or address residential segregation. So what can be done to improve urban youths' access to potentially beneficial social interactions? Cook and colleagues' work has exposed the isolation of city-dwelling young people, but solutions to the problem are yet to be found. Given the strong correlation between residential segregation and experienced isolation[2], reducing neighbourhood segregation is an obvious target.

Beyond that, there are three key avenues to improving social opportunities: enhancing mobility, optimizing venues and reshaping preferences. The first involves finding creative ways to encourage youths from disadvantaged groups to venture outside their home neighbourhood — for example, by offering discounted ride-sharing services[5]. Second, specific venues could be conducive to social opportunities, either owing to their location or because they attract a diverse demographic. These venues might be schools, churches or even large shopping centres, if they are located at socio-economic intersections[6].

Finally, a hypothesis known as intergroup-contact theory suggests that repeated exposure to diverse populations can help to change people's social preferences[7]. In that case, encouraging overlapping visits to shared spaces by people from different backgrounds could increase tolerance, reduce social biases and generate further social inclusion[8]. Each of these avenues for mitigating experienced isolation forms an active research area inspired by Cook and colleagues' findings. Equipped with clear insights into which groups face the most isolation, future research should investigate the root causes of the disparities, and develop policies to remedy them.

Victor Couture is in the Vancouver School of Economics, University of British Columbia, Vancouver, British Columbia V6T 1L4, Canada.
e-mail: victor.couture@ubc.ca

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Environmental science

Groundwater decline is global but not universal

Donald John MacAllister

Measurements of groundwater levels in 170,000 wells reveal the global extent of groundwater decline. But the data also show that such depletion is not inevitable in a changing climate, providing hope for a resilient water future. **See p.715**

Groundwater is crucial for water and food security because it acts as a climate buffer, sustaining communities and ecosystems that are vulnerable to changes in water availability as a result of climate change. Groundwater is therefore likely to become more important as these changes accelerate[1]. However, humans are affecting its availability, both indirectly through changes in rainfall, driven by anthropogenic climate change, and directly, through overuse[2]. An estimated 70% of all groundwater is used for irrigation[3], a practice that has rapidly increased in the past 40 years[3,4], leading to serious concerns about depletion[5,6]. Satellite observations[7] and models[5] have been used to study changes in groundwater storage, but these approaches have inherent limitations[8,9]. On page 715, Jasechko *et al.*[10] report direct measurements of groundwater levels around the world — a timely and welcome contribution to our understanding of the state of groundwater resources globally.

Jasechko and colleagues have compiled an impressive global data set of groundwater levels over the past four decades from around 170,000 monitoring wells installed in 1,693 aquifer systems, which the authors define as areas underlain by one or more aquifers (Fig. 1). The data are concentrated in roughly 40 countries in which there has been consistent monitoring, but they nonetheless cover about 75% of global groundwater withdrawal. The authors ensured that the data analysed captured real groundwater-level trends by excluding wells measured over a timespan of fewer than eight years. They then used various statistical

