inappropriately normal serum concentrations of PTH, and normal brisk increases in plasma cAMP in response to PTH infusion, which indicates normal sensitivity of the PTH receptor. The patients also had bilateral sensorineural deafness. The renal abnormalities consisted mainly of bilateral cysts that compressed the glomeruli and tubules and led to renal impairment in some patients. Cytogenetic abnormalities were not detected,[11] except in two unrelated patients, who had abnormalities affecting chromosome 10p14–10pter.[12] These two patients did not have immunodeficiency or heart defects, which are key features of DiGeorge type 2 syndrome, which is due to an abnormality on 10p13–14. Deletion-mapping in other HDR patients defined a critical region that contained GATA3, and DNA sequence analysis in additional HDR patients identified mutations that resulted in a haploinsufficiency and loss of GATA3 function.[12]

GATA3 belongs to a family of zinc-finger transcription factors that are involved in vertebrate embryonic development, and the HDR phenotype is consistent with the expression pattern of GATA3 during human and mouse embryogenesis in the developing kidney, otic vesicle, and parathyroids. However, GATA3 is also expressed in the developing central nervous system and the haemopoietic organs in man and mice,[13] which suggests that GATA3 may have a more complex role. Indeed, homozygous GATA3-knockout mice have defects of the central nervous system and a lack of T-cell development.[13]

The basis of these inter-species differences remain to be elucidated. However, the absence of immunodeficiency in HDR patients with GATA3 haploinsufficiency contrasts with the immune abnormalities observed in some patients with 10p deletions, which suggests that immunodeficiency is likely to be caused by other genes on 10p. These studies of HDR patients clearly indicate the importance of GATA3 in parathyroid development and hypoparathyroidism.

These advances are also important for patient care. The recognition that hypoparathyroidism encompasses a heterogeneous group of disorders, some of which may also affect organs, indicates the need to look for associated abnormalities because early treatment of endocrinopathies in APECED, and of renal failure or deafness in HDR, may improve the outlook for these patients. Also, the recognition that ADHH patients with activating CaSR mutations do not require vitamin D treatment to restore normocalcaemia will help to prevent nephrocalcinosis and renal failure. Indeed, this subgroup of hypocalcaemic patients would benefit most from PTH injections, which may become available in the future. Thus, the hypoparathyroid disorders remain a challenge, with the genetic advances providing important clues for management.

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Are some public-health problems better neglected?

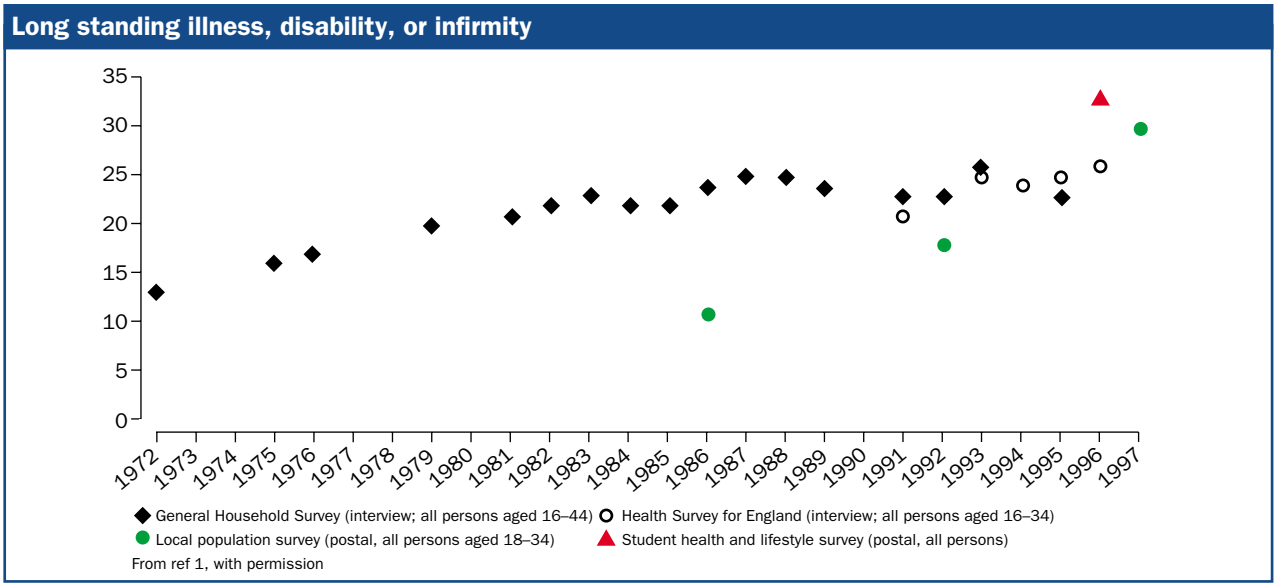
The finding of yet another "important and neglected public health problem" will probably make the hearts of everyone involved in health-care delivery sink, though perhaps not those of journalists and journal editors. Now the health of university students has been added to the list.[1]

