THIS WEEK

EDITORIALS

HISTORY DNA discovery kicks off memorable blasts from the past **p.270**

WORLD VIEW Economic crisis triggering a modern Greek tragedy **p.271**

TICK TOCK The bacteria that keep time for the underwater squid **p.273**

Look after the pennies

Government decisions about where to spend and where to cut should be based on evidence, not ideology.

When a nation's expenses grossly exceed its income, as they routinely do in the United States, the most foolish way to curb the resulting deficit is to slash spending wildly. Yet that is the path that the US government has chosen to follow with this year's 'sequester'. A smarter way is to follow the path pioneered by evidence-based medicine: fund what works and cut what doesn't. That is the approach being pursued in the budget submitted last week by US President Barack Obama (see page 277).

In a budget chapter rarely mentioned in the media hoopla over proposed tax rises and spending cuts, the administration has laid out a blueprint to implement evidence-based decision-making throughout the government — in effect, bringing the methods of science to bear on policy.

This reform effort began under Obama's predecessor, George W. Bush, but it has accelerated greatly with the need to do much more with significantly less. The White House Office of Management and Budget (OMB) signalled the way that things were going in May last year when it instructed government agencies to incorporate evidence-based strategies throughout their operations.

The White House mandate applies to every agency in the executive branch, including those that fund science. But the most urgent target is the government's vast array of social services, which range from early-childhood enrichment projects to the home care of elderly patients. All were created with good intentions; few have had their effectiveness evaluated with any kind of rigour, or by anything that resembles peer review.

The OMB memorandum suggests several ways to change that situation. One is to fund social services through a 'tiered' approach not unlike the stages followed in clinical trials. At the lowest tier, agencies would allocate seed money to promising, but unproven, ideas, provided that the research programme builds in a rigorous assessment of outcomes by independent investigators — usually academic social scientists or non-profit research firms.

In the higher tiers, more funding would be available for programmes that are supported by stronger evidence (and with built-in assessment protocols). The highest tier would be reserved for large-scale, multi-million-dollar programmes that are already supported by multiple gold-standard, controlled trials.

Federal agencies are already using the tiered model for six evidence-based programmes — ranging from teen-pregnancy prevention to education — with budgets totalling about US$1 billion in 2012. Obama's new budget proposes to boost that funding by 44% for 2014.

Another suggested strategy, pioneered in the United Kingdom, is a model known as 'social impact bonds' or 'pay for success'. It sees philanthropic organizations and private companies fund preventative services, with the government paying them back only if rigorous assessments show that the services save taxpayers' money. US federal agencies have tried this approach on a small scale with job-training programmes and projects to reduce recidivism in newly released prisoners. In 2014, Obama proposes to spend up to $195 million to expand these initiatives into areas such as housing and education.

Such strategies for data-driven decision-making have the potential to radically improve the US government's efficiency and effectiveness, and deserve vigorous support from Congress — with one caveat: both Congress and president must be equally vigorous about supporting research into what success actually means and how to measure it. These are still open questions in most areas of policy. Most parents, for instance, probably think that there is more to a good education than getting their child to score well on standardized tests. It can be difficult to quantify such intangible benefits, but that is no excuse not to try.

"A smarter way is to follow the path pioneered by evidence-based medicine."

Everyone favours government effectiveness as a concept. But every existing programme is also someone's livelihood. When those judged ineffective — by whatever measure — are cut or consolidated, the protests and the lobbying are fierce. If officials can resist that pressure, evidence-based policy initiatives could help to bring about a much-needed shift in the inflamed fiscal debate, from ideology to pragmatism.

The OMB memorandum captured that spirit in a refreshingly unbureaucratic call to arms: "Where evidence is strong, we should act on it. Where evidence is suggestive, we should consider it. Where evidence is weak, we should build the knowledge to support better decisions in the future."

That is easy to say; it is harder to do. But to say it is a start. ■

Smoke and mirrors

Italy's parliament must listen to expert advice before deregulating stem-cell therapies.

Just weeks after the white smoke from the Vatican signalled the election of a new pope, a grimmer pall hangs over the Eternal City — a fog of confusion and misrepresentation about stem-cell therapy. Those who have lit the fire beneath the debate say that they are promoting the translation of stem-cell research into the clinic so that currently incurable diseases can be treated. Nothing could be further from the truth.

The Second International Vatican Adult Stem Cell meeting, held on 11–13 April in Vatican City, was a shamelessly choreographed performance. Sick children were paraded for television, sharing the stage with stem-cell companies and scientists desperate to hawk a message that their therapies must be speeded to clinical use.

A kilometre away at the Italian senate, meanwhile, parliamentarians further eroded protection for vulnerable patients targeted by stem-cell companies. On 10 April, they amended an already controversial ministerial decree (see *Nature* **495,** 418–419; 2013) with a clause that would redefine stem-cell therapy as tissue transplantation, thereby releasing it from any regulatory oversight. If the second parliamentary chamber endorses this amendment, Italy will be out of step with the rules of the European Union and the US Food and Drug Administration, both of which define stem cells modified outside the body as medicines.

Many scientists around the world were appalled by the events in Rome, and rightly so. It is wrong to exploit the desperation of the disabled and the terminally ill and to raise false hopes of quick fixes, as some at the Vatican meeting tried to do. It is also wrong to try to use such patients as experimental animals by bypassing regulatory agencies, as the Italian parliament seems to want to do.

Reputable stem-cell companies insist that stringent regulatory control is necessary, and that patients should be exposed to experimental treatments only when safety and efficacy is assured. Failures in the clinic will hold back the field. But not all of the cell-therapy industry is so tolerant.

