

What's trending at the *Medical Journal of Australia*? The current top 10 most-cited articles

Authors and other experts reflect on the articles that made Journal history

From flares to hotpants to shoulder pads, we all know how fashions change over time: but what about trends in citations? Ten years ago, as part of the 90th birthday celebrations of the *Medical Journal of Australia*, then Deputy Editor Ann Gregory examined the top 10 most-cited articles as of 2004.¹ Now celebrating our 100th birthday, the current editorial team have looked again at the most-cited articles, using the Web of Science (Thomson Reuters) citation analysis tool, which examines citations from 1949 to 2014 (Box). Since 2004, Cade² has been supplanted in the number one position by the Quality in Australian Health Care Study,³ although Cade remains in the top 10. The new entrants in many ways reflect current issues in health care: the rise in awareness of non-communicable diseases such as obesity and mental illness; the challenge of innovation in health care delivery; and the greater value placed on quality

evidence from clinical trials in medicine. Several authors of the top 10 articles and other experts in their respective fields have submitted short perspectives on their top 10 articles. We invite you to toast their success: a glass of *Helicobacter pylori* is optional.

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- 1 Gregory AT. Jewels in the crown: *The Medical Journal of Australia's* 10 most-cited articles. *Med J Aust* 2004; 181: 9-12.
- 2 Cade JFJ. Lithium salts in the treatment of psychotic excitement. *Med J Aust* 1949; 2: 349-352.
- 3 Wilson RM, Runciman WB, Gibberd RW, et al. The Quality in Australian Health Care Study. *Med J Aust* 1995; 163: 458-471. □

Helicobacter pylori: what does it taste like?

The Journal's early support for a *Helicobacter* pioneer allowed publication of key results

The title above is the most common question people ask me about the spiral bug. By the time this article comes to press the answer might even be published. But the question leads back to my paper in the *MJA* 29 years ago.¹ It described the deliberate self-administration of *Helicobacter pylori* and the observation that it caused an acute upper gastrointestinal illness with vomiting, halitosis and an underlying achlorhydria. Embarrassed to admit that it was a self-experiment, I wrote the paper in the third person at the suggestion of my coauthors, but they at least had witnessed my sufferings over a 14-day period, so it was not entirely subjective and anecdotal. It came to be published in the Journal because I had received a letter from the Editor at the time, Alistair Brass, saying how much he liked the *Lancet* paper I had coauthored with Robin Warren,² and did I have

any others up my sleeve on the subject? Warren and I had had such a bad run with editors by then that it seemed a breath of fresh air to meet an editor who actually liked original material. So I finished the paper and submitted it to the Journal in about September 1984. However, then showing his true colours, the Editor sent it out to scrupulous reviewers who asked for a complete rewrite, which made it a much better paper, but delayed its publication until April 1985.¹

I obtained incredible value from the *MJA* publication. Who knew that so many people were following the *MJA*? In a *Lancet* editorial soon afterwards, then Editor David Sharp "re-tweeted" the *MJA* paper, agreeing that *H. pylori* infection explained a mysterious illness that was spreading from time to time in gastroenterology laboratories performing acid secretion studies.³ An unnoticed infectious agent was contaminating their equipment and infecting many of the volunteers.^{4,5}

Re-reading that paper every few years, I am impressed by how far the *MJA* Editor was "sticking his neck out" in allowing me to publish a hypothesis

as to the cause of peptic ulcer. It was a further 5 years before journals allowed the word "cure" to appear in articles about duodenal ulcer,⁶ and almost a decade before mainstream United States journals could accept it as proven.⁷

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- 2 Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1984; 1: 1311-1315.
- 3 Pyloric *Campylobacter* finds a volunteer [editorial]. *Lancet* 1985; 1: 1021-1022.
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After the Quality in Australian Health Care Study, what happened?

Milestones in Australia's journey to high-quality care

The 1995 Quality in Australian Health Care Study (QAHCS) demonstrated the potential to improve the quality and safety of health care.¹⁻³ Using a modified version of the earlier Harvard Medical Practice Study on medical negligence, the QAHCS focused on the more useful measure of preventability of medical error. The incidence of adverse events was higher than in the Harvard study, and at first the Australian rates were queried by government: 16.6% of hospital admissions were associated with an adverse event, of which 51.2% were judged to have high preventability. Many countries replicated the Australian study, using one medical reviewer rather than two as in the QAHCS, which reduced the estimate by about 3%. Overall, a consistent rate of about 10% of hospital admissions associated with an adverse event was seen in New Zealand, Japan, Singapore, the United Kingdom and Denmark. In 2012, a World Health Organization study on adverse events in developing countries showed a similar result.⁴

The Australian Government responded with a succession of initiatives: the Australian Council for Safety and Quality in Health Care was established by Australian health ministers in 2000 and operated until 2005; the Australian Commission on Safety and Quality in Health Care (ACSQHC) was created in 2006 and written into legislation with the *National Health Reform Act 2011*. The ACSQHC promulgated 10 national quality and safety standards as part of national accreditation processes. Health reform has also included the Independent Hospital Pricing Authority, the National Health Funding Body and the National Health Performance Authority. Linking costs to quality outcomes, combined with national comparative performance measures of safety, efficiency, access and patient experience, has to be considered a milestone in Australia's journey to high-quality care.

