intern Med* 2014; **161**: 711–23.
- 4 Dempster DW, Zhou H, Recker RR, et al. A longitudinal study of skeletal histomorphometry at 6 and 24 months across four bone envelopes in postmenopausal women with osteoporosis receiving teriparatide or zoledronic acid in the SHOTZ trial. *J Bone Miner Res* 2016; **31**: 1429–39.

- 5 Hansen S, Hauge EM, Beck Jensen JE, Brixen K. Differing effects of PTH 1-34, PTH 1-84, and zoledronic acid on bone microarchitecture and estimated strength in postmenopausal women with osteoporosis: an 18-month open-labeled observational study using HR-pQCT. *J Bone Miner Res* 2013; **28**: 736–45.
- 6 Keaveny TM, Donley DW, Hoffmann PF, Mitlak BH, Glass EV, San Martin JA. Effects of teriparatide and alendronate on vertebral strength as assessed by finite element modeling of QCT scans in women with osteoporosis. *J Bone Miner Res* 2007; **22**: 149–57.
- 7 Keaveny TM, McClung MR, Wan X, Kopperdahl DL, Mitlak BH, Krohn K. Femoral strength in osteoporotic women treated with teriparatide or alendronate. *Bone* 2012; **50**: 165–70.
- 8 Hadji P, Zanchetta JR, Russo L, et al. The effect of teriparatide compared with risedronate on reduction of back pain in postmenopausal women with osteoporotic vertebral fractures. *Osteoporos Int* 2012; **23**: 2141–50.
- 9 Gluer CC, Marin F, Ringe JD, et al. Comparative effects of teriparatide and risedronate in glucocorticoid-induced osteoporosis in men: 18-month results of the EuroGIOPs trial. *J Bone Miner Res* 2013; **28**: 1355–68.
- 10 Saag KG, Shane E, Boonen S, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med* 2007; **357**: 2028–39.
- 11 Kendler DL, Marin F, Zerbini CAF, et al. Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial. *Lancet* 2017; published online Nov 9. [http://dx.doi.org/10.1016/S0140-6736\(17\)32137-2](http://dx.doi.org/10.1016/S0140-6736(17)32137-2).
- 12 Miller PD, Delmas PD, Lindsay R, et al. Early responsiveness of women with osteoporosis to teriparatide after therapy with alendronate or risedronate. *J Clin Endocrinol Metab* 2008; **93**: 3785–93.
- 13 Tsai JN, Uihlein AV, Burnett-Bowie SA, et al. Comparative effects of teriparatide, denosumab, and combination therapy on peripheral compartmental bone density, microarchitecture, and estimated strength: the DATA-HRpQCT Study. *J Bone Miner Res* 2015; **30**: 39–45.
- 14 Miller PD, Hattersley G, Riis BJ, et al. Effect of abaloparatide vs placebo on new vertebral fractures in postmenopausal women with osteoporosis: a randomized clinical trial. *JAMA* 2016; **316**: 722–33.
- 15 Langdahl BL, Libanati C, Crittenden DB, et al. Romosozumab (sclerostin monoclonal antibody) versus teriparatide in postmenopausal women with osteoporosis transitioning from oral bisphosphonate therapy: a randomised, open-label, phase 3 trial. *Lancet* 2017; **390**: 1585–94.
- 16 Cosman F, Crittenden DB, Grauer A. Romosozumab treatment in postmenopausal osteoporosis. *N Engl J Med* 2017; **376**: 396–97.
- 17 Bone HG, Wagman RB, Brandi ML, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. *Lancet Diabetes Endocrinol* 2017; **5**: 513–23.
- 18 Saag KG, Petersen J, Brandi ML, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis. *N Engl J Med* 2017; **377**: 1417–27.



Inclusion health: addressing the causes of the causes

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The social gradient in health describes a graded association between an individual's position on the social hierarchy and health: the lower the socioeconomic position of an individual, the worse their health.¹ The fact that the social gradient extends from the highest echelons of society to the lowest suggests that everyone is affected to a greater or lesser extent by the social determinants of health. One component of social cohesion is making common cause between people at various points on the social ladder. However, people at the extremes can appear to be on a different scale to the rest of

society. F Scott Fitzgerald famously began his story *The Rich Boy*, "Let me tell you about the very rich. They are different from you and me".² In societies with substantial inequality, the considerable gap between the top 0.1% of income earners and the rest of society threatens social cohesion.

Different, too, are socially excluded populations: the homeless, people with substance use disorders, sex workers, and prisoners. These individuals can seem to be off the scale of the social hierarchy completely, which represents a further challenge to social cohesion. For example, in the first of two papers on inclusion

health in *The Lancet*, Robert Aldridge and colleagues³ found that socially excluded populations have a mortality rate that is nearly eight times higher than the average for men, and nearly 12 times higher for women. By contrast, individuals (aged 15–64 years) in the most deprived areas of England and Wales have a mortality rate that is 2.8 times higher in men and 2.1 times higher in women than in individuals in the least deprived areas. To adapt Jeremy Bentham's turn of phrase,⁴ social exclusion is deprivation upon stilts.

To put it less colourfully, the causes of excess morbidity and mortality in socially excluded populations (ie, the social determinants of health) are not so much different from the causes of health inequalities more generally but differ in their degree. Multiple intersecting causes and multiple forms of morbidity characterise social exclusion. The result is people with little hope or prospects and considerably shortened lives. The challenge is to bring socially excluded populations in from the cold—literally and metaphorically—and to provide them with the opportunity to be part of a diverse and flourishing society. The concerned practitioner might despair at achieving such social inclusion.