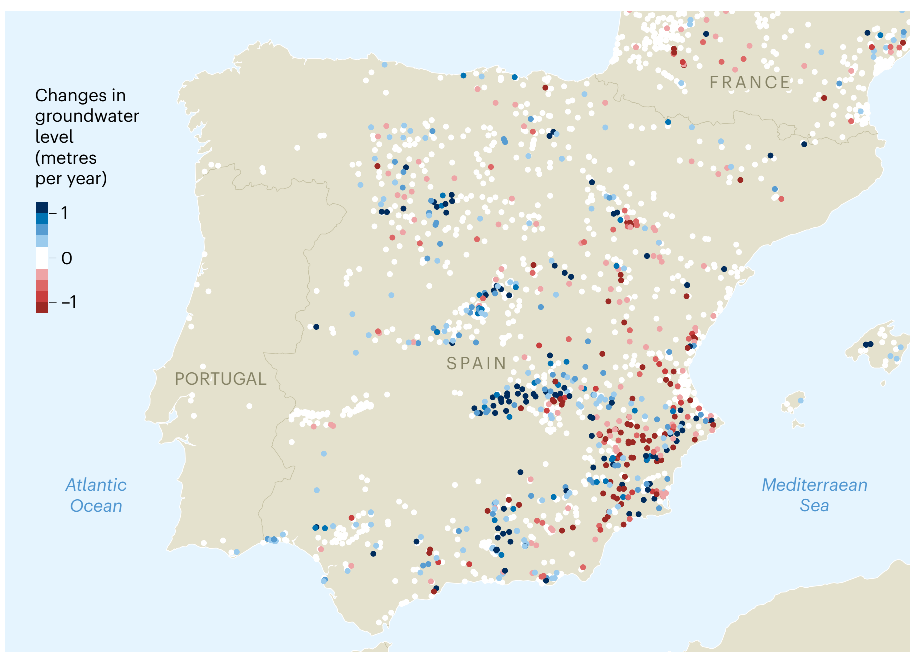

Figure 1 | Groundwater levels across the Iberian peninsula. Jasechko *et al.*[10] compiled measurements of groundwater levels over the past four decades from wells around the world. They found declining levels globally, but also noted that the decline slowed or reversed, or that levels rose continuously in around half of the aquifer systems where monitoring data was available. This variability is evident in this map of groundwater levels measured across Spain, Portugal and France. (Adapted from Supp. Fig. 54 in ref. 10.)

methods to determine whether groundwater levels were declining, stable or increasing, and at what rate (Fig. 2). In 542 of the aquifer systems, they compared trends in the twenty-first century with those from 1980 to 2000.

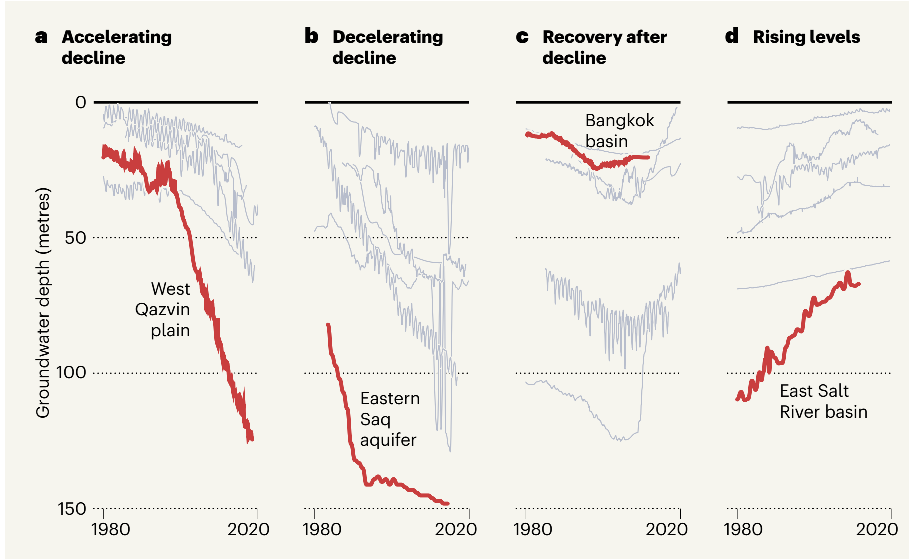

Figure 2 | Trends in groundwater levels around the world. **a**, In 30% of the wells studied by Jasechko and colleagues[10], the decline of groundwater levels accelerated during 1980–2020, as shown by these six representative cases, including measurements from the West Qazvin plain in Iran. **b**, However, declines slowed in 20% of the wells measured, for example, in the Eastern Saq aquifer in Saudi Arabia. **c**, In 16% of wells measured, declining trends were reversed, as was the case in the Bangkok basin in Thailand. **d**, Groundwater levels rose continuously in 13% of the wells, including those in the East Salt River basin in Arizona. (Adapted from Extended Data Figs 1–4 in ref. 10.)

In 30% of the aquifer systems, the decline of groundwater levels accelerated in the twenty-first century. Depletion was most common and rapid in cultivated drylands. The authors found significant declines in India and California, where threats to groundwater are well understood, but they also found accelerating declines in areas where the problem is less well known, for example, in the West Qazvin plain in Iran. Accelerating declines were explained in part by reduced recharge — the process by which surface water moves downwards to replenish groundwater reserves — and increased extraction as a result of changing rainfall patterns.

But there is also some good news. Jasechko and colleagues' analysis reveals that groundwater-level declines have slowed in 20% of aquifer systems, reversed in 16% and that levels have risen continuously in 13%. Together, these represent almost half of the aquifer systems studied. This is an important finding, because most studies have focused on areas in which groundwater is under severe threat, such as India and California.