Have the rates of adverse events declined? A repeat of the same study would be costly, and the changed

context of health care would complicate interpretation. However, there have been significant process changes that reflect an increasing attention to quality. Federal and state governments are reporting infection rates and triage times. The Australian Council on Healthcare Standards reports annually on 360 indicators in Australasia and, for the years 2005–2012, more indicators improved (125) than worsened (38), with no significant trend for 62 indicators.⁵ For example, the proportions of emergency department presentations meeting the triage benchmarks increased by about 6% over the 8-year period.

Quality principles have been introduced into medical and health professional education and expanded as a research theme. Early on, the University of Newcastle introduced a quality-of-care project, winning Australian Council on Healthcare Standards student quality improvement awards.⁶ Other schools have followed, and national and international curricula have been developed from Australia.

Notwithstanding the good progress, there remains much to do to improve health care systems. There is increasing focus on process re-engineering, applications of reliability science, human factor mitigation strategies, teamwork, communication, patient-based care and greater application of evidence-based medicine.

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Improving the mental health of the population: where to next?

The need for a national strategy on preventing mental disorders

During the 1990s, two national surveys were carried out in Australia that were very influential in guiding thinking about population mental health. The first was the National Survey of Mental Health and Wellbeing, which showed that mental disorders were common, disabling and undertreated.¹ The second was the National Survey of Mental Health Literacy, which showed that many members of the public had negative views of the standard psychiatric treatments that were endorsed as effective by clinical practice guidelines and mental health clinicians.^{2,3}

This “treatment gap” suggested a clear path to improving population mental health: we needed to get more people with mental disorders to seek help and receive evidence-based treatments.⁴ In Australia, efforts to achieve these aims were successful. There is now a greater willingness to be open about mental disorders and to seek help,⁵ and the Australian public's beliefs about treatment of mental disorders have become much closer to those of professionals.⁶ Further, we have seen considerable increases in use of pharmacological and psychological treatments.⁷

However, the expected gains in population mental health have not been seen. Repeat population surveys since the

1990s, using screening tests for mental disorders, show no detectable reduction in symptoms.^{7,8} The one population gain that has been found is a reduction in the suicide rate, which roughly coincided with the introduction of the National Suicide Prevention Strategy in 1999.⁹

These observations raise the question of “where to next?” One option would be to continue to expand the reach of clinical services and reduce the treatment gap further. However, it could be argued that the marginal gains of reducing the treatment gap will become progressively smaller as treatment is applied to milder cases.

An alternative strategy is to have a greater emphasis on prevention.¹⁰ The prevalence of mental disorders is a function of incidence and duration. Prevention aims to reduce incidence, whereas treatment aims to reduce duration. We need a two-pronged effort aimed at both prevention and treatment, but the prevention prong is largely missing. It is notable that the reduction in suicide corresponded to the introduction of a strategy focused on population prevention. We need to build on this approach by developing a national strategy for the prevention of mental disorders.

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The current top 10 most-cited articles*

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archives of the Journal is to be expected. But perhaps what is truly remarkable is the fact that lithium has recently strengthened its clinical profile in the pharmacological armamentarium presently used to treat bipolar disorder.⁴ This resurgence of interest reflects lithium's enduring efficacy — put bluntly, it works. Lithium is arguably the best agent for the most critical phase of bipolar disorder, long-term prophylaxis, and as such it is the only true mood stabiliser.⁵ Boosting its profile further, lithium is both antisuicidal⁶ and neuroprotective.⁴

Unfortunately, lithium can be toxic, acutely so at high doses, but also at low doses when administered chronically, although the true risks have been somewhat exaggerated.⁷ As the only antimanic agent, it would be useful to understand its mechanism of action, so as to target those patients most likely to respond and to develop mimetics that can replicate lithium's specific actions without reproducing its tolerability problems. Recent studies have identified genetic variations associated with lithium response,⁸ and potential lithium-like molecules are undergoing development.⁹ These ambitious endeavours aim to advance the treatment of bipolar disorder and, in doing so, will provide more robust means for defining the illness and equating diagnoses to disease. A lithium-responsive and lithium-defined subtype of bipolar disorder representing a biologically anchored phenotype could be called Cade's

Cade's lithium: an extraordinary experiment with a not-so-ordinary element

Lithium research continues to yield benefits for treatment of bipolar disorder

To those familiar with the properties of lithium, it was no surprise that John Cade's seminal article¹ was, in 2004, the most cited in the history of the Journal, and was aptly described as a jewel in the crown.² After all, lithium has long had royal status in clinical practice guidelines and is very much in its element in blue blood.³ Hence, the fact that another decade later Cade's groundbreaking study has retained regal standing in the

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Study (AusDiab). *Med J Aust* 2003; 178: 427-432.