In 1996 Sarah Stewart-Brown and colleagues[1] did a survey of students in three UK higher-education institutions. 1208 responses were received, a response rate of 49%, which as the investigators admit, questions the validity of the findings. The main outcome reported was the scores on the SF-36, the quality-of-life measure that by now has become almost de rigueur for these sort of studies. Because of its ubiquity, numerous comparison groups are available, and it is these comparisons that are the most interesting part of the study.

The study found that 33% of students reported long-standing illness. The researchers draw attention to, and are clearly surprised by, this percentage, which is higher than found in other surveys that provide comparable data from the same questionnaire (figure). What ought to be made of this finding?

What comes across most strongly is that the prevalence of self-reported illness has increased in a short space of time. General health, energy, mental health, pain, and physical function were poorer when these students were compared with the local population in 1991/92. The survey has uncovered an important and neglected public-health problem, but is it the one that Stewart-Brown and colleagues acknowledge? All Western societies seem to be facing a rising tide of symptoms, illness, and disability,[2–4] which has been labelled the "paradox of health"—ie, although all objective indices of health have improved beyond recognition over the past 50 years, instead of an improvement in subjective measures of health, people feel less well.[5,6]

There is an analogy with the concerns of medical and social authorities at the end of the 19th century. Numerous commentators drew attention to an apparent epidemic of both neurasthenia and mental illness. This epidemic was partly blamed on changing patterns of work and education, such as the increasing demands made by the spread of mass education and the introduction of new business techniques and practices. But these concerns gradually receded, with



editorialists concluding that the the relation between these conditions and unwelcome features of modern life was more spurious than real,[7] and that "we had become more tender in our ills".[8]

There is an additional factor. The letter accompanying the questionnaire provided details of the institutions' counselling services "in case any student needed support as a result of any issues raised by completing the questionnaire". As researchers we appreciate why such a statement was included (perhaps it was imposed by a local ethics committee), but would the act of filling in a questionnaire uncover an issue of such magnitude as to necessitate consulting a professional? Leaving aside the important question of whether or not counselling would help, what impact might this statement have had on the way students approached the questionnaire? There is good evidence that health perceptions and symptoms are affected by expectations, and cognitive schema[9] framing the questionnaire in this way may have increased symptom reporting.

So what should be done about the findings? According to Stewart-Smith and colleagues, public-health practitioners should support the concept of "health promoting universities". Few people would support universities that set out to endanger health, so what does their suggestion mean? The researchers speculate that because the levels of stress (whatever that ambiguous term means[10]) are so high, students may end up assuming that high levels of stress and anxiety are normal and unavoidable, and thus miss out on opportunities to take up "low stress" jobs. Not only will doing so jeopardise their mental health, but, the researchers remind readers, their immune and cardiovascular systems as well.

Work stress is indeed an "epidemic". Yet, as a recent thoughtful paper discussed,[11] the epidemiological perspective is lacking. Exposure to asbestos causes disease in a quantifiable and reproducible way, but exposure to "stress" does not cause illness, let alone disease, in the same manner. Any effects of stress on health depends on its context, and what is lacking in much of the publications on stress at work is a realisation of the way in which social factors, meanings, and interpretations affect this link, and the way in which socially constructed explanations may be the mediator variable. If expectations change, as they seem to be doing, then so does the relationship. What may be happening is not an epidemic of stress, or of disability, but a change in people's identities, their views of themselves, and their views of work.[12]

If so, how might this alarming situation be remedied?. Should these "at risk" students be protected? Should someone be told on the basis of an SF-36 score that he or she is unsuited for "high stress" occupations, and pointed in the direction of "low stress" jobs, as Stewart and colleagues imply? Do such jobs exist? Journals are overflowing with surveys of virtually every occupation, and any that do not report high stress are hard to find. It is not too far fetched to envisage a time when people thought to be at risk will be advised against, or even denied (because of the threat of litigation), work. Yet the most powerful and established association of mental ill health and occupation is not work, but the absence of work.[13] There is therefore a risk of scoring a serious "own goal."[14]

Before more measures are proposed for managing stress at work, some humility is needed. Employers and others, out of a mixture of good intentions and defensive practice, are introducing means of treating and preventing workplace stress. Yet there is an unhappy history of similar Panglossian interventions doing more harm than good, whether they be for reducing delinquency[15] or for preventing post-traumatic stress disorder.[16] The rising level of self-reported disability among apparently healthy students is a prime example of a situation in which it will be far easier to accelerate the rate in which people view themselves as ill rather than the converse. Sometimes public-health problems should stay neglected lest they are made worse.