There are a range of possible reasons for there being positive changes in about 50% of the aquifers. For instance, in the Eastern Saq aquifer in Saudi Arabia, slowing groundwater depletion could be a result of policies aimed at curbing water demand. In the Bangkok basin, rising groundwater levels are thought to be a response to increased regulation of groundwater use. In Tucson, Arizona, aquifer recharge projects have improved the outlook for systems with dwindling reserves. The situation has also improved for the Abbas-e Shargi basin in Iran, which was replenished by transferring water from other basins in the region. All of these cases offer valuable lessons on how to reverse losses in areas where groundwater decline seems unmanageable.

Similar interventions could be used, along with integrated surface and groundwater management, to slow or reverse declining groundwater levels elsewhere. Increased precipitation can also slow down declines or raise groundwater levels, as has been revealed by satellite data[2]. However, typical rates of groundwater-level increase (5 centimetres per year) are much slower than declines (20 centimetres per year), emphasizing the precarious nature of groundwater in a changing climate, even in regions where the outlook seems more positive.

Jasechko and colleagues' use of high-resolution data from monitoring wells complements lower-resolution global analyses using satellite data[2,11], and the two approaches produce broadly consistent results (excluding some notable exceptions, such as South India). The increased spatial resolution that can be achieved using well data enables a more nuanced interpretation of hydrological processes and management interventions. It also reveals areas in which rising and falling groundwater levels occur in close proximity, for example in North India and Pakistan[12].

Although Jasechko and co-workers' analysis incorporates an unprecedented number of monitoring wells from around the world, the authors' data set covers only a small proportion of Earth's surface, in part because groundwater use is dominated by a relatively small number of countries. Notable gaps include central China, much of southeast Asia and Latin America and almost all of Africa. These areas are currently experiencing rapid population growth, and their dependence on groundwater is likely to increase to meet people's basic needs and for the countries' wider economic development. Furthermore, the partial coverage highlights areas where our understanding of groundwater is relatively poor, the variable quality of much of the available groundwater data and the urgent need to improve monitoring of this essential resource[13].

Although the authors considered groundwater decline, they did not assess whether such decline is unsustainable. This is a key direction for further study, because although groundwater pumping inevitably leads to decline, groundwater levels can eventually reach an equilibrium without groundwater vanishing completely[14]. Another topic for future investigation is the quality of groundwater, which is often more of a risk to water security than is depletion[12,15], and is particularly important considering that about half of the world's population relies on groundwater for drinking[13]. Finally, groundwater is often neglected in global water-security or scarcity assessments, so Jasechko and colleagues' work provides a basis to incorporate it in these types of study in future.

Jasechko *et al.* have shown that groundwater-level decline is accelerating in many areas across the world. Given the importance of groundwater as a climate buffer and resilient water resource, these findings provide a timely warning, as the world prepares for a 1.5 °C or greater temperature increase and the changes to drought and rainfall patterns that will follow. However, the authors' analyses also reveal areas in which groundwater declines are slowing or have been reversed, or where levels have continuously risen through the late twentieth and early twenty-first century. Lessons must be learnt from these areas to help to halt or reverse accelerating groundwater decline elsewhere, and to prepare for the future impacts of climate change.

Donald John MacAllister is in the British Geological Survey, Edinburgh EH14 4AP, UK.
e-mail: donmac@bgs.ac.uk

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Women's health

Pregnancy sickness linked to hormone from fetus

Alice E. Hughes & Rachel M. Freathy

Maternal sensitivity to a hormone produced by the fetus might underlie the risk of severe nausea and vomiting in human pregnancy – a finding that could open up strategies for the treatment of this debilitating condition. **See p.760**

Nausea and vomiting are reported in about two-thirds of pregnancies[1]. Although pregnancy sickness is often mild and transient, some people experience persistent and severe nausea and vomiting that presents a serious health problem. This condition, known as hyperemesis gravidarum (HG), occurs in 0.3–3% of pregnancies[2] and can cause dehydration, nutrient deficiencies and weight loss. It frequently leads to hospitalization, and, at its most extreme, can result in termination of wanted pregnancies and maternal death. Even though excessive vomiting in pregnancy has been recognized for centuries[3,4], the cause of HG has remained elusive. On page 760, Fejzo *et al.*[5] describe a link between sickness during pregnancy and sensitivity to a hormone called growth differentiation factor 15 (GDF15). The findings open up potential avenues for research aimed at preventing or treating HG.

In 2018, a genome-wide analysis of more than 53,000 women identified a link between the *GDF15* gene and nausea and vomiting in pregnancy across the whole spectrum of severity[6]. Although GDF15 had not previously been implicated in pregnancy sickness, it was a promising candidate for investigation, because evidence suggested that it acts on a part of the brainstem that controls vomiting[7], and its overproduction had already been linked to chronic nausea and weight loss in people with cancer[8,9].