With their ability to differentiate into various cell types, stem cells hold enormous potential to repair damaged tissues. Human embryonic stem cells can turn into any cell type, but many groups, including the Catholic Church, find their derivation from embryos unethical.

The current controversy concerns adult stem cells. These exist in several tissues, but can replace only those particular tissues. Big claims are being made for them, with many trials of therapies under way worldwide for conditions as diverse as Alzheimer's and heart disease. Some stem-cell therapies are approved by regulatory agencies; others sneak under the radar by exploiting rules allowing compassionate therapy, for example, or by operating in countries such as China or Mexico — and perhaps now Italy — where regulation is less strict.

The scientifically naive Vatican finds the concept of adult stem cells attractive simply because embryos are not involved — yet it ignores the ethical implications of false hope.

The main organizer of last week's conference was the non-profit Stem for Life Foundation, launched by the stem-cell company NeoStem, both based in New York. The foundation says that it is in favour of strict regulation of stem-cell therapies. But its conference programme, which left no room for questions, included many speakers who clearly were not. It was framed as a fight for reason and fairness against an uncaring and intransigent scientific community.

"A lot more research into the deep biology of stem cells is needed."

Adult stem cells have already had clinical success, such as in bone-marrow transplantation for leukaemia treatment, growing new skin layers to treat burns and regenerating corneas. More ambitious hopes need to be tempered, however. Many trials involve infusing patients with mesenchymal stem cells from bone marrow, which are relatively easy to extract and grow. These can make only bone, cartilage and fat cells, but trials targeting other tissues use the rationale that other, non-stem properties of mesenchymal stem cells apply. It remains to be seen how effective these properties will be outside the normal biological home of the stem cells.

Given the burden of incurable disease, rapid bench-to-bedside translation is unquestionably crucial. But a lot more research into the deep biology of stem cells is needed. Some trials approved by regulatory agencies may yield useful results, but that is a long shot without strong research data. At least they are safer under regulatory eyes. Unregulated treatment — such as that issued on a compassionate basis by the Stamina Foundation in Brescia, Italy, which led to the current ministerial decree — is more worrying. The second parliamentary chamber needs to heed independent expert advice before voting to deregulate stem-cell therapies.

Stem cells will help to develop treatments for currently incurable diseases. But we are not there yet, whatever the smoke signals may say. ■

Due credit

Nature's podcast charts 12 landmark discoveries in the history of science.

Even the greatest scientific discoveries come with an element of the mundane. A humble paperclip was biophysicist Raymond Gosling's choice. Late one night in May 1952, in a chemistry lab in London, the PhD student wrapped DNA around a paperclip to keep the molecule's fibres stretched taut in front of an X-ray source so that he could analyse their structure. The result was the celebrated 'photograph 51' — the image that told James Watson that DNA strands curl around each other like a twisted ladder, and that the specific pairings in the rungs are key to the mechanism of inheritance.

The rest of that story is legend. Based on their work at the University of Cambridge, UK, Watson and Francis Crick published their paper in the pages of this journal, including a beautiful diagram of the double helix that was hand-drawn by Odile Crick, Francis' wife (J. D. Watson and F. H. C. Crick *Nature* **171,** 737–738; 1953).

Next week marks the 60th anniversary of the publication of the famous Watson and Crick paper — and that of two other papers on DNA that appeared in the same issue. Neither was so high profile, but each was essential to the structure's discovery. Both were written by scientists at King's College London: one by Maurice Wilkins and his colleagues Alec Stokes and Herbert Wilson, and the other by Gosling and his PhD supervisor, Rosalind Franklin.

Only Gosling (now 86) and Watson survive from that group of seven scientists. Watson has never been shy, and his compelling swagger helped to establish another colossus of biology, the Human Genome Project. But the supporting cast matters too, even on the biggest stages.

Gosling is a *Nature* author, even if he is largely forgotten when the story of DNA is told. To mark the anniversary of his paperclip-inspired contribution, *Nature* has interviewed him. You can hear the results at go.nature.com/lizfik, in the first of a series of monthly podcasts to highlight 12 key scientific discoveries from the pages of this journal. (Future episodes in the 'Pastcast' series will plunder the *Nature* archive to investigate the discovery of X-rays in 1896, the early days of quantum theory in the 1920s and the first report of the ozone hole in 1985.)

In the interview, a humble Gosling fondly recalls that Franklin's response to Crick and Watson's model of the double helix was gracious and sanguine: "She didn't use the word 'scooped'. What she actually said was, 'We all stand on each other's shoulders.'"

All three papers appeared with no peer review — unthinkable now. The head of the King's College biophysics unit, John Randall, belonged to the same London gentleman's club — the Athenaeum — as Lionel ('Jack') Brimble, co-editor of *Nature*. Randall convinced Brimble to publish Wilkins' paper alongside Watson and Crick's; Franklin's paper was added only after she petitioned for its inclusion.

This cavalier approach to submissions extended to the awarding of credit. Watson and Crick's paper features only a glancing concession to being "stimulated by a knowledge of the general nature of [Wilkins and Franklin's] unpublished experimental results and ideas". There is no mention of Gosling by name. Gosling left research soon after, with no bitterness; in his words, he "was no good at it".

Discoveries take ego, genius, conflict, inspiration and fierce ambition. But they also need the hard graft of PhD students who beaver away late into the night and improvise with what they find in the stationery cupboard. They do not always receive the recognition that they deserve. Raymond Gosling is a good place to start to reverse that trend. ■

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