The second of the two papers on inclusion health in *The Lancet*, by Serena Luchenski and colleagues,⁵ provides evidence to banish despair. The authors report that intervention is possible and can make a difference to the lives of the four excluded groups included in their Review: homeless individuals, prisoners, sex workers, and people with substance use disorders. These four populations, of course, overlap—eg, substance use disorder is common in the other three socially excluded groups.

The methods used in both papers are of high quality. But therein lies a problem. As identified by Luchenski and coworkers, the effect of basing their work on systematic reviews is a focus on proximate interventions on individuals—eg, the Review includes many papers on pharmacological treatment of substance use disorder. These downstream interventions have been covered, for the most part, in the scientific literature. There has been much less focus on structural interventions. If one went purely by the numbers of papers published, one would put effort into pharmacological treatment and would ignore housing; emphasise case management and ignore poverty. Much of the literature included in Luchenski and coworkers' Review was from populations with substance use disorders, with few publications about



Giacomo Pirazzi/Panos Pictures

homeless people and prisoners, and almost no studies on sex workers. For individuals committed to evidence-based policies, this poses a dilemma: efforts that promote social inclusion have to be encouraged, but the fact that sex workers have not been included in systematic reviews, and prisoners have only been included rarely, should not result in inaction.

The focus on systematic reviews of interventions in Luchenski and colleagues' Review is encouraging because it means that much can be done, now and relatively quickly, to promote inclusion health. Building on the authors' claim that structural interventions have been underemphasised, the causes of the causes should also be focused on.

A focus on the health of prisoners shows how a societal approach must take different forms. Aldridge and colleagues report that prisoners have shockingly high all-cause mortality and mortality from injuries and poisonings. Part of the reason will not be prison itself but the multiple problems that prisoners have. For example, prisoner's involvement in drugs might have resulted in their imprisonment. It is also well known that exposure to adverse childhood experiences increases the risk of substance use disorder, mental illness, and violent behaviour—all of which increase an individual's risk of imprisonment.⁶ But, prison might well be the worst place imaginable in which to detain young people who are damaged. The public need to be protected, of course, which is one reason for imprisoning people,⁷ but by what stretch of the imagination is it appropriate to detain young people

with disordered behaviour, mental illnesses, or multiple morbidities in a place that foments violence, promotes drug use, and labels people for life, such that their chances of being socially included on release are drastically reduced? Deciding whether people are damaged by prison or whether they brought all their problems with them into prison is not straightforward.

On the assumption that prison does have negative effects, then it is of concern that societies have markedly different rates at which they imprison individuals. In Japan, the prevalence of imprisonment is 48 per 100 000 individuals compared with 148 per 100 000 in the UK and 698 per 100 000 in the USA.⁸ These differences, in part, reflect differences in crime rates; but they also reflect variation in the operation of the criminal justice system, in policing practices, and the availability of guns.

A welcome feature of the inclusion health approach advocated by Luchenski and colleagues⁵ is user involvement, which aims to enable people to improve their own health. We need the involvement of society as a whole to tackle the causes of the causes of social exclusion and its dramatic health consequences. This approach might save money and it is the right thing to do.

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I declare no competing interests.

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- 1 Marmot M. *The Health Gap*. London: Bloomsbury; 2015.
- 2 F Scott Fitzgerald. *The rich boy*. New York: Scribner, 1926.
- 3 Aldridge RW, Story A, Hwang SW, et al. Morbidity and mortality in homeless individuals, prisoners, sex workers, and individuals with substance use disorders in high-income countries: a systematic review and meta-analysis. *Lancet* 2017; published online Nov 11. [http://dx.doi.org/10.1016/S0140-6736\(17\)31869-X](http://dx.doi.org/10.1016/S0140-6736(17)31869-X).
- 4 Schofield P. Jeremy Bentham's 'Nonsense upon Stilts'. 2013. <https://www.cambridge.org/core/services/aop-cambridge-core/content/view/S0953820800003745> (accessed Oct 27, 2017).
- 5 Luchenski S, Maguire N, Aldridge RW, et al. What works in inclusion health: overview of effective interventions for marginalised and excluded populations. *Lancet* 2017; published online Nov 11. [http://dx.doi.org/10.1016/S0140-6736\(17\)31959-1](http://dx.doi.org/10.1016/S0140-6736(17)31959-1).
- 6 Bellis MA, Lowey H, Leckenby N, Hughes K, Harrison D. Adverse childhood experiences: retrospective study to determine their impact on adult health behaviours and health outcomes in a UK population. *J Public Health* 2014; **36**: 81–91.
- 7 Nussbaum M. *Anger and forgiveness: resentment, generosity, and justice*. New York: Oxford University Press; 2016.
- 8 Walsmsley R. World prison population list. http://www.prisonstudies.org/sites/default/files/resources/downloads/world_prison_population_list_11th_edition_0.pdf (accessed Sept 22, 2017).



The Lancet–CAMS Health Summit 2018: a call for abstracts

The Lancet and the Chinese Academy of Medical Sciences (CAMS) have held three successful health summits in 2015–17 in Beijing, China. We continue to support China's health science research communities and invite abstract

submissions from China for the 2018 *The Lancet–CAMS* Health Summit, to be held on Oct 27–28 in Beijing. Submissions are invited from all aspects of health science, including, but not limited to: translational medicine; clinical medicine; public health; global health; health policy; the environment and ecological systems; primary care; maternal, newborn, child, and adolescent health, health professionalism; and medical education.

The event will consist of keynote presentations by leading researchers from China and beyond, oral and poster presentations of selected abstracts, launch of *The Lancet's* annual China themed issue, and writing and publishing sessions with editors. *The Lancet* will publish accepted abstracts online and in a conference booklet. Abstracts must be relevant to health science in China.

The conference language will be English. Abstracts should be written in English, up to 300 words in length, with no references, tables, or figures. Submissions should be structured and include the following sections: background (including context and aim); methods;