In the latest study, Fejzo and colleagues found that the levels of GDF15 in the maternal bloodstream increase steadily in the first 12 weeks of pregnancy, but are higher on average in women who experience nausea, vomiting and HG than in those who do not (Fig. 1a). These results were important because they confirmed observations from previous studies, which used a method of assessing the levels of GDF15 in the blood that was subsequently found to be unreliable[10]. Those measurements were confounded by the inability of the assays to detect a common genetic variant of *GDF15* known as H202D.

What makes the study by Fejzo *et al.* a major advance is that it goes beyond establishing a correlation between GDF15 and nausea and vomiting in pregnancy, and provides genetic evidence for a potential causal mechanism. Using the H202D genetic variant to their advantage, the authors developed a mass-spectrometry-based method to distinguish between GDF15 carrying a histidine (H) amino-acid residue at position 202 and the variant carrying an aspartate (D) residue at this position. They then studied pairs of mothers and babies in which the mother and the baby had different genotypes – for example, a mother who did not have the 'D' variant of the *GDF15* gene (an 'HH' genotype) and a baby who had one copy of the 'D' variant and one copy of the 'H' variant (an 'HD' genotype). In this way, the researchers could assess how much of the GDF15 in the mother's blood was maternal in origin, and how much was fetal. They found that most of the circulating GDF15 in pregnancy came from the fetus.

The team focused next on variants in or near the *GDF15* locus that are linked with a predisposition to HG. They showed that, in the blood of non-pregnant individuals, these genetic variants were associated with circulating levels of GDF15 that were lower – not higher, as might be expected – than those observed in people who did not have the HG-predisposing variants (Fig. 1b). The finding that a high risk of HG is related to genetic variants that are associated with low levels of GDF15 in the non-pregnant state is consistent with a causal relationship, because genotypes cannot be changed by lifestyle factors that might normally confound a correlation between exposure to something in the environment and a disease[11]. Furthermore,

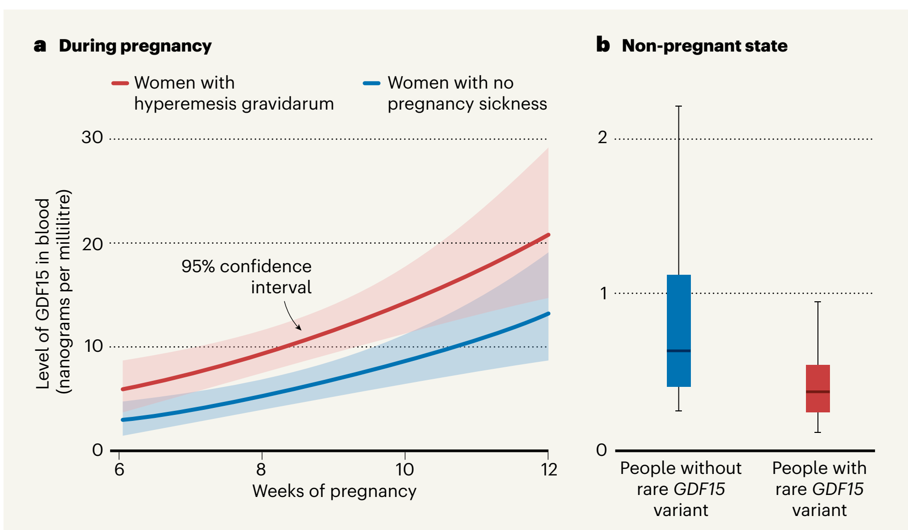

Figure 1 | The hormone GDF15 is responsible for excessive nausea and vomiting during pregnancy. **a**, Fejzo *et al.*[5] find that the levels of GDF15 in the mother's bloodstream increase during the first 12 weeks of pregnancy, and that most of this GDF15 originates from the fetus and placenta. Women with a condition called hyperemesis gravidarum (HG), who experience severe nausea and vomiting, have higher levels of GDF15 than those who don't experience pregnancy sickness – suggesting that high levels of GDF15 are linked to symptoms of HG. Graph adapted from Fig. 1c of ref. 5. **b**, People with a rare *GDF15* variant have lower basal levels of GDF15 than those who do not have the variant. Individuals with this genetic variant are predisposed to HG. Lower levels of GDF15 in the non-pregnant state could explain why these people are sensitive to the increase in GDF15 during pregnancy, and so experience HG. Graph adapted from Fig. 3c of ref. 5.