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* As at 12 May 2014. Source: Web of Science (Thomson Reuters).

disease.¹⁰ Alas, although this would be a tremendous acknowledgement, perhaps the eponym would be better suited to describing the remedy that he discovered.

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What will it take to curb the rise in obesity?

Shifting a whole population towards a healthy weight requires action targeting the root causes of obesity

The headline finding from our 2003 paper was a 2.5-times increase in the prevalence of obesity since 1980, with 20.8% of Australian adults found to be obese. Reporting the national obesity prevalence for the first time since 1995, this paper was one of the key outcomes from the Australian Diabetes, Obesity and Lifestyle study (AusDiab).¹ AusDiab was the first Australian national diabetes study; it showed an adult prevalence of diabetes of 7.4% and that of prediabetes (elevated blood glucose levels but below the cut-point for diabetes) at 16.4%.² These figures meant that prevention of the twin epidemics of obesity and diabetes was placed very much on the national agenda. AusDiab went on to become a longitudinal study, with the follow-ups of the cohort at 5 and 12 years providing invaluable data for studying obesity, diabetes, prediabetes, hypertension and kidney disease in individuals as they age. The more than 200 papers now published using data from this

study have played an important role in influencing national public health policy and action.

With the prevalence of obesity continuing to climb since the baseline AusDiab survey (28.3% in the 2011-12 National Health Survey³), it is becoming clear that the lifestyle change programs and medical interventions that are often successful in trials and for individuals are effectively individual sandbags against the flood of obesity. Successfully shifting a whole population towards a healthy weight is likely to also require action targeting some of the root causes of obesity. Our increasingly sedentary and inactive lifestyles in combination with an environment full of cheap, tasty, heavily marketed and energy-dense foods make us highly susceptible to weight gain. Although we are each responsible for our own behaviour, these environmental and cultural factors combine to effectively conspire against healthy choices.⁴ In addition, a focus on adult lifestyles, although important, ignores the increasing body of data suggesting that the genesis of adult obesity is biological and cultural factors operating very early in life.⁵

A promising next generation of environmental obesity prevention initiatives include the excellent work done to improve the school food environment in many countries (now championed in the United States by First Lady Michelle Obama⁶), whole-of-community interventions such as the Healthy Together Communities program in Victoria⁷ and excellent work by researchers,⁸ retailers⁹ and others¹⁰ to change the way food is marketed and sold. Obesity prevention in mothers and in infants¹¹ and prevention of excess gestational weight gain are further promising approaches. The combination of initiatives such as these will hopefully mean that when the Journal celebrates another decade, we will also be finally able to celebrate a reduction in Australia's obesity prevalence.

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Child health — how is Australia doing and what more do we need to do for our kids?

Focusing on the health and wellbeing of our children is the most important investment Australia can make

Australia is similar to other wealthy Western democracies for many aspects of child and youth health and wellbeing but, despite our material wealth, Australian rates of vaccination, obesity, child abuse and neglect do not compare well, and youth unemployment and the gap between rich and poor are increasing.^{1,2} Canadian researchers suggest that an unwanted outcome of economies focusing heavily on wealth creation is an impoverishment of the health and wellbeing of children, which will affect adult health and the human capability of nations — so-called modernity's paradox.³

Problems including developmental delays, substance misuse, child maltreatment and obesity and overweight are occurring at such high rates that they are already putting pressure on our health and welfare services. Most of these problems do not have effective treatments, hence they demand an urgent preventive approach. With a third of Australian children now overweight or obese, baby boomers may be the last generation to live longer than their parents, given the disease complications that will result.⁴

Further, mental health problems including substance misuse and autism appear to be increasing, or at least increasingly diagnosed.⁵ The impact on children of increasing mental health problems and substance misuse in their parents is hard to quantify and likely to be enormous.⁶ In a healthy country like Australia, it is unacceptable that many child health problems are much more prevalent in Aboriginal populations.

Can we replicate the successes of population interventions such as folate supplementation for preventing neural tube defects^{7,8} and supine sleeping for preventing sudden infant death syndrome?⁹ Surely some measures, such as improved

vaccination coverage and prevention of prenatal alcohol exposure, are achievable. Most interventions will require collaborative action on multiple fronts outside health and with increased attention to social, economic and health inequalities. No issue is more urgent than climate change, which will have a disproportionately greater effect on child health.¹⁰ Let's hope the dithering, delaying, denying and disparaging of the scientific evidence does not mean it is too late.

Australia really is a lucky country, but if we want future prosperity, then focusing on the health and wellbeing of our children is one of the most important investments we can make.

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