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Should quality-of-life needs influence resource allocation?

Patients' self-reported health-related quality of life (HRQL) is commonly assessed as a major outcome in clinical trials and considered with other outcomes such as cure rate, clinical response, or survival. Costs, too, are sometimes combined with these outcomes, to evaluate the cost-effectiveness of the treatment policies. Health-economic analyses can be applied across different disease areas, in attempts to contrast the benefits of increased spending within different specialties so as to guide macrolevel decisions about resource allocation.[1–3]

In a novel approach, Mirjam Sprangers and colleagues have compared HRQL data from several studies in a wide range of chronic disorders, to identify needs for increased resources in research, training, and health care.[4] Instead of attempting to examine the cost-benefit of treatments, the investigators show how HRQL data can be used merely to pinpoint areas that may be worthy of extra attention. They gathered data from eight studies, representing over 15 000 patients, that had used the SF-36 questionnaire or the closely related SF-24. Results were presented showing, to take a few examples, that "patients with cerebrovascular/neurologic conditions reported relatively favourable levels of pain, but were found to have the poorest levels of social functioning and mental health", and "patients with musculoskeletal conditions reported the poorest levels of physical functioning, role functioning and pain, while patients with renal disease reported the poorest level of general health". The investigators note that their results are generally in line with published work, and propose that these comparisons might be used to identify disease areas or specialties in which there is a high prevalence of poor HRQL or functioning. They conclude that "research funds can be allocated to patient groups with those chronic diseases and/or sociodemographic characteristics who are in greatest need".

Sprangers and colleagues acknowledge limitations of their review. Their data were collected from completed studies, solely in the Netherlands, and some disease categories were either under-represented or missing (for example, psychiatric patients with psychoses or schizophrenia and patients with AIDS were not included). Some of the studies had poor rates of response from patients, with fewer than half the patients completing questionnaires. The investigators note the need for a planned prospective study in another country to validate the results.

Although this report is fascinating and thought-provoking, one is left with several unresolved questions. Some studies included patients in only limited age-ranges or with specified severities of disease. Thus the results from this dataset may not apply to all age-groups or may exaggerate the severity in certain chronic disorders. For example, all those patients with hypertension or with gastrointestinal disorders were from studies of patients aged 57 or more, whereas nearly all with rheumatoid arthritis, multiple sclerosis, and psychiatric disorders were under 60. Patients with asthma or chronic obstructive pulmonary disease were excluded if they were "under active treatment of a specialist", but for other disorders there is no information about severity of disease or whether the patients are receiving treatment. Other reviews synthesising data from HRQL studies have noted similar concerns about interpretation.[5]

For some disorders the grouping together of patients may be inappropriate. In this paper, 87% of patients with diabetes were from studies of the elderly. However, although diabetes is a common disease in elderly obese females, the medical implications can be minor, with little need for extensive changes to lifestyle. By contrast, a young person faced with a lifetime of diabetes could be severely disadvantaged. It does not seem appropriate to use average values across all patients with diabetes; they are a heterogeneous group with clinically distinct characteristics. However, the investigators group the disorders with abandon; they combine thyroid-gland impairments with diabetes, to form a "disease cluster" of endocrinological disorders, and multiple sclerosis, a debilitating illness with no prospect of recovery, together with migraine.

Some of these issues might be addressed in future studies, and in particular by more extensive tabulation of subgroups of patients. But the problems of case-mix will always be an issue—for some diseases, population surveys will commonly be characterised by many cases of low severity, which may make average HRQL values seem close to those of the normal population, even though for a common disease the small proportion of severely ill patients could represent a large number of individuals who urgently need attention. Conversely, in some disease areas, surveys based on hospital attenders could distort the results by emphasising the few patients whose disorder is most critical. Perhaps what is really needed is not average values for HRQL, but simply estimates of the prevalence of problems in the community. For each disease, subdivided where appropriate by severity or age or other factors, an estimate of the number of patients (rate per 100 000 population) with seriously reduced HRQL would indicate those areas in greatest need of further research, training, or resources